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Chronic Myeloid Leukemia: In Detail

A companion to the booklet CML: The Basics

Revised **2025**

Formerly titled Chronic Myeloid Leukemia

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Inside This Booklet

Acknowledgement

The Leukemia & Lymphoma Society appreciates the review of this material by

Lindsay A.M. Rein, MD
Hematologic Oncologist
Duke Blood Cancer Center
Associate Professor of Medicine
Duke University School of Medicine
Durham, NC

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Introduction

Chronic myeloid leukemia (CML) is a type of blood cancer in which the bone marrow makes too many white blood cells called granulocytes. It is also known as chronic myelogenous leukemia, chronic granulocytic leukemia and chronic myelocytic leukemia.

For easy-to-read, general information about CML for yourself, family or friends, visit www.LLS.org/booklets to view *CML: The Basics*.

Since the introduction of tyrosine kinase inhibitor (TKI) therapy in 2001, CML has been transformed from a life-threatening disease to a manageable chronic condition for most patients. People with CML are living longer and experiencing fewer treatment side effects. Some patients who meet specific criteria may even have the option of discontinuing TKI treatment once their CML is in a deep remission.

The more you know about your disease, the better you can take care of yourself—your mind, your body and your health. This booklet provides information about the diagnosis, staging and treatment of CML. It also includes brief descriptions of normal blood and bone marrow, as well as a glossary of health terms related to CML.

We hope that you will keep this booklet handy and that, should you ever feel alone in confronting problems, you will turn to it for information and guidance to find the support and resources you need.

We are here to help.

Visit www.LLS.org/booklets to view these two booklets: *Managing Stress: How stress affects you and ways to cope* and *Each New Day*.

All LLS publications mentioned in this booklet are free and can be viewed, downloaded or ordered online at www.LLS.org/booklets.

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Leukemia

The human body is made up of trillions of cells. Normally these cells grow and multiply to form new cells as the body needs them. When cells become damaged or grow old, they usually die, and new cells take their place.

Sometimes cells start collecting mistakes in their DNA (deoxyribonucleic acid). DNA is like an instruction manual for your body, telling cells how to grow, function, and make you who you are. A gene mutation is a change in the sequence of the DNA in a cell.

Cancer starts when a gene or several genes in a cell mutate and create a cancerous cell. This abnormal cancer cell grows and divides instead of dying. Cancer cells spread into, or invade, other areas of the body, disrupting how the body works.

As cancer cells multiply, many types of cancers form solid tumors, but cancers of the blood, such as leukemia, generally do not. Instead leukemia cells affect the amount of blood cells in the body, and they may accumulate in organs such as the liver or spleen.

Cancer can happen in almost any cell anywhere in the body. Leukemia is a cancer of blood cells. It begins in the bone marrow, the spongy tissue in the center of bones where most blood cells are formed. Blood cells begin as hematopoietic (blood) stem cells in the bone marrow. These stem cells develop into immature cells called blasts that go through many stages before they eventually develop into mature red blood cells, white blood cells and platelets.

Leukemia occurs when one of the immature cells in the bone marrow mutates at some point in its development and becomes a leukemia cell. Leukemia cells do not mature into healthy functioning blood cells. They grow more quickly and live longer than normal blood cells. They divide and copy themselves to make more and more leukemia cells. Over time, the leukemia cells crowd out and suppress the development of healthy blood cells in the bone marrow. When this happens, the body may not have enough red blood cells, white blood cells and/or platelets.

Red blood cells carry oxygen throughout the body. White blood cells help fight infections. Platelets help stop bleeding by clotting (clumping together) at the site of an injury. Without sufficient red blood cells, the body's organs and tissues may not receive enough oxygen to work properly. Low white blood cell counts can lead to serious and frequent infections, and low platelet counts can cause excessive bleeding and bruising.

Medical term	Description
Anemia	Low number of red blood cells
Thrombocytopenia	Low number of platelets ("thrombocyte" is another word for platelet)
Neutropenia	Low number of neutrophils (a neutrophil is type of white blood cell)

Leukemia is classified as either “acute” or “chronic.” The two terms describe how the disease progresses without treatment. Acute leukemias progress rapidly and produce cells that are not fully developed. These immature cells cannot perform their normal functions. Chronic forms of leukemia usually progress slowly, and patients have greater numbers of mature cells. In general, the more mature cells can carry out some or all of their normal functions.

Leukemia is further classified by the type of blood cell, either “myeloid” or “lymphoid,” that becomes cancerous. A blood stem cell may become a lymphoid stem cell or a myeloid stem cell. Lymphoid stem cells develop into white blood cells called “lymphocytes.” Myeloid stem cells can develop into red blood cells, platelets or certain other types of white blood cells. Leukemia is classified as “lymphocytic” or “lymphoblastic” if it originates in a lymphoid cell. It is classified as “myeloid” or “myelogenous” if the cancerous changes start in a myeloid cell. See **Figure 6** on page 50, for an illustration of blood cell development.

The names of the four major types of leukemia indicate how the disease progresses either acute (quickly) or chronic (slowly). It also identifies the type of blood cell involved, either myeloid or lymphoid. The four major types of leukemia are:

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

What Is CML?

Chronic myeloid leukemia (CML) is a type of leukemia that progresses slowly and involves myeloid white blood cells in the bone marrow. The World Health Organization (WHO) classifies CML as a “myeloproliferative neoplasm,” a group of blood cancers in which the bone marrow makes too many blood cells.

In CML, the bone marrow produces too many white blood cells called granulocytes. Heathy granulocytes help the body fight infection and disease. Granulocytes include the white blood cells known as neutrophils, eosinophils and basophils.

CML usually gets worse slowly over time, as the extra cells build up in the bone marrow making less room for healthy blood cells to develop. Without treatment, CML can become life threatening.

CML starts with a genetic mutation in a myeloid stem cell that is developing in the bone marrow. Normally, these cells form into mature granulocytes. The mutation is called the *BCR::ABL1* fusion gene. It results from a translocation between parts of chromosome 9 and chromosome 22, known as the Philadelphia chromosome. See **Figure 1** on page 6.

Figure 1. The Philadelphia Chromosome and the *BCR::ABL1* Fusion Gene

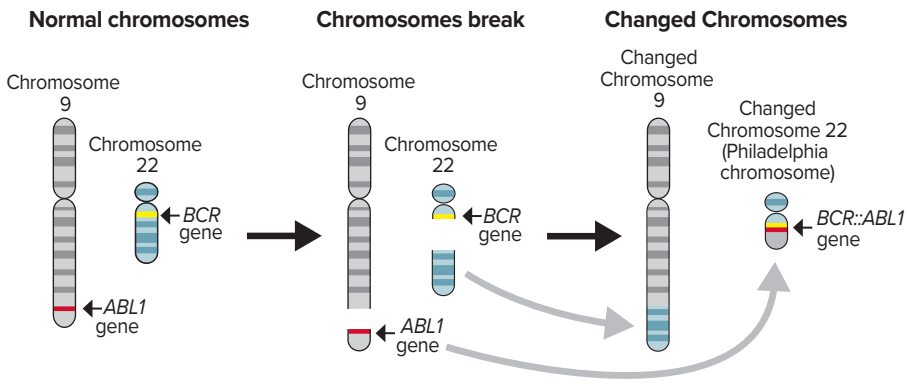
The human body is made up of trillions of cells. In the nucleus of most cells, the genetic material is packaged into thread-like structures called chromosomes. Chromosomes are made of DNA. Human cells normally contain 23 pairs of chromosomes, for a total of 46 chromosomes. A person's "karyotype" is their complete set of chromosomes. The term also refers to a laboratory-produced image of a person's chromosomes from an individual cell and arranged in numerical order. See **Figure 3** on page 12, for an illustration of a normal karyotype.

Cells in the body make copies of themselves to replace worn out cells. This process is called "cell division." In cell division, a cell first duplicates all of its contents, including its chromosomes, and then splits and forms two cells. Sometimes errors occur during chromosome duplication. One type of error is a translocation. This occurs when a piece of one chromosome breaks off and attaches to another chromosome.

In CML, a translocation occurs between parts of chromosomes 9 and 22 in a single myeloid bone marrow cell during cell division. Part of chromosome 9 attaches to chromosome 22, and part of chromosome 22 attaches to chromosome 9. As a result, chromosome 9 is longer than normal and chromosome 22 is shorter than normal. The abnormal chromosome 22 is known as the "Philadelphia chromosome" (because it was discovered at the Wistar Institute in Philadelphia). The disease is referred to as Ph positive (Ph+) CML, in which "Ph" is the abbreviation for the Philadelphia chromosome, and the plus sign (+) indicates the presence of the abnormal Ph chromosome.

CML is caused by a specific abnormal fusion gene on the Philadelphia chromosome. The break on chromosome 22 involves a gene called *BCR*. Part of the *ABL1* gene from chromosome 9 moves to chromosome 22 and fuses with the *BCR* gene. The leukemia-causing fusion gene that results from this translocation is called *BCR::ABL1*.

Translocation of Chromosomes 9 and 22



Genes provide cells with instructions for making proteins. The *BCR::ABL1* fusion gene is not found in normal blood cells. It turns the myeloid stem cell into a CML stem cell. This genetic mutation causes the CML stem cell to make too much of a protein called BCR::ABL1 tyrosine kinase, which stimulates CML stem cells to divide faster than normal myeloid stem cells. This, in turn, leads to a constant overproduction of granulocytes. These granulocytes all have the abnormal fusion gene *BCR::ABL1*, and they do not become healthy white blood cells. They are also called "leukemia cells," "myeloblasts" or "CML cells."

As the leukemia cells multiply and accumulate in the bone marrow, they slow down the production of normal, healthy red blood cells, white blood cells and platelets. As a result, there are too many leukemia cells and too few mature, functioning red blood cells, white blood cells and platelets. Over time, leukemia cells spill out of the bone marrow into the bloodstream. This causes high white blood cell counts. Once leukemia cells are in the blood, they can spread to other parts of the body such as the spleen, causing swelling and pain.

There is another, similar type of blood cancer in which too many granulocytes are made in the bone marrow, called MDS/MPN with neutrophilia (previously referred to as atypical CML). But MDS/MPN with neutrophilia is caused by other genetic mutations. The cancer cells in these patients do not have the Ph chromosome or the *BCR::ABL1* gene. People with this disease generally have poorer responses to treatment and shorter survival times.

MDS/MPN with neutrophilia is treated with different medications than CML. Therefore, it is very important to obtain an accurate diagnosis from an experienced pathologist — a doctor who specializes in identifying diseases by studying cells under a microscope. Classic Philadelphia-chromosome CML looks similar to MDS/MPN with neutrophilia and other myeloproliferative neoplasms when the cells are examined under a microscope. But an experienced pathologist with familiarity with both diseases will be better able to make an accurate diagnosis.

Visit www.LLS.org/booklets to view *Understanding Genetics*.

Signs and Symptoms

Signs and symptoms are changes in the body that may indicate an illness or disease. A sign is a change that the doctor sees during a physical exam or in a laboratory test. A symptom is a change that a patient feels or experiences.

In the United States, many people with CML are diagnosed with the disease before they have any symptoms. An abnormal white blood cell count during a routine blood test is often the first sign of CML.

For those with symptoms, they typically develop gradually. As CML progresses, a person may experience symptoms due to low blood cell counts because the CML cells crowd out the normal blood-making cells in the bone marrow. As a result, people with CML may not have enough red blood cells, platelets and functioning white blood cells.

Symptoms of anemia (low red blood cell count) include:

- Weakness
- Fatigue
- Shortness of breath during basic everyday activities

Symptoms of neutropenia (low number of mature neutrophils, a type of white blood cell important in fighting infections) include:

- Fever
- Infections

Symptoms of thrombocytopenia (low platelet count) include:

- Bruising easily
- Prolonged bleeding from minor cuts
- Bleeding gums
- Frequent or severe nosebleeds

Other general symptoms of CML include:

- Bone pain
- Unexplained weight loss
- Pain or a feeling of fullness below the ribs on the left side, due to an enlarged spleen
- Night sweats

The symptoms of CML may be like those of other blood disorders or medical conditions. Speak with your doctor if you have any of these symptoms to ensure proper diagnosis and treatment.

Diagnosis

While certain signs and/or symptoms may indicate that a person has CML, laboratory tests are needed to confirm the diagnosis. It is important to have an accurate diagnosis because it helps the doctor to:

- Estimate how the disease will progress
- Determine the appropriate treatment

Talk to your doctor about:

- The diagnostic tests that are being done
- What the results mean
- Getting copies of test results

To diagnose CML, doctors use a variety of tests to analyze blood and bone marrow cells. A pathologist will examine the blood cells and the bone marrow cells. The samples should also be examined by a hematopathologist, a doctor who has special training in identifying blood and bone marrow diseases.

Tests done to diagnose CML include:

Medical History. Your doctor will take a thorough medical history. The history may include information about past illnesses, injuries, treatments and medications. Some illnesses run in families, so the doctor may also ask about the health of your blood relatives.

Physical Examination. Your doctor will want to know about your current symptoms and will conduct a physical examination. During the exam, the doctor may listen to your lungs and heart and carefully examine your body for signs of infection and disease. To check your internal organs, the doctor may feel different parts of your body. For example, your doctor may feel your abdomen to see if you have an enlarged liver or spleen, and check the lymph nodes in your neck, armpits and groin (the top inner part of the thigh). Your doctor will also look for signs of other problems, such as bruising.

Complete Blood Count (CBC) With Differential. This test measures the number of red blood cells, white blood cells and platelets in a sample of blood. It also measures the amount of hemoglobin (a protein that carries oxygen) in the red blood cells, and the percentage of red blood cells in the sample. The CBC should include a "differential," which measures the different types of white blood cells in the sample. People with CML often have:

- Increased white blood cell count, often a very high level
- Decreased hemoglobin levels, a sign of anemia
- Increased or decreased platelet count, depending on the severity of the disease

Peripheral Blood Smear. In this test, blood cell samples are stained (dyed) and examined under a microscope. These samples show the:

- Number, size, shape and type of blood cells
- Composition of white blood cells
- Proportion of immature cells (blast cells) compared to the proportion of maturing and fully matured white blood cells. Blast cells are not normally present in the blood of healthy individuals.

Most people with CML have too many white blood cells in the blood. If there are blasts in the blood, further tests will be done to determine if you have the Philadelphia chromosome or the *BCR::ABL1* gene.

Bone Marrow Aspiration and Biopsy. Leukemia starts in the bone marrow. If leukemia is suspected, based on the results of blood tests, your doctor will order a bone marrow aspiration and biopsy to see whether your bone marrow is healthy

and making normal amounts of blood cells. Doctors use the results from these tests to diagnose and monitor blood and bone marrow diseases, including leukemia.

Bone marrow has both a liquid and a solid component.

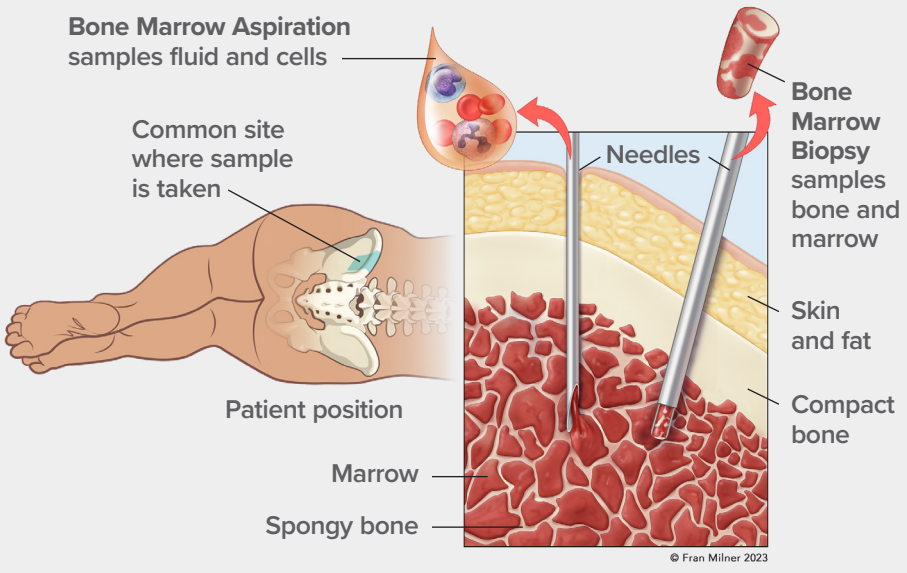
- A bone marrow aspiration is a procedure to remove a sample of the liquid part of the bone marrow.
- A bone marrow biopsy is a procedure to remove a small sample of the solid, spongy part of the bone marrow.

Many people have both tests at the same time. Bone marrow aspiration and biopsy are often performed at the doctor's office or in the hospital. Both samples are usually taken from the hip bone in the lower back. You will likely lie on your stomach or side.

For many patients, this is a painful procedure, so you will receive medicine to numb the skin and the surface of the bone. You may also have the option to take medicine before the procedure to help you relax. Some patients may be given a sedative so that they will feel less pain and have no memory of the procedure.

For a bone marrow aspiration, a special hollow needle is inserted through the back of the hip bone and into the bone marrow to remove a liquid sample of cells. For a bone marrow biopsy, a wider needle is used to remove a sample of a solid piece of marrow. See **Figure 2** below for an illustration of the bone marrow tests.

Figure 2. Bone Marrow Aspiration and Biopsy



Left: The place on the back of the patient's hip bone where a bone marrow aspiration or biopsy is done. **Right:** One needle goes into bone marrow to get a liquid sample for aspiration (left) and the other needle goes inside the bone for a bone biopsy (right). The needle for aspiration is thinner than the one for biopsy.

Both samples are sent to the laboratory where they are viewed under a microscope. The various types of blood cells are counted and examined to check their composition and determine whether the cells look abnormal. Additional biomarker testing may be done on the bone marrow samples.

Visit www.LLS.org/3D and click on "Bone Marrow Biopsy and Aspiration" to view an interactive 3D image which will help you visualize and better understand the bone marrow aspiration and biopsy procedures.

Biomarker Testing. These laboratory tests look for biomarkers, which are molecules found in the blood, other body fluids or tissues that are signs of a normal or abnormal process, or of a condition or disease. Biomarkers provide information about a person's cancer. Each person's cancer has a unique pattern of biomarkers.

Biomarker testing is used to help diagnose some types of cancer. It may also be used to help plan treatment, make a prognosis or monitor treatment. Important tests may include:

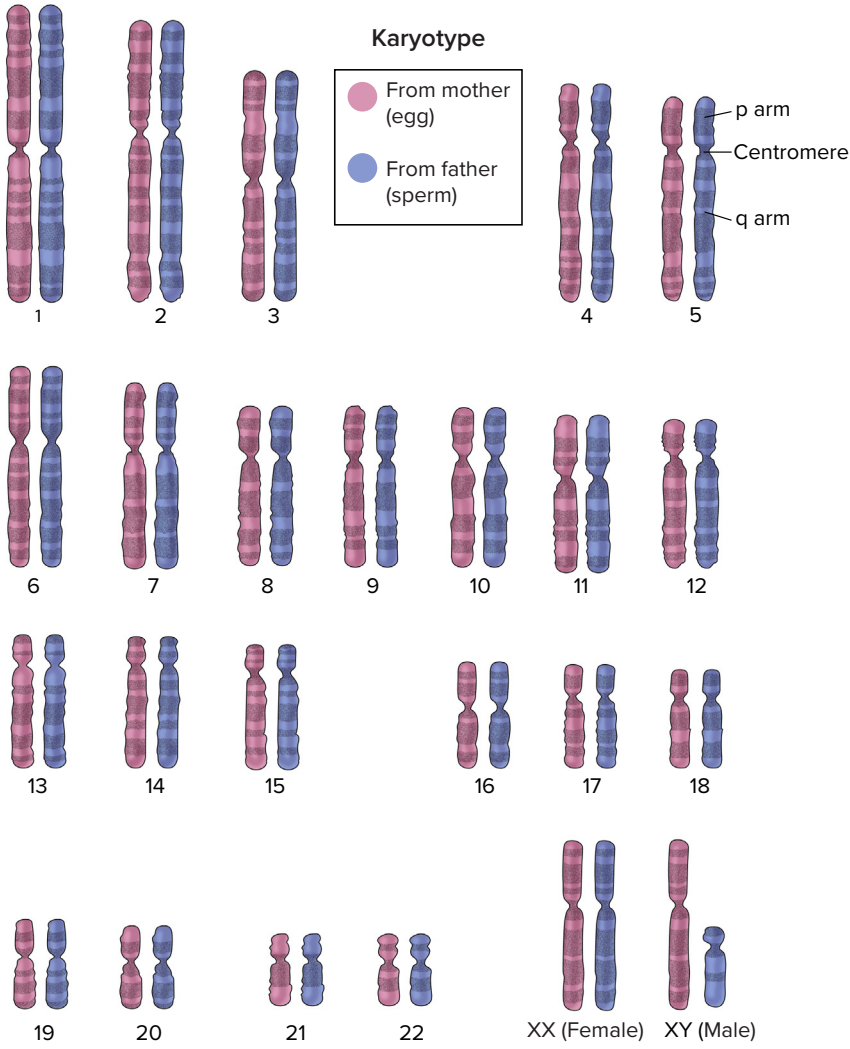
Cytogenetic Analysis (Karyotyping). This test is used to examine chromosomes in a sample of cells. Normal human cells contain 23 pairs of chromosomes, each made up of one chromosome from each parent, for a total of 46 chromosomes. Each pair of chromosomes is a certain size, shape and structure. A "karyotype" is a picture of the chromosomes. See **Figure 3** on page 12 for an illustration of a normal karyotype.

For the test, cells from a bone marrow or blood sample are grown in the laboratory. The cells are then stained and viewed under a microscope to examine the size, shape and number of chromosomes. Cytogenetic testing checks the chromosomes in the sample of cells to:

- See whether there are 46 chromosomes
- Look for changes in the structure of chromosomes, such as broken, missing or extra pieces

The presence of the Ph chromosome in bone marrow cells, along with a high white blood cell count and other characteristic blood and bone marrow test findings, confirm the diagnosis of CML. In about 95 percent of people with CML, the Ph chromosome in bone marrow cells is detectable by cytogenetic analysis. In a small percentage of people with clinical signs of CML, the Ph chromosome cannot be detected by cytogenetic analysis. However, these patients almost always test positive for the *BCR::ABL1* fusion gene on chromosome 22, found with the other types of tests, such as fluorescence in situ hybridization (FISH) (see page 12) and quantitative polymerase chain reaction (qPCR) (see page 13).

Figure 3. Normal Karyotype



Fluorescence In Situ Hybridization (FISH). This test is another way to examine the chromosomes and genes in leukemia cells. It is a slightly more sensitive method for detecting CML than the standard cytogenetic tests used to identify the Ph chromosome. FISH tests can identify the presence of the *BCR::ABL1* gene. A bone marrow sample is often used in FISH testing but testing on blood is also possible.

Doctors use this test to detect certain abnormal changes in the chromosomes and genes of leukemia cells. These tests use color probes that bind to DNA to locate the *BCR* and *ABL1* genes in chromosomes. The *BCR* and *ABL1* genes are marked with two different chemicals, each of which emits a different color. The color

shows up on the chromosome that contains the gene—normally chromosome 9 for *ABL1* and chromosome 22 for *BCR*—so FISH can detect the pieces of chromosomes 9 and 22 that were translocated or switched. The *BCR::ABL1* fusion gene is shown by the overlapping colors of the two probes.

FISH can also detect some changes that are too small to be seen with basic cytogenetic testing. However, FISH is not used as a general screening tool, and this test has one disadvantage—the doctor must select the specific chromosomes or genes to examine before the test is performed.

Next-Generation Sequencing (NGS). Next-generation sequencing, also called "molecular testing" or "genomic testing," refers to a number of different laboratory tests that examine the exact sequence (order) of DNA or RNA (ribonucleic acid). This makes it possible to identify a variety of genetic changes in a patient's cancer cells. There are targeted sequencing tests (also called multigene panels) that look for specific mutations in the cancer cells. These tests focus on specific sets of genes or areas of DNA. There are also broad DNA sequencing tests (genomic screening tests) that analyze the sequence of large regions of DNA, rather than looking for mutations of specific genes. Doctors may also order sequencing of all the DNA in the cancer cells, and/or normal cells in the body. This test is known as whole genome sequencing.

Quantitative Polymerase Chain Reaction (qPCR). This test can identify cancer cells based on their characteristic genetic abnormalities, such as mutations or chromosomal changes. qPCR essentially increases or "amplifies" small amounts of specific pieces of either DNA or RNA to make them easier to detect and count. As a result, qPCR can detect genetic abnormalities even when a very small number of cancer cells remain. The test is done with a bone marrow or blood sample. With qPCR, it is possible to identify one cancer cell among 100,000 to 1 million healthy cells.

In CML, qPCR is used to determine the amount of *BCR::ABL1* compared to normal cells in a bone marrow or blood sample. It can detect very small amounts of the *BCR::ABL1* gene, even when the Ph chromosome cannot be detected in blood or bone marrow cells with less sensitive tests such as cytogenetic analysis or FISH.

Doctors use qPCR to monitor a patient's response to treatment. The amount of the *BCR::ABL1* gene found in the blood is compared to baseline (the pre-treatment amount) using a measure called the International Scale (IS). The International Scale has been established to standardize PCR testing across different laboratories. For more information on the International Scale, see page 34.

Visit www.LLS.org/booklets to view the LLS booklets *Understanding Lab and Imaging Tests*, *Understanding Genetics* and *Biomarker Testing for Cancer Treatment*.

Treatment Planning

Choosing a Hospital and Doctor. When you find out that you have cancer, you want to get the best possible medical care and treatment. CML is a rare disease. So, you may want to seek treatment at a center with hematologist-oncologists who have significant experience in caring for people with CML. A hematologist is a doctor who has special training in treating blood disorders. An oncologist is a doctor who has special training in treating cancer. A hematologist-oncologist specializes in treating blood cancers.

A local or community-based oncologist may only see a few CML patients. In large medical centers, there are hematologist-oncologists who specialize in treating CML. These specialists develop experience and expertise in diagnosing and treating CML. They can also better anticipate treatment-related side effects of CML and provide therapies to prevent or manage side effects. If your local medical center does not have a hematologist-oncologist, ask your cancer specialist to consult with a hematologist-oncologist at another medical center.

Getting a Second Opinion. If you have been diagnosed with CML, you may want to consult one or more CML specialists before proceeding with a treatment plan to make sure that you receive the therapy that is right for you. You may also want to seek a second opinion from another doctor. A second opinion may help you feel more confident about the recommended treatment plan. The second opinion should come from another hematologist-oncologist, preferably one who treats CML. Some CML specialists may conduct telehealth visits, so you may have the opportunity to see an expert without traveling.

When you go to the appointment for a second opinion, make sure that all your medical records are available for examination. Upon review of your medical records, the specialist you see for a second opinion can confirm a proposed treatment plan and/or suggest modifications, as well as potentially offer a clinical trial that may only be available at certain institutions. This review will also reassure you that you have explored all of your treatment options.

If you are either unsure about getting a second opinion or feel uncomfortable about how to tell your doctor you are seeking one, call our Information Specialists at (800) 955-4572 to discuss an approach that makes you feel comfortable. You may also want to check with your insurance company to be sure that your plan covers the cost of getting a second opinion and to see if specific doctors or centers are recommended.

Visit www.LLS.org/booklets to view *Choosing a Specialist or Treatment Center.*

Fertility. If you are of child-bearing age, you should be aware that some cancer treatments, including tyrosine kinase inhibitor (TKI) therapy, may affect fertility (the ability to have children in the future). Before you begin your CML treatment,

it is important to talk with your doctor about whether your treatment could affect your fertility.

Those who want to have children in the future may want to speak with a fertility specialist. The fertility specialist can talk to you about possible options for preserving your fertility. You may be able to take steps before treatment begins to preserve your fertility. However, delaying cancer treatment to address fertility options may not always be recommended. For more information, see *Fertility, Pregnancy and TKIs* on page 42.

Visit www.LLS.org/booklets to view *Fertility and Cancer.*

CML Phases and Prognostic Factors

Your doctor will discuss with you how your phase of CML and your prognostic factors will affect your treatment plan.

CML Phases. To help plan treatment for many types of cancers, doctors will determine the stage of cancer, which refers to the extent of cancer in the body.

For most types of cancer, doctors assign a stage based on the size of the tumor and whether the cancer has spread to the lymph nodes or other parts of the body. Blood cancers such as leukemia, however, are staged differently. Leukemia cells spread throughout the body as they circulate in the bloodstream and typically do not produce a tumor that can be measured. Therefore, the stages of CML are determined differently based on blood cell counts in the patient's blood and bone marrow.

In CML, the stages are called "phases." There are three phases of CML. They are:

- Chronic phase
- Accelerated phase
- Blast phase (also called blast crisis phase)

Chronic Phase. In the United States, most people have chronic phase CML at the time of diagnosis. People with chronic phase CML:

- Have an increased number of white blood cells in the blood and bone marrow at various stages of maturation
- May or may not have symptoms
- Usually respond very well to standard treatment
  - Specifically, symptoms go away, white blood cell counts and spleen size return to normal, and hemoglobin concentration improves

If untreated, chronic phase CML will eventually progress to accelerated phase and/or blast phase CML.

Accelerated Phase. In the accelerated phase, the number of immature myeloblasts is higher than in chronic phase, and often new chromosomal changes or other mutations occur, in addition to the Ph chromosome. The International Consensus Classification (ICC) criteria for accelerated phase CML include:

- Bone marrow or peripheral blood blasts of 10% to 19%
- Peripheral blood basophils (a type of white blood cell) in the blood equal to or greater than 20%
- Presence of additional chromosomal abnormalities in CML cells (such as second Ph, trisomy 8, isochromosome 17q, trisomy 19, complex karyotype, or chromosome 3q26.2 abnormalities)

In the accelerated phase, the number of CML cells grows faster and causes symptoms such as fatigue, fever, weight loss, bone pain and night sweats. If untreated, accelerated phase CML will eventually transform into blast phase CML.

Blast Phase (also called Blast Crisis Phase). The blast phase looks and behaves like a fast growing acute leukemia, which can be either of myeloid or lymphoid origin.

The ICC criteria for diagnosing blast phase CML include:

- Bone marrow or peripheral blood blasts greater than or equal to 20%
- Myeloid sarcoma, a buildup of myeloblasts that form a tumor outside the bone marrow. This is also called extramedullary disease.
- Bone marrow or peripheral blood lymphoblasts (immature lymphoid cells) greater than 5%, suggesting lymphoblastic crisis. The increased number of lymphoblasts can affect treatment.

People who have blast phase CML may have signs and symptoms such as fever, fatigue, shortness of breath, abdominal pain, bone pain, enlarged spleen, poor appetite and weight loss, night sweats, bleeding and/or infections.

Prognostic Factors. Certain factors can affect a patient's prognosis—the probable outcome of their cancer. These are called prognostic factors. Doctors use prognostic factors to help predict how a person's disease is likely to respond to treatment. These factors help doctors plan the most appropriate initial treatment for each patient.

The following prognostic factors at the time of diagnosis are associated with a less favorable prognosis:

- Accelerated or blast phase CML
- Age 60 years or older
- Enlarged spleen

- Very high or very low platelet counts
- High number of circulating blast cells in the blood
- Increased numbers of basophils and eosinophils (types of white blood cells) in the blood

Doctors use prognostic scoring systems, which take these factors into account, to predict outcomes for patients with CML. There are three main prognostic scoring systems used to determine the risk profile of patients with chronic phase CML at the time of diagnosis:

- Sokal scoring system: This score is based on the patient's age, spleen size, platelet count and the percentage of blast cells in the blood.
- Hasford (Euro) scoring system: This score uses the same factors as the Sokal score but also includes the number of basophils and eosinophils circulating in the blood.

  To calculate your Sokal and Hasford (Euro) scores, go to: https://www.leukemia-net.org/leukemias/cml/euro__and_sokal_score/
- European Treatment and Outcome Study for CML (EUTOS) Long-Term Survival scoring system (ELTS): The ELTS score also uses the same factors as the Sokal scoring system but looks specifically at long-term survival in CML patients. This is important because CML treatment is so effective that many patients are living longer and therefore die from other causes common in older people, such as heart disease.

  To learn about calculating your ELTS score, go to: https://www.leukemia-net.org/leukemias/cml/elts_score/

Doctors use risk scores to help guide treatment decisions. The Sokal, Hasford and ELTS scoring systems categorize CML patients into three groups: low risk, intermediate risk and high risk. Generally, patients in the low-risk categories are likely to respond better to treatment.

Treatment Options

New treatments may have been approved since this booklet was printed. Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Before you begin treatment, you and your doctor will discuss your treatment options. One option may be a clinical trial. A clinical trial is a type of research study that tests how well new medical approaches work in people. Like all treatment options, clinical trials have possible risks and benefits. By considering all of your treatment options, including clinical trials, you will be

taking an active role in a very important decision that affects you. For more information on clinical trials, see page 43.

Talk to your doctor about:

- Your treatment options and the results you can expect from treatment
- The possibility of participating in a clinical trial

In choosing treatment options, your doctor will take into account your:

- Phase of CML
- Risk group
- Age and other health conditions
- Results of biomarker testing on your CML cells (chromosome abnormalities and DNA mutations)

Treatment typically begins with a targeted therapy called a tyrosine kinase inhibitor (TKI). For most, TKIs have changed CML from a life-threatening illness to a chronic, manageable condition. Most people diagnosed with CML in the chronic phase can expect to have a near normal life span. Some people who are able to maintain deep remissions on TKIs may even be able to stop treatment under careful monitoring (see *Treatment-Free Remission* on page 38).

Tyrosine Kinase Inhibitor Therapy. Tyrosine kinase inhibitors (TKIs) are a type of targeted therapy. Targeted therapies target specific molecules that cancer cells need to grow, divide and spread.

TKIs block a protein called tyrosine kinase. In CML, the leukemia cells have the abnormal *BCR::ABL1* gene that makes a protein called BCR::ABL1 tyrosine kinase. This abnormal tyrosine kinase signals the CML cells to divide more quickly and live longer than normal blood cells. TKIs block this signaling which stops the uncontrolled growth of the CML cells.

CML treatment has improved dramatically since the introduction of TKIs. Imatinib mesylate (Gleevec®) was the first TKI approved for CML in 2001. Subsequently second- and third-generation TKIs have been approved. Second- and third-generation TKIs are generally more potent and better at targeting certain mutations. See **Table 1** on page 19 for a list of TKIs used to treat CML. However, not all patients respond to TKIs, and some patients develop resistance to these drugs.

TKIs are oral medications that are taken as pills or capsules by mouth. Generic equivalents of TKIs have been available since 2016. A generic drug is a medication created to be the same—in terms of dosage, form, safety, strength, route of administration, quality, performance characteristics and intended

use—as a brand-name drug that is already on the market. These similarities allows generic drugs to demonstrate "bioequivalence," which means that a generic medicine works in the same way and provides the same clinical benefit as its brand-name version. In other words, you can take a generic medicine as an equal substitute for its brand-name counterpart. The FDA employs strict standards to ensure that generic drugs are bioequivalent to brand name drugs in the United States. Generic drugs typically cost less than brand-name versions. Talk to your doctor about whether a generic TKI is best for you.

Patients with a history of cardiac disease or peripheral vascular disease need to be monitored carefully and frequently during TKI treatment and after completion of therapy, depending on which TKI was given. Some patients treated with TKIs have developed serious cardiac side effects, including heart attacks and changes in heartbeat rhythm. Some have developed narrowing of the arteries in the extremities of the brain, which can cause a stroke. Many patients who develop these adverse effects also have other health problems and risk factors, including older age, high blood pressure, high cholesterol levels, diabetes or a history of cardiac disease, so careful monitoring is very important.

CML treatment can cause side effects and some may negatively affect your quality of life. It is important to talk to your doctor if you are experiencing any side effects from your TKI. Most patients can manage their side effects without stopping treatment; however, changing to another treatment may be an option to lessen side effects and improve quality of life.

For more information, see the package insert and/or full prescribing information for each medication (available on the internet).

Table 1. TKIs Used in the Treatment of CML

Name FDA Approval Date	Approved for
Imatinib mesylate (Gleevec®) 2001; 1st generation TKI	1. Newly diagnosed adult and pediatric patients with Philadelphia chromosome positive chronic myeloid leukemia (Ph+ CML) in chronic phase 2. Patients with Ph+ CML in blast crisis, accelerated phase, or in chronic phase after failure of interferon-alfa therapy
Dasatinib (Sprycel®) 2006; 2nd generation TKI	1. Newly diagnosed adults with Ph+ CML in chronic phase 2. Adults with chronic, accelerated or myeloid or lymphoid blast phase Ph+ CML with resistance or intolerance to prior therapy including imatinib 3. Pediatric patients 1 year of age and older with Ph+ CML in chronic phase

Table 1. TKIs Used in the Treatment of CML (continued)

Name FDA Approval Date	Approved for
Nilotinib (Tasigna®, Danziten™) 2007; 2nd generation TKI	Nilotinib (Tasigna®) 1. Adult and pediatric patients greater than or equal to 1 year of age with newly diagnosed Ph+ CML in chronic phase 2. Adult patients with chronic phase and accelerated phase Ph+ CML resistant to or intolerant to prior therapy that included imatinib 3. Pediatric patients greater than or equal to 1 year of age with Ph+ CML in chronic phase or accelerated phase with resistant to or intolerant to prior TKI therapy --- Nilotinib (Danziten™) 1. Adult patients with newly diagnosed Ph+ CML in chronic phase 2. Adult patients with chronic phase and accelerated phase Ph+ CML resistant to or intolerant to prior therapy that include imatinib
Bosutinib (Bosulif®) 2012; 2nd generation TKI	1. Adult and pediatric patients 1 year of age and older with chronic phase Ph+ CML, newly diagnosed or resistant or intolerant to prior therapy 2. Adult patients with accelerated or blast phase Ph+ CML with resistance or intolerance to prior therapy
Ponatinib (Iclusig®) 2012; 3rd generation TKI	1. Adult patients with chronic phase CML with resistance or intolerance to at least two prior kinase inhibitors 2. Adult patients with accelerated phase or blast phase CML for whom no other kinase inhibitors are indicated 3. Adult patients with T315I-positive CML (chronic phase, accelerated phase, or blast phase)
Asciminib (Scemblix®) 2021; TKI: STAMP (Specifically Targeting the ABL Myristoyl Pocket) Inhibitor	1. Adult patients with newly diagnosed Ph+ CML in chronic phase 2. Adult patients with previously treated Ph+ CML in the chronic phase 3. Adult patients with Ph+ CML in chronic phase with the T315I mutation
The following drugs were used as initial therapy before TKIs were introduced and continue to be used in select patients: **Interferon alfa (Roferon®-A, Intron® A) (immunotherapy)** **Pegylated interferon alfa (immunotherapy)** **Hydroxyurea (Hydrea®) (chemotherapy)** **Cytarabine (Cytosar-U®) (chemotherapy)** **Busulfan (Myleran®) (chemotherapy)**	

New treatments may have been approved since this booklet was printed.
Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Choosing a TKI. Each TKI has risks and benefits. Patients should talk with their doctor to determine which TKI to use for initial and subsequent treatment as needed. Choosing a TKI is based on many factors including:

Patient Factors

- Patient age
- Treatment goals (survival versus treatment-free remission). Among older patients, survival may be the primary goal, and treatment-free remission a secondary goal. In younger patients, treatment-free remission may be pursued more aggressively. For more information on treatment-free remission, see page 38.
- Preexisting comorbidities (medical conditions being treated alongside CML) and medications. Some comorbidities that can influence the choice of a TKI include chronic lung disease, high blood pressure, diabetes, and liver or kidney disease. See **Table 2** below.

Table 2. Suggestions for TKI Selections for First-Line Therapy Based on Selected Comorbidities

Comorbidity	Preferred	Less preferred
Diabetes	Imatinib, dasatinib, bosutinib, asciminib	Nilotinib
Pulmonary disease/pulmonary arterial hypertension	Imatinib, bosutinib, nilotinib, asciminib	Dasatinib
Gastrointestinal issues	Nilotinib, dasatinib, asciminib	Imatinib, bosutinib
Cardiovascular	Imatinib, bosutinib	Nilotinib, dasatinib
Peripheral arterial	Imatinib, bosutinib (dasatinib?)	Nilotinib
Liver	Imatinib, dasatinib (nilotinib?)	Bosutinib
Kidney	Nilotinib, dasatinib, asciminib	Imatinib, bosutinib

Adapted from: Cortes J. How to manage CML patients with comorbidities. *Blood.* 2020; 136(22):2507-2512.

Oehler VG. (2024). The future of CML treatment: what's next? [Webinar]. The Leukemia & Lymphoma Society. https://www.lls.org/patient-education-webcasts/future-cml-treatment-whats-next

Disease Factors

- Phase of CML
- Risk score (as defined by the Sokal or other risk models)
- Drug-resistant mutations in the *BCR::ABL1* gene
- Additional chromosomal abnormalities or gene mutations in the CML cells

Cost Considerations

- Insurance coverage
- Out-of-pocket costs
- Potential use of generic options

Below is additional information about the TKIs used to treat CML. For a full listing of side effects, please see the package insert and/or full prescribing information for each medication (available on the internet). See **Table 1** on page 19, for drug approval information.

Imatinib mesylate (Gleevec®)

- Imatinib should be taken with a meal and a large glass of water.
- Grapefruit and grapefruit products may increase the amount of imatinib in the blood. Patients should avoid consuming grapefruit, grapefruit juice and any supplement containing grapefruit extract while taking imatinib.
- This highly effective therapy brings about a stable remission in most people with chronic phase CML.
- The drug is generally well tolerated by the majority of both younger and older patients, although most people experience some side effects. It is important for patients to tell their healthcare team about any side effects because most side effects can be managed. Common side effects of imatinib are:
  - Nausea, vomiting and/or diarrhea
  - Muscle cramps and bone pain
  - Fatigue
  - Rashes
  - Edema (fluid retention that causes swelling around the eyes, feet, lungs or heart)
- Although rare, serious side effects of imatinib include:
  - Low blood cell counts. Having low levels of red blood cells, white blood cells or platelets can increase a patient's risk of anemia, infection and/or bleeding.
  - Congestive heart failure in the setting of fluid retention (impaired ability of the heart to pump blood) and left ventricular dysfunction (impaired functioning of the left side of the heart), particularly in patients with other health issues and risk factors. (Note: Patients with heart disease or risk factors for heart disease should be monitored and treated for heart disease.)
  - Severe liver problems
- Some CML patients are not able to tolerate the side effects of imatinib, and in some others the drug stops working. These problems are known as drug "intolerance" and drug "resistance." For some patients the drug will work with an increase in the dosage; other patients may need to take a different TKI. Fortunately, there are other approved therapies for people with imatinib intolerance or resistance. When imatinib is not a treatment option, doctors decide, along with their patients, which of the other treatment options is the best alternative.

Dasatinib (Sprycel®)

- Dasatinib is taken once daily, either in the morning or evening, either with or without food. Patients taking antacid medicine should take the antacid at least 2 hours after taking dasatinib.

- Grapefruit products may increase the amount of dasatinib in the blood. Patients should avoid consuming grapefruit, grapefruit juice and any supplement containing grapefruit extract while taking dasatinib.
- Studies of dasatinib have shown that it is more potent than imatinib and that it induces faster and deeper molecular responses. However, dasatinib has not been shown to increase survival compared to imatinib.
- Common side effects of dasatinib include:
  - Nausea
  - Diarrhea
  - Headache
  - Fatigue
  - Shortness of breath, usually due to accumulation of fluid in the lungs (known as a "pleural effusion")
  - Rash
  - Fever
- Serious side effects of dasatinib include:
  - Low blood cell counts. Having low numbers of red blood cells, white blood cells and platelets increase a patient's risk of anemia, infection and/or bleeding.
  - Fluid retention around the lungs (pleural effusion) or the heart. Patients should call the doctor immediately if they have any of the following symptoms: swelling all over the body, weight gain, shortness of breath, and cough (especially during low levels of physical activity or at rest), or chest pain when taking a deep breath.
  - In rare instances, dasatinib may increase the risk of developing a serious condition called "pulmonary arterial hypertension" (PAH), which is high blood pressure in the arteries of the lungs.

Doctors should check the heart and lungs of patients both before and during treatment with dasatinib. If a patient is diagnosed with PAH while taking dasatinib, the medication should be discontinued permanently. PAH may be reversible after dasatinib is discontinued.

Nilotinib (Tasigna,®Danziten™)

- Nilotinib is usually taken twice a day. Tasigna® should be taken on an empty stomach. Patients should avoid eating food for at least 2 hours before and at least 1 hour after the dose is taken. In 2024, the FDA approved a new formulation of nilotinib tablets (Danziten™) with no mealtime restrictions.
- Grapefruit products increase the amount of nilotinib in the blood. Patients should avoid consuming grapefruit, grapefruit juice and any supplement containing grapefruit extract while taking nilotinib.

- Studies have shown that nilotinib is more potent than imatinib and that it induces faster and deeper molecular responses. However, nilotinib has not been shown to increase survival compared to imatinib.
- One serious side effect of nilotinib is that it may cause heart rhythm problems in some patients. This is sometimes caused by nilotinib interacting with other drugs or supplements, so it is very important for patients to tell their doctors about any supplements or medicines they are taking, including over-the-counter medicines.
- Patients who take histamine type 2 (H2) receptor antagonists/blockers should take these medicines either about 10 hours before or about 2 hours after taking nilotinib. Patients taking over-the-counter (OTC) antacids containing aluminum hydroxide, magnesium hydroxide or simethicone, should take these medicines about 2 hours before or about 2 hours after taking nilotinib. OTC drugs can be obtained without a prescription.
- Common side effects of nilotinib include:
  - Nausea, vomiting, diarrhea
  - Rash
  - Headache
  - Fatigue
  - Itching
  - Cough
  - Constipation
  - Muscle and joint pain
  - Runny or stuffy nose, sneezing, sore throat
  - Fever
  - Night sweats
- Serious side effects include:
  - Low blood cell counts. Having low numbers of red blood cells, white blood cells and platelets can increase a patient's risk of anemia, infection and/or bleeding.
  - QT interval prolongation, a serious heart problem that causes a change in heartbeat rhythm that can be fatal. The patient should contact the doctor immediately if feeling lightheaded, faint or having an irregular heartbeat while taking nilotinib. Before starting and during treatment with nilotinib, the doctor should check the patient's heart with a test called an "electrocardiogram" (ECG, also abbreviated EKG).
  - Blood clots which cause decreased blood flow to the legs, heart or brain.
  - Liver damage symptoms, including yellow skin and eyes (jaundice).

- Pancreatitis (inflammation of the pancreas).
- Hyperglycemia, a higher-than-normal amount of glucose (sugar) in the blood.
- Fluid retention with symptoms including shortness of breath, rapid weight gain and swelling.

Bosutinib (Bosulif®)

- Bosutinib is taken once daily with food.
- Grapefruit and grapefruit products may increase the amount of bosutinib in the blood. Patients should avoid consuming grapefruit, grapefruit juice and any supplement containing grapefruit extract while taking bosutinib.
- Side effects include:
  - Stomach pain, diarrhea, nausea and/or vomiting
  - Fluid retention
  - Rash
  - Fatigue
- Serious side effects include:
  - Low blood cell counts. Low levels of red blood cells, white blood cells and platelets can increase a patient's risk of anemia, infection and/or bleeding.
  - Liver problems
  - Fluid retention around the lungs, heart and stomach
  - Kidney problems

Ponatinib (Iclusig®)

- Ponatinib may be taken either with or without food.
- The most common side effects include:
  - Rash
  - Abdominal (stomach-area) pain
  - Fatigue
  - Headache
  - Dry skin
  - Fever
  - Constipation
  - High blood pressure (hypertension)
- Serious side effects and/or life-threatening risks include:
  - Low blood cell counts. Low levels of red blood cells, white blood cells and platelets can increase a patient's risk of anemia, infection and/or bleeding.

- Blood clots or blockages in blood vessels (arteries and veins). Patients should get medical help right away if they have any of the following symptoms: chest pain or pressure; pain in the arms, legs, back, neck or jaw; shortness of breath; numbness or weakness on one side of the body; leg swelling; headaches; severe stomach pain; dizziness; decreased vision and/or loss of vision; trouble talking.
- Heart problems, including heart failure; irregular, slow or fast heartbeats; and heart attack. Doctors will check a patient's heart function, both before and during treatment with ponatinib. Patients who have cardiovascular risk factors should be referred to a cardiologist. Get medical help right away if you have any of the following symptoms: shortness of breath, chest pain, fast or irregular heartbeats, dizziness or feeling faint.
- Liver problems, including liver failure. Symptoms may include yellowing of the skin or white part of the eyes (jaundice), dark-colored urine, bleeding or bruising, loss of appetite and sleepiness.
- High blood pressure (hypertension)
- Pancreatitis (inflammation of the pancreas)
- Neuropathy (damage to the nerves in the arms, brain, hands, legs or feet)
- Serious eye problems that can lead to blurred vision and/or blindness
- Severe bleeding
- Fluid retention

Asciminib (Scemblix®)

- Asciminib is taken once or twice daily, as directed by your healthcare team.
- Asciminib should be taken on an empty stomach. Patients should avoid eating food for at least 2 hours before and at least 1 hour after the dose is taken.
- Studies have shown that asciminib is more potent than bosutinib and that it induces faster and deeper molecular responses.
- The most common side effects include:
  - Upper respiratory tract infections
  - Musculoskeletal pain
  - Fatigue
  - Nausea
  - Rash
  - Diarrhea
- Serious side effects and/or life-threatening risks include:
  - Low blood cell counts. The healthcare team will check your blood cell counts every 2 weeks for the first 3 months of treatment and then monthly

or as needed. Tell the healthcare team if you notice unexpected bleeding or bruising, blood in your urine or stool, fever, or signs and/or symptoms of infection.

- Pancreatitis (inflammation of the pancreas)
- High blood pressure (hypertension)
- Allergic reaction
- Heart and blood vessel (cardiovascular) problems. This drug can cause heart problems including heart attack, stroke, blood clots, blockage of arteries, heart failure and abnormal heartbeat. Tell the healthcare team right away if you have any of the following symptoms: shortness of breath, chest pain or pressure, a feeling like your heart is beating too fast or you feel abnormal heartbeats, swelling in your ankles or feet, dizziness, weight gain, numbness or weakness on one side of your body, decreased vision or loss of vision, trouble talking, headache, severe stomach-area pain, or pain in your arms, legs, back, neck or jaw.

Ask your healthcare team these questions about your TKI treatment:

- How can I best communicate with my healthcare team if my TKI is affecting my quality of life?
- What modifications can safely be made to my current TKI to reduce side effects?
- Are there changes I can make to how I take my TKI to reduce side effects? (for example, dissolving the pill in juice, avoiding taking it before lying flat in bed at night, splitting up the dose, etc.)
- What are the long-term side effects of my current TKI?
- When should I consider changing my TKI based on side effects and how my treatment is affecting my daily activities?
- Are there any tools or tips to help me track my side effects and the effect on my quality of life?
- If I switch my TKI but find the new one less tolerable, can I go back to my current TKI?

Drug Interactions. Certain drugs, herbal supplements and even some foods can affect the way TKIs work in the body. Corticosteroids, antiseizure medications, antacids and the herbal supplement called St. John's Wort can make some TKIs less effective. Other products, including certain antibiotics, antifungal medications and grapefruit compounds, may increase the amount of TKIs in the blood to high, unsafe levels.

In addition, TKIs can have serious or even deadly interactions with other prescription medications, over-the-counter products, supplements and even certain foods. Patients should always provide their doctors with a list of any medications, herbal supplements and vitamins they are taking to be certain that it is safe to take these products while taking a TKI. It is also important to ask the doctor about any foods that should be avoided.

TKI Adherence. It is important for you to take your TKI exactly as prescribed by the doctor. "Adherence" to an oral therapy means that you:

- Take the correct dose of medication
- Take the medication at the correct time
- Never or rarely miss a dose
- Never take an extra dose
- Do not take a dose with foods, liquids or other medications that are not allowed

TKI therapy can control CML in most patients, but you must take your medication exactly as prescribed for it to work. You should never skip doses or stop taking your medication unless instructed to do so by your doctor. Not adhering to a medication regimen is a primary reason for poor response to the prescribed treatment. If you are experiencing side effects from your TKI, talk to your doctor. Your doctor can provide supportive treatment to help manage your side effects or can change your TKI. If you cannot afford your medication and are not taking the prescribed amount, talk to your healthcare team. They may be able to help you find financial assistance. Or visit www.LLS.org/finances to learn more about LLS financial assistance programs.

Visit www.LLS.org/booklets to view *Oral Treatment Adherence Facts.*

TKI Resistance. Drug resistance is the term used when a disease has not responded to treatment. Drug resistance in CML occurs when a patient is taking a TKI but the number of leukemia cells in their blood increases.

"Primary resistance" is the term that describes resistance to a drug that is being taken for the first time. "Secondary resistance" occurs when cancer cells initially respond to a treatment, but then stop responding.

In CML, resistance is often caused by mutations in the *BCR::ABL1* gene. Sometimes, resistance to a TKI can be overcome by increasing the dose of the TKI or by switching to another type of TKI. Second-generation TKIs can be effective in treating patients with mutations that are resistant to imatinib.

BCR::ABL1 kinase domain mutation analysis is a test that identifies the mutations in the *BCR::ABL1* gene that are frequently responsible for TKI resistance (see *BCR::ABL1 Kinase Domain Mutation Analysis* on page 36). This information can help a doctor decide which TKI to prescribe.

Before modifying treatment, the doctor should determine if the patient is taking the TKI as prescribed. The doctor should also find out if the patient is taking other drugs that may interact with the TKI.

Allogeneic Stem Cell Transplantation. Allogeneic stem cell transplantation is a type of treatment that destroys cells in the patient's bone marrow and then replaces them with new, healthy blood-forming stem cells from either a matched or partially matched donor. While certain people with CML may be cured with an allogeneic stem cell transplantation, not everyone can receive one. It is an intense and complex treatment that can cause life-threatening side effects in some patients. It is often not a good option for older patients or for patients who have other health problems.

The decision to pursue allogeneic transplantation has become more complicated because many patients have very good responses to TKIs. It is true that stem cell transplantation has been proven to be curative for some CML patients; but today, treatment with TKIs may control the disease for very long periods and preserve quality of life without the serious side effects of transplantation.

Doctors consider many important factors when deciding if an allogeneic transplant is the preferred choice of treatment for a patient. These factors include the patient's age, general health, phase of CML, history of poor response to other treatments, and the availability of a well-matched donor. Stem cell transplantation is considered a treatment option for patients who have resistance to at least two types of TKIs, for patients whose CML is in accelerated or blast phase, and for patients who are intolerant to all TKIs.

The most important prognostic factor for post-transplant survival is the patient's phase of CML. Approximately 80 percent of patients with chronic phase CML will be disease-free for 5 years after transplant. In patients with accelerated phase CML, approximately 40 to 50 percent are disease-free after 5 years, and only 10 to 20 percent of blast phase patients are alive and disease-free after 5 years.

Visit www.LLS.org/booklets to see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.

Immunotherapy. Immunotherapy is a type of therapy that uses substances to stimulate or suppress the immune system to help the body fight cancer and other diseases. Interferon, a type of immunotherapy, is a substance made naturally by the immune system, but it can also be made in the laboratory. Interferon reduces the growth and division of cancer cells.

Prior to the introduction of TKIs, interferon was considered the first-line treatment for patients who were not candidates for an allogeneic stem cell transplant. Today, interferon therapy is rarely used as a treatment for CML because TKIs are more effective and have fewer side effects than interferon. But interferon may be an option for patients who cannot tolerate the side effects of TKI therapy or for patients who are pregnant.

Interferon can cause significant side effects, including:

- Trouble with concentration and memory
- Mood changes including anxiety and depression
- Flu-like symptoms, such as muscle aches, fatigue, fever, chills, headaches, nausea and vomiting
- Low red blood cell, white blood cell and platelet counts

These side effects continue as long as a patient takes interferon, but over time, they may become easier to tolerate. However, many patients cannot cope with these side effects every day and will need to talk with their doctor about discontinuing interferon treatment.

Treating CML by Phase

Before treatment, some patients need short-term management to lower excessively high white blood cell counts. A very high white blood cell count can impair blood flow to the brain, lungs, eyes and other areas of the body. Even if the diagnosis of CML has not been confirmed, it can still be important to lower the white blood cell count quickly.

- Hydroxyurea (Hydrea®), a chemotherapy drug, is sometimes given to lower a very high white blood cell count quickly, until a suspected CML diagnosis can be confirmed. Hydroxyurea is taken orally as a capsule and can also help reduce the size of the spleen. Once a diagnosis of CML is confirmed, doctors usually start TKI therapy and discontinue hydroxyurea.
- "Leukapheresis" is a procedure that uses a machine (similar to a dialysis machine) to remove white blood cells (WBCs) from the blood. It can lower WBC counts immediately in all patients who have a dangerously high WBC count that causes symptoms such as confusion or shortness of breath. It may also be used to lower WBC counts in female patients diagnosed with chronic phase CML during the first months of pregnancy, when other treatments may be harmful to fetal development.

Treatment for Chronic Phase CML. Most people with CML are diagnosed during the chronic phase of the disease. The goals of treatment are to eliminate all cells that contain the *BCR::ABL1* gene, to prevent progression to more aggressive accelerated or blast phase CML and to allow patients to achieve a life expectancy similar to the general population with good quality of life.

TKI therapy is the standard treatment for chronic phase CML. TKIs are often successful at managing CML for long periods of time. The first therapy given for a disease is called "first-line" treatment. The following TKIs are approved as first-line treatment for chronic phase CML:

- Asciminib
- Bosutinib
- Dasatinib
- Imatinib
- Nilotinib

Some people with CML have a *BCR::ABL1* gene mutation called T315I. The following TKIs have been approved to treat CML with the T315I:

- Asciminib
- Ponatinib

After treatment starts, doctors will monitor patients to evaluate treatment response. Patients who are responding will stay on their current TKI. If the patient is not meeting treatment milestones, the doctor will need to find out why.

The initial treatment may not work because of drug intolerance (intolerable side effects from a particular drug), or because of drug resistance (meaning the disease does not respond to the drug). If a patient is adhering to their prescribed treatment regimen and their current treatment is not working, a *BCR::ABL1* kinase domain mutation analysis should be done to check for mutations of the *BCR::ABL1* gene (see *BCR::ABL1 Kinase Domain Mutation Analysis* on page 36).

When a first-line treatment does not work or stops working, the doctor may:

- Advise patients who have not been taking their TKIs as prescribed about the importance of adhering to their medication regimen
- Increase the dosage of the current drug (if possible)
- Switch to another TKI: for example, switching from imatinib to dasatinib, nilotinib, bosutinib, asciminib or ponatinib
- Assess whether an allogeneic stem cell transplant is an option

Treatment for Accelerated Phase CML. The treatment goal for accelerated phase CML is the same as it is for the chronic phase: eliminate all cells that contain the *BCR::ABL1* gene, leading to a remission. If this is not possible, the goal is to return the disease to the chronic phase. Patients with accelerated phase CML should be treated at a specialized center by doctors who have expertise in treating CML. In the accelerated phase of CML, the leukemia cells often acquire new genetic mutations that may make treatments less effective. Patients should undergo *BCR::ABL1* gene mutation analysis before starting treatment, to determine which treatment option is best for them (see *BCR::ABL1 Kinase Domain Mutation*

Analysis on page 36). Treatment options for accelerated phase CML depend on the patient's previous treatments.

If CML is diagnosed in the accelerated phase and the patient has not yet received a TKI, the best treatment option is to begin TKI therapy. Drugs used to treat accelerated phase CML may include:

- Bosutinib
- Dasatinib
- Nilotinib
- Ponatinib

If CML progresses from chronic phase to accelerated phase during TKI therapy, a doctor may increase the dosage of the current TKI (if possible) or prescribe another TKI that the patient has not received before. Other options include:

- An allogeneic stem cell transplant
- Treatment in a clinical trial (See *Clinical Trials for Blood Cancers* on page 43)

See **Table 1** on page 19 for drug approval information.

Treatment for Blast Phase CML. Blast phase CML is similar to acute leukemia, with higher blasts in the blood and bone marrow and more severe symptoms. Patients with blast phase CML should be treated at specialized centers by doctors who have expertise in treating CML. Before treatment for blast phase CML, patients will need multiple tests to learn more about their leukemia cells, including the following tests on the bone marrow sample:

- Flow cytometry. This test determines whether the leukemia cells involve myeloid or lymphoid blast cells. The type of blast cells is a factor in treatment decisions.
- *BCR::ABL1* kinase domain mutation analysis. This test checks for mutations in the part of the *BCR::ABL1* gene that is targeted by TKIs (see *BCR::ABL1 Kinase Domain Mutation Analysis* on page 36). Different mutations can make the BCR::ABL1 protein either more or less resistant to certain TKIs. Ponatinib and asciminib can be prescribed for patients who have the *BCR::ABL1* gene with the T315I mutation. Doctors will often do next-generation sequencing panels to look for new mutations to the CML cells.

One option for patients with blast phase CML is to receive treatment in a clinical trial. Patients should talk to their doctors about the potential benefits and risks of participating in a clinical trial. See *Clinical Trials for Blood Cancers* on page 43.

Another treatment option is for patients to receive TKI therapy, either with or without chemotherapy, and then proceed to an allogeneic stem cell transplant, which offers the best chance of a long-term remission. In general, the more potent second-generation or third-generation TKIs are preferred treatments for blast phase CML. An allogeneic stem cell transplant is more likely to be successful if the disease can be returned to the chronic phase before transplantation.

Monitoring Treatment Response

After patients begin treatment, their doctors will order periodic blood tests to determine whether they are responding to treatment. Monitoring is usually done with blood tests only; bone marrow tests are done on an as-needed basis. A bone marrow aspiration and biopsy are recommended at the start of treatment and when disease progression or resistance is a concern.

Treatment Response. A treatment response is an improvement in a disease that is associated with the patient's treatment. Monitoring treatment response is one of the key strategies for managing CML.

Below are different levels of response to treatment.

Hematologic Response. This response is classified as either "partial" or "complete," depending on the results of a complete blood count (CBC) with differential. This test measures the number of red blood cells, white blood cells (including the different types of white blood cells) and platelets in the blood.

- Partial hematologic response—The number of each type of blood cell begins to return to a normal level.
- Complete hematologic response (CHR)—The blood cell counts have returned to normal, there are no blasts in the peripheral blood, and there are no signs or symptoms of the disease including the spleen returning to normal size. Most patients receiving TKI therapy will have a complete hematologic response within 1 month of beginning treatment.

Cytogenetic Response. This response is identified based on the percentage of cells in the bone marrow that contain the Philadelphia chromosome (Ph+ cells). Either cytogenetic analysis or a FISH test is used to measure the number of these cells. If a reliable qPCR test is not available, cytogenetic analysis of bone marrow cells (bone marrow cytogenetics) is done at 3-month intervals to check the patient's response to treatment.

- Minor cytogenetic response—The Ph chromosome is found in more than 35 percent of cells in the bone marrow.
- Major cytogenetic response (MCyR)—There are 35 percent or fewer cells with the Ph chromosome. This term is sometimes used to describe either a complete or partial cytogenetic response.
  - Complete cytogenetic response (CCyR)—No cells with the Ph chromosome can be detected in the bone marrow.
  - Partial cytogenetic response (PCyR)—The Ph chromosome is found in 1 to 35 percent of bone marrow cells.

Molecular Response. A molecular response is a decrease in the amount of the *BCR::ABL1* gene that can be detected in the blood. This is measured using a qPCR test.

A patient's initial molecular response to treatment is significant in predicting outcome and in determining further treatment options. Molecular response is the most sensitive method of monitoring *BCR::ABL1* levels in the blood and is most commonly used in clinical practice.

- Early molecular response (EMR)—The *BCR::ABL1* (IS) level is 10 percent or less at 3 and 6 months after the start of treatment. This means that the leukemia cells have been reduced by 90 percent or more.
- Major molecular response (MMR)—At least a 3-log reduction in *BCR::ABL1* (IS) levels or *BCR::ABL1* ≤ 0.1%. This means that the leukemia cells have been reduced by 99.9 percent or more.
- Deep molecular response (DMR)/Undetectable—At least a 4-log reduction: *BCR::ABL1* (IS) ≤0.01%; 4.5-log reduction *BCR::ABL1* (IS) ≤0.0032%; or 5-log reduction: ≤0.001% *BCR::ABL1* (IS).

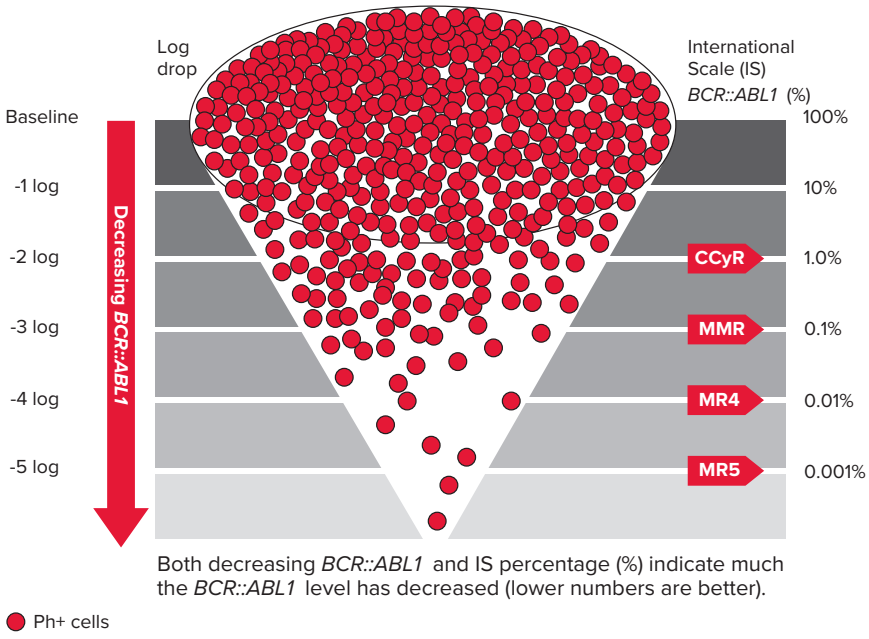
International Scale (IS). A molecular response is measured with qPCR using the International Scale. In the past, labs used different standards to measure and report qPCR results, making results difficult to compare. The International Scale was developed to provide a standard approach for reporting qPCR results. The qPCR test reflects the amount of the *BCR::ABL1* gene detectable in the blood.

The International Scale defines the standard baseline value as 100%. The baseline refers to the start of treatment. (The baseline was developed from the IRIS clinical trial, by testing a large number of patients' pretreatment samples and averaging patient results to create this baseline). The baseline is the value that your test results are measured against. Changes in qPCR scores are often described as log changes. Log changes can increase or decrease.

Log Reduction. A log reduction indicates that the *BCR::ABL1* level has decreased by a certain amount from the standard baseline. For example, a 1-log reduction indicates the *BCR::ABL1* level has decreased by 90 percent, a 2-log reduction by 99 percent, and so forth as described here and on **Figure 4** on page 35.

- 1-log reduction means that the *BCR::ABL1* level has decreased to 10 times below the standardized baseline. This means that 10 percent of cells (10 out of every 100 cells) have the *BCR::ABL1* gene. This reduction is equivalent to an early molecular response when achieved within 3 to 6 months of starting treatment.
- 2-log reduction means that the *BCR::ABL1* level has decreased to 100 times below the standardized baseline. This means that 1 percent of cells (1 out of every 100 cells) have the *BCR::ABL1* gene.
- 3-log reduction means that the *BCR::ABL1* level has decreased to 1,000 times below the standardized baseline. This means that 0.1 percent of cells (1 out of every 1,000 cells) have the *BCR::ABL1* gene. It is also referred to as a major molecular response (MMR).
- 4-log reduction means that 0.01% of cells (1 out of every 10,000 cells) have the *BCR::ABL1* gene.

Figure 4. Treatment Response by Log Reduction



Key: CCyR, complete cytogenic response; IS, International Scale; log, logarithm; MMR, major molecular response; MR4, molecular response 4; MR5, molecular response 5; Ph+, Philadelphia chromosome positive.

- 4.5-log reduction is referred to as a "complete molecular response (CMR)" or a "deep molecular response (DMR)." Doctors may refer to this reduction as "MR4.5." A 4.5 log reduction indicates that 0.0032% of cells (1 out of every 32,000 cells) have the *BCR::ABL1* gene. Achieving a deep molecular response is a sign of disease remission. Patients who achieve and then sustain a deep molecular response for a significant period of time may be considered candidates for discontinuing TKI therapy under careful medical supervision. See *Treatment-Free Remission* on page 38.
- 5-log reduction means that 0.001% of cells (1 out of every 100,000) have the *BCR::ABL1* gene. By reaching a 5-log reduction, patients have achieved undetectable *BCR::ABL1*.

Unfortunately, qPCR tests cannot be completely standardized from laboratory to laboratory. Laboratories establish their own standardized baseline values. Slightly different results may be obtained at different labs based on the same patient sample. To receive consistent results it is best to have samples sent to the same laboratory each time. This will help patients and members of the healthcare team monitor treatment response more effectively.

Response Milestones. The goal of CML treatment is to reach certain response milestones within a certain time period and maintain those responses.

Important milestones in CML are:

- Early Molecular Response (EMR) means that *BCR::ABL1* (IS) is less than 10% at 3 months.
- Complete Cytogenetic Response (CCyR) means that the *BCR::ABL1* (IS) is less than 1% or less within 12 months of treatment.
- Major Molecular Response (MMR) means that the *BCR::ABL1* (IS) is less than 0.1%.
- Deep Molecular Response (DMR) means that *BCR::ABL1* (IS) is 0.01 percent or less.

See **Table 3** on page 37 for early treatment milestones.

In general, the greater the response to the TKI, the longer the disease will be controlled. Having a major molecular response, however, is not the same as being cured. Even if qPCR tests cannot detect any trace of CML cells, the disease may return. That is why monitoring is very important.

It is recommended that patients have a qPCR test done every 3 months initially. After 2 years of achieving and maintaining a *BCR::ABL1* (IS) level of 0.1 percent or less, the test should be done every 3 to 6 months.

Not Meeting Treatment Milestones. If you are not meeting certain milestones during treatment, then it is possible that your CML is resistant to the TKI that you are taking. You may have *BCR::ABL1* mutation analysis before continuing treatment.

***BCR::ABL1* Kinase Domain Mutation Analysis.** In CML, mutations in the *BCR::ABL1* gene alter the shape of the BCR::ABL1 protein. This can affect the blocking action of the TKI on *BCR::ABL1*, allowing cancer cells to grow again. A *BCR::ABL1* kinase domain mutation analysis is a test that looks for mutations in the *BCR::ABL1* gene that may cause certain TKIs to stop working. This test should be performed if there is:

- An inadequate response to the initial TKI therapy
- A failure to meet a treatment milestone
- A loss of hematologic, cytogenetic or major molecular response, or a 1-log increase in the *BCR::ABL1* level, in the context of continuous therapy
- Progression to accelerated phase or blast phase CML

Mutation testing does not need to be done in patients who are switching medication because of side effects.

Among the *BCR::ABL1* mutations:

- A337T, P465S, M244V and F539V/I/C are resistant to asciminib
- T315I, V299L, G250E and F317L are resistant to bosutinib
- T315I/A, F317L/V/I/C and V299L are resistant to dasatinib
- T315I, Y253H, E255K/V and F359V/C/I are resistant to nilotinib

For people with CML that stops responding to a TKI, or who do not achieve the expected response within a given period of time (see **Table 3** on page 37), the most common options are switching to a different TKI or participating in a clinical trial.

Table 3. Early Treatment Response Milestones

BCR::ABL1 (IS)	3 months	6 months	12 months[a]
>10%	YELLOW	RED	
>1% – 10%	GREEN		ORANGE
>0.1% – 1%	GREEN		LIGHT GREEN
≤0.1%	GREEN		

Color	Concern	Treatment Team Considerations	Recommendations
RED	TKI-resistant disease	• Evaluate patient adherence and drug interactions • Consider *BCR::ABL1* kinase mutational analysis • Consider bone marrow cytogenetic analysis to assess additional chromosomal abnormalities	• Switch to alternate TKI • Evaluate for allogeneic stem cell transplantation
YELLOW	Possible TKI resistance	• Evaluate patient adherence and drug interactions • Consider *BCR::ABL1* kinase mutational analysis	• Switch to alternate TKI ***OR*** • Continue same TKI (other than imatinib)
ORANGE	Possible TKI resistance	• Evaluate patient adherence and drug interactions • Consider *BCR::ABL1* kinase mutational analysis • Consider bone marrow cytogenetic analysis to assess for CCyR response at 12 months	• Consider switch to alternate TKI ***OR*** • Continue the same TKI if CCyR is achieved
LIGHT GREEN	TKI-sensitive disease	• If treatment goal is long-term survival: ≤1% optimal • If treatment goal is treatment-free remission: ≤0.1% optimal	• If optimal: continue same TKI • If not optimal: shared decision-making with patient[b]
GREEN	TKI-sensitive disease	• Monitor response and manage side effects	• Continue same TKI[c]

Adapted from: National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology: Chronic Myeloid Leukemia*; version 3.2025.

[a]*BCR::ABL1* (IS) ≤0.1% at 12 months is associated with a very low probability of disease progression and a high likelihood of achieving a subsequent deep molecular response (MR4.0; ≤0.01% *BCR::ABL1* IS), which may allow for discontinuation of TKI therapy.

[b]Switching from imatinib to a second-generation TKI improves response but is associated with increased toxicity.

[c]Discontinuation of TKI with careful monitoring is possible in select patients.

Key: MCyR, major cytogenetic response; CCyR, complete cytogenetic response; IS, International scale: TKI, tyrosine kinase inhibitor.

Treatment-Free Remission

In recent years, stopping TKI therapy is a potential goal for some CML patients. Treatment-free remission (TFR) allows some patients who have a achieved a deep molecular response (DMR) to stop taking their TKIs. These patients do not require further TKI treatment, although there may still be some remaining leukemia cells in their body. Unfortunately, TFR is not yet achievable in all patients, although research is in progress to make this a feasible objective for all CML patients.

The feasibility and safety of discontinuing TKI therapy has been evaluated in several studies. Patients with CML in chronic phase who achieve and maintain a stable, deep molecular response for at least 2 years are considered good candidates for TKI therapy discontinuation, under careful medical supervision.

The National Comprehensive Cancer Network (NCCN) guidelines recommend the following as patient criteria for discontinuation: Outside of a clinical trial, discontinuation of TKI therapy should be considered only if all of the criteria included in the following list are met:

- Age 18 years and older
- Chronic phase CML. No prior history of accelerated or blast phase CML
- On an approved TKI therapy for at least 3 years
- Prior evidence of quantifiable *BCR::ABL1* transcript
- Stable molecular response (*BCR::ABL1* ≤0.01% IS) for 2 or more years, as documented on at least 4 tests performed at least 3 months apart
- Access to a reliable qPCR test with a sensitivity of detection of at least MR4.5 (*BCR::ABL1* ≤0.0032% IS) and that provides results within 2 weeks
- Monitoring with qPCR every 1-2 months for the first 6 months following discontinuation, bimonthly during months 7-12 and quarterly thereafter (indefinitely) for patients who remain in MMR (MR3; *BCR::ABL1* ≤0.1% IS)
- Prompt resumption of TKI therapy within 4 weeks of a loss of MMR with monthly molecular monitoring until MMR is re-established. Every 3 months thereafter is recommended indefinitely for patients who have reinitiated TKI therapy after a loss of MMR. If MMR is not achieved after 3 months of TKI resumption, *BCR::ABL1* kinase domain mutation testing should be performed, and monthly molecular monitoring should be continued for another 6 months.

CML patients have many reasons to attempt treatment-free remission. Motivations may include:

- Reducing the risk of TKI side effects and future drug interactions. Although TKIs are generally well tolerated, they do produce side effects that may affect health and quality of life.

- Reducing the risk of potential long-term side effects
- Having treatment-free periods for female patients considering becoming pregnant
- Easing the inconvenience of taking daily medication
- Eliminating patient co-pays and insurance costs for ongoing treatment, reducing expenses for both patients and the healthcare system

After discontinuing TKI therapy, some patients may experience TKI withdrawal syndrome which includes muscle and joint pain and possible development of a rash. Although this syndrome can last for months, it can often be controlled with nonprescription drugs or nonsteroidal anti-inflammatory drugs (NSAIDs), and in more severe cases, with corticosteroids. TKI withdrawal syndrome has been reported in about 10 to 30 percent of patients who discontinued TKI therapy.

CML patients may be reluctant to try TFR due to fear of relapse or disease progression. In the case of relapse, nearly all patients who restart therapy are able to obtain and maintain a major molecular response again. Treatment-free remission periods may last from a few months to many years. Other patients may feel they do not have enough information to decide whether to try TFR. Ask your doctor questions and ask for additional information. Make sure all questions are answered before making the decision to proceed. Review **Table 4**, below, for psychosocial and emotional recommendations for patients.

Table 4. Psychosocial and Emotional Prerequisites for TKI Therapy Discontinuation

Recommendations for the patient
• Be well informed about treatment-free remission (TFR) and well motivated to discontinue treatment.
• Do not feel pressure to stop TKI therapy.
• Understand that relapse is possible; this does not mean it was a mistake to try for TFR.
• Understand the need for frequent monitoring, especially during the first year.
• Have access to proper monitoring with reliable qPCR tests that have a sensitivity of detection of at least MR4.5 and that also provide results within 2 weeks.
• Be reassured that in case of disease relapse, treatment can be restarted promptly and successfully.
• Understand the risk of TKI withdrawal syndrome.

Monitoring During TFR. Frequent and highly sensitive molecular testing is essential for ensuring the safety of patients attempting TFR, particularly during the first year of TKI discontinuation and during re-treatment, if needed.

Following discontinuation, the NCCN Guidelines recommend qPCR testing:

- Every 1-2 months for the first 6 months
- Every 2 months during months 7 to 12
- Every 3 months thereafter (indefinitely)

Doctor appointments are important because they provide the opportunity for the healthcare team to address patient concerns, discuss qPCR results and adjust monitoring tests and schedules as needed.

What Happens if Relapse Occurs? Approximately 40 to 60 percent of patients who discontinue TKI therapy after achieving deep molecular response do experience a recurrence within 12 months of stopping treatment, in some cases as early as 1 month into discontinuing TKI therapy. Restarting therapy immediately after recurrence results in returning to undetectable disease in almost all patients. Late molecular responses do occur; it is important for patients to adhere to monitoring during TFR so that the doctor can detect a relapse and prevent the disease from progressing.

Several factors may help predict the risk of relapse after stopping TKI therapy. These include:

- Higher Sokal risk score (see page 17)
- Being female
- Lower natural killer cell counts
  - Natural killer cells are white blood cells. This test is not routinely done in clinical care.
- Suboptimal response or resistance to imatinib
- Shorter duration of TKI therapy
- Shorter duration of deep molecular response prior to stopping treatment

Patients should discuss with their doctor whether attempting TFR is a potential option for them. Consultation with an experienced CML doctor is essential.

CML in Children and Young Adults

Most cases of CML occur in adults. CML accounts for less than 3 percent of all pediatric leukemias. Due to its rarity, there are no standardized recommendations for the treatment of CML in children. It often follows guidelines developed for

adults, even though there are differences between CML in children and adults in terms of disease presentation and progression. Some studies indicate that children and young adult patients have lower rates of complete cytogenetic and major molecular responses compared with older adults. Children and young adults may have a slightly higher risk of transformation to accelerated and blast phases. Children with CML should be treated by pediatric hematologist-oncologists, doctors who specialize in treating children with blood cancers.

The following medications are used in the treatment of children with CML:

- Bosutinib
- Dasatinib
- Imatinib
- Nilotinib

See **Table 1** on page 19 for full prescribing information.

Although there are not a great number of studies focused on the treatment of pediatric patients with CML, there is evidence that imatinib may slow physical growth, particularly in children who are treated before they reach puberty. Other rare side effects of imatinib seen in adults, such as thyroid dysfunction, appear to be very rare in children.

Because children with CML may receive TKI therapy during periods of active growth, follow-up care is very important. In addition to evaluating treatment response, your child's doctor should also monitor:

- Height and weight—consider a bone scan and a bone density scan if there is evidence of abnormal growth
- Puberty—refer patients to an endocrinologist if there is a delay in puberty
- Thyroid function
- Heart—an annual echocardiogram is recommended

Poor adherence to therapy, particularly in adolescents and young adults, is an additional concern. With oral TKIs, it is essential to follow the doctor's directions exactly and keep taking the medication for as long as prescribed. Nonadherence to TKI treatment (meaning the patient does not take the medication as scheduled) increases the risk that treatment will not work well, or possibly at all. See *TKI Adherence* on page 28.

Considering the potential concerns of lifelong TKI treatment, researchers are studying TKI discontinuation in children and young adults. Treatment-free remission is now considered a goal of treatment for select patients in various ongoing clinical trials (see *Treatment-Free Remission* on page 38). Intermittent TKI dosing is another potential method to reduce long-term side effects in children, but more studies are needed to evaluate this approach.

An allogeneic stem cell transplant is an additional treatment option, but it is used only in cases of relapse or accelerated/blast phase CML. Due to the small number of pediatric patients, there have been no randomized, controlled trials comparing a stem cell transplant with imatinib use in children. Because of this, decisions about treatment approaches in children with CML must be individualized. The complications of stem cell transplantation must be weighed against the complications associated with lifelong TKI use. For more information on allogeneic stem cell transplantation, see page 29.

A clinical trial may be the best treatment option. Talk to your child's doctor about the best option for your child and any concerns regarding the risks associated with your child's treatment.

Visit www.LLS.org/booklets to view the LLS booklet *Choosing a Specialist or Treatment Center*.

Visit www.LLS.org/FamilyWorkbook and www.LLS.org/ChildhoodYAresources for additional resources to help children and their families cope with blood cancer.

Visit www.LLS.org/CTSC to learn more about clinical trials and to contact a Clinical Trial Nurse Navigator.

Fertility, Pregnancy and TKIs

CML patients of childbearing age, as well as the parents of children with CML, should ask their doctor to explain how treatment may affect fertility (the ability to have children). People with CML who will be taking TKIs should discuss fertility preservation with their doctors before they start TKI therapy.

Growing numbers of CML patients of childbearing age are living in stable remissions and are considering having children while being treated for CML. There is no risk that parents will pass the Ph chromosome onto their children.

Generally, there are no concerns for males taking TKIs that are associated with having children. For females who want to become pregnant, however, the issues are more complex and there is limited data. Imatinib, dasatinib and nilotinib are known to cause embryonic or fetal toxicities in animal studies. In some instances, patients receiving TKI therapy at the time of conception have had miscarriages or babies born with congenital abnormalities. Therefore, it is strongly suggested not to become pregnant while taking a TKI. Patients who can become pregnant should use effective contraception while on TKI therapy.

If a patient is considering pregnancy during TKI therapy, early consultation with a hematologist-oncologist, as well as a high-risk obstetrician, is important. They need to discuss the potential risks of discontinuing TKI therapy during pregnancy, versus the potential risks to the fetus of continuing TKI therapy.

Doctors may advise planning the pregnancy when the patient's response to therapy is as deep as possible, at least a major molecular response. The patient would suspend TKI therapy prior to conception and during the pregnancy, then resume it immediately after the birth of the child and refrain from breastfeeding. The patient should be closely monitored with qPCR tests for signs of disease progression during pregnancy by a hematologist-oncologist and an obstetrician, both of whom specialize in high-risk pregnancies.

At present, no data suggest that either imatinib or any other TKI drug can be taken safely during pregnancy. Leukapheresis may be used to lower white blood counts during the first months of pregnancy, when other treatments may be harmful to fetal development. If treatment is needed during pregnancy, interferon alfa is safe to use throughout pregnancy.

Talk to your doctor about the:

- Risk of relapse when discontinuing TKI therapy during pregnancy
- Risk of congenital abnormalities for babies exposed to TKIs during pregnancy
- Need for patients on TKI therapy to refrain from breastfeeding their babies
- Treatment options, both during and after pregnancy

Treatment-free remission is now a treatment goal for many patients with CML who have achieved a deep, stable response to treatment. Patients who are interested in becoming pregnant should discuss all their options with their treatment team, including the possibility of TKI discontinuation to try for treatment-free remission. See *Treatment-Free Remission* on page 38.

Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called "clinical trials." Researchers use them to find better ways to care for and treat people with cancer. In the United States, the FDA requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat cancer. Researchers use cancer clinical trials to study new ways to

- Treat cancer using:
  - A new drug
  - An approved drug to treat a different kind of cancer
  - A new combination of drugs
  - A new way of giving a drug (by mouth, intravenously (IV), etc)

- Manage cancer symptoms and treat side effects
- Find and diagnose cancer
- Keep cancer from coming back after treatment
- Manage long-term treatment side effects

By taking part in a clinical trial, patients can see doctors who are experts in their disease, gain access to new, cutting-edge therapies, and provide helpful information for future patients. The treatments and information we have today are due in large part to patients who have been willing to join clinical trials. Anyone interested in participating in a clinical trial should talk to their hematologist-oncologist about whether a clinical trial might be right for them. During this conversation it may help to:

- Have a list of questions to ask about the risks and benefits of each trial (visit www.LLS.org/WhatToAsk for lists of suggested questions)
- Ask a family member or friend to go with you to your doctor visit—both for support and to take notes

Clinical trials can be difficult to navigate and figure out, but The Leukemia & Lymphoma Society is here to help. Patients and caregivers can work with **Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome the barriers to enrollment and provide support throughout the entire clinical-trial process.

Our Clinical Trial Nurse Navigators are registered nurses who are experts in adult and pediatric blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals
- Help you to understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (such as past treatments, treatment responses, and your cancer genetic profile), your current health and your medical history. This information is taken into account and may factor into your eligibility to participate in certain clinical trials
- Help you to understand how your finances, insurance coverage, and support network, as well as your ability and willingness to travel might impact your choice of a clinical trial
- Guide you and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites
- Help deal with any problems you might have as you participate in a trial
- Support you throughout the clinical-trial process

Call an LLS Information Specialist at (800) 955-4572 or visit www.LLS.org/CTSC for more information about clinical trials and the Clinical Trial Support Center at LLS.

Visit www.LLS.org/booklets to view *Understanding Clinical Trials for Blood Cancers.*

Financial Concerns

People with CML are living longer, primarily because of the development of TKIs. While this progress is exciting, the financial costs associated with therapy can become an obstacle to treatment. Paying for healthcare is a major concern for many people who are living with blood cancer. The high cost of cancer can lead to significant financial and emotional stress for both patients and their families.

Even if you have health insurance, cancer can still take a toll on your finances. You may have new expenses such as co-payments or travel for treatment. You may also have less income if you need to take time off from work.

Speak with your healthcare team if you have any concerns about being able to afford your treatment. They may be able to provide information and resources that can help. Health insurance plans may not cover all the costs of cancer care, but there are many resources available to help with prescription drug payment. In addition, several major drug manufacturers currently provide patient assistance or prescription assistance programs. These programs can provide both insured and uninsured patients free or reduced-cost medications.

LLS offers financial assistance programs and medical debt case management for eligible patients. You can call an LLS Information Specialist at (800) 955-4572 for more information about these programs.

Visit www.LLS.org/booklets to view *Cancer and Your Finances.*

Follow-Up Care

CML follow-up care varies from patient to patient. However, you are encouraged to:

- Maintain regular follow-up appointments with your hematologist-oncologist. The doctor will check your blood cell counts and molecular response to treatment using qPCR tests, and possibly perform bone marrow tests.
- Keep a record of your cancer diagnosis, treatment and follow-up care. This is often called a “survivorship care plan.” Ask your doctor for a written survivorship care plan. Share this information with any new healthcare providers you see. The plan should include:
  - A list of all healthcare providers
  - A diagnosis summary with specifics such genetic biomarkers and phase of CML

- A treatment summary with specifics such as the names, dates and dosages of drugs, transplantation information, response to treatment and side effects
- A list of possible side effects and late effects
- A schedule of ongoing monitoring with recommended tests, frequency and coordinating provider
- Health and wellness recommendations, such as nutrition guidelines and suggested exercise regimens, as well as other appropriate disease screening

- Receive certain vaccinations for influenza, pneumococcal pneumonia, shingles and COVID-19. Immunizations using live organisms or with high viral loads should not be administered. Speak to your doctor for more information.
- Should seek medical and psychosocial support for fatigue, depression and other long-term effects, if needed.
- Consider cancer risk-reduction strategies, such as stopping smoking, protecting skin against prolonged exposure to the sun, healthy eating and exercising.

Visit www.LLS.org/booklets to see the free LLS booklet *Navigating Life During and After a Blood Cancer Diagnosis.* There are versions for adults, young adults, and children and adolescents.

Nutrition and Cancer. Eating well is important for patients receiving treatment for blood cancer. Proper nutrition plays a key role in keeping the body strong, supporting the immune system and reducing the risk for diseases. Patients who eat well and maintain a healthy weight usually manage treatment and its side effects better. It is also important for patients with weakened immune systems to follow all food safety guidelines to reduce the risk of food-borne illness. Speak to your healthcare team about food and nutrition and for a referral to an oncology registered dietitian (RD) for specific nutrition advice and guidance.

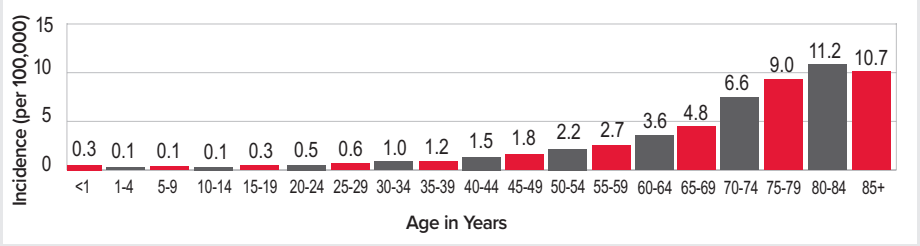
LLS registered dietitians have expertise in oncology nutrition and provide patients, parents and caregivers with free nutrition consultations by phone. Call (877) 467-1936 or visit www.LLS.org/nutrition to schedule a consult.

Visit www.LLS.org/booklets to view *Food and Nutrition During Cancer Treatment* and *Nutrition Handbook: Feeding your family from meal planning to meal time.*

Incidence, Causes and Risk Factors

Incidence. CML is a relatively rare disease. In the United States, approximately 9,280 new cases of CML were expected to be diagnosed in 2024. As of 2020, the latest year for which statistics are available, an estimated 63,479 people are either living with or in remission from CML. This disease is slightly more common in men than in women, and most cases of CML occur in adults. CML is most frequently diagnosed in people over the age of 75 (see **Figure 5** below). The median age at diagnosis is 65 years. A small number of children develop CML.

Figure 5. Age-Specific Incidence Rates for CML, 2016-2020



Source: SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute; 2023 Apr 19. [updated: 2023 Nov 16; cited 2024 Feb 21]. Available from: https://seer.cancer.gov/statistics-network/explorer/. Data source(s): SEER Incidence Data, November 2022 Submission (1975-2020), SEER 22 registries.

Causes and Risk Factors. CML is not passed from parent to child, so no one is born with CML. Rather, it occurs when there is a mutation to the DNA of a single bone marrow cell. Although in most cases it is not clear what caused the genetic changes that lead to CML, there are some known risk factors. A risk factor is anything that increases a person's chance of developing a disease. Having a risk factor, however, does not mean that person will develop CML. Some people with several risk factors for CML never develop the disease, while others with no known risk factors may develop the disease. You cannot catch CML from someone else.

The following risk factors are associated with an increased risk of developing CML:

- Sex—CML is slightly more common in males than females.
- Age—The risk of developing CML increases with age.
- Radiation exposure—In a small number of patients, CML is caused by exposure to very high doses of radiation (such as being a survivor of an atomic bomb blast or a nuclear reactor accident).
  - A slight increase in risk also occurs in some individuals treated with high-dose radiation therapy for other cancers, such as lymphoma. But most people treated for cancer with radiation do not develop CML, and most people who have CML have not been exposed to high doses of radiation.

- Exposures to diagnostic dental or medical X-rays have not generally been associated with an increased risk of CML. CML has been reported in individuals undergoing excessive diagnostic X-rays or computed tomography (CT) scans, so use of imaging modalities such as X-rays and CT scan needs to be justified to minimize the risk of CML and other types of blood cancers.

Normal Blood and Bone Marrow

Blood. Blood is the liquid that flows through a person's arteries and veins. It carries oxygen and nutrients throughout the body. It also carries away waste products. Blood is composed of plasma and cells.

Plasma. Plasma is largely made up of water in which many chemicals are dissolved. These chemicals each have a special role. They include:

- Proteins
  - Albumin. This is the most common blood protein.
  - Blood-clotting proteins (coagulation factors). They are made by the liver.
  - Erythropoietin. It is made by the kidneys and stimulates red blood cell production.
  - Immunoglobulins. These are cells that fight infection.
- Hormones, such as thyroid and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B_{12}
- Electrolytes, such as calcium, potassium and sodium

Blood Cells. Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis" (see **Figure 6** on page 50). The blood cells are suspended in the plasma.

Once the blood cell is created, it will develop into one of the three types of blood cells.

These are:

1. Red blood cells are the cells that carry oxygen; they
   - Make up a little less than half of the body's total blood volume
   - Are filled with hemoglobin, the protein that picks up oxygen from the lungs and takes it around the body. It binds with carbon dioxide (CO_2) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO_2 is removed from the lungs.

2. Platelets are cells that help blood clot; they
    - Are small cells (one-tenth the size of red blood cells)
    - Help stop bleeding from an injury or cut
    - Stick to the torn surface of the vessel, clump together, and plug up the bleeding site. They form a clot, with the help of proteins, such as fibrin, and electrolytes, such as calcium.
3. White blood cells (WBCs) are cells that fight infections. The several types of WBCs include:
    - Neutrophils and monocytes. These are “phagocytes” (eating cells) that ingest and destroy bacteria and fungi. Unlike red blood cells and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
    - Eosinophils and basophils. These WBCs respond to allergens or parasites.
    - Lymphocytes. WBCs found mostly in the lymph nodes, spleen and lymphatic channels, lymphocytes are a key part of the immune system. Some enter the bloodstream. There are three major types of lymphocytes:
        - T lymphocytes (T cells)
        - B lymphocytes (B cells)
        - Natural killer (NK cells)

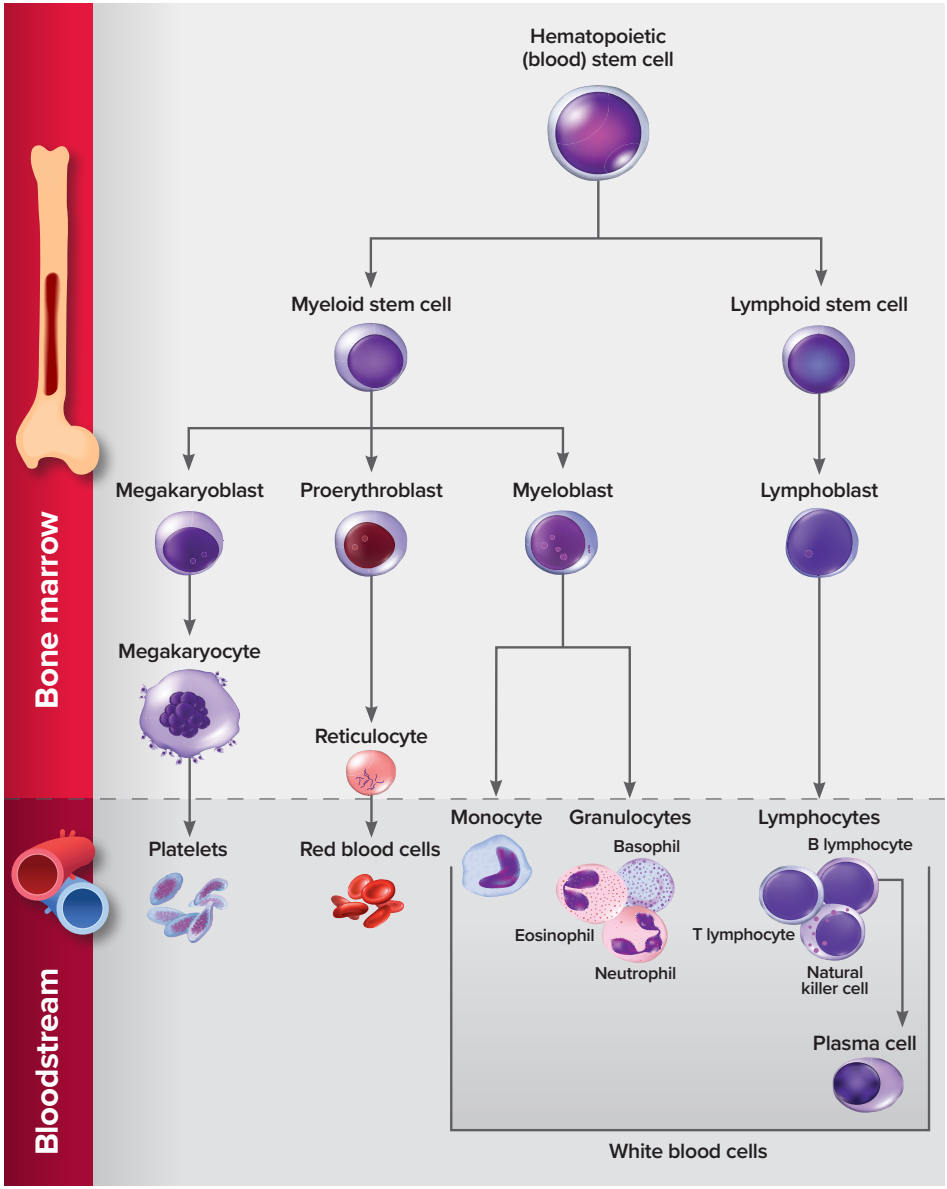
In healthy people, stem cells in the bone marrow produce new blood cells continuously. When blood cells are fully developed, they enter the bloodstream as it passes through the bone marrow and then circulates throughout the body.

In babies, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have blood-forming marrow. In adults, bone marrow is only found in the spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull.

Hematopoietic stem cells are found in the bone marrow. These stem cells are important because they can be transplanted. Some stem cells enter the bloodstream and circulate; there are not enough of them to be counted in standard blood tests. Doctors know how to stimulate the growth of these cells in the bone marrow and have them migrate into the bloodstream. Then a special technique called “apheresis” is used to separate them from the circulating blood so they can be collected and stored. Stem cells from the placenta and the umbilical cord of a newborn infant can also be harvested and used for future transplantation.

Figure 6. Blood Cell & Lymphocyte Development

Most blood cells start as hematopoietic (blood) stem cells in the bone marrow. Hematopoietic stem cells are the most immature blood-forming cells. They must mature (go through many stages) to become a red blood cell, white blood cell or platelet. Some blood cells mature in the bone marrow. Other blood cells leave the bone marrow and travel to other parts of the body to develop into mature blood cells.



Additional Resources

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, visit www.LLS.org/ResourceDirectory to view the directory.

Language Services. Let members of your healthcare team know if you need translation or interpreting services because English is not your native language, or if you need other assistance, such as a sign language interpreter. Often these services are free.

Information for Veterans. Veterans who were exposed to Agent Orange while serving in Vietnam; to airborne hazards and burn pits while serving in Iraq, Afghanistan and other areas of Southwest Asia; to contaminated water at Camp Lejeune between 1953-1987; or to ionizing radiation during service may be able to get help from the United States Department of Veterans Affairs. For more information, please

- Call: the VA (800) 749-8387
- Visit: https://www.va.gov/disability/eligibility/hazardous-materials-exposure/

Information for Firefighters. Firefighters are at an increased risk of developing cancer. There are steps that firefighters can take to reduce the risk. Please visit www.LLS.org/FireFighters for resources and information.

World Trade Center Health Program. People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get help from the World Trade Center (WTC) Health Program. People eligible for help include:

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area and those who lived, worked or were in school in that area
- Responders to the Pentagon and the Shanksville, PA, crashes

For more information, please

- Call: WTC Health Program at (888) 982-4748
- Visit: www.cdc.gov/wtc/faq.html

Mental Health. Caring for your mental health has benefits for cancer patients. Seek medical advice if you are struggling. For more information, please:

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov

If you or your loved is experiencing a mental health crisis, call 988 to talk to a trained mental health professional. The 988 Suicide and Crisis Lifeline is free, confidential and always available. For the Crisis Text Line, text HOME to 741741.

Health Terms

Allogeneic Stem Cell Transplantation. A treatment that uses stem cells from a healthy donor to restore a patient's damaged or diseased cells in the bone marrow. **See the free LLS booklet *Blood and Marrow Stem Cell Transplantation.***

Anemia. A condition in which the number of red blood cells is below normal. This results in a diminished ability of the blood to carry oxygen. Severe anemia can cause a pale complexion, weakness, fatigue and shortness of breath.

Basophil. A type of white blood cell that has granules (small particles) with enzymes that are released during allergic reactions.

BCR::ABL1. The abnormal fusion gene found in most patients with CML. The exchange of DNA between chromosomes 9 and 22 results in the creation of a cancer-causing gene called *BCR::ABL1* on chromosome 22.

Blast. An immature (undeveloped) blood cell.

Bone Marrow. The spongy tissue in the hollow central cavity of bones where blood cells form.

Bone Marrow Aspiration. A procedure in which a liquid sample of bone marrow is removed for examination by a pathologist. After medication is given to numb the skin and outer bone, a special hollow needle is used to remove the sample. It is normally done at the same time as a bone marrow biopsy.

Bone Marrow Biopsy. A procedure in which a sample of bone containing bone marrow is removed for examination by a pathologist. After medication is given to numb the skin and outer bone, a special wider hollow needle is used to remove the sample.

Chemotherapy. Treatment with chemical agents (medication) that stops the growth of cancer cells, either by killing the cancer cells or by preventing them from dividing.

Chromosomes. Threadlike structures within cells that contain genes arranged in a linear order. Human cells have 23 pairs of chromosomes.

Complex Karyotype. Three or more unrelated chromosomal abnormalities in more than one cell.

Cytogenetic Analysis. The process of analyzing the number and size of the chromosomes in cells. It detects chromosome alterations and, in some cases, may identify the actual genes that have been affected. These findings help doctors diagnose specific types of blood cancer, determine treatment approaches and monitor a patient's response to treatment.

DNA. Abbreviation for deoxyribonucleic acid, the molecule inside cells that contain the genetic information needed for a person to develop and grow and is passed from one generation to the next.

Drug Intolerance. Inability to tolerate the side effects of a drug.

Drug Resistance. The failure of cancer cells, viruses or bacteria to respond to a drug that is supposed to kill or weaken them.

Eosinophil. A type of white blood cell that promotes inflammation during allergic reactions and helps fight certain parasitic infections.

FDA. The abbreviation used to refer to the United States Food and Drug Administration. The FDA makes sure that drugs, medical devices and medial equipment are safe and effective.

Flow Cytometry. A test that measures the number of cells and certain characteristics of cells, such as size and shape, in a blood or bone marrow sample. The presence of tumor markers on the surface of cells is also measured.

Fluorescence In Situ Hybridization (FISH). A technique for studying abnormal chromosomes in cells and tissues. Pieces of DNA that contain fluorescent molecules are added to cell or tissue samples on a slide. The pieces of DNA bind to specific genes or chromosomes and they light up when viewed under a specialized “fluorescence” microscope.

Granulocyte. A type of white blood cell with many particles (granules) in the cell body. Neutrophils, eosinophils and basophils are types of granulocytes.

Hasford Scoring System. A prognostic scoring system that estimates survival of patients who have chronic phase CML. The system categorizes patients into three groups: low risk, intermediate risk or high risk. Hasford scores are calculated based on the following factors for each patient at diagnosis: spleen size, platelet count, age, percentage of blast cells circulating in the bloodstream and number of eosinophils and basophils circulating in the bloodstream.

Hematologic. Of, or relating to, blood.

Hematologist. A doctor who specializes in blood cell diseases.

Hematopathologist. A doctor who has special training in identifying diseases of the blood cells by examining blood, bone marrow, lymph and other tissue samples under a microscope.

Hemoglobin. A protein inside red blood cells that carries oxygen from the lungs to tissues and organs in the body and carries carbon dioxide back to the lungs.

Immunotherapy. A treatment that uses the body's immune system to treat cancer and other diseases.

Isochromosome. An abnormal chromosome with two identical arms. Normal chromosomes have one long (q) arm and one short (p) arm, but isochromosomes have either two long arms or two short arms.

Lymph Node. A bean-shaped structure that is part of the body's immune system. There are hundreds of lymph nodes located throughout the body. They contain lymphocytes (white blood cells) that help fight infection and disease.

Lymphoblast. An immature cell that can develop and develop into a mature lymphocyte.

Lymphocyte. A type of white blood cell that is important to the body's immune system. There are three major types of lymphocytes: 1) B lymphocytes (B cells) that produce antibodies to fight infections; 2) T lymphocytes (T cells) that help protect the body from infections and may help the body fight cancer; and
3) natural killer (NK) cells, which can attack virus-infected cells or tumor cells.

Macrophage. A type of white blood cell that surrounds and kills microorganisms, removes dead cells and stimulates the action of other immune system cells. Also referred to as a "scavenger cell." See Monocyte.

Monocyte. A type of white blood cell that forms in the bone marrow and travels through the bloodstream to tissues in the body; in tissue, monocytes become macrophages. See Macrophage.

Mutation. A change in the DNA of a cell. A mutation may be caused by an error in cell division, or it may be caused by contact with DNA-damaging substances in the environment.

Myeloblast. A type of immature white blood cell that forms in the bone marrow. Myeloblasts become mature white blood cells called granulocytes (neutrophils, basophils and eosinophils).

Myeloproliferative Neoplasm. A type of disease in which the bone marrow makes too many red blood cells, platelets or certain white blood cells. Myeloproliferative neoplasms usually get worse over time as the number of extra cells build up in the blood and/or bone marrow.

Neutrophil. A type of white blood cell and the principal type of phagocyte (microbe-eating cell), in the blood. It is the main type of cell that combats infection. Patients with certain blood cancers and those who have received certain treatments, such as chemotherapy, often have a low neutrophil count, which makes them very susceptible to infections.

Oncologist. A doctor who has extensive training in diagnosing and treating cancer.

Pathologist. A doctor who detects and identifies diseases by examining body tissues and fluids under a microscope.

Peripheral Blood. The blood that circulates throughout the body in the arteries, capillaries and veins.

Phagocyte. A type of white blood cell that protects the body from infection by eating and killing micro-organisms, such as bacteria and fungi. The two main types of phagocytes are neutrophils and monocytes. Once an infection occurs, phagocytes travel to the site of the infection through the bloodstream and enter the infected tissue.

Philadelphia Chromosome (Ph Chromosome). An abnormality of chromosome 22 found in the bone marrow and blood cells of most patients with CML. It is formed when parts of chromosomes 9 and 22 break off and trade places. As a result, chromosome 22 is shorter than normal. The exchange of DNA between chromosomes 9 and 22 results in the creation of a cancer-causing gene called *"BCR::ABL1"* on chromosome 22.

Platelet. A small, colorless cell fragment that helps control bleeding. Platelets travel to and then collect at the site of a wound, where their sticky surface helps them form clots and stop bleeding. Also called "thrombocyte."

Prognosis. The probable outcome or expected course of a disease; the likelihood of recovery or recurrence of a disease.

Quantitative Polymerase Chain Reaction (qPCR). A technique used to expand trace amounts of DNA (deoxyribonucleic acid), so that the specific type of the DNA can be examined. This technique has become useful in detecting a very low concentration of residual blood cancer cells that cannot be seen with a microscope. A qPCR test can detect the presence of one blood cancer cell among 100,000 to 1 million healthy cells.

Red Blood Cell. A type of blood cell that contains hemoglobin, which carries oxygen to the tissues of the body. Red blood cells make up about 40 to 45 percent of blood volume in healthy people. Also called "erythrocyte."

Relapse. When a disease returns after a period of improvement.

Remission. When signs of a disease disappear, usually following treatment. The remission is sometimes further defined as complete or partial. "Complete remission" means that all evidence of the disease is gone. "Partial remission" means that the disease is markedly improved by treatment, but evidence of the disease is still present in the body.

Resistance (to Treatment). When cancer cells continue to grow even after administration of strong drugs and/or treatments. The cancer cells may be resistant to the drug at the beginning of treatment or may become resistant after being exposed to the drug over time.

Response (to Treatment). An improvement in a disease related to treatment.

RNA. Abbreviation for ribonucleic acid, a molecule in cells that carries out the DNA instructions for making proteins.

Sokal Scoring System. A prognostic scoring system used to estimate the survival of patients with chronic phase CML. Patients are categorized into risk groups (low risk, intermediate risk and high risk) based on their spleen size, platelet count, age and the percentage of blast cells in their blood.

Spleen. An organ in the left upper portion of the abdomen, just under the left side of the diaphragm. The spleen acts as a blood filter.

Stem Cell. A cell from which other types of cells develop. In the bone marrow, blood-forming stem cells mature into red blood cells, white blood cells and platelets. Stem cells can be collected, preserved and used for stem cell transplantation.

Stem Cell Transplantation. See Allogeneic Stem Cell Transplantation.

Translocation. A genetic abnormality in which a piece of one chromosome breaks off and attaches to another chromosome. Sometimes genetic material is exchanged between two different chromosomes. When a translocation takes place, the gene at which the break occurs is altered. **Visit LLS.org/booklets to view the free LLS booklet *Understanding Genetics.***

Trisomy. The presence of three or more copies of a specific chromosome in some or all of the body's cells instead of the usual two copies.

Tyrosine Kinase. A type of enzyme that plays a key role in cell functions, including cell growth and division. It is normally present in cells, and certain genes (such as the *ABL1* gene on chromosome 9) direct its production. In CML, an alteration in the DNA results in the abnormal fusion gene called *BCR::ABL1,* which produces an abnormal tyrosine kinase. This abnormal enzyme signals blood stem cells to produce too many granulocytes (white blood cells).

Tyrosine Kinase Inhibitor (TKI). A type of drug that blocks the action of enzymes called tyrosine kinases. Tyrosine kinases are a part of many cell functions, including cell signaling, growth and division. These enzymes may

be too active or found at high levels in some types of cancer cells, and blocking them may help keep cancer cells from growing.

White Blood Cell. A type of blood cell that is part of the body's immune system. The five types of these infection-fighting blood cells are neutrophils, eosinophils, basophils, monocytes and lymphocytes. Also called "leukocyte."

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NOTES

A six-word narrative about living with blood cancer from patients in our LLS Community

Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/ happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith, and optimism. Finding joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.

Discover what thousands already have at **www.LLS.org/Community**

Join our online social network for people who are living with or supporting someone who has a blood cancer. Members will find

- Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff
- Accurate and cutting-edge disease updates
- The opportunity to participate in surveys that will help improve care.

LEUKEMIA & LYMPHOMA SOCIETY®

For more information, please contact our Information Specialists **800.955.4572** (Language interpreters available upon request).

The Leukemia & Lymphoma Society Mail Center 1201 15th Street N.W., Suite 410 Washington, D.C. 2005

The mission of The Leukemia & Lymphoma Society (LLS) is to cure blood cancer and improve the quality of life of all patients and their families. Find out more at www.LLS.org.

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