Learning that you have cancer can be overwhelming. The goal of this book is to help you get the best care. It explains which tests and treatments are recommended by experts in chronic myelogenous leukemia.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 26 of the world’s leading cancer centers. Experts from NCCN® have written treatment guidelines for doctors who treat leukemia. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of chronic myelogenous leukemia. Key points of this book are summarized in the NCCN Quick Guide™ series for Chronic Myelogenous Leukemia. NCCN also offers patient resources on breast cancer, kidney cancer, melanoma, and many other cancer types. Visit NCCN.org/patients for the full library of patient books, summaries, as well as other patient and caregiver resources.
NCCN aims to improve the care given to patients with cancer. NCCN staff work with experts to create helpful programs and resources for many stakeholders. Stakeholders include health providers, patients, businesses, and others. One resource is the series of books for patients called the NCCN Guidelines for Patients®. Each book presents the best practice for a type of cancer. The patient books are based on clinical practice guidelines written for cancer doctors. These guidelines are called the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Clinical practice guidelines list the best health care options for groups of patients. Many doctors use them to help plan cancer treatment for their patients. Panels of experts create the NCCN Guidelines®. Most of the experts are from NCCN Member Institutions. Panelists may include surgeons, radiation oncologists, medical oncologists, and patient advocates. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors. For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

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LLS is dedicated to developing better outcomes for blood cancer patients through research, education and patient services and is happy to have this comprehensive resource available to patients with chronic myelogenous leukemia. www.LLS.org/informationspecialists

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Chronic Myelogenous Leukemia (CML)

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Who should read this book?

The information in this book is about chronic myelogenous leukemia—a slow-growing cancer that starts in blood-forming cells in the bone marrow. Patients and those who support them—caregivers, family, and friends—may find this book helpful. It may help you discuss and decide with your doctors what care is best.

Where should I start reading?

Starting with Part 1 may be helpful for many people. It explains what chronic myelogenous leukemia is. Knowing more about this cancer may help you better understand its treatment. Parts 2 and 3 explain how doctors assess for this type of cancer and plan treatment. Some of the tests described in Part 2 are also used to check treatment results. Part 4 describes the types of treatments that may be used. Part 5 is a guide to treatment options. Part 6 offers some helpful tips for anyone making treatment decisions.

Making sense of medical terms

In this book, many medical words are included. These are words that you will likely hear from your treatment team. Most of these words may be new to you, and it may be a lot to learn.

Don’t be discouraged as you read. Keep reading and review the information. Be sure to ask your treatment team to explain a word or phrase that you don’t understand.

Words that you may not know are defined in the text or in the Dictionary. Words in the Dictionary are underlined when first used on a page. Acronyms are defined in the text when first used and are also defined in the Glossary. Acronyms are words formed from the first letters of other words. One example is CBC for complete blood count.

Does the whole book apply to me?

This book includes information for many situations. Thus, you will likely not get every test and treatment listed. Your treatment team can point out what applies to you and give you more information. As you read through this book, you may find it helpful to make a list of questions to ask your doctors.

The recommendations in this book are based on science and the experience of NCCN experts. However, each patient is unique and these recommendations may not be right for you. Your doctors may suggest other tests or treatments based on your health and other factors. If other suggestions are given, feel free to ask your treatment team questions.
1

About CML
Learning that you have cancer can be overwhelming and confusing. Part 1 explains some basics about chronic myelogenous leukemia that may help you better understand this disease. These basics may also help you start planning for treatment.

What are blood cells?

Blood is made of many types of cells, called blood cells. The three main types of blood cells are platelets, red blood cells, and white blood cells. Each type of blood cell has a certain job in the body. Platelets help control bleeding. Red blood cells carry oxygen throughout the body. White blood cells are part of the immune system and help fight infections in the body. The immune system is the body’s natural defense against infection and disease.

Blood cells are made from immature blood-forming cells in the bone marrow. Bone marrow is the soft, sponge-like tissue in the center of most bones. See Figure 1.1. These blood-forming cells are called blood stem cells or hematopoietic stem cells.

Blood stem cells go through a series of changes as they grow and develop to make new blood cells. See Figure 1.2. A blood stem cell may become a myeloid stem cell or a lymphoid stem cell. Each type of blood
stem cell then makes blast cells. Blast cells are new, immature blood cells that grow into mature blood cells over time.

Lymphoid stem cells make immature cells called lymphoblasts. Lymphoblasts become a type of white blood cells called lymphocytes. Myeloid stem cells make red blood cells, platelets, and immature cells called myeloblasts. Myeloblasts become a type of white blood cells called granulocytes. Neutrophils, eosinophils, and basophils are granulocytes.

Often, the cells formed by lymphoid stem cells are referred to as lymphoid cells. Likewise, the cells formed by myeloid stem cells are referred to as myeloid cells.
What is CML?

Cancer is a disease of cells—the building blocks that form tissue in the body. Leukemia is a cancer that starts in blood-forming cells in the bone marrow. There is more than one type of leukemia. Each type of leukemia is named based on how fast it grows and the type of blood cell in which it begins. This book focuses on CML (chronic myelogenous leukemia). “Chronic” means the leukemia grows and progresses slowly. “Myelogenous” means it starts in immature white blood cells called myeloid cells.

Normally, the amount and type of new blood cells made is very controlled and balanced. Normal blood cells grow and divide to make new red blood cells, white blood cells, and platelets as the body needs them. When normal blood cells grow old or get damaged, they die. New blood cells are then made to replace the old ones. In a person with CML, too many white blood cells are made.

How does CML start?

Inside of all cells are coded instructions called genes. Genes tell cells how to behave and what to do in the body. Genes are also needed for building new cells. Genes tell cells when to grow and divide to make new cells and how long the cells should live. Abnormal changes in genes cause normal cells to become cancer cells.

Genes are a part of DNA (deoxyribonucleic acid). DNA is grouped into bundles called chromosomes. See Figure 1.3. Every cell has 23 pairs of chromosomes. Each pair looks different from the others and is labeled by a number.

Before a cell divides to make two new cells, it first must make a copy of its DNA and chromosomes. Sometimes there are mistakes in the new copies.

---

**Figure 1.3**
Chromosomes and genes in cells

Genes are sets of coded instructions in cells for making new cells and controlling how cells behave. Genes are a part of DNA, which is bundled into long strands called chromosomes. Every cell has 23 pairs of chromosomes.

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One type of mistake is when parts of two chromosomes break off and switch with each other. This is called a translocation. It can result in a fusion gene—an abnormal gene that is formed when two genes are joined (fused) together.

CML is caused by the BCR-ABL fusion gene. This gene is not found in normal blood cells and is not passed down from parents to children. The BCR-ABL gene is formed by a translocation between parts of chromosomes 9 and 22. See Figure 1.4. The short bottom piece of chromosome 9 has the ABL gene. The ABL gene codes for a protein called a tyrosine kinase. The short top piece of chromosome 22 has the BCR gene. These short pieces attach to each other. As a result, the two genes join (fuse) together and form the BCR-ABL fusion gene.

This also results in a longer chromosome 9 and a shorter chromosome 22. The shorter chromosome 22 is called the Philadelphia chromosome. The Philadelphia chromosome is the hallmark of CML. It contains the BCR-ABL gene. If you do not have the Philadelphia chromosome or the BCR-ABL gene, then you do not have CML.

**Figure 1.4**
Philadelphia chromosome and BCR-ABL gene

The Philadelphia chromosome is formed by a translocation between parts of chromosomes 9 and 22. It contains the abnormal BCR-ABL fusion gene.
How does CML spread?

Cells that contain the **BCR-ABL gene** are called **leukemia cells** or **CML cells**. These cells are different from normal blood cells in a few key ways. The changes in their genes cause CML cells to make new cells that aren’t needed. The cells also live too long and don’t work as they should.

The **BCR-ABL** gene makes the abnormal **BCR-ABL protein** that helps CML cells grow and survive. It is a type of **protein** called a **tyrosine kinase**. These proteins send signals that tell cells when to grow and divide. The BCR-ABL protein is not normal. It is locked in the “on” position so that it is always sending signals for cells to grow and divide. This causes **blood stem cells** to make too many **white blood cells** called **granulocytes**.

White blood cells made by the BCR-ABL protein aren’t normal. They all are CML cells and contain the **BCR-ABL** gene. These cells don’t mature into healthy, normal cells. They may make new cells too quickly. The cells also don’t die when they should. Over time, the CML cells can build up in the **bone marrow**. They can overcrowd the bone marrow so there isn’t room for healthy white blood cells, **red blood cells**, and **platelets**. Over months or years, the CML cells can spill out of bone marrow into the **bloodstream**. Without treatment, the CML cells can eventually reach and collect in other organs such as the **spleen**. This can damage organs and cause **symptoms**.
Symptoms of CML

A symptom is a health problem a person experiences that may indicate a disease. CML can cause a number of symptoms. But, because it is a slow-growing cancer, many people do not have symptoms when CML is first found (diagnosed). Instead, CML may cause symptoms as it progresses over time.

Some common symptoms that may be caused by CML include:

- Severe tiredness (fatigue),
- Weakness,
- Fever,
- Unusual sweating at night,
- Unexplained weight loss, and
- Feeling pain or fullness in the upper, left part of the belly beneath the ribs.

Symptoms of CML may result from a shortage of healthy blood cells. Symptoms may also result from CML cells collecting in organs such as the spleen. However, these symptoms can also be caused by many other common health conditions.
Review

- Blood cells are made in the soft tissue in the center of most bones called bone marrow.
- A blood stem cell is a cell from which all other types of blood cells are made.
- White blood cells fight disease and infections in the body.
- Leukemia is a cancer that starts in blood-forming cells in the bone marrow.

- CML is a slow-growing type of leukemia in which too many white blood cells called granulocytes are made.
- People with CML have the Philadelphia chromosome, which contains the abnormal BCR-ABL gene.
- The BCR-ABL gene causes white blood cells to grow in an abnormal, uncontrolled way, causing leukemia.
Testing for CML
Treatment planning starts with testing. This section describes the tests that are used to confirm (diagnose) CML, plan treatment, and check treatment results. This information can help you use the *Treatment guide* in Part 5. It may also help you know what to expect during testing. Not every person with CML will receive every test listed.

**Medical history**

Your medical history includes any health events in your life and any medications you’ve taken. A medical history is needed for treatment planning. Your doctor will ask about illnesses, injuries, and health problems that you have had. Your doctor will also ask about any symptoms you’ve had that may be due to CML. This information may affect which cancer treatment is best for you. It may help to make a list of old and new medications while at home to bring to your doctor’s office.
Physical exam

Doctors usually perform a physical exam along with taking a medical history. A physical exam is a review of your body for signs of disease such as infection and areas of unusual bleeding or bruising.

Your doctor may listen to your lungs, heart, and intestines. Your doctor may also feel different parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched. For example, your doctor will feel your belly area (abdomen) to check for signs of an enlarged spleen.

Checking the size of your spleen is a key part of the physical exam. Your spleen is found in the upper, left part of your belly underneath your ribs. A normal-sized spleen often cannot be felt during a physical exam. But, the spleen can be felt when it is enlarged. The spleen filters blood, stores blood cells, and destroys old blood cells. CML may cause an enlarged spleen due to extra white blood cells being stored in this organ.

Blood tests

Doctors test blood to look for signs of disease and to check your general health. Blood tests are done along with other initial tests to help confirm (diagnose) CML. They are also used to check how well treatment is working and check for side effects. For a blood test, your doctor will insert a needle into a vein to remove a sample of blood. The blood sample will then be sent to a lab for testing. At the lab, a pathologist will examine the blood sample with a microscope and perform other tests.
Bone marrow tests

Bone marrow is the soft, sponge-like tissue in the center of most bones where blood cells are made. Bone marrow tests are used to confirm CML and to check how well treatment is working. The two types of bone marrow tests used for CML are a bone marrow biopsy and bone marrow aspiration.

A biopsy is the removal of tissue from your body to test for disease. A biopsy is generally a safe test and can often be done in about 30 minutes. After the samples are collected, they are sent to a lab for testing.

A bone marrow biopsy removes a small piece of solid bone along with a small amount of soft bone marrow inside the bone. A bone marrow aspiration removes a small amount of liquid bone marrow from inside the bone. Often, both tests are done at the same time on the back of the hip bone or on the breastbone.

These bone marrow tests are done as outpatient tests—this means you don’t have to spend the night in the hospital. First, you may be given a sedative injected with a needle into your vein. Your doctor will then clean the area of skin where the biopsy will be performed. Next, you will receive local anesthesia to numb the area of skin and bone beneath. After the area is numbed, a hollow needle will be inserted into your skin and then pushed into the bone to remove the liquid bone marrow with a syringe. Then, a wider needle will be inserted into the bone and twisted to remove the solid bone and marrow sample. See Figure 2.1. You may feel some pain while the samples are being removed and your skin may be bruised afterward.

**Figure 2.1**

**Bone marrow biopsy**

Doctors use a bone marrow biopsy and aspiration to remove a sample of bone marrow for testing. These tests are often done at the same time on the hip bone.
Lab tests

To confirm if you have CML, a sample of blood and/or bone marrow must be removed from your body. The samples will be sent to a lab for testing by a pathologist. This is a doctor who’s an expert in testing cells and tissue for signs of disease. At the lab, the pathologist will examine the samples with a microscope. A number of tests will be done to check for signs of CML.

Signs of CML may be found in blood. This includes too many white blood cells and abnormal levels of certain chemicals. Signs of CML may also be found in bone marrow. This includes the Philadelphia chromosome and the BCR-ABL gene.

It often takes several days before the lab results are known. If you do not have the Philadelphia chromosome or the BCR-ABL gene, then you do not have CML. Chart 2.1 lists the different lab tests that are used for CML. Read the next pages to learn more about these tests, including when each is recommended.

CBC with differential
A CBC (complete blood count) is a test that measures the number of white blood cells, red blood cells, and platelets in a sample of blood. The CBC should include a differential. The differential measures the different types of white blood cells in the sample. A high number of white blood cells and a low number of red blood cells may be signs of CML. This is because CML causes too many white blood cells to be made. These white blood cells may overcrowd the bone marrow so that too few normal blood cells are made. A CBC with differential is given along with other initial tests when CML is first suspected. This test is also repeated during and after treatment to check treatment results.

Chart 2.1 Lab tests for CML

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Blood chemistry profile

A blood chemistry profile measures the levels of a number of different chemicals in a sample of blood. Different organs and tissues in the body naturally release chemicals into the blood. Abnormal levels of certain chemicals in the blood may be a sign that an organ isn't working well. A blood chemistry profile helps doctors assess if certain organs and body systems are working well. This test is done along with other initial tests when CML is first found. It may also be repeated during and after cancer treatment.

Cell assessment

A microscope is used to look at the cells in the blood and bone marrow samples. This lab test is simply called cell assessment. For this test, special dyes may be used to stain the samples. This helps to show the differences between parts of a single cell and differences between many cells.

The pathologist will look at the size, shape, type, and other features of the cells. This is to see if the cells look more like normal, mature cells or more like abnormal, immature cells. The number of immature blood cells (blast cells) and basophils should be noted. Basophils are a type of white blood cell.

In a person without CML, there are no blast cells in the bloodstream and the number of basophils is very low. In a person with CML, the number of basophils is often increased. And, in advanced phases of CML, many blast cells are found in the bone marrow or bloodstream.

Bone marrow cytogenetics

Cytogenetics is the study of chromosomes—long strands of DNA that contain genes. Genes are sets of coded instructions for making and controlling cells. Cytogenetic testing uses a microscope to examine the chromosomes inside cells. This type of test is used to look for abnormal changes in the chromosomes. It is often done on a sample of bone marrow. This is called bone marrow cytogenetics.

Bone marrow cytogenetics is used to find the Philadelphia chromosome and measure the number of cells that have it. For this test, a pathologist will look at a “map” of the chromosomes under a microscope. He or she will assess the size, shape, number, and placement of the chromosomes to check for abnormal changes.

Bone marrow cytogenetics is used to confirm CML and find out the disease phase. It is also used to check how well treatment is working—called a treatment response. Cytogenetic testing can also be done on a sample of blood, but bone marrow is preferred. A blood sample may be used in some cases if a bone marrow sample can’t be collected.

FISH

FISH (fluorescence in situ hybridization) can also be used to look for the BCR-ABL gene, which is on the Philadelphia chromosome. This test uses special color dyes—called probes—that attach to the BCR gene and the ABL gene in chromosomes. The BCR-ABL gene is shown by the overlapping colors of the two probes.

FISH can be performed on a sample of blood. Thus, this test may be used to help confirm CML if a sample of bone marrow can’t be collected. But, FISH is not used to check treatment results.
**QPCR**

QPCR (quantitative reverse transcriptase polymerase chain reaction) is a test that is used to find and measure the **BCR-ABL** gene. It can be done on a sample of blood or bone marrow. This test is used to confirm (diagnose) CML. It is also used to check how well treatment is working.

QPCR measures the number of cells in the blood or bone marrow that have the **BCR-ABL** gene. QPCR is very sensitive and can find one CML cell among more than 100,000 normal cells. This test should always be done at the same lab. A lab that uses the IS (International Scale) is preferred. See page 46 for more details about the IS and how QPCR is used to check treatment results.

**Cytochemistry**

A cytochemistry test uses chemical stains (dyes) to show which types of cells are present in a blood sample. Each dye reacts with a chemical that is found in only one type of cell. This reaction causes a color change that can be seen with a microscope.

This test can be used to check if leukemia cells are mostly myeloid or lymphoid cells. This test is not used for all patients with CML. It is only used to help guide treatment options for CML in blast phase.

**Flow cytometry**

Flow cytometry looks at certain substances on the surface of cells to find out the type of cells present. This test is used to show if the leukemia cells are mostly myeloid cells or lymphoid cells. It is used for CML in advanced phases to help guide treatment choices. Flow cytometry can be done on a sample of blood or bone marrow. This test is important because the cell type may affect which treatment is best for you.

**BCR-ABL gene mutation analysis**

Sometimes new changes (mutations) happen in the part of the **BCR-ABL** gene that makes the BCR-ABL protein. These mutations change the shape of the BCR-ABL protein. This affects how and which targeted cancer drugs can bind to it to block the growth signals.

New mutations in the **BCR-ABL** gene may occur over time. New mutations can happen as CML progresses to advanced phases. They can also happen during treatment for CML. **BCR-ABL gene mutation analysis** is a test that looks for these new mutations. This test can be done on a sample of blood or bone marrow. It may be done after the start of treatment based on how well treatment is working. This test is important because new or different gene mutations can affect which treatment option is best for you.

**HLA testing**

HLAs (human leukocyte antigens) are special proteins found on the surface of most cells in the body. These proteins help the body to tell its own cells apart from foreign cells. The HLA type is the unique set of HLA proteins on a person’s cells.

HLA types differ among people just like blood types differ among people. HLA proteins can be thought of as a “bar code” that uniquely identifies a person. All cells in a single person have the same HLA “bar code.”

**HLA testing** is a blood test that finds a person’s HLA type. This test must be done before treatment that transfers blood stem cells from another person to the patient. (See Part 4 on page 34 for details about this treatment). The patient’s HLA type and the donor’s HLA type must be a near-perfect match for this treatment to work. This is because the HLA type affects how the body responds to foreign substances.
### Review

- Cancer tests are used to plan treatment and check how well treatment is working.
- To confirm if you have CML, a sample of bone marrow and/or blood must be removed from your body for testing.
- The removal of tissue from your body for testing is called a biopsy.
- Blood tests are used to look for signs of disease and to assess your general health.
- Cytogenetic testing is used to check for the Philadelphia chromosome.
- QPCR is a very sensitive test that is used to find and measure the \textit{BCR-ABL} gene.
Phases of CML
To help plan treatment, doctors classify CML into three groups called phases. The phase is based on the number of immature white blood cells (blasts) in the blood and bone marrow. The phase of CML helps predict the likely outcome (prognosis). Part 3 describes each phase of CML as well as the other factors doctors use to plan treatment.

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**Chronic phase**

The first phase of CML is called the *chronic phase*. In this phase, there is an increased number of white blood cells in the blood and/or bone marrow. Immature white blood cells (blast cells) make up less than 10% of cells in the blood and/or bone marrow. This means that less than 10 out of every 100 cells are blasts.

Most often, CML does not cause any symptoms in the chronic phase. But, it may cause some mild symptoms like fatigue or a feeling of fullness under the left side of the ribs. The body can still fight infections since the changes in blood cells are not severe.

In this phase, the cancer progresses very slowly. It may take several months or years to reach the next phase, called *accelerated phase*. Compared to other phases, CML in the chronic phase tends to respond better to treatment.

**Accelerated phase**

The second phase of CML is called the accelerated phase. In this phase, the number of blast cells in the blood and/or bone marrow is higher than normal. The number of white blood cells is also high. Other features may include a high number of basophils or a very low number of platelets in the blood. New chromosome changes may also be found.

In this phase, the leukemia cells (CML cells) grow faster and may cause symptoms. Such symptoms may include fever, weight loss, not feeling hungry, and an enlarged spleen. A few different criteria groups can be used to define accelerated phase. The main ones are the WHO (World Health Organization) Criteria and the criteria from MD Anderson Cancer Center. But, the WHO Criteria is used most often. The WHO defines accelerated phase as the presence of any of the following features:

- 10% to 19% blasts in the bloodstream and/or bone marrow
- >20% basophils in the bloodstream
- Very high or very low platelet count that is not related to treatment
- Increasing spleen size and white blood cell count despite treatment
- New chromosome changes (mutations)
Blast phase

The third and final phase of CML is called blast phase. It is also referred to as “blast crisis.” Once CML is in blast phase, it can be life-threatening. In this phase, the number of blast cells in the blood and/or bone marrow is very high. Another key feature of blast phase is that the blast cells have spread outside the blood and/or bone marrow to other tissues. In this phase, CML may cause more symptoms. This may include infections, bleeding, belly pain, and bone pain.

In this phase, the leukemia cells become more abnormal. CML in blast phase often acts similar to acute leukemia. Acute leukemia is a type of leukemia that grows and progresses very fast. In contrast, chronic leukemia progresses slowly over months or years. In blast phase, the leukemia cells may behave more like AML (acute myeloid leukemia) or more like ALL (acute lymphoblastic leukemia).

Blast phase can be defined by the WHO Criteria or the International Bone Marrow Transplant Registry. The key difference between these definitions is the number of blasts in the blood or bone marrow. The WHO defines blast phase as >20% blast cells in the bloodstream or bone marrow. The International Bone Marrow Transplant Registry defines blast phase as >30 blast cells in the blood and/or bone marrow. A defining feature included by both groups is the presence of blast cells outside of the blood or bone marrow.

Risk assessment

Along with the phase of CML, there are other key factors that affect treatment options and the likely outcome (prognosis) of CML. Something that affects and helps predict prognosis is called a prognostic factor.

Prognostic scoring systems use many factors to determine a patient’s risk score. Such factors include a person’s age, spleen size, and blood counts. Based on the risk score, patients are classified into risk groups—low-, intermediate-, or high-risk. People in the same risk group are similar in certain ways and will likely respond to certain treatments in the same way. Therefore, doctors often use risk scores to help guide treatment decisions. In general, a person classified as low-risk is more likely to have a better response to treatment.
Review

- To help plan treatment, CML is classified into three groups called phases.
- The phase of CML is based on the number of immature white blood cells (blasts) in the blood and bone marrow.
- A prognostic factor is something that affects and helps predict the likely outcome (prognosis) of a disease.
- Prognostic scoring systems help predict the likely outcome (prognosis) and guide treatment decisions.
Overview of cancer treatments
Part 4 describes the main types of treatment for CML. This information may help you better understand the treatment options listed in the Treatment guide in Part 5. It may also help you know what to expect during treatment. Not every person with CML will receive every treatment listed.

Tyrosine kinase inhibitor therapy

TKI (tyrosine kinase inhibitor) therapy is a type of targeted therapy. Targeted therapy is treatment with drugs that target a specific or unique feature of cancer cells. Because these drugs target cancer cells, they may be less likely to harm normal cells.

TKIs target the abnormal BCR-ABL protein that helps CML cells grow. The BCR-ABL protein is made by the abnormal BCR-ABL gene. It is a type of protein called a tyrosine kinase. TKIs block (inhibit) the BCR-ABL protein from sending the signals that cause too many CML cells to form.

The FDA (U. S. Food and Drug Administration) approved the first TKI for the treatment of CML in 2001. Since then, four other TKIs have been approved to treat CML. These newer drugs are called “second-generation” TKIs. The TKIs used to treat CML are described next. These drugs are made in the form of a pill that is swallowed. The dose of the drug is measured in mg (milligrams).
**TKI drugs**

**Imatinib**
Imatinib was the first TKI approved by the FDA to treat CML. Thus, it is called a “first-generation” TKI. Imatinib works by binding to the active site on the BCR-ABL protein to block it from sending signals to make new abnormal white blood cells (CML cells). See Figure 4.1.

**Dasatinib**
Dasatinib is a second-generation TKI that was approved for the treatment of CML in 2006. Dasatinib is more potent than imatinib and can bind to the active and inactive sites on the BCR-ABL protein to block growth signals.

**Nilotinib**
Nilotinib was first approved to treat CML in 2007. It is a second-generation TKI that works in almost the same way as imatinib. However, nilotinib is more potent than imatinib and it more selectively targets the BCR-ABL protein.

**Bosutinib**
Bosutinib is a second-generation TKI that was approved to treat CML in 2012. This drug is only approved to treat CML in patients after another TKI has stopped working or caused very bad side effects. (For more details, read TKI drug resistance on page 31.)

**Ponatinib**
Ponatinib was approved to treat CML in 2012. Ponatinib is a multitargeted TKI. This means that it targets all of the changes (mutations) on the BCR-ABL protein that are resistant to imatinib and other TKIs. (See TKI drug resistance on page 31 for details.) But, this drug can cause severe side effects and is not a good option for all patients. Ponatinib is only approved for patients with a T315I mutation or CML that is resistant or intolerant to other TKIs.

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**Figure 4.1 How imatinib works**

Imatinib was the first TKI approved to treat CML. It works by binding to a part of the BCR-ABL protein that sends signals for CML cells to grow. This stops new CML cells from being made.
Side effects of TKIs

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Each TKI for CML can cause side effects. How your body will respond to treatment can’t be fully known. You may have different side effects than someone else. Side effects of TKIs depend on the drug, the amount taken, the length of treatment, and the person. Some side effects listed below are caused by only one TKI. Others are caused by all or most TKIs but differ in how likely they are to occur.

Most side effects can be managed or even prevented. Be sure to tell your treatment team about any side effects that you have. This way you can receive the supportive care you need. Supportive care is the treatment of symptoms caused by CML or side effects caused by CML treatment. Managing symptoms and side effects is important for your quality of life and CML treatment outcome.

Common side effects of TKIs for CML include:

- Low blood cell counts
  - Low red blood cell counts
  - Low platelet counts
  - Low neutrophil counts
- Abnormal bleeding
- Swelling due to fluid buildup (edema)
- Fluid buildup around the lungs (pleural effusion)
- Nausea and vomiting
- Muscle cramps or spasms
- Muscle, bone, and joint pain
- Skin rash and/or dry, itchy skin
- Fatigue
- Diarrhea
- Low levels of the mineral phosphorus in the blood
- Headache
- Stomach or belly pain

Low numbers of blood cells may be treated by lowering the TKI dose. Stopping TKI therapy for a short time may also help.

All TKIs have the capacity to cause a serious heart problem called QT interval prolongation. This heart problem causes a change in heartbeat rhythm and can be fatal. But, this side effect can be managed by giving a lower dose of the TKI. Your doctor may give a test called an ECG (electrocardiogram) to check for this side effect. An ECG is a test that shows the activity of the heart with a line graph. This test may be given before and during TKI treatment.

Pleural effusion is when there is fluid buildup around the lungs. It is a serious side effect that can be caused by dasatinib. A history of heart problems and high blood pressure may increase the risk of pleural effusion.

Nilotinib may cause the amount of sugar (glucose) in the blood to be higher than normal. This condition is called hyperglycemia.

Severe side effects of ponatinib include heart problems, blood clots, narrowing of blood vessels, heart attack, and stroke. Liver problems or swelling of the pancreas may also happen, but they can often be managed by lowering the dose of ponatinib.
Drug interactions
Certain medicines (drugs) and substances can change the way TKIs work in the body. This is called a drug interaction. TKIs are broken down and made active by proteins in the liver. Some drugs and substances can increase or decrease the amount of these proteins in the body.

Drugs that increase these proteins may make TKIs less effective. Such drugs include steroids, St. John’s wort, and drugs used to treat seizures. Drugs that decrease these proteins can cause higher, unsafe levels of TKIs in the blood. Such drugs include certain antibiotics and anti-fungals. Grapefruit juice may also increase TKI levels in the body.

Drugs that reduce acid in the stomach and intestines may reduce the amount of dasatinib or nilotinib in the blood. Such drugs include H2 (histamine-2) blockers and proton pump inhibitors. These drugs should not be used during treatment with dasatinib or nilotinib.

TKI drug resistance
A treatment response is an outcome or improvement caused by treatment. It means that a treatment or drug is working well to kill the cancer. Drug resistance is when CML doesn’t respond to a drug. There is more than one type of drug resistance.

Primary resistance is when CML doesn’t respond at all to a drug taken for the first time. This type is rare in patients with CML. Secondary resistance is when CML responds to a drug at first and then stops responding after a period of time. This is the most common type of resistance that happens in patients with CML.

A number of factors may cause or lead to secondary resistance. Most often, it is caused by changes (mutations) in the part of the BCR-ABL gene that makes the BCR-ABL protein. These mutations change the shape of the BCR-ABL protein so that certain TKIs can’t bind to it as well. New mutations can happen as CML progresses. They can also happen over time during TKI therapy. This can cause the TKI to stop working.

But, each TKI drug works in a slightly different way. One TKI drug may be able to work against a mutation that another TKI can’t. Therefore, switching to a different TKI may result in a treatment response after a prior TKI stops working.

Second-generation TKIs can work against many of the mutations that are resistant to imatinib. Dasatinib, nilotinib, and bosutinib appear to work against all but one of the mutations that are resistant to imatinib. But, ponatinib is currently the only TKI that works against the more difficult T315I mutation. The chemotherapy drug omacetaxine can also work against this mutation.
TKI adherence
Medication adherence—in this case, TKI adherence—is the extent to which you take your TKI as prescribed and by your doctor. Good adherence means that you always take your TKI exactly the way your doctor asked you to. This means taking the right number of pills, at the right time, on the right day, every day. When you don’t take your TKI the right way, it is called nonadherence or poor adherence.

Taking your TKI the right way is very important—it affects how well treatment works. This means that you must always take your TKI the right way for it to work best. A treatment response is an outcome or improvement caused by treatment. Studies show that good TKI adherence is linked with reaching and keeping a good treatment response. Not taking your TKI the right way can lower the chance of reaching or keeping a good treatment response.

TKI therapy can control CML for long periods of time. But, it must be taken indefinitely or until it stops working. You should never stop taking your TKI on your own. Only stop taking it if your doctor tells you to or as part of a clinical trial.

There are many things that might make it hard to take your TKI as you should. At times, you may miss a dose due to forgetfulness. Or, you may decide to skip a dose to try to lessen the side effects. No matter the cause, don’t keep it to yourself. Tell your doctor or nurse right away so they can help you with the problem. This is even more important if it’s the side effects that make it hard to take your TKI. These side effects can and should be managed. There are many ways your treatment team can help you.
Immunotherapy

The immune system is the body’s natural defense against infection and disease. Immunotherapy is treatment with drugs that boost the immune system response against cancer cells. Interferon is a substance naturally made by the immune system. Interferon can also be made in a lab to be used as immunotherapy for CML. PEG (pegylated) interferon is a long-acting form of the drug. Interferon is not used as initial treatment for CML. But, it may be an option for certain patients who can’t tolerate the side effects of TKI therapy. Interferon is a liquid that is injected under the skin or in a muscle with a needle.

Side effects of immunotherapy

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Most side effects can be managed or even prevented with the right supportive care. Supportive care is the treatment of symptoms caused by CML or side effects caused by CML treatment. Be sure to tell your treatment team about any side effects that you have. Treating side effects is important for your quality of life and CML treatment outcome. Possible side effects of interferon include:

- Trouble with concentration or memory,
- Mood changes, and
- Flu-like symptoms
  - Fever
  - Chills
  - Fatigue
  - Body aches
  - Nausea/vomiting
  - Not feeling hungry

Chemotherapy

Chemotherapy is the use of drugs to kill cancer. Many people refer to this treatment as “chemo.” Chemotherapy drugs kill fast-growing cells throughout the body, including cancer cells and normal cells.

Different types of chemotherapy drugs attack leukemia cells in different ways. Therefore, more than one drug is often used. When only one drug is used, it’s called a single agent. A combination regimen is the use of two or more chemotherapy drugs.

Chemotherapy is given in cycles. A cycle includes days of treatment followed by days of rest. Giving chemotherapy in cycles gives the body a chance to recover before the next treatment. Often, the cycles are 14, 21, or 28 days long. The cycles vary in length depending on which drugs are used. The number of treatment days per cycle and the total number of cycles given also varies.

Omacetaxine is the newest chemotherapy drug for CML. In 2012, the FDA approved omacetaxine for the treatment of CML in patients with resistance and/or intolerance to two or more TKIs. Resistance is when CML does not respond to a treatment. Intolerance is when treatment with a drug must be stopped due to severe side effects. Studies have shown that omacetaxine is active against all of the mutations resistant to TKIs. A mutation is an abnormal change in the instructions in cells for making and controlling cells. (Read TKI drug resistance on page 31 for details).

Omacetaxine is given as a liquid that is injected under the skin with a needle. Other chemotherapy drugs may be injected into a vein. Or, they may be given as a pill that is swallowed.
Side effects of chemotherapy

A **side effect** is an unhealthy or unpleasant physical or emotional condition caused by treatment. Each treatment for CML can cause side effects. How your body will respond to treatment can’t be fully known. Some people have many side effects. Others have few. Some side effects can be very serious while others can be unpleasant but not serious.

The side effects of chemotherapy depend on many factors. This includes the drug, the dose, and the person. In general, side effects are caused by the death of fast-growing cells, which are found in the intestines, mouth, and blood. As a result, common side effects include nausea, vomiting, numbness in hands and feet, hair loss, and low blood cell counts. The most common side effects of omacetaxine include:

- Low **platelet** counts,
- Low **red blood cell** counts,
- Low **white blood cell** counts,
- Diarrhea,
- Nausea,
- **Fatigue**,  
- Weakness or lack of energy,  
- Injection site reaction,  
- Fever, and  
- Infection.

Hematopoietic cell transplant

High-dose chemotherapy followed by an HCT (hematopoietic cell transplant) may be a treatment option for some patients with CML. For this treatment, high-dose chemotherapy is given first to destroy normal cells and CML cells in your bone marrow. An HCT is a procedure that replaces the destroyed cells in your bone marrow with new, healthy blood-forming cells. The blood-forming cells are called **blood stem cells** or hematopoietic stem cells. Thus, this treatment is also referred to as a stem cell transplant.

For the treatment of CML, the blood stem cells are collected from another person, called a donor. This is called an allogeneic HCT. Before the transplant, special testing must be done to make sure the donor is a good match for you. HLA testing is used to find a person’s tissue type, called an HLA type. (See page 19 for more details on HLA testing.)

High-dose chemotherapy, and sometimes radiation therapy, is given before the transplant to destroy the CML cells in your bone marrow. The high-dose chemotherapy also destroys normal blood cells in your bone marrow. This greatly weakens your **immune system** so that your body doesn’t attack the transplanted blood stem cells. Once the high-dose chemotherapy is complete, the donated blood stem cells are put into your body with a **transfusion**. A transfusion is when you receive whole blood or parts of blood put directly into your bloodstream through a **vein**. This process can take 1 to 5 hours to complete.

The transplanted blood stem cells then travel to your bone marrow and grow to make new healthy blood cells. This is called engraftment and it usually occurs about 2 to 4 weeks after the transplant. Until then you will have little or no immune defense, and so you are at high risk for infection and bleeding. Therefore, you will likely need to stay in a hospital in a very clean environment.
Overview of cancer treatments

Hematopoietic cell transplant

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Chronic Myelogenous Leukemia, Version 1.2016

(stereile) unit for about 2 weeks. It may take a few weeks or months for blood cells to fully recover so that your immune system is back to normal.

An allogeneic HCT creates a new immune system for your body. The immune system is the body’s natural defense against infection and disease. This transplant also causes the GVL (graft-versus-leukemia) effect. The GVL effect is when the transplanted blood stem cells (the graft) see the leukemia cells in your body as foreign and attack them.

Considering allogeneic HCT

Before TKIs, an HCT was considered the treatment of choice for CML. However, an allogeneic HCT is a complex treatment and can cause very serious side effects. Thus, it may not be a good treatment choice for every patient with CML. Many treatment centers will only consider this treatment option for patients younger than 65 years of age.

Your doctor will consider many important factors when deciding if an allogeneic HCT is a good choice for you. These factors include your age and general health, the phase of CML, how well prior TKIs worked, and whether a well-matched donor is available.

An allogeneic HCT is not used as the first treatment for CML. But, it may be used as second-line treatment or follow-up treatment for certain patients. Doctors may also consider an allogeneic HCT if prior treatments fail or stop working.

Side effects of allogeneic HCT

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Common side effects of chemotherapy, which is given before the transplant, are described on page 34. You will likely feel tired and weak shortly after the transplant while waiting for the new blood stem cells to grow in the bone marrow.

Allogeneic transplants have a high risk of GVHD (graft-versus-host disease). GVHD is when the donated cells (the graft) see the cells in your body (the host) as foreign and attack them. The parts of the body most commonly damaged by GVHD include the skin, intestines, and liver. GVHD is a serious side effect that can cause the transplant to fail by stopping the donated blood stem cells from growing in your bone marrow. GVHD can develop within a few weeks after the transplant or much later. Your doctor may give you medications that lessen (suppress) the immune response to try to prevent this side effect.

Many side effects can be managed or even prevented. Be sure to tell your treatment team about any side effects that you have. Managing side effects is important for your quality of life and CML treatment outcome.
Donor lymphocyte infusion

**DLI** (donor lymphocyte infusion) is a procedure in which the patient receives lymphocytes from the same person who donated blood stem cells for the HCT. A lymphocyte is a type of white blood cell that helps the body fight infections. The purpose of a DLI is to stimulate an immune response called the **GVL effect**. The GVL effect is when the transplanted cells (the graft) see the leukemia cells in your body as foreign and attack them. This treatment may be used after an allogeneic HCT for CML that didn’t respond to the transplant or that came back after an initial response.

Because a DLI starts an immune response in your body, the main risk of this treatment is **GVHD**. Some other side effects of a DLI are myelosuppression and an increased risk of infection. Myelosuppression is when the bone marrow is weakened (suppressed) and, as a result, fewer red blood cells, white blood cells, and platelets are made.

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**Complementary and alternative medicine**

**CAM** (complementary and alternative medicine) is a group of treatments that aren’t often given by doctors. There is much interest today in CAM for cancer. Many CAMs are being studied to see if they are truly helpful.

Complementary medicines are treatments given along with usual medical treatments. While CAMs aren’t known to kill cancer cells, they may improve your comfort and well-being. Two examples are acupuncture for pain management and yoga for relaxation.

Alternative medicine is used in place of usual medicine. Some alternative medicines are sold as cures even though they haven’t been proven to work. If there was good proof that CAMs or other treatments cured cancer, they would be included in this book.

It is important to tell your treatment team if you are using any CAMs. They can tell you which CAMs may be helpful and which CAMs may limit how well treatments work.
Clinical trials

New tests and treatments aren’t offered to the public as soon as they’re made. They need to be studied first. New uses of tests and treatments also need to be studied.

A clinical trial is a type of research that studies a test or treatment. Clinical trials study how safe and helpful tests and treatments are. When found to be safe and helpful, they may become tomorrow’s standard of care. Because of clinical trials, the tests and treatments in this book are now widely used to help patients.

Tests and treatments go through a series of clinical trials to make sure they’re safe and work. Without clinical trials, there’s no way to know if a test or treatment is safe or helpful. Clinical trials are done in a series of steps, called phases. The four phases of clinical trials are described next using the example of a new drug treatment:

**Phase I trials** aim to find the best dose and way to give a new drug with the fewest side effects. If a drug is found to be safe, it will be studied in a phase II trial.

**Phase II trials** assess if a drug works for a specific type of cancer. They are done in larger groups of patients with the same type of cancer.

**Phase III trials** compare a new drug to the standard treatment. These are randomized, meaning patients are put in a treatment group by chance.

**Phase IV trials** test new drugs approved by the FDA to learn about short-term side effects, long-term side effects, and safety. They involve many patients with different types of cancer.

Joining a clinical trial has benefits. First, you’ll have access to the most current cancer care. Second, you will receive the best management of care. Third, the results of your treatment—both good and bad—will be carefully tracked. Fourth, you may help other patients with cancer.

Clinical trials have risks, too. Like any test or treatment, there may be side effects. Also, new tests or treatments may not work better than current treatments. Another downside may be that paperwork or more trips to the hospital may be needed.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial often have a similar cancer type and general health. This helps ensure that any response is because of the treatment and not because of differences between patients.

You also must review and sign a paper called an informed consent form to join a clinical trial. This form describes the study in detail, including the risks and benefits. Lastly, many insurance companies will not pay the costs of a clinical trial. This information will be outlined in your health insurance policy.

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you’re getting treatment or at other treatment centers nearby.
Review

- Primary treatment is the main treatment used to rid the body of cancer.
- TKI therapy is used as the primary treatment for CML.
- TKI therapy is treatment with drugs that block the signals that tell CML cells to grow.
- Immunotherapy is treatment with drugs that boost the body’s natural defense against infection and disease.
- Chemotherapy is treatment with drugs that kill fast-growing cells, including cancer cells and normal cells.
- A hematopoietic cell transplant replaces damaged or diseased cells in the bone marrow with healthy blood stem cells.
- A clinical trial studies a test or treatment to see how safe it is and how well it works.
5 Treatment guide

42 5.1 Chronic phase primary treatment

Presents the initial treatments recommended for CML in the first phase of progression.

44 5.2 Checking treatment results

Presents the tests that are recommended during treatment to check how well it is working—called a treatment response. The types of treatment responses are also explained.

50 5.3 Chronic phase follow-up treatment

Presents the next options that are recommended for chronic phase CML at each follow-up point based on how well treatment has worked so far.

60 5.4 Accelerated and blast phase treatment

Presents the tests and treatments that are recommended for CML in the advanced phases of progression.

64 5.5 Allogeneic HCT (hematopoietic cell transplant)

Presents the recommendations for treatment with an allogeneic HCT, also called allogeneic stem cell transplant. This treatment replaces damaged cells in the bone marrow with healthy blood stem cells from another person.
Part 5 is a guide through the treatment options for people with CML (chronic myelogenous leukemia). It shows which tests and treatments are recommended under which conditions. This information is taken from the treatment guidelines written by NCCN experts for doctors who treat CML.

The treatment options in Part 5 are organized by the phase of CML. The initial or main treatment used is called the primary treatment. Much effort has been made to make this guide easy to read. Charts list the treatment options and map the steps through the treatment process. The text along with each chart explains the information presented in the chart. Some words that you may not know are defined on the page and in the Dictionary on page 78. Words defined in the Dictionary are underlined when first used on a page. More details about the tests, CML phases, and treatments in this guide can be found in Parts 2 through 4.
5.1 Chronic phase primary treatment

Chart 5.1 shows the primary treatment options for newly diagnosed CML in the chronic phase. Chronic phase is the first phase of CML. In this phase, less than 10 out of 100 cells in the bone marrow are blast cells. Primary treatment is the main treatment used to rid your body of cancer.

Before you start treatment for CML, a member of your treatment team will discuss the treatment options with you. This person will explain the benefits and risks of each treatment. There are three main options for primary treatment for CML in the chronic phase. Options include TKI therapy, allogeneic HCT, and joining a clinical trial. (See Part 4 on page 28 for details about each treatment option.)

TKI therapy is by far the most preferred primary treatment option for chronic phase CML. TKIs are drugs that block the BCR-ABL protein from sending signals that cause CML cells to grow. TKIs are often very good at controlling CML for long periods of time. Three TKIs are approved as primary treatment for chronic phase CML. Imatinib was the first TKI approved for CML. Thus, it is called a first-generation TKI. Nilotinib and dasatinib came later and are called second-generation TKIs. Each TKI drug works by blocking the BCR-ABL protein, but each TKI also affects a unique set of other proteins. Your doctor will look at many factors to decide which is best for you.

After you start TKI therapy, your doctor will give follow-up tests to check how well it is working. An outcome or improvement caused by treatment is called a treatment response. The follow-up tests, test schedule, and types of treatment responses are explained in the next section, Part 5.2.

Next steps:

See Chart 5.2.1 on page 44 to read about the types of treatment responses. Then, see Chart 5.2.2 on page 48 for the schedule of follow-up tests that are needed based on the treatment response.
My notes
5.2 Checking treatment results

<table>
<thead>
<tr>
<th>Type of response</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hematologic response</strong></td>
<td>Complete hematologic response: Blood counts completely back to normal; no blasts or other immature cells in blood; no signs or symptoms of disease, including no enlarged spleen</td>
</tr>
<tr>
<td><strong>Cytogenetic response</strong></td>
<td>Complete cytogenetic response: No Philadelphia chromosomes are found with bone marrow cytogenetics</td>
</tr>
<tr>
<td></td>
<td>Partial cytogenetic response: 1% to 35% of cells have the Philadelphia chromosome on bone marrow cytogenetics</td>
</tr>
<tr>
<td></td>
<td>Major cytogenetic response: 0% to 35% of cells have the Philadelphia chromosome on bone marrow cytogenetics</td>
</tr>
<tr>
<td></td>
<td>Minor cytogenetic response: More than 35% of cells have the Philadelphia chromosome on bone marrow cytogenetics</td>
</tr>
<tr>
<td><strong>Molecular response</strong></td>
<td>Early molecular response: At 3 and 6 months, $BCR-ABL \leq 10%$ found by QPCR using the International Scale</td>
</tr>
<tr>
<td></td>
<td>Major molecular response: At least a 3-log reduction in $BCR-ABL$ levels, or $BCR-ABL \leq 0.1%$ by QPCR using the International Scale</td>
</tr>
<tr>
<td></td>
<td>Complete molecular response: No $BCR-ABL$ copies are found by QPCR using the International Scale</td>
</tr>
<tr>
<td><strong>Relapse</strong></td>
<td>Any relapse: Tests show any signs of loss of a treatment response</td>
</tr>
<tr>
<td></td>
<td>Hematologic relapse: Loss of a complete hematologic response; when blood counts become more abnormal again</td>
</tr>
<tr>
<td></td>
<td>Cytogenetic relapse: Loss of a complete cytogenetic response; when there’s an increase in the number of cells that have the Philadelphia chromosome</td>
</tr>
</tbody>
</table>

Chart 5.2.1 shows the different types of treatment responses for CML. A treatment response is an outcome or improvement caused by treatment. The return or worsening of cancer after a period of improvement is called a relapse or loss of response. Some of the tests used to find and confirm CML are repeated during treatment to check for a response. (See page 14 for more test details.)
Hematologic response

A CBC with differential measures the numbers of the different types of blood cells. This test is used to check for a hematologic response—when the numbers of each type of blood cells begin to go back to a normal level. A complete hematologic response is when the blood counts have completely returned to normal and all signs and symptoms of CML are gone.

Cytogenetic response

Bone marrow cytogenetics measures the number of cells in the bone marrow that have the Philadelphia chromosome. This test is used to check for a cytogenetic response—a decrease in the number of bone marrow cells that have the Philadelphia chromosome. A complete cytogenetic response is when no Philadelphia chromosomes are detected.

A partial cytogenetic response is when the Philadelphia chromosome is found in 1% to 35% of bone marrow cells. This means that 1 to 35 out of every 100 cells in the bone marrow have the Philadelphia chromosome. A major cytogenetic response is when 0% to 35% of the cells have the Philadelphia chromosome. A minor cytogenetic response is when the Philadelphia chromosome is found in more than 35% of cells in the bone marrow.

Molecular response

QPCR measures the number of cells in the blood that have the BCR-ABL gene. This test is used to check for a molecular response—a decrease in the number of cells that have the BCR-ABL gene. An early molecular response is when the BCR-ABL level is \( \leq 10\% \) at 3 and 6 months after the start of treatment. This means that no more than 10% of cells—10 out of every 100 cells—have the BCR-ABL gene.

A major molecular response is when the level has decreased to BCR-ABL 0.1% using the IS. This means that 0.1% of cells—1 out of every 1,000 cells—have the BCR-ABL gene. This is also referred to as a 3-log reduction. A complete molecular response is when no cells with the BCR-ABL gene are found by QPCR using the IS. This is often called MR4.5 since it is 4.5 logs below the standardized baseline. (See page 46 to read more about QPCR using the IS.)

Relapse

A relapse is when tests show signs of loss of a treatment response. This means that there are signs that the cancer has worsened or returned after a period of improvement. A hematologic relapse is the loss of a complete hematologic response. This is when blood cell counts become more abnormal again. A cytogenetic relapse is the loss of a complete cytogenetic response. This is when there’s an increase in the number of cells that have the Philadelphia chromosome. A 1-log increase in the BCR-ABL level with loss of a major molecular response alone is not defined as a relapse. But, it should prompt bone marrow tests to check for loss of a complete cytogenetic response.

Next steps:

See Chart 5.2.2 on page 48 for follow-up tests that are needed at each follow-up point based on the treatment response.
QPCR using the International Scale

What is the IS?

The IS (International Scale) is a standardized scale for measuring and reporting QPCR test results. QPCR is an important test that is used to check how well treatment is working. It is used to check if treatment response goals (response milestones) are reached.

Why is it important to use the IS?

Different labs sometimes use different scales to measure and report QPCR test results. Without the IS, test results from different labs can vary. This is similar to the way currencies in different countries vary. For example, $1 in the United States is not equal to €1 in Europe.

By using an exchange rate, currencies from different countries can be compared. Likewise, a conversion factor (like an exchange rate) is used to convert a lab’s QPCR results to the IS. This way, all test results are consistent and can be compared between labs. Using the IS also allows all treatment responses and milestones to be consistent and compared between different patients and labs.

How is QPCR used to check the treatment response?

QPCR measures the number of cells that have the BCR-ABL gene. The change in the BCR-ABL level is an accurate indicator of the treatment response.

The IS defines the standardized baseline as BCR-ABL 100%. This means that 100 out of 100 cells have the BCR-ABL gene. A log reduction means the BCR-ABL level has decreased by a certain amount from the baseline. The remaining number of cells with the BCR-ABL gene is written as a percentage.

**BCR-ABL 10% IS:** The BCR-ABL level is 10% using the IS. This means that 10% of cells—10 out of every 100 cells—have the BCR-ABL gene. This is also called a 1-log reduction.

**BCR-ABL 1% IS:** The BCR-ABL level is 1% using the IS. This means that 1% of cells—1 out of every 100 cells—have the BCR-ABL gene. This is also called a 2-log reduction. A decrease in the BCR-ABL level to 1% IS is about equal to a complete cytogenetic response.

**BCR-ABL 0.1% IS:** The BCR-ABL level is 0.1% using the IS. This means that 0.1% of cells—1 out of every 1,000 cells—have the BCR-ABL gene. This is also called a 3-log reduction. A decrease in the BCR-ABL level to 0.1% IS is a major molecular response.
My notes
Chart 5.2.2 Follow-up testing

<table>
<thead>
<tr>
<th>Test</th>
<th>When test is recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bone marrow cytogenetics</strong></td>
<td>• At 3-month and 6-month follow-up to check the response to TKI therapy, if QPCR is not available</td>
</tr>
<tr>
<td></td>
<td>• At 12-month follow-up if you haven’t had either a complete cytogenetic response or a major molecular response</td>
</tr>
<tr>
<td></td>
<td>• Any time BCR-ABL levels increase by 1 log without a major molecular response</td>
</tr>
<tr>
<td></td>
<td>• At any scheduled follow-up if QPCR isn’t available to check the treatment response</td>
</tr>
<tr>
<td><strong>QPCR</strong></td>
<td>• Every 3 months after the start of treatment, including 3-month and 6-month follow-up</td>
</tr>
<tr>
<td></td>
<td>• After a complete cytogenetic response is reached, every 3 months for 2 years, then every 3 to 6 months</td>
</tr>
<tr>
<td></td>
<td>• If BCR-ABL levels increase by 1 log with a major molecular response</td>
</tr>
<tr>
<td><strong>BCR-ABL gene mutation analysis</strong></td>
<td>• At any follow-up point if response milestone is not reached:</td>
</tr>
<tr>
<td></td>
<td>◦ Lack of partial cytogenetic response or BCR-ABL &gt;10% IS at 3- or 6-month follow-up</td>
</tr>
<tr>
<td></td>
<td>◦ Less than complete cytogenetic response or BCR-ABL &gt;1% IS at 12-month follow-up</td>
</tr>
<tr>
<td></td>
<td>• If tests show a hematologic relapse or cytogenetic relapse</td>
</tr>
<tr>
<td></td>
<td>• If there is a 1-log increase in BCR-ABL levels with loss of major molecular response</td>
</tr>
<tr>
<td></td>
<td>• If CML progresses to accelerated phase or blast phase</td>
</tr>
</tbody>
</table>

Chart 5.2.2 shows the follow-up tests that are recommended after starting TKI therapy. These tests are used to check how well treatment is working or why it isn’t working. A treatment response is an outcome or improvement due to treatment. Which tests are needed at each follow-up visit depends on the treatment response so far. This includes whether or not the response goal (response milestone) for a certain follow-up point has been reached. See Chart 5.2.1 on page 44 for details on each type of treatment response.
Response milestones

In general, there are two main goals of TKI therapy. One goal is to reach a complete cytogenetic response within 12 months of starting treatment. The other goal is to stop CML from progressing to accelerated phase or blast phase.

Most patients on TKI therapy will have a complete hematologic response within 3 months of the start of treatment. Most will also then have a complete cytogenetic response within 6, 12, or 18 months of the start of TKI therapy. **BCR-ABL levels** often fall slowly after a complete cytogenetic response is reached. Lack of a major molecular response in the presence of a complete cytogenetic response is not viewed as a treatment failure. But, it is a reason for close, frequent monitoring.

Follow-up tests

**Bone marrow cytogenetics** measures the number of cells in the bone marrow that have the Philadelphia chromosome. Bone marrow cytogenetics is needed at the 3-month follow-up if QPCR is not available. It should be done at the 12-month visit if at least one of the two response goals has not been reached. The response goal at the 12-month follow-up is to have either a complete cytogenetic response or a major molecular response.

This test is also needed any time QPCR shows a 1-log increase in **BCR-ABL levels** when you don’t currently have a major molecular response. This includes whether you had a major molecular response and lost it or never had it at all.

**QPCR** measures the number of cells that have the **BCR-ABL gene**. This test is recommended every 3 months as long as CML is still responding to treatment. QPCR should be done every 3 months for 3 years. After 3 years, the test can be done every 3 to 6 months. If **BCR-ABL levels** increase by 1 log and you still have a major molecular response, then QPCR should be repeated in 1 to 3 months. (See page 46 for more details on QPCR using the IS.)

**BCR-ABL gene mutation analysis** is a test that checks for changes (mutations) in the **BCR-ABL gene** that are linked with TKI resistance. (See page 31 for more about TKI resistance.) This test is needed any time the response milestone for a follow-up period is not reached. **BCR-ABL gene mutation analysis** is also needed if a milestone is reached and then lost.

This test should be done any time follow-up tests show a relapse—loss of a treatment response. A hematologic relapse is when blood cell counts get more abnormal again. A cytogenetic relapse is when tests find more cells with the Philadelphia chromosome after a point when none were detected.

Mutation testing is also useful if there’s a 1-log increase in **BCR-ABL levels** and loss of a major molecular response. This means that **BCR-ABL levels** are no longer 3 logs below the standardized baseline. This test is also needed if CML progresses to accelerated phase or blast phase.

Next steps:

- For chronic phase CML, see Chart 5.3.1 on page 50 for the next options.
- For accelerated phase CML, see Chart 5.4.1 on page 60 for the next options.
- For blast phase CML, see Chart 5.4.2 on page 62 for the next options.
### 5.3 Chronic phase follow-up treatment

#### Chart 5.3.1 Chronic phase 3-month follow-up treatment

<table>
<thead>
<tr>
<th>Test results</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BCR-ABL ≤10% by QPCR using the International Scale</strong> or Partial cytogenetic response on bone marrow cytogenetics</td>
<td>Stay on same dose of current TKI (imatinib, nilotinib, or dasatinib)</td>
</tr>
<tr>
<td><strong>BCR-ABL &gt;10% by QPCR using the International Scale</strong> or Lack of partial cytogenetic response on bone marrow cytogenetics</td>
<td>Had imatinib as primary treatment</td>
</tr>
<tr>
<td></td>
<td>Clinical trial</td>
</tr>
<tr>
<td></td>
<td>Switch to a different TKI</td>
</tr>
<tr>
<td></td>
<td>Increase imatinib dose up to 800 mg (if other TKI is not a good option)</td>
</tr>
<tr>
<td></td>
<td>And, discuss HCT</td>
</tr>
<tr>
<td></td>
<td>Had nilotinib or dasatinib as primary treatment</td>
</tr>
<tr>
<td></td>
<td>Clinical trial</td>
</tr>
<tr>
<td></td>
<td>Stay on same dose of current TKI</td>
</tr>
<tr>
<td></td>
<td>Switch to a different TKI (other than imatinib)</td>
</tr>
<tr>
<td></td>
<td>And, discuss HCT</td>
</tr>
</tbody>
</table>

**Chart 5.3.1** shows the options that are recommended 3 months after starting TKI therapy for CML in the chronic phase. The next options depend on how well treatment has worked so far. An outcome or improvement caused by treatment is called a treatment response. The types of treatment responses are described in Chart 5.2.1 on page 44. The treatment response is based on the results of follow-up tests described in Chart 5.2.2 on page 48.

**Follow-up test results**

Based on the results of follow-up tests, your doctors will know if the response milestone has been reached. The response milestone at 3 months is to have **BCR-ABL ≤10% by QPCR using the IS**. This test measures the number of cells that have the **BCR-ABL gene**. But, not all labs use the IS for QPCR. In this case, the milestone is to have a partial cytogenetic response...
on bone marrow cytogenetics. This test measures the number of cells that have the Philadelphia chromosome. (See page 46 for more details about QPCR using the IS and page 14 for more details about other tests.)

**Treatment options**

**If tests show BCR-ABL ≤10% IS or a partial cytogenetic response,** then the response milestone has been reached. Since treatment is working well, you will stay on the same dose of your current TKI. And, QPCR using the IS should be done every 3 months to check the response. You should stay on the TKI therapy indefinitely or until it stops working.

**If tests show BCR-ABL >10% IS or lack of a partial cytogenetic response,** then the response milestone has not been reached. Since treatment isn’t working as well as it should, your doctor will try to find out why.

**BCR-ABL gene mutation analysis** should be done to check for mutations in the BCR-ABL gene. These gene mutations change the shape of the BCR-ABL protein and can affect how well TKI treatments work. Your doctor will also talk to you about taking your TKI the right way. Treatment may not work as well if you don’t take your TKI the right way. Taking certain other medicines can also affect how well TKI treatments work. For more details, read TKI adherence on page 32 and Drug interactions on page 31.

The follow-up treatment options differ slightly depending on which TKI you received as primary treatment. But, treatment on a clinical trial is an option for all patients. A clinical trial is research on a test or treatment to assess its safety or how well it works.

If you had primary treatment with imatinib, then one option is to switch to a different TKI such as dasatinib, nilotinib, or bosutinib. Other TKI drugs might not be good options for you because of their side effects. In this case, another option is to increase the dose of imatinib up to 800 mg unless side effects are very bad. Side effects are often worse when higher doses are given and some patients may not be able to tolerate them. In addition to the options above, your doctor may also assess if an allogeneic HCT is a good treatment option for you. (See page 28 for more details about each treatment.)

If you had primary treatment with nilotinib or dasatinib, then one option is to stay on the same dose of your current TKI. Another option is to switch to a different TKI (besides imatinib) that you haven’t had before. In addition to the options above, your doctor may also assess if an allogeneic HCT is a good treatment option for you.

**Next steps:**

- If you are on TKI therapy, see Chart 5.3.2 on page 52 for 6-month follow-up recommendations.

- If you will switch to a different TKI, see Chart 5.3.4 on page 58 for recommended options.

- If you will receive an allogeneic HCT, see Chart 5.5 on page 64 for the next options.

- If the CML progressed, see Chart 5.4.1 on page 60 for accelerated phase or Chart 5.4.2 on page 62 for blast phase.
Chart 5.3.2 shows the options that are recommended 6 months after starting TKI therapy for CML in the chronic phase. The next options depend on how well treatment has worked so far. An outcome or improvement caused by treatment is called a treatment response. The types of treatment responses are described in Chart 5.2.1 on page 44. The treatment response is based on the results of follow-up tests described in Chart 5.2.2 on page 48.

Follow-up test results

Based on the results of follow-up tests, your doctors will know if the response milestone has been reached. The response milestone at 6 months is to have *BCR-ABL* \( \leq 10\% \) by QPCR using the IS. This test measures the number of cells that have the *BCR-ABL* gene. But, not all labs use the IS for QPCR. In this case, the milestone is to have at least a partial cytogenetic response on bone marrow cytogenetics. This test measures the number of cells that have the Philadelphia chromosome. (See page 46 for more details about QPCR using the IS and page 14 for more details about other tests.)

Treatment options

If tests show *BCR-ABL* \( \leq 10\% \) IS or at least a partial cytogenetic response, then the response milestone has been reached. Since treatment is working well, you will stay on the same dose of your current TKI. And, QPCR using the IS should be done every 3 months to monitor the response. You should stay on the TKI therapy indefinitely or until it stops working. You will follow the test schedule in Chart 5.2.2 on page 48 until your 12-month follow-up visit.
If tests show BCR-ABL >10% IS or lack of a partial cytogenetic response, then the response milestone has not been reached. Since treatment isn’t working as well as it should, your doctor will try to find out why.

BCR-ABL gene mutation analysis should be done to check for mutations in the BCR-ABL gene. These gene mutations change the shape of the BCR-ABL protein and can affect how well TKI treatments work. (See TKI drug resistance on page 31 for details.) Your doctor will also talk to you about taking your TKI the right way. Treatment may not work as well if you don’t take your TKI the right way. Taking certain other medicines can also affect how well TKI treatments work. For more details, read TKI adherence on page 32 and Drug interactions on page 31.

After the gene mutation test and talking with your doctor, you have a few follow-up treatment options to choose from. One option is to receive treatment on a clinical trial. A clinical trial is research on a test or treatment to assess its safety or how well it works. Another option is to switch to a different TKI, other than imatinib, that you haven’t had before. Other TKI options may include dasatinib, nilotinib, or bosutinib. See Chart 5.3.4 on page 58 for the next TKI options.

If you experience resistance or intolerance with two or more TKIs, then the chemotherapy drug omacetaxine is an option. In addition to the options above, your doctor may also assess if an allogeneic HCT is a good treatment option for you. (See page 28 for details about each type of treatment.)

**Next steps:**

- If the response milestone was reached based on QPCR, see Chart 5.2.2 on page 48 for recommended follow-up tests.

- If the treatment response was based on bone marrow cytogenetics or the response milestone was not reached, see Chart 5.3.3 on page 54 for 12-month follow-up recommendations.

- If you will switch to a different TKI, see Chart 5.3.4 on page 58 for recommended options.

- If you will receive an allogeneic HCT, see Chart 5.5 on page 64 for the next options.

- If the CML progressed, see Chart 5.4.1 on page 60 for accelerated phase or Chart 5.4.2 on page 62 for blast phase.
### Chart 5.3.3 Chronic phase follow-up treatment at 12 months and beyond

<table>
<thead>
<tr>
<th>Test results</th>
<th>Treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete cytogenetic response or $\text{BCR-ABL} &lt; 1% \text{ but } &gt; 0.1%$ by QPCR using the International Scale</td>
<td>Stay on same dose of current TKI</td>
</tr>
<tr>
<td>Partial cytogenetic response or $\text{BCR-ABL} \leq 10% \text{ but } &gt; 1%$ by QPCR using the International Scale</td>
<td>Maybe $\text{BCR-ABL}$ gene mutation test, and discuss taking your TKI the right way and all medicines you take. Switch to different TKI other than imatinib (preferred). Stay on same dose of current TKI. Increase imatinib dose up to 800 mg as tolerated (if other TKI or omacetaxine isn’t a good option)</td>
</tr>
<tr>
<td>Less than a partial cytogenetic response or $\text{BCR-ABL} &gt; 10%$ by QPCR using the International Scale</td>
<td>Need $\text{BCR-ABL}$ gene mutation test, and discuss taking your TKI the right way and all medicines you take. Switch to a different TKI other than imatinib. Clinical trial. And, discuss HCT</td>
</tr>
<tr>
<td>Cytogenetic relapse</td>
<td>Need $\text{BCR-ABL}$ gene mutation test, and discuss taking your TKI the right way and all medicines you take. Switch to different TKI other than imatinib (preferred). Increase imatinib dose up to 800 mg as tolerated (if other TKI or omacetaxine isn’t a good option). Clinical trial. And, discuss HCT</td>
</tr>
</tbody>
</table>

**Chart 5.3.3** shows the options that are recommended 12 months after starting TKI therapy for CML in the chronic phase. The next options depend on how well treatment has worked so far. An outcome or improvement caused by treatment is called a *treatment response*. The types of treatment responses are described in Chart 5.2.1 on page 44. The treatment response is based on the results of follow-up tests described in Chart.5.2.2 on page 48.
Follow-up test results

Based on the results of follow-up tests, your doctors will know if the response milestone has been reached. The response milestone at 12 months and beyond is to have $\text{BCR-ABL} < 1\%$ by QPCR using the IS. This test measures the number of cells that have the $\text{BCR-ABL}$ gene. But, not all labs use the IS for QPCR. In this case, the milestone is to have a complete cytogenetic response on bone marrow cytogenetics. This test measures the number of cells in the bone marrow that have the Philadelphia chromosome. This test should be done at the 12-month follow-up if you haven’t had either a complete cytogenetic response or a major molecular response so far. (See page 46 for more about QPCR using the IS and page 14 for more details about other tests.)

Treatment options

If tests show a complete cytogenetic response or $\text{BCR-ABL} \leq 1\%$ IS but $>0.1\%$ IS, then the response milestone has been reached. Since treatment is working well, you will stay on the same dose of your current TKI. And, you will have a QPCR test every 3 months as long as the CML is responding to treatment. You should stay on the TKI therapy indefinitely or until it stops working. Follow the test schedule in Chart 5.2.2 on page 48 to check treatment results.

If tests do not show a complete cytogenetic response or at least $\text{BCR-ABL} \leq 1\%$ IS, then the response milestone has not been reached. Since treatment isn’t working as well as it should, your doctor will try to find out why. $\text{BCR-ABL}$ gene mutation analysis should be done to check for mutations in the $\text{BCR-ABL}$ gene. (Read TKI drug resistance on page 31 for details.) Your doctor will also talk to you about taking your TKI the right way. Treatment may not work as well if you don’t take your TKI the right way. Taking certain other medicines can also affect how well TKI treatments work. For more details, read TKI adherence on page 32 and Drug interactions on page 31.

Based on the gene mutation test results and talking with your doctor, there are a few follow-up treatment options to choose from. But, the options differ slightly depending on the extent of the treatment response. (See page 28 for details about each type of treatment.)

If tests show a partial cytogenetic response or $\text{BCR-ABL} \leq 10\%$ IS but $>1\%$ IS, then you have three options to choose from. The preferred option is to switch to a different TKI, other than imatinib, that you haven’t had before. (See Chart 5.3.4 on page 58 for the next TKI options.)

Another option is to stay on the same dose of your current TKI. You should stay on the TKI therapy indefinitely or until it stops working. If you experience resistance or intolerance with two or more TKIs, then the chemotherapy drug omacetaxine is an option. Intolerance is when treatment with a drug must be stopped due to severe side effects. Resistance is when CML doesn’t respond to a treatment. The types of resistance are described on page 31.

You may not be able to take other TKI drugs or omacetaxine because of their side effects. In this case, another option is to increase the dose of imatinib up to 800 mg unless side effects are very bad. Side effects are often worse when higher doses are given and some patients may not be able to tolerate them.

If tests show less than a partial cytogenetic response or $\text{BCR-ABL} > 10\%$ IS, then you have three options to choose from. One option is to switch to a different TKI, other than imatinib, that you haven’t had before. (See Chart 5.3.4 on page 58 for
the next TKI options.) If you experience resistance or intolerance with two or more TKIs, then the chemotherapy drug omacetaxine is an option.

Another option is to receive treatment on a clinical trial. A clinical trial is research on a test or treatment to assess its safety or how well it works. In addition to these options, your doctor may also assess if an allogeneic HCT is a good treatment option for you.

If tests show a cytogenetic relapse, then you have four main options to choose from. The preferred option is to switch to a different TKI, other than imatinib, that you haven’t had before. (See Chart 5.3.4 on page 58 for the next TKI options.) You may not be able to take other TKI drugs or omacetaxine because of their side effects. In this case, another option is to increase the dose of imatinib up to 800 mg as long as the side effects aren’t too severe. The third option is to receive treatment within a clinical trial. In addition to the options above, your doctor may also assess if an allogeneic HCT is a good treatment option for you.

Next steps:

- If you will switch to a different TKI, see Chart 5.3.4 on page 58 for recommended options.

- If you will receive an allogeneic HCT, see Chart 5.5 on page 64 for the next options.

- If the CML progressed, see Chart 5.4.1 on page 60 for accelerated phase or Chart 5.4.2 on page 62 for blast phase.

Next options

If the 12-month response milestone wasn’t reached, then bone marrow cytogenetics will be done again 3 months after changing treatment. This is to check how well treatment is working. The goal is to have a complete cytogenetic response. If tests show less than that, the next treatment options are the same as those described above for less than a partial cytogenetic response or BCR-ABL >10%.
My notes
Chart 5.3.4 shows the next TKI options that are recommended after a prior TKI had to be stopped. Primary treatment is the first or main treatment used to rid the body of disease. Second-line treatment is the next treatment given after the first treatment failed or had to be stopped.

You may have had to stop taking a TKI because of its severe side effects. This is called intolerance. Or, you may have had to stop taking a TKI because of resistance. Resistance is when CML doesn’t respond to a drug. There is more than one type of resistance. The most common type is when CML responds to a drug at first, but stops responding over time. See page 31 for more details.

TKI therapy with imatinib, dasatinib, or nilotinib is most often used as primary treatment for CML. The second-line treatment options depend on which TKI you received as primary treatment. In general, you can switch to a TKI that you haven’t had before, other than imatinib. But, BCR-ABL gene mutation analysis may also be helpful in choosing second-line TKI therapy. (See page 19 for details.)

After three or more TKIs have been tried, your doctor may want to consider other treatment options. At this point, there are three main options to choose from. The first option is to receive treatment within a clinical trial. A clinical trial is research on a test or treatment to assess its safety or how well it works. Based on the response to TKI therapy, another option is to receive an allogeneic HCT. This type of treatment replaces damaged or diseased bone marrow in your body with healthy blood stem cells taken from another person. The third option is to receive the chemo drug omacetaxine. (See page 30 for more details on each type of treatment.)
Next steps:

- If you will receive an allogeneic HCT, see Chart 5.5 on page 64 for the next options.

- If the CML progressed see Chart 5.4.1 on page 60 for accelerate phase or Chart 5.4.2 on page 62 for blast phase.
## 5.4 Accelerated and blast phase treatment

### Chart 5.4.1 Accelerated phase treatment

<table>
<thead>
<tr>
<th>Tests before treatment</th>
<th>Treatment options</th>
<th>Relapse treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>• BCR-ABL gene mutation analysis</td>
<td>Clinical trial</td>
<td>Clinical trial</td>
</tr>
<tr>
<td></td>
<td>TKI therapy: imatinib, dasatinib, nilotinib, bosutinib, or ponatinib</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Omacetaxine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Consider HCT based on response</td>
<td></td>
</tr>
</tbody>
</table>

**Chart 5.4.1** shows the tests and treatment options for CML in accelerated phase. In this phase, the number of blast cells in the blood and/or bone marrow is higher than normal. Symptoms may also be more severe. It is strongly recommended that patients with CML in accelerated phase receive treatment in specialized centers.

### Tests before treatment

Before you start treatment, *BCR-ABL gene mutation analysis* is needed. This test is used to check for mutations in the part of the *BCR-ABL* gene that makes the BCR-ABL protein. New mutations can happen over time as CML progresses. They can also happen during TKI therapy. These mutations can affect how well certain TKI drugs work. Thus, doctors use this test to help decide which TKI is the best option for you. (Read *TKI drug resistance* on page 31 for details.)

### Treatment options

There are four main treatment options for CML in accelerated phase. The first option is to receive treatment within a clinical trial. A clinical trial is a type of research that studies how safe and helpful a treatment is.

The second option is to begin, or change, TKI therapy. If the CML was in accelerated phase when first diagnosed and you haven’t had a TKI before, then there are four TKIs to choose from. This includes imatinib (600 mg daily), dasatinib (140 mg once daily), nilotinib (400 mg twice daily), or bosutinib (500 mg once daily).

If the CML progressed to accelerated phase during TKI therapy, then you can receive a TKI other than imatinib that you haven’t had before. Options include dasatinib, nilotinib, bosutinib, and ponatinib. But, ponatinib is only an option for patients with a T315I
mutation or CML that hasn’t responded to two or more TKIs. Results of the BCR-ABL gene mutation analysis can also help guide TKI therapy choices. See Chart 5.3.4 on page 58 for TKI options based on prior treatment and mutation test results.

The third option is to receive the chemo drug omacetaxine. But, this is only an option if you have resistance or intolerance with two or more TKIs.

An allogeneic HCT is the only curative option for CML that progresses to accelerated phase during TKI therapy. In such cases, you and your family members should receive HLA testing to check for a well-matched donor for the transplant. If a family member is not a good match, then a search for an unrelated donor may be done.

Relapse treatment

If follow-up tests show that the CML has not improved or that it has worsened, then the next option is to join a clinical trial. An outcome or improvement due to treatment is called a treatment response. The return or worsening of cancer after treatment is called a relapse. Read page 44 for details about each type of treatment response and relapse.

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Next steps:

- If you will have an allogeneic HCT, see Chart 5.5 on page 64 for the next options.
- If the CML progressed to blast phase, see Chart 5.4.2 on page 62 for the next options.
- For TKI options based on prior TKI therapy, see Chart 5.3.4 on page 58.
Chart 5.4.2 shows the tests and treatments that are recommended for CML in blast phase. This phase of CML has the highest number of immature blood cells (blast cells) in the blood and bone marrow. CML in blast phase may cause more severe symptoms and can be life-threatening. It is strongly recommended that patients with CML in blast phase receive treatment in specialized centers.

### Tests before treatment

Two important tests are needed before starting treatment. Blast phase CML can involve either myeloid or lymphoid white blood cells. Cytochemistry is a test that is used to find out the type of white blood cell that is affected. This test is needed because the cell type is a factor that is used to decide treatment options for blast phase CML.

**BCR-ABL gene mutation analysis** is also needed before starting treatment. This test is used to check for mutations in the part of the *BCR-ABL* gene that makes the *BCR-ABL* protein. These mutations can affect how well TKI therapy works. Different mutations can make the BCR-ABL protein more or less resistant to certain TKIs. Thus, doctors use this test to help decide which TKI is the best option for you. (See page 14 for more test details and page 31 to read more about TKI resistance.)

<table>
<thead>
<tr>
<th>Tests before treatment</th>
<th>Cell type</th>
<th>Treatment options</th>
<th>Relapse treatment</th>
</tr>
</thead>
</table>
| • BCR-ABL gene mutation analysis  
• Cytochemistry         | Lymphoid  | Clinical trial  
ALL-type chemotherapy + TKI followed by HCT if possible  
TKI followed by HCT if possible | Clinical trial |
|                        | Myeloid   | Clinical trial  
AML-type chemotherapy + TKI followed by HCT if possible  
TKI followed by HCT if possible | Clinical trial |
Treatment options

There are three main treatment options for CML in blast phase. The first option for all patients is to receive treatment within a clinical trial. A clinical trial is a type of research that studies how safe and helpful a treatment is.

The second option is to have high-dose chemotherapy and a TKI, followed by an allogeneic HCT if possible. The type of chemotherapy you will have depends on the type of leukemia cells found—lymphoid or myeloid. If the leukemia cells are mostly lymphoid cells, then you will have chemotherapy that is used for ALL. This is called ALL-type chemotherapy. If the leukemia cells are mostly myeloid cells, then you will have chemotherapy that is used for AML. This is called AML-type chemotherapy.

The third option for all patients is to receive TKI therapy and then an allogeneic HCT if possible. Which TKI you will have depends on the TKIs you’ve had before. It also depends on results of the BCR-ABL gene mutation analysis. See Chart 5.3.4 on page 58 for TKI options based on prior treatment and mutation test results. (See page 28 to read more about TKI therapy.)

Relapse treatment

If follow-up tests show that the CML has not improved or that is has worsened, then the next option is to join a clinical trial. An outcome or improvement due to treatment is called a treatment response. The return or worsening of cancer after treatment is called a relapse. Read page 44 for details about each type of treatment response and relapse.
## 5.5 Allogeneic HCT

**Chart 5.5 Allogeneic HCT**

<table>
<thead>
<tr>
<th>HCT results</th>
<th>Follow-up tests</th>
<th>Follow-up treatment options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete cytogenetic response</td>
<td>QPCR blood test</td>
<td>TKI therapy (imatinib, dasatinib, nilotinib, bosutinib, or ponatinib) or omacetaxine or DLI or Interferon/PEG-interferon or Clinical trial</td>
</tr>
<tr>
<td></td>
<td>Every 3 months for 2 years, then</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td>Every 3 to 6 months thereafter</td>
<td>Negative</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Continue scheduled follow-up tests</td>
</tr>
<tr>
<td>Did not have a complete cytogenetic</td>
<td>Slowly stop treatments that lower</td>
<td>TKI therapy (imatinib, dasatinib, nilotinib, bosutinib, or ponatinib) or omacetaxine or DLI or Interferon/PEG-interferon or Clinical trial</td>
</tr>
<tr>
<td>response, or had a relapse</td>
<td>(suppress) the immune system</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
</tr>
</tbody>
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**Chart 5.5** shows the tests and treatments that are recommended after an allogeneic HCT. An allogeneic HCT replaces damaged or diseased bone marrow in your body with healthy blood stem cells taken from another person. This creates a new immune system for your body. (See page 34 for more details about this type of treatment.)

**HCT results**

Follow-up options after an allogeneic HCT depend on how the CML responded. A treatment response is an outcome or improvement due to treatment. A complete cytogenetic response is when no Philadelphia chromosomes are found with bone marrow cytogenetics. A relapse is when there are any signs of loss of treatment response. (See page 44 for more details on the types of treatment responses and relapse.)
Follow-up tests and treatment options

If you had a complete cytogenetic response, then the next option is to begin follow-up testing with QPCR. The schedule for follow-up QPCR testing is listed in the chart. A positive test result means that QPCR found copies of the BCR-ABL gene. A negative test result means that QPCR did not find any copies of the BCR-ABL gene. This is defined as a complete molecular response. You will follow this schedule of follow-up testing as long as the QPCR tests are negative. For patients with prior accelerated phase or blast phase CML who have a complete cytogenetic response, TKI therapy should be considered for at least one year following the transplant.

If the QPCR test result is positive, then the next step is to discuss follow-up treatment options with the transplant team. One option is TKI therapy with imatinib, dasatinib, nilotinib, bosutinib, or ponatinib. But, ponatinib is only an option for patients with a T315I mutation or CML that hasn’t responded to two or more TKIs.

Omacetaxine is an option if you’ve had resistance or intolerance to two or more TKIs. Resistance is when CML doesn’t respond to a treatment. The types of resistance are described on page 31. Intolerance is when treatment with a drug must be stopped due to severe side effects.

Another option is to receive lymphocytes from the same person who donated blood stem cells for the allogeneic HCT. This type of treatment is called a DLI. The third option is to receive immunotherapy with interferon or PEG-interferon. The fourth option is to receive treatment within a clinical trial—a type of research that studies the safety and effectiveness of a test or treatment.

If you did not have a complete cytogenetic response or you had a relapse, then you still have four main follow-up treatment options to choose from. But, you cannot start follow-up treatment right away. The first step is to slowly stop treatment with the drugs used to suppress your immune system for the transplant.

Your doctors will give you lower and lower doses of these drugs over time until they are stopped completely. Your doctors will carefully monitor you during this process. Next, the transplant team will go over the follow-up treatment options with you. The follow-up treatment options are the same as those described for patients who had a complete cytogenetic response.
My notes
Making treatment decisions
### Chapter 6: Making treatment decisions

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Having cancer can feel very stressful. While absorbing the fact that you have cancer, you must also learn about tests and treatments. And, the time you have to decide on a treatment plan may feel short. Parts 1 through 5 aimed to teach you about CML, its treatment, and other challenges. Part 6 aims to help you talk with your doctors and make treatment decisions that are right for you.

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**Have a treatment plan**

Learning you have cancer starts an unplanned journey to an unknown place. A treatment plan is like having a roadmap for your journey. It is a written course of action through treatment and beyond. It can help you, your loved ones, and your treatment team.

A treatment plan addresses all cancer care needs while respecting your beliefs, wishes, and values. It is likely to change and expand as you go through treatment. The plan will include the role of your doctors and how you can help yourself. A treatment plan often has the following parts:

**Cancer information**

Cancer can greatly differ even when people have cancer in the same organ. Test results that describe the cancer are reported in the treatment plan. Such test results include the cancer site, cell type, and important gene and chromosome changes. See Part 2 on page 14 to read more about the tests used for CML.
Your treatment team
Treating CML takes a team approach. Your team will likely include a number of doctors and health professionals who are experts in different areas of cancer care. A hematologist is a doctor who is an expert in diseases of the blood. A medical oncologist is a doctor who’s an expert in treating cancer with drugs. A pathologist is an expert in testing cells and tissue to find disease.

Your primary care doctor can also be part of your team. He or she can help you express your feelings about treatments to the team. Treatment of other medical problems may be improved if he or she is informed of your cancer care. Besides doctors, you may receive care from nurses, social workers, and other health experts. Ask to have the names and contact information of your health care providers included in the treatment plan.

Cancer treatment
There is no single treatment practice that is best for all patients. There is often more than one treatment option, including clinical trials. Clinical trials study how well a treatment works and its safety.

A guide to CML treatment options can be found in Part 5. The treatment that you and your doctors agree on should be reported in the treatment plan. It is also important to note the goal of treatment and the chance of a good treatment outcome. All known side effects should be listed and the time required to treat them should be noted. See Part 4 for a list of some of the possible side effects of CML treatments.

Your treatment plan may change because of new information. You may change your mind about treatment. Tests may find new results. How well the treatment is working may change. Any of these changes may require a new treatment plan.

Stress and symptom control
Cancer and its treatments can cause bothersome symptoms. The stress of having cancer can also cause symptoms. There are ways to treat many symptoms, so tell your treatment team about any that you have.

You may lose sleep before, during, and after treatment. Getting less sleep can affect your mood, conversations, and ability to do daily tasks. If possible, allow yourself to rest, let people do things for you, and talk with your doctor about sleep medication. Behavioral sleep medicine—a type of talk therapy—may also help.

Feelings of anxiety and depression are common among people with cancer. At your cancer center, cancer navigators, social workers, and other experts can help. Help can include support groups, talk therapy, or medication. Some people also feel better by exercising, talking with loved ones, or relaxing.

You may be unemployed or miss work during treatment. Or, you may have too little or no health insurance. Talk to your treatment team about work, insurance, or money problems. They will include information in the treatment plan to help you manage your finances and medical costs.

Survivorship care
Cancer survivorship begins on the day you learn of having CML. For many survivors, the end of active treatment signals a time of celebration but also of great anxiety. This is a very normal response. You may need support to address issues that arise from not having regular visits with your cancer care team. In addition, your treatment plan should include a schedule of follow-up tests, treatment of long-term side effects, and care of your general health.
Advance care planning
Talking with your doctor about your prognosis can help with treatment planning. If the cancer can’t be controlled or cured, a care plan for the end of life can be made. However, such talks often happen too late or not at all. Your doctor may delay these talks for fear that you may lose hope, become depressed, or have a shorter survival. Studies suggest that these fears are wrong. Instead, there are many benefits to advance care planning. It is useful for:

- Knowing what to expect,
- Making the most of your time,
- Lowering the stress of caregivers,
- Having your wishes followed,
- Having a better quality of life, and
- Getting good care.

Advance care planning starts with an honest talk between you and your doctors. You don’t have to know the exact details of your prognosis. Just having a general idea will help with planning. With this information, you can decide at what point you’d want to stop chemotherapy or other treatments, if at all. You can also decide what treatments you’d want for symptom relief, such as surgery or drugs.

Another part of the planning involves hospice care. Hospice care doesn’t include treatment to fight the cancer but rather to reduce symptoms caused by cancer. Hospice care may be started because you aren’t interested in more cancer treatment, no other cancer treatment is available, or because you may be too sick for cancer treatment. Hospice care allows you to have the best quality of life possible. Care is given all day, every day of the week. You can choose to have hospice care at home or at a hospice center. One study found that patients and caregivers had a better quality of life when hospice care was started early.

An advance directive describes the treatment you’d want if you weren’t able to make your wishes known. It also can name a person whom you’d want to make decisions for you. It is a legal paper that your doctors have to follow. It can reveal your wishes about life-sustaining machines, such as feeding tubes. It can also include your treatment wishes if your heart or lungs were to stop working. If you already have an advance directive, it may need to be updated to be legally valid.
Your role in planning

The role patients want in treatment planning differs. Your doctors and treatment team will give you the information you need to make informed choices. But, you may prefer to let others take the lead in deciding your treatment. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may have never heard the words used to describe CML, tests, or treatments. Likewise, you may think that your judgment isn’t any better than your doctors’. You may rely on your doctors alone to make the right decisions. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, you still have to agree by signing a consent form.

On the other hand, you may prefer to take the lead or share in decision-making. In shared decision-making, you and your doctors share information, weigh the options, and agree on a treatment plan. Your doctors know the science of treating CML. But, you know your personal concerns and goals. By working together, you may feel more comfortable and satisfied with your care and treatment plan. You’ll likely get the treatment you want, at the place you want, and by the doctors you want.

Getting a 2nd opinion

The time around a cancer diagnosis can be very stressful. People with cancer often want to start treatment as soon as possible. They want to make the cancer go away before it spreads any farther. While cancer can’t be ignored, there is time to think about and choose which treatment plan is best for you.

You may wish to have another doctor review your test results and the treatment plan your doctor has recommended. This is called getting a 2nd opinion. You may completely trust your doctor, but a 2nd opinion on which treatment is right for you can help. Copies of all of the test results need to be sent to the doctor giving the 2nd opinion. Some people feel uneasy asking for copies from their doctors. However, a 2nd opinion is a normal part of cancer care.

When doctors have cancer, most will talk with more than one doctor before choosing their treatment. What’s more, some health plans require a 2nd opinion. If your health plan doesn’t cover the cost of a 2nd opinion, you have the choice of paying for it yourself. Choosing your cancer treatment is a very important decision. It can affect length and quality of life.
Questions about **CML**

1. Where did the cancer start? In what type of cell?
2. What phase of CML do I have? What does this phase mean?
3. Is this a fast- or slow-growing leukemia?
4. What is the prognosis?
5. Will I be on cancer therapy forever?

Questions about **testing**

1. What tests will I have?
2. How often will I be tested?
3. Where will the tests take place? Will I have to go to the hospital?
4. How do I prepare for testing? Should I bring a list of my medications?
5. Should I bring someone with me?
6. How often will I have bone marrow tests?
7. How soon will I know the test results?
8. Who will explain the test results to me?
9. Who will talk with me about the next steps? When?
Questions about treatments

1. What treatments do you recommend?
2. Will I have more than one treatment?
3. What are the risks and benefits of each treatment? What about side effects?
4. Will my age, general health, and other factors limit my treatment choices?
5. Would you help me get a 2nd opinion?
6. Do I have to get treated?
7. How soon should I start treatment?
8. How long does cancer treatment last? Will I need to stay on cancer treatment forever?
9. Where will I be treated? Will I have to stay in the hospital or can I go home after each treatment?
10. What can I do to prepare for treatment?
11. How much will the treatment cost? How can I find out how much my insurance company will cover?
12. How likely is it that I’ll be cancer-free after treatment?
13. What is the chance that the cancer will come back?
14. Are there supportive services that I can get involved in? Support groups?
Questions about stem cell transplants

1. Am I a candidate for an allogeneic stem cell transplant?

2. If I will have an allogeneic stem cell transplant, how should my family members be tested to see if their bone marrow matches mine?

3. When should an allogeneic stem cell transplant be considered?

4. What are the risks of this type of stem cell transplant, both short-term and long-term?

5. How long would this type of treatment control the cancer, and what are the chances of long-term control or even cure?

6. Will I receive other treatments, such as chemotherapy, along with the stem cell transplant?
Questions about **clinical trials**

1. Is there a clinical trial that I could take part in?
2. What is the purpose of the study?
3. What kinds of tests and treatments does the study involve?
4. What does the treatment do?
5. Has the treatment been used before? Has it been used for other types of cancers?
6. Will I know which treatment I receive?
7. What is likely to happen to me with, or without, this new treatment?
8. How might the study change my daily life?
9. What side effects can I expect from the study? Can the side effects be controlled?
10. Will the study cost me anything? Will any of the treatment be free?
11. What type of long-term follow-up care is part of the study?
Websites

American Cancer Society
www.cancer.org/cancer/leukemia-chronicmyeloidcml/index

www.cancer.org/Treatment/FindingandPayingforTreatment/index

National Cancer Institute
www.cancer.gov/types/leukemia/patient/cml-treatment-pdq

Leukemia & Lymphoma Society
www.lls.org/leukemia/chronic-myeloid-leukemia/

My PCR
www.mypcr.org

Be The Match
www.bethematch.org

National Coalition for Cancer Survivorship
www.canceradvocacy.org/toolbox

NCCN
www.nccn.org/patients/resources/life_with_cancer/default.aspx

Review

• A treatment plan can help you through treatment and beyond.

• A treatment plan covers many issues—test results, treatments, and supportive programs.

• You can choose how active a role to have in planning your treatment.

• You may wish to get a 2nd opinion on your treatment plan.
Glossary

Dictionary

Acronyms
Dictionary

**abdomen**
The belly area between the chest and pelvis.

**accelerated phase**
The second phase of chronic myelogenous leukemia progression, when the number of immature blood cells (blast cells) is increased.

**acute leukemia**
a fast-growing cancer that starts in blood forming cells in the bone marrow—the soft, sponge-like tissue in the center of most bones where blood cells are made.

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

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

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

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

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

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

**baseline**
an initial, starting point measurement to which future test results are compared.

**basophil**
a type of white blood cell that helps fight infections and has small particles (granules).

**BCR-ABL gene**
an abnormal gene (set of coded instructions for controlling cells) that is formed when the BCR gene and ABL gene join together on the Philadelphia chromosome. Also called BCR-ABL fusion gene.

**BCR-ABL gene mutation analysis**
a test that looks for abnormal changes (mutations) in the BCR-ABL gene that change the shape of the BCR-ABL protein.

**BCR-ABL level**
the number of copies of the BCR-ABL gene found in your body by tests. It reflects the amount of leukemia or CML cells in your body.

**BCR-ABL protein**
an abnormal protein that is made by the BCR-ABL fusion gene and causes too many abnormal white blood cells (leukemia cells) to be made.

**biopsy**
removal of small amounts of tissue from the body to be tested for disease.
**blast cell**  
An immature blood cell.

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

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

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

**bloodstream**  
Blood that flows throughout the body in small tubes called blood vessels.

**blood test**  
A test done on a sample of blood to check for signs of disease.

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

**bone marrow aspiration**  
The removal of a small amount of liquid bone marrow (soft tissue in the center of most bones where blood cells are made) to test for disease.

**bone marrow biopsy**  
The removal of a small amount of solid bone and bone marrow (the soft tissue in the center of most bones where blood cells are made) to test for disease.

**bone marrow cytogenetics**  
Test of a sample of bone marrow (soft tissue in the center of most bones where blood cells are made) to look for changes in the cells’ chromosomes (strands of bundled instructions for making and controlling cells).

**cell assessment**  
Use of a microscope and special dyes to assess the features—size, shape, type, maturity—of cells in a sample of blood or bone marrow.

**chemotherapy (chemo)**  
Drugs that kill fast-growing cells, including cancer cells and normal cells.

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

**chronic myelogenous leukemia (CML)**  
A slow-growing cancer that starts in the bone marrow and causes too many white blood cells called granulocytes to form.

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

**clinical trial**  
Research on a test or treatment to assess its safety or how well it works.

**CML cell**  
Abnormal white blood cell that contains the BCR-ABL gene or the Philadelphia chromosome. Also called leukemia cell.

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

**complete cytogenetic response**
When tests don’t find any copies of the Philadelphia chromosome—the abnormal chromosome that contains the *BCR-ABL* gene.

**complete hematologic response**
When blood cell counts in the bloodstream have completely returned to normal. There are no immature cells in the blood and there are no signs or symptoms of disease.

**complete molecular response**
No copies of the abnormal *BCR-ABL* gene are found using a very sensitive test.

**cytochemistry**
A test that uses special chemical dyes to identify the specific type of leukemia cell present in a blood or bone marrow sample.

**cytogenetic relapse**
Tests show an increase in the number of cells with the Philadelphia chromosome—the abnormal chromosome that contains the *BCR-ABL* gene—after a period of improvement when no cells with the Philadelphia chromosome were found.

**cytogenetic response**
Tests show a decrease in the number of cells that have the Philadelphia chromosome—the abnormal chromosome that contains the *BCR-ABL* gene.

**cytogenetic testing**
A test that uses a microscope to examine a cell’s chromosomes—long strands of coded instructions in cells for making and controlling cells.

**cytogenetics**
The study of chromosomes, which are long strands in cells that contain bundles of coded instructions for making and controlling cells.

**deoxyribonucleic acid (DNA)**
A chain of chemicals in cells that contains genes (coded instructions in cells for making and controlling cells) and is bundled into long strands called chromosomes.

**diagnose**
To confirm or identify a disease or health condition.

**donor**
A person who gives their organs, tissues, or cells to another person.

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

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

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

**eosinophil**
A type of white blood cell that helps fight infections and has small particles (granules).

**fatigue**
Severe tiredness despite getting enough sleep that limits one’s ability to function.

**first-generation tyrosine kinase inhibitor (TKI)**
The first TKI drug that was approved to treat chronic myelogenous leukemia.
flow cytometry
A test that looks at certain substances on the surface of cells to identify the type of cells present.

fluorescence in situ hybridization (FISH)
A lab test that uses special dyes to look for abnormal changes in a cell’s genes (coded instructions for controlling cells) and chromosomes (long strands of genes).

follow-up test
Tests done after the start of treatment to check how well treatment is working.

follow-up treatment
The next treatment given after a prior treatment failed or had to be stopped. Also called second-line treatment.

fusion gene
A gene (set of coded instructions for making and controlling cells) that is made when parts of two separate genes join (fuse) together.

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

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

graft-versus-leukemia (GVL) effect
An attack on cancer cells by transplanted blood stem cells (immature blood-forming cells).

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

hematologic relapse
Tests show that blood cell counts have become more abnormal again after a period of improvement when they were completely normal.

hematologic response
Tests show that the numbers of different blood cells in the bloodstream are returning to a normal level as a result of treatment.

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

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

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

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

human leukocyte antigen (HLA) testing
A blood test that finds a person’s HLA type—the unique set of proteins on the surface of cells that help the body to tell its own cells apart from foreign cells.

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

immune response
The action of the body’s natural defense against infections and disease in response to foreign substances.
immune system
The body’s natural defense against infection and disease.

immunotherapy
Treatment with drugs that boost the body’s natural defense against infection and disease (immune system) to attack cancer cells.

interferon
A drug used to treat cancer by activating the body’s natural defense against infection and disease (immune system).

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

intestine
The organ that food passes through after leaving the stomach.

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

leukemia
A type of cancer that starts in blood-forming cells in the bone marrow—the soft, sponge-like tissue in the center of most bones where blood cells are made.

leukemia cell
Abnormal, immature white blood cell that grows and divides all the time without control. Also called a CML cell.

liver
An organ that removes waste from the blood and helps to digest food.

local anesthesia
A controlled loss of feeling in a small area of the body caused by drugs.

log reduction
A decrease in the number of cells that have the BCR-ABL gene.

lymphoblast
An immature cell that becomes a mature white blood cell called a lymphocyte.

lymphocyte
A type of white blood cell that helps protect the body from infection and disease.

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

lymphoid stem cells
Immature blood-forming cells in the bone marrow (soft tissue in the center of bones where blood cells are made) that make a type of white blood cell called a lymphocyte.

major cytogenetic response
An improvement related to treatment, when tests detect the Philadelphia chromosome in 0 to 35 cells out of 100.

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

medical history
All health events and medications taken to date.
microscope
A tool that uses lenses to see things the eyes can’t.

minor cytogenetic response
An improvement related to treatment, when tests detect the Philadelphia chromosome in more than 35 cells out of 100.

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

mutation
An abnormal change in the coded instructions in cells for making and controlling cells.

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

myeloblast
An immature blood cell that develops into a mature white blood cell called a granulocyte.

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

myeloid stem cells
Immature blood-forming cells in the bone marrow (soft tissue in the center of bones where blood cells are made) that make a type of white blood cell called a granulocyte.

neutrophil
A type of white blood cell that helps fight infections and has small particles (granules).

partial cytogenetic response
An improvement related to treatment, when tests detect the Philadelphia chromosome in 1 to 35 cells out of 100.

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

phase
A rating or description of the progression of chronic myelogenous leukemia in the body.

Philadelphia chromosome
An abnormal, short chromosome 22 that is formed when parts of chromosomes 9 and 22 switch with each other. It is the hallmark of chronic myelogenous leukemia and contains the BCR-ABL gene.

physical exam
A review of the body by a health expert for signs of disease.

platelet
A type of blood cell that helps control bleeding.

potent
Degree of strength or intensity.

primary resistance
When the cancer doesn’t respond at all to a drug taken for the first time.

primary treatment
The main treatment used to rid the body of cancer.

prognosis
The likely or expected course and outcome of a disease.
prognostic factor
Something that affects and helps predict the likely outcome of a disease.

prognostic scoring system
A system used to help gauge the likely outcome of a disease based on certain factors.

protein
A chain of small chemical compounds important to every cell in the body.

quantitative reverse transcriptase polymerase chain reaction (QPCR)
A very sensitive test that measures the number of cells in the blood or bone marrow that have the BCR-ABL gene.

red blood cell
A type of blood cell that carries oxygen from the lungs to the rest of the body.

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

resistance
When cancer does not respond to a drug treatment.

response milestone
The target or goal for the level of treatment response—an improvement in disease—to be reached in a certain amount of time after starting treatment.

risk group
Grouping of patients who will likely have a similar treatment outcome.

risk score
A rating of the likely chance of a good treatment outcome based on certain factors.

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

second-generation tyrosine kinase inhibitor (TKI)
A TKI drug that was developed after imatinib, the first TKI approved for chronic myelogenous leukemia.

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

sedative
A drug that helps a person to relax or go to sleep.

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

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

St. John’s wort
An herbal product that is sometimes used to treat depression and that can affect how well certain cancer drugs work in the body.

standardized baseline
A standardized starting point (baseline) for measuring changes in the number of cells that have the BCR-ABL gene.

stem cell transplant
Treatment that replaces damaged or diseased cells in the bone marrow with healthy blood-forming cells called blood stem cells. Also called hematopoietic cell transplant.

steroid
A drug used to reduce swelling, pain, and redness.
supportive care
Treatment for the symptoms or health conditions caused by cancer or cancer treatment.

symptom
A new or changed health problem a person experiences that may indicate a disease.

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

transfusion
Replacing lost blood with new blood.

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

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

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

tyrosine kinase inhibitor (TKI)
A type of drug that targets and blocks the protein made by the BCR-ABL gene so that it can’t tell leukemia cells (CML cells) to grow and make new cells.

U.S. Food and Drug Administration (FDA)
A federal government agency that regulates drugs and food.

vein
A small tube that carries blood to the heart from anywhere in the body.

white blood cell
A type of blood cell that helps fight infections in the body.
Acronyms

CBC  
complete blood count

CML  
chronic myelogenous leukemia

DLI  
donor lymphocyte infusion

DNA  
deoxyribonucleic acid

FDA  
U.S. Food and Drug Administration

FISH  
fluorescence in situ hybridization

GVHD  
graft-versus-host disease

GVL  
graft-versus-leukemia

HCT  
 hematopoietic cell transplant

HLA  
human leukocyte antigen

IS  
International Scale

QPCR  
quantitative reverse transcriptase polymerase chain reaction

TKI  
tyrosine kinase inhibitor

WHO  
World Health Organization

NCCN Abbreviations and Acronyms

NCCN®  
National Comprehensive Cancer Network®

NCCN Patient Guidelines  
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