NCCN Guidelines for Patients®

Chronic Myelogenous Leukemia

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About this booklet

Its purpose
Learning that you have cancer can be overwhelming. The goal of this booklet is to help you get the best cancer treatment. It has a step-by-step guide of the tests and treatments recommended by experts in chronic myelogenous leukemia.

Supported by the NCCN Foundation
The NCCN Foundation supports the mission of the National Comprehensive Cancer Network® (NCCN®) to improve the care of patients with cancer. One of its aims is to raise funds to create a library of booklets for patients. Learn more about the NCCN Foundation at NCCN.org/foundation.

The source of the information
NCCN is a not-for-profit network of 23 of the world’s leading cancer centers. Experts from NCCN have written treatment guidelines for chronic myelogenous leukemia doctors. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient booklet is based on the guidelines written for doctors. For more information, visit NCCN.org/clinical.asp.

For more information
This booklet focuses on the treatment of chronic myelogenous leukemia. NCCN also offers patient booklets on breast, lung, and pancreatic cancer, as well as many other cancer types. Visit NCCN.org/patients for the full library of booklets as well as additional patient and caregiver resources.
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How to use this booklet

Who should read this booklet?
This booklet is about a slow-growing cancer of the blood in which too many white blood cells are made. This booklet may be helpful for patients, caregivers, family, and friends dealing with this cancer.

Does the whole booklet apply to me?
This booklet includes important information for many situations. Thus, not everyone will get every test and treatment listed. The first parts of the booklet cover basic information that will make it easier to understand later parts. Each topic is described at the start of Parts 1 through 6. Page numbers are listed so you can flip right to the topic of interest. Your treatment team can also point out the parts that apply to you and give you more information. As you read through this booklet, you may find it helpful to make a list of questions to ask your doctor.

The treatment guide in Part 5 includes the recommendations that NCCN doctors agree are most useful for most patients. However, each patient is unique and these specific recommendations may not be right for you. Your doctor may suggest other tests or treatments based on your medical history and other factors. This booklet does not replace the knowledge and suggestions of your doctors.

Making sense of medical terms
In this booklet, many medical words are included that describe cancer, tests, and treatments. These are words that you will likely hear your treatment team use in the months and years ahead. Some of this information may be new to you, and it may be a lot to learn.

Words that you may not know are defined in the text or the sidebar. Words with sidebar definitions are underlined when first used on a page. All definitions are listed in the Dictionary in Part 7. Acronyms are also listed in the text or the sidebar. Acronyms are words formed from the first letters of other words. One example is CBC for complete blood count.
Part 1: What is chronic myelogenous leukemia?

You’ve learned that you have chronic myelogenous leukemia. It’s common to feel shocked and confused. Part 1 reviews some basics about chronic myelogenous leukemia that may help you better understand this disease. These basics may also help you start planning for treatment.

6 1.1 – What are blood cells?
Describes the different types of blood cells and what they do in the body.

7 1.2 – How does chronic myelogenous leukemia start?
Describes how and where this type of cancer begins.

9 1.3 – Symptoms of chronic myelogenous leukemia
Describes the signs and health conditions that may be caused by this type of cancer.

10 1.4 – Tools
Lists webpages with basics about chronic myelogenous leukemia.
1.1 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. 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.

Blood cells are made from stem cells in the bone marrow—the soft, sponge-like tissue in the center of most bones. See Figure 1. These are called blood stem cells or hematopoietic stem cells.

Blood stem cells make many different types of blood cells. See Figure 2. Blast cells, such as myeloblasts and lymphoblasts, are immature blood cells that become mature white blood cells. There are three main types of white blood cells: monocytes, lymphocytes, and granulocytes. Lymphoid stem cells form lymphocytes. Myeloid stem cells form red blood cells, platelets, monocytes, and granulocytes. Neutrophils, eosinophils, and basophils are granulocytes.

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Figure 1. Blood cells in bone marrow
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Figure 2. ‘Family tree’ of blood cells
Illustration Copyright © 2013 Nucleus Medical Media, All rights reserved.
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1.2 How does chronic myelogenous leukemia start?

Leukemia is a cancer that starts in the blood-forming cells in the bone marrow. CML (chronic myelogenous leukemia) is a leukemia that grows slowly and causes too many white blood cells to form.

Normal blood cells grow and divide to form new blood cells as the body needs them. When normal cells grow old or get damaged, they die. CML cells don’t do this. Instead, they make new cells that aren’t needed and don’t die quickly when old or damaged.

Genes are the coded instructions in cells for making new cells and controlling how cells behave. Cancer is caused by an abnormal change in genes. CML is believed to be caused by the BCR-ABL gene. This gene is not found in normal blood cells and is not passed down from parents to children. The BCR-ABL gene is a fusion gene—a new gene that is formed when two genes are joined together.

Genes are carried in the DNA (deoxyribonucleic acid) of every cell. DNA is bundled together into long strands called chromosomes. See Figure 3.

**Definitions:**

- **DNA:** Molecules in cells that contain genes
- **Granulocyte:** A type of white blood cell that has small particles (granules)
- **Immune system:** The body’s natural defense against infection and disease
- **Lymphocyte:** A type of cell that fights infections—called white blood cells
- **Monocyte:** A type of cell that fights infections—called white blood cells
- **Stem cell:** An immature cell from which other types of cells develop

![Figure 3. Chromosomes, DNA, and genes](Illustration Copyright © 2013 Nucleus Medical Media, All rights reserved. www.nucleusinc.com)
1.2 How does chronic myelogenous leukemia start?

Every cell has 23 pairs of chromosomes. Each pair looks different from the others and is labeled by a number. Sometimes pieces of chromosomes break off and switch with each other. This is called a translocation.

The \textit{BCR-ABL} gene is formed by the translocation between parts of chromosomes 9 and 22. See Figure 4. The short bottom piece of chromosome 9 has the \textit{ABL} gene. It attaches to the short top piece of chromosome 22, which has the \textit{BCR} gene. As a result, these two genes join (fuse) together and form the \textit{BCR-ABL} fusion gene.

This translocation creates 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 and it contains the \textit{BCR-ABL} gene. If you do not have the Philadelphia chromosome or the \textit{BCR-ABL} gene, then you do not have CML.

The \textit{BCR-ABL} gene makes the BCR-ABL protein, a type of protein called a tyrosine kinase. Tyrosine kinases are proteins that are located on or near the surface of cells and send signals telling cells when to grow and divide. The BCR-ABL protein is abnormal. It is locked in the “on” position so that it always sends signals for cells to keep growing and dividing. This causes blood stem cells to make too many white blood cells called granulocytes. White blood cells made by the BCR-ABL protein are called leukemia cells or CML cells and they contain the \textit{BCR-ABL} gene. These cells aren’t normal. They don’t mature into healthy, normal cells. They don’t die when they should. They also may reproduce too quickly. Over time, these abnormal white blood cells (CML cells) can overcrowd the bone marrow so there isn’t room for healthy white blood cells, red blood cells, and platelets.
1.3 Symptoms of chronic myelogenous leukemia

Because CML is a slow-growing cancer, many people do not have symptoms of CML when it is first found (diagnosed) by a doctor. A symptom is a physical sign of a disease.

Possible symptoms that may be caused by CML include:

- Feeling unusually tired,
- Unexplained weight loss,
- Unusual sweating at night,
- Fever,
- Pale skin, and
- Pain or a feeling of fullness on the upper, left side of the belly area (abdomen) under the ribs.

However, these symptoms may be caused by other health conditions.

Definitions:

**Blood stem cell:** An immature cell from which other types of blood cells develop.

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

**Chromosomes:** Long strands of bundles of coded instructions in cells for making and controlling cells.

**Gene:** Set of coded instructions in cells for making and controlling cells.

**Platelet:** Type of blood cell that helps control bleeding.

**Red blood cell:** Type of blood cell that carries oxygen from the lungs to the rest of the body.

**White blood cell:** A type of cell that helps fight infections in the body.
1.4 Tools

Webpages

American Cancer Society

Leukemia and Lymphoma Society
www.lls.org/#/diseaseinformation/leukemia/chronicmyeloidleukemia/

National Cancer Institute
www.cancer.gov/cancertopics/pdq/treatment/CML/Patient/page1

Review of Part 1

- White blood cells fight disease and infections in the body.
- Blood cells are made in the soft tissue in the center of bones called bone marrow.
- CML is a leukemia that grows slowly and causes too many white blood cells to form.
- People with CML have the Philadelphia chromosome.
- The Philadelphia chromosome contains the \textit{BCR-ABL} gene.
Part 2: Testing for chronic myelogenous leukemia

Treatment planning starts with testing. The tests used for chronic myelogenous leukemia are described on the next pages. Many of the tests used to confirm (diagnose) chronic myelogenous leukemia and plan treatment are also used to check how well treatment is working. 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 chronic myelogenous leukemia will receive every test listed.

12  2.1 – General health tests
Describes a medical history and a physical exam.

13  2.2 – Blood and bone marrow tests
Describes the removal of blood and bone marrow from your body for testing.

15  2.3 – Lab tests
Describes the lab tests performed on samples of blood and bone marrow to check for signs of chronic myelogenous leukemia.

19  2.4 – Tools
Lists helpful webpages along with questions about testing to ask your doctor.
2.1 General health tests

Medical history
Before and after cancer treatment, your doctor will assess your medical history. Your medical history includes any health events in your life and any medications you've taken. Your doctor will ask about any symptoms and health conditions that you have had. 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. During this exam, your doctor may listen to your lungs, heart, and gut. 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.

A key part of the physical exam is assessing the size of your spleen. Your spleen is located on the upper, left part of your belly area (abdomen) underneath your ribs. The spleen filters blood, stores blood cells, and destroys old blood cells. A normal-sized spleen typically cannot be felt during a physical exam. But, the spleen can be felt when it is enlarged. CML may cause an enlarged spleen due to extra blood cells being stored in this organ.
2.2 Blood and bone marrow tests

Blood Tests
Blood tests are used to look for signs of CML in peripheral blood. Blood tests are done along with other initial tests to help diagnose CML. They are also used to monitor how well treatment is working—called a treatment response—and to check for side effects. For a blood test, your doctor will insert a needle into a vein to remove a sample of blood. A pathologist will examine the sample with a microscope and may perform other tests.

Bone marrow tests
Bone marrow tests are used to diagnose CML and to monitor how well treatment is working. Bone marrow is the soft, sponge-like tissue in the center of most bones where blood cells are made. The two types of bone marrow tests used for CML are a bone marrow biopsy and a bone marrow aspiration. A biopsy is a medical procedure that removes samples of tissue to be tested for disease. A biopsy is generally a safe test and can typically 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 (called an aspirate) from inside the bone. Usually both tests are done at the same time on the hip or breastbone.
2.2 Blood and bone marrow tests

The bone marrow tests are done as outpatient tests—this means you do not 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 rotated to remove the solid bone and marrow sample. See Figure 5. You may feel some pain while the samples are being removed and your skin may be bruised afterward.

Figure 5. Bone marrow biopsy
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2.3 Lab tests

The peripheral blood and bone marrow samples removed from your body are sent to the lab for testing. At the lab, a pathologist will examine the samples with a microscope and perform a number of different tests. A pathologist is a doctor who’s an expert in testing cells and tissue for signs of disease. The blood sample will be tested for signs of CML, such as too many white blood cells and abnormal levels of certain chemicals in the blood. The bone marrow sample will be tested for signs of CML such as the Philadelphia chromosome and the BCR-ABL gene. It usually 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. The lab tests used for CML are listed in Table 1 and are described on the following pages.

Table 1. Lab tests for CML

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<tr>
<td>BCR-ABL gene mutation analysis</td>
<td>Peripheral blood or bone marrow</td>
</tr>
</tbody>
</table>

Definitions:

**BCR-ABL gene**: Abnormal gene formed when the BCR and ABL genes join.

**Biopsy**: Removal of small amounts of tissue for testing.

**Bone marrow**: Soft tissue in the center of most bones where blood cells are made.

**Chromosome**: Strand of bundled instructions for making and controlling cells.

**Gene**: Instructions for making and controlling cells.

**Local anesthesia**: A loss of feeling in a small area of the body caused by drugs.

**Microscope**: A tool that uses lenses to see things the eyes can’t.

**Peripheral blood**: Blood outside of the bone that circulates in the body.

**Sedative**: Drug that helps a person relax or go to sleep.
2.3 Lab tests

**Complete blood count with differential**
A CBC (complete blood count) measures the number of white blood cells, red blood cells, and platelets in a sample of blood. For CML, the CBC should include a differential. The differential measures the different types of white blood cells in the sample. A high white blood cell count and low red blood cell count 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.

**Blood chemistry profile**
A blood chemistry profile measures the levels of different chemicals in the blood. Organs such as the liver and kidneys 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. This test is done along with other initial tests when CML is first diagnosed.

**Cytochemistry**
A cytochemistry test uses chemical stains (dyes) to show which types of leukemia cells—myeloid or lymphoid—are present in a blood sample. The chemical dyes cause a color change in one type of leukemia cell and not another. This color change can be seen with a microscope—a tool that uses lenses to see things the eyes can’t. Myeloperoxidase is a chemical found in myeloid cells but not in lymphoid cells. TdT (terminal deoxynucleotidyl transferase) is a chemical found in lymphoid cells but not in myeloid cells. For CML, cytochemistry tests use dyes that only react with these two chemicals. This type of test may be used to help guide treatment options once CML is in advanced phases. This type of test is not used to diagnose CML.

**Human leukocyte antigen testing**
HLAs (human leukocyte antigens) are special proteins on the surface of white blood cells. These proteins help the body to identify its own cells from foreign cells. An HLA type is a unique set of HLA proteins on a person’s white blood cells. HLA types differ among people just like blood types differ among people. HLA testing is used to determine a person’s HLA type. HLA testing is done before a type of treatment that transfers blood stem cells from another person to the patient (See Part 4). It’s very important that their HLA types are a near-perfect match for this treatment to work. This is because the HLA type affects how the body responds to foreign substances.

**Cell assessment**
The pathologist will examine the blood and bone marrow samples with a microscope to assess the features of the cells. A pathologist is a doctor who’s an expert in testing cells and tissue for signs of disease. Staining the samples with dyes helps show the differences between parts of a single cell and differences between multiple cells. The pathologist will assess the size, shape, type, and maturity of the cells. The number of immature blood cells (blasts) 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 circulating (peripheral)
2.3 Lab tests

blood and the number of basophils is very low. But in the advanced phases of CML, the number of basophils is increased and many blast cells are found in the bone marrow or peripheral blood.

**Bone marrow cytogenetics**

Cytogenetics is the study of chromosomes—long strands of bundles of coded instructions for making and controlling cells. Bone marrow cytogenetics, also called conventional cytogenetics, involves examining the bone marrow sample with a microscope to look for changes in the cells’ chromosomes. This type of test is used to detect the Philadelphia chromosome and measure the number of cells that have it. The pathologist will use a microscope to examine a “map” of the chromosomes, called a karyotype. The pathologist will assess the size, shape, number, arrangement, and structure of the chromosomes on the karyotype to look for any abnormal changes.

Cytogenetic testing can also be performed on cells from the peripheral blood, but bone marrow is preferred. This is because the yield from peripheral blood is very poor. Analysis of peripheral blood may be used if a bone marrow sample cannot be collected (see below). Bone marrow cytogenetics is used to diagnose CML and determine the disease phase (discussed in Part 3). It is also used to monitor how well treatment is working—called a treatment response.

**Fluorescence in situ hybridization**

FISH (fluorescence in situ hybridization) is another test used to detect the Philadelphia chromosome and the BCR-ABL fusion gene. This test may be used on a peripheral blood sample if a bone marrow sample can’t be collected. FISH uses color “probes” to find the BCR gene and the ABL gene in chromosomes. The BCR-ABL fusion gene, located on the Philadelphia chromosome, is shown by the overlapping colors of the two probes. FISH analysis of peripheral blood may be used to diagnose CML when bone marrow cytogenetics isn’t possible. But, FISH is not recommended for monitoring the response to treatment.
2.3 Lab tests

Quantitative reverse transcriptase polymerase chain reaction

QPCR (quantitative reverse transcriptase polymerase chain reaction) is a very sensitive test that detects and measures the \textit{BCR-ABL} gene. QPCR makes thousands of copies of the DNA in cells from a blood or marrow sample to see how many cells have the \textit{BCR-ABL} gene. Copies of \textit{BCR-ABL} found by QPCR are also called \textit{BCR-ABL} transcripts. The number of \textit{BCR-ABL} copies detected by QPCR is called the transcript level. The \textit{BCR-ABL} transcript level reflects the number of \textit{BCR-ABL} genes in your body. Changes in \textit{BCR-ABL} levels are measured in logs—a log reduction means the \textit{BCR-ABL} level has decreased by a certain amount.

QPCR can detect one CML cell among more than 100,000 normal cells. This test is used to confirm (diagnose) CML as well as to monitor the treatment response. The QPCR test should always be done in the same lab, preferably a lab that uses the International Scale. The International Scale is a standardized scale for measuring and reporting QPCR test results using a standardized baseline level of \textit{BCR-ABL} copies.

QPCR test results from different labs are converted to the International Scale so that all test results are consistent and can be compared between labs. Using the International Scale is important because test results from different labs can vary similar to the way currencies in different countries vary—$1 in the United States is not equal to €1 in Europe.

Flow cytometry

Flow cytometry looks at certain substances on the outside surface of cells to identify the specific type of cells present. This test is used for advanced phases of CML to determine if the leukemia cells are mostly myeloid or lymphoid cells. This test is important because the cell type may affect which treatment option is best for you. Flow cytometry can be performed on a sample of bone marrow or peripheral blood. Bone marrow is the soft, sponge-like tissue in the center of most bones where blood cells are made. Peripheral blood is located outside the bone and circulates throughout the body in veins.

\textit{BCR-ABL} gene mutation analysis

Sometimes new changes (mutations) develop in the part of the \textit{BCR-ABL} gene that makes the \textit{BCR-ABL} protein. These mutations change the shape of the \textit{BCR-ABL} protein, affecting how and which targeted cancer drugs can bind to it to block the growth signals.

A mutation analysis is a test that looks for new mutations in the \textit{BCR-ABL} gene that may occur during treatment for CML. This test may be performed on a peripheral blood or bone marrow sample after months of treatment based on how well treatment is working. Mutational analysis is important because new or different gene mutations can affect which treatment option is best for you.
2.4 Tools

Questions about testing to ask your doctor

- What tests will I have? How often will I be tested?
- Where will the tests take place? Will I have to go to the hospital?
- How long will it take? Will I be awake?
- Will it hurt? Will I need anesthesia?
- What are the risks? What are the chances of infection or bleeding afterward?
- How do I prepare for testing? Should I not take aspirin? Should I not eat beforehand?
- Should I bring a list of my medications? Should I bring someone with me?
- How long will it take for me to recover? Will I be given an antibiotic or other drug afterward?
- If a biopsy is done, will I get a copy of the results?
- How often will I have bone marrow tests? Will you remove the sample of bone marrow from the hip or from another bone?
- How soon will I know the test results and who will explain them to me?
- Who will talk with me about the next steps? When?

Definitions:

**Baseline**: Starting point to which future test results are compared

**BCR-ABL gene**: Abnormal set of instructions in cells, formed when the BCR and ABL genes join (fuse)

**BCR-ABL protein**: Abnormal protein that causes too many white blood cells to be made

**DNA**: Molecules that contain genes—coded instructions in cells for making and controlling cells

**Lymphoid**: Referring to a type of white blood cell called a lymphocyte

**Myeloid**: Referring to a type of white blood cell called a granulocyte

Acronyms:

**DNA** = Deoxyribonucleic acid
2.4 Tools

Webpages

American Cancer Society

Leukemia and Lymphoma Society
www.lls.org/#/diseaseinformation/leukemia/chronicmyeloidleukemia/diagnosis/
www.lls.org/#/resourcecenter/freeeducationmaterials/treatment/labandimagingtests

National Cancer Institute
www.cancer.gov/cancertopics/pdq/treatment/CML/Patient/page1#Keypoint4

Review of Part 2

• Cancer tests are used to plan treatment and check how well treatment is working.
• To confirm if you have CML, a sample of blood and/or bone marrow must be removed from your body for testing.
• The removal of tissue from your body for testing is called a biopsy.
• Cytogenetic tests check for abnormal changes in chromosomes, such as the Philadelphia chromosome.
• QPCR is a very sensitive test that detects and measures the BCR-ABL gene.
• Blood tests check for signs of CML in the blood.
Part 3: Phases of chronic myelogenous leukemia

Chronic myelogenous leukemia is divided into three groups of progression called phases. The treatments doctors recommend for chronic myelogenous leukemia depend on the phase of the cancer. The phase is based on the amount of immature white blood cells, called blasts, in the blood and bone marrow as well as the severity of symptoms. The cancer phase and other factors affect the likely outcome (prognosis). Part 3 describes the different phases of chronic myelogenous leukemia as well as the scoring systems used to help predict prognosis. This information will help you use the treatment guide in Part 5.

3.1 – Chronic phase
Describes the first phase of progression, when the number of white blood cells is increased but may not cause symptoms.

3.2 – Accelerated phase
Describes the second phase of progression, when the number of blast cells is increased and more likely to cause symptoms.

3.3 – Blast phase
Describes the third and final phase of progression, when the number of blast cells is the highest and can be life-threatening.

3.4 – Risk assessment
Describes the scoring systems used to help gauge the likely outcome of chronic myelogenous leukemia and treatment.

3.5 – Tools
Lists webpages with helpful information about the phases of chronic myelogenous leukemia.
3.1 Chronic phase

The chronic phase is the first phase of CML. In this phase, the number of white blood cells is increased and immature white blood cells (blasts) make up less than 10% of cells in the peripheral blood and/or bone marrow. This means that less than 10 out of every 100 cells are blasts. CML in the chronic phase may cause mild symptoms, but most often it does not cause any symptoms. Possible symptoms include feeling unusually tired and a feeling of fullness near the belly. The body can still fight infections since the changes in blood cells are not severe. In this phase, the cancer progresses very slowly. Thus, CML in the chronic phase may progress over several months or years. In general, people with CML in the chronic phase respond better to treatment.

3.2 Accelerated phase

The accelerated phase is the second phase of CML. In this phase, the number of blast cells in the peripheral blood and/or bone marrow is usually higher than normal. Other aspects of accelerated phase can include increased basophils, very low platelets, or new chromosome changes. The number of white blood cells is also high. In this phase, the leukemia cells grow more quickly and may cause symptoms such as anemia and an enlarged spleen. A few different criteria groups can be used to define accelerated phase. However, the two most commonly used are the World Health Organization Criteria and the criteria from MD Anderson Cancer Center. See Table 2.

Definitions:

Anemia: A health condition in which the number of red blood cells is low

Basophil: A type of white blood cell that helps fight infection in the body

Bone marrow: Soft tissue in the center of most bones where blood cells are made

Chromosome: Long strand of bundles of coded instructions in cells for making and controlling cells

Peripheral blood: Blood outside of the bone that travels throughout the body

Platelet: Blood cell that helps control bleeding

Promyelocyte: Immature blood cell that forms a type of mature white blood cell

Spleen: An organ to the left of the stomach that helps protect the body from disease
### 3.2 Accelerated phase

<table>
<thead>
<tr>
<th>MD Anderson¹</th>
<th>World Health Organization²</th>
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<td>≥15% blasts in peripheral blood</td>
<td>10% to 19% blasts in peripheral blood and/or bone marrow</td>
</tr>
<tr>
<td>≥30% blasts and promyelocytes in peripheral blood</td>
<td>≥20% basophils in peripheral blood</td>
</tr>
<tr>
<td>≥20% basophils in peripheral blood</td>
<td>Very high or very low platelet count that is unrelated to treatment</td>
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<td>Very low platelet count that is unrelated to treatment</td>
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<td>New chromosome changes (mutations)</td>
<td>New chromosome changes (mutations)</td>
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</table>


² Adapted from Swerdlow SH, Campo E, Harris NL, et al. (Eds.): *WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues*. Lyon, France: IARC Press; 2008.
3.3 Blast phase

The blast phase is the final phase of CML progression. Also referred to as “blast crisis,” CML in this phase can be life-threatening. There are two criteria groups that may be used to define blast phase. See Table 3. In this phase, the number of blast cells in the peripheral blood and/or bone marrow is very high. Another defining feature of blast phase is that the blast cells have spread outside the blood and/or bone marrow into other tissues. CML in the blast phase may cause more symptoms such as infections, bleeding, abdominal 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 rapidly, whereas chronic leukemia progresses slowly over months or years. In blast phase, the leukemia cells may be more similar to AML (acute myeloid leukemia) or more similar to ALL (acute lymphoblastic leukemia). AML causes too many immature white blood cells called myeloblasts to be made. ALL results in too many immature white blood cells called lymphoblasts.

### Table 3. Criteria for blast phase

<table>
<thead>
<tr>
<th>World Health Organization¹</th>
<th>International Bone Marrow Transplant Registry ²</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥20% blasts in peripheral blood or bone marrow</td>
<td>≥30% blasts in peripheral blood or bone marrow</td>
</tr>
<tr>
<td>Blasts found outside of blood or bone marrow</td>
<td>Blasts found outside of blood or bone marrow</td>
</tr>
<tr>
<td>Large groups of blasts found in bone marrow</td>
<td></td>
</tr>
</tbody>
</table>

¹ Adapted from Swerdlow SH, Campo E, Harris NL, et al. (Eds.): WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Lyon, France: IARC Press; 2008.

3.4 Risk assessment

In addition to the phase of CML, other factors can affect and help predict the likely outcome (prognosis) of CML treatment. These are called prognostic factors. Prognostic scoring systems use these factors to determine a patient's risk score. 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.

Sokal and Hasford are the two prognostic scoring systems used for patients with CML. The Sokal score is based on your age, spleen size, platelet count, and the percentage of blasts in the peripheral blood. In addition to these four factors, the Hasford score also includes the number of eosinophils and basophils in the peripheral blood.

**Definitions:**

- **Basophil:** A type of white blood cell that helps fight infections and has small particles (granules)
- **Blast cell:** An immature blood cell
- **Bone marrow:** The soft, sponge-like tissue in the center of most bones where blood cells are made
- **Eosinophil:** A type of white blood cell that helps fight infections and has small particles (granules)
- **Peripheral blood:** Blood outside of the bone that circulates throughout the body
- **Platelet:** A type of blood cell that helps control bleeding
- **Spleen:** An organ to the left of the stomach that helps protect the body from disease
3.5 Tools

**Webpages**

American Cancer Society

European LeukemiaNet
www.leukemia-net.org/content/leukemias/cml/cml_score/index_eng.html

Leukemia and Lymphoma Society
www.lls.org/#/diseaseinformation/leukemia/chronicmyeloidleukemia/cmlphases/

National Cancer Institute
www.cancer.gov/cancertopics/pdq/treatment/CML/Patient/page2

National Marrow Donor Program

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**Review of Part 3**

- CML is divided into three groups (phases) of progression.
- The phase of CML is based on the number of immature white blood cells, called blasts, in the peripheral blood and bone marrow.
- Prognostic scoring systems use certain factors to help predict the likely outcome (prognosis) and guide treatment decisions.
Part 4: Overview of cancer treatments

There is more than one treatment for chronic myelogenous leukemia. Which treatment you will receive depends on many factors such as your age, general health, and the cancer phase. The main types of treatments for chronic myelogenous leukemia are described on the next pages. This information may help you better understand your treatment options and use the treatment guide in Part 5. It may also help you know what to expect during treatment. Not every person with chronic myelogenous leukemia will receive every treatment listed.

4.1 – Tyrosine kinase inhibitor therapy
Describes the use of drugs that specifically target chronic myelogenous leukemia cells.

4.2 – Immunotherapy
Describes the use of drugs that boost the body’s natural defense against infection and disease—immune system—to fight cancer cells.

4.3 – Chemotherapy
Describes the use of drugs that kill rapidly dividing cells to treat chronic myelogenous leukemia.

4.4 – Stem cell transplant and donor lymphocyte infusion
Describes a treatment that replaces damaged bone marrow with healthy stem cells and a treatment that gives you more white blood cells to help your body fight the cancer.

4.5 – Clinical trials
Describes a type of research that may be a treatment option.

4.6 – Tools
Lists helpful webpages as well as questions about treatment to ask your doctor.
4.1 Tyrosine kinase inhibitor therapy

TKI (tyrosine kinase inhibitor) therapy is a type of targeted therapy used to treat CML. Targeted therapy is treatment with drugs that target a specific or unique feature of cancer cells not generally present in normal cells. Because these drugs specifically target cancer cells, they may be less likely to harm normal cells throughout your body.

TKIs target the abnormal BCR-ABL protein that causes the overgrowth of abnormal white blood cells (CML cells). The BCR-ABL protein, made by the BCR-ABL gene, is a type of protein called a tyrosine kinase. Tyrosine kinases are proteins located on or near the surface of cells and they tell cells when to grow and divide to make new cells. TKIs block (inhibit) the BCR-ABL protein from sending the signals that cause too many abnormal white blood cells to form. However, each TKI works in a slightly different way.

The FDA (Food and Drug Administration) approved the first TKI for the treatment of CML in 2001. Since then, several new TKIs have been developed to treat CML. These newer drugs are referred to as “second-generation” TKIs. The TKIs used to treat CML are listed in Table 4 and described on the following pages. These drugs are made in the form of a pill that is swallowed. The dose of the drug is measured in mg (milligrams).

Order of treatments

Some people with CML will have more than one treatment. When and why treatments are given can be hard to understand. Part 5 gives full details. Here, the terms that describe the order of treatments are explained.

**Primary treatment** is the main treatment used to rid your body of cancer. TKIs are often used as primary treatment for CML. **First-line treatment** is the first set of treatments given. If first-line treatment fails, **second-line treatment** is the next treatment or set of treatments given. This is also referred to as **follow-up treatment** since it is given after follow-up tests show that the previous treatment failed or stopped working.
4.1 Tyrosine kinase inhibitor therapy

### Table 4. TKI drugs used to treat CML

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Brand name (sold as)</th>
<th>Approved for</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imatinib</td>
<td>Gleevec</td>
<td>First-line treatment</td>
</tr>
<tr>
<td>Dasatinib</td>
<td>Sprycel</td>
<td>First-line treatment</td>
</tr>
<tr>
<td>Nilotinib</td>
<td>Tasigna</td>
<td>First-line treatment</td>
</tr>
<tr>
<td>Bosutinib</td>
<td>Bosulif</td>
<td>Second-line treatment</td>
</tr>
</tbody>
</table>

### Definitions:

**BCR-ABL gene**: An abnormal gene formed when the BCR gene and the ABL gene join (fuse) together on the Philadelphia chromosome.

**BCR-ABL protein**: A protein that is made by the abnormal BCR-ABL gene and causes too many white blood cells to be made.

**FDA**: A federal government agency that regulates drugs and food.

**Gene**: Set of coded instructions in cells for making and controlling cells.
4.1 Tyrosine kinase inhibitor therapy

**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 6.

**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. Dasatinib also blocks another protein in addition to the BCR-ABL protein.

**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 was approved to treat CML in 2012. However, this second-generation TKI is only approved to treat patients who experienced intolerance or resistance to prior TKI therapy. Read about this in TKI drug resistance on page 34. Bosutinib also blocks another protein in addition to the BCR-ABL protein.

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**Figure 6. How imatinib works**

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Version 1.2014
4.1 Tyrosine kinase inhibitor therapy

Side effects of TKIs
Side effects are new or worse unplanned physical or emotional conditions 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 in this section 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 experience so that 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 with appropriate supportive care is important for your quality of life and CML treatment outcome.

Definitions:

- **BCR-ABL protein**: An abnormal protein that causes too many white blood cells to be made
- **FDA**: A federal government agency that regulates drugs and food
- **Intolerance**: When a drug treatment must be stopped due to severe side effects
- **Potent**: Degree of strength or intensity
- **Resistance**: When cancer doesn’t respond to treatment

Acronyms:

- **FDA** = Food and Drug Administration
- **TKI** = Tyrosine kinase inhibitor
4.1 Tyrosine kinase inhibitor therapy

Common side effects of TKI therapy for CML include:

- Low blood cell counts (cytopenia)
  - Low red blood cell counts (anemia)
  - Low platelet counts (thrombocytopenia)
  - Low neutrophil counts (neutropenia)
- 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
- Abdominal pain
4.1 Tyrosine kinase inhibitor therapy

Managing common side effects of TKIs

Low numbers of blood cells may be treated by lowering the TKI dose or with another medication. However, medications that stimulate growth of blood cells for anemia or neutropenia are not recommended for patients with CML.

All TKIs have the capacity to cause a serious heart problem called QT interval prolongation. This condition causes an irregular heartbeat and can be fatal. However, it may be managed by lowering the dose of the TKI. Your doctor may monitor for this side effect using a test called an ECG (electrocardiogram) before and during TKI treatment. An ECG is a test that shows the activity of the heart with a line graph.

Pleural effusion—fluid buildup around the lungs—is a possible serious side effect of dasatinib. A history of heart problems and high blood pressure may increase the risk of pleural effusion.

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

Definitions:

**Fatigue:** Severe tiredness despite getting enough sleep that limits one’s ability to function

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

**Phosphorus:** A substance found in blood, muscles, nerves, bones, and teeth

**Platelet:** Type of blood cell that helps control bleeding

**Red blood cell:** A type of blood cell that carries oxygen from the lungs to the rest of the body

Acronyms:

**TKI** = Tyrosine kinase inhibitor
4.1 Tyrosine kinase inhibitor therapy

TKI drug resistance

A treatment response is an outcome or improvement related to treatment. Drug resistance is when CML doesn’t respond to a drug. Primary resistance is when CML doesn’t respond at all to a drug taken for the first time. This type of resistance is rare in CML. Secondary resistance is when CML responds to a drug at first and then stops responding after a period of time. Secondary resistance occurs more often in patients with CML and there are a number of possible causes.

Most often, secondary resistance 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 effectively. 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 overcome a mutation that another TKI can’t. Therefore, switching to a different TKI may result in a treatment response after CML stops responding or becomes resistant to a prior TKI.

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, the chemotherapy drug omacetaxine is the only treatment currently recommended that works against the more difficult T315I mutation.

Drug interactions

Certain medications 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 certain proteins in the liver. Certain medications and substances may increase or decrease the amount of these proteins in the body.

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

In addition, medications that reduce acid in the stomach and intestines may reduce the amount of dasatinib or nilotinib in the blood. Such medications include H2 (histamine-2) blockers and proton pump inhibitors and are not recommended during treatment with dasatinib or nilotinib.
4.2 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 recommended as a first-line treatment option for patients with newly diagnosed CML. But, it may be considered for patients unable to tolerate TKIs. Interferon is often given as a liquid that is injected under the skin or in a muscle with a needle.

**Side effects of immunotherapy**

Side effects are new or worse unplanned physical or emotional conditions caused by treatment. Most side effects can be managed or even prevented with appropriate 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 experience. Managing side effects is important for your quality of life and CML treatment outcome. Possible side effects of interferon include:

- Concentration and memory difficulties,
- Mood changes, and
- Flu-like symptoms
  - Fever
  - Chills
  - Fatigue
  - Body aches
  - Nausea/vomiting
  - Loss of appetite

**Definitions:**

- **Fatigue:** Severe tiredness despite getting enough sleep that limits one’s ability to function
- **First-line treatment:** The first set of treatments given to treat a disease
- **Intestines:** The organs that food travels through after leaving the stomach
- **Liver:** Organ that removes waste from the blood
- **St. John’s wort:** An herbal product sometimes used to treat depression
- **Steroid:** Drug that reduces swelling, pain, and redness

**Acronyms:**

- TKI = Tyrosine kinase inhibitor
4.3 Chemotherapy

Chemotherapy is a type of drug commonly used to treat cancer. Many people refer to this treatment as “chemo.” Chemotherapy drugs kill cells that grow rapidly, including cancer cells and normal cells. Different types of chemotherapy drugs attack cancer cells in different ways. Therefore, more than one drug is often used.

Omacetaxine is the latest chemotherapy drug to be used 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. Omacetaxine works in part by blocking cells from making some of the proteins, such as the BCR-ABL protein, needed for cell growth and division. This may slow or stop the growth of new CML cells. 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 34 for details.

Omacetaxine is given as a liquid that is injected under the skin with a needle. Other chemotherapy drugs may be given as a pill that is swallowed. Chemotherapy is given in cycles of treatment days followed by days of rest. The number of treatment days per cycle and the total number of cycles varies depending on the chemotherapy drug given. Often, the cycles are 14, 21, or 28 days long.

Side effects of chemotherapy

All chemotherapy drugs can cause side effects—unplanned or unwanted physical or emotional conditions caused by treatment. The side effects of chemotherapy depend on many factors. How your body will respond to treatment can’t be fully known. You may have different side effects than someone else. Most side effects can be managed or even prevented with appropriate 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 experience. Managing side effects is important for your quality of life and CML treatment outcome. In general, common side effects of chemotherapy drugs may 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 (thrombocytopenia),
- Low red blood cell counts (anemia),
- Low white blood cell counts,
- Diarrhea,
- Nausea,
- Severe tiredness (fatigue),
- Weakness or lack of energy,
- Injection site reaction,
- Fever, and
- Infection.
4.4 Stem cell transplant and donor lymphocyte infusion

Stem cell transplant
An HSCT (hematopoietic stem cell transplant) is a medical procedure that kills damaged or diseased blood stem cells in your body and replaces them with healthy stem cells. HSCT is currently the only treatment for CML that may cure rather than control the cancer. However, the excellent results with TKIs have challenged the role of HSCT as first-line treatment—the first set of treatments given to treat a disease.

For the treatment of CML, healthy blood stem cells are collected from another person, called a donor. This is called an allogeneic HSCT. An allogeneic HSCT creates a new immune system for your body. The immune system is the body’s natural defense against infection and disease. For this type of transplant, HLA testing is needed to check if you and the donor are a good match. (See page 16 to read about HLA testing.)

High-dose chemotherapy, and sometimes radiation therapy, is given before the transplant to destroy the CML cells and normal blood cells in the bone marrow. This greatly weakens (suppresses) the immune system so your body doesn’t attack the transplanted stem cells. Once the high-dose chemotherapy is complete, the donated 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 stem cells then travel to the 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 (sterile) 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.

Definitions:

- **BCR-ABL protein**: Protein that causes too many white blood cells to be made
- **Blood stem cell**: Immature cell from which all other blood cells develop
- **Bone marrow**: Soft tissue in the center of most bones where blood cells are made
- **Radiation therapy**: Use of high-energy rays to destroy cancer cells
- **TKI**: A type of drug that targets and blocks (inhibits) certain proteins that cause too many white blood cells to be made

Acronyms:

- **FDA** = Food and Drug Administration
- **HLA** = Human leukocyte antigen
- **TKI** = Tyrosine kinase inhibitor
4.4 Stem cell transplant and donor lymphocyte infusion

Considering allogeneic HSCT

An allogeneic HSCT may not be a good treatment option for every patient with CML. Your doctor will consider many important factors when deciding if an allogeneic HSCT is a good option for you. These factors include your age, your general health, the current phase of CML, response to prior TKI therapy, and whether a well-matched donor is available. This treatment can cause severe side effects, so many treatment centers will only consider this treatment option for patients younger than 65 years of age.

Side effects of allogeneic HSCT

Side effects are unplanned or unwanted physical or emotional conditions caused by treatment. Common side effects of chemotherapy, which is given before the transplant, are described on page 36. 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 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.

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

Donor lymphocyte infusion

A DLI (donor lymphocyte infusion) is a procedure in which the patient receives lymphocytes from the same person who donated blood stem cells for the HSCT. 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 GVT (graft-versus-tumor) effect or GVL (graft-versus-leukemia) effect. The GVT effect is when the transplanted cells (the graft) see the cancer cells (the tumor or leukemia) in your body as foreign and attack them. This treatment may be used after HSCT for CML that didn’t respond to the transplant or that came back after an initial response.

Possible side effects of a DLI are similar to those associated with an allogeneic HSCT. Because this treatment induces an immune response in your body, you are at risk for GVHD as previously described. Other possible side effects of a DLI include 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.
4.4 Stem cell transplant and donor lymphocyte infusion

Complementary and alternative medicine

You may hear about other treatments from your family and friends. They may suggest using CAM (complementary and alternative medicine). CAM 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 treatment that is used in place of the standard or 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 booklet.

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.

Definitions:

Allogeneic HSCT: A treatment that transfers healthy blood stem cells from a person to the patient

Blood stem cell: Immature cell from which all other blood cells develop

Immune response: Action of the body’s natural defense against disease

Phase: Rating of CML progression in the body

TKI: A drug that targets and blocks certain proteins that cause too many white blood cells to be made

Acronyms:

HSCT = Hematopoietic stem cell transplant

TKI = Tyrosine kinase inhibitor
A clinical trial is a type of research that studies a test or treatment. Because of clinical trials, the tests and treatments in this booklet are now widely used to help patients. Tests and treatments aren't offered to all patients as soon as they're made. They must be tested in clinical trials first. When tests and treatments are found to be safe and helpful, they may become tomorrow’s standard of care. However, there is no way to know this before the trial is done.

Clinical trials are done in a series of steps, called phases. This is to fully study how safe and helpful a test or treatment is for patients. There may be an open clinical trial that you can join. 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.

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 or a fake treatment (placebo). 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 and long-term side effects and safety. They involve many patients with different types of cancer.
Questions about treatment to ask your doctor

- What are my treatment options?
- Will I have more than one treatment?
- What are the risks and benefits of each treatment for CML?
- Will my age, general health, phase of CML, and other medical conditions limit my treatment choices?
- Do I have to get treated?
- Where will I be treated? Will I have to stay in the hospital or can I go home after each treatment?
- What can I do to prepare for treatment? Should I stop taking my medications? Should I store my blood in case I need a transfusion?
- How soon should I start treatment? How long does treatment take?
- How much will the treatment cost? How can I find out how much my insurance company will cover?
- How likely is it that I'll be cancer-free after treatment?
- What symptoms should I look out for while being treated for CML?
- When will I be able to return to my normal activities?
- What is the chance that the cancer will come back and/or spread?
- What should I do after I finish treatment?
- Are there supportive services that I can get involved in? Support groups?
Questions about *stem cell transplants* to ask your doctor

- Am I a candidate for an allogeneic stem cell transplant? If so, how should my family members be tested to see if their bone marrow matches mine?

- When should an allogeneic stem cell transplant be considered?

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

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

- Will I receive other treatments, such as targeted therapy or chemotherapy, along with the stem cell transplant? If so, will I receive the other treatments before the transplant, afterward, or both?
4.6 Tools

**Webpages**

**American Cancer Society**

**Leukemia and Lymphoma Society**
www.lls.org/#/diseaseinformation/leukemia/chronicmyeloidleukemia/treatment/

**National Cancer Institute**
www.cancer.gov/cancertopics/pdq/treatment/CML/Patient/page4

**National Marrow Donor Program**
www.bethematch.org/For-Patients-and-Families/Learning-about-your-disease/Chronic-myelogenous-leukemia/How-transplant-can-treat-CML/

**NCCN**
www.nccn.org/patients/resources/clinical_trials/default.aspx

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**Review of Part 4**

- Targeted therapy drugs specifically target cancer cells.
- TKIs are targeted drugs that block the signals that cause CML cells to grow out of control.
- 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 throughout the body.
- A stem cell transplant replaces damaged or diseased bone marrow with healthy blood stem cells.
- An allogeneic transplant transfers healthy stem cells from another person, called a donor, to the patient.
- A clinical trial studies a test or treatment to see how safe it is and how well it works.
Part 5 is a guide through treatment for people with chronic myelogenous leukemia. It shows what tests and treatments are recommended under which conditions. This information is taken from the treatment guidelines written by NCCN experts for chronic myelogenous leukemia doctors.

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 in Part 7. More information about the tests and treatments in this guide can be found in Parts 2 through 4.

5.1 – Initial testing
Presents the first set of tests recommended to confirm chronic myelogenous leukemia and plan treatment.

5.2 – Chronic phase primary treatment
Presents the initial treatments recommended for CML in the first phase of progression.

5.3 – Follow-up tests and treatment responses
Presents the tests that are recommended after starting treatment to assess how well treatment is working—called a treatment response. The different types of treatment responses are also presented along with the criteria for each.

5.4 – Chronic phase follow-up treatment
Presents the next set of treatments and tests that are recommended for chronic phase CML based on how well treatment has worked so far.

5.5 – Accelerated and blast phase tests and treatment
Presents the recommended tests and treatments for CML in the advanced phases of progression.

5.6 – Hematopoietic stem cell transplant
Presents the recommendations for treatment with an allogeneic hematopoietic stem cell transplant, which replaces bone marrow with healthy blood stem cells from another person.
5.1 Initial testing

Initial tests to confirm CML

<table>
<thead>
<tr>
<th>Tests</th>
<th>Test results</th>
<th>Next steps</th>
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<tbody>
<tr>
<td>Medical history and physical exam, including spleen size</td>
<td>Negative for Philadelphia chromosome and BCR-ABL gene</td>
<td>Evaluate for other diseases (not CML)</td>
</tr>
<tr>
<td>CBC with differential and platelets</td>
<td>Positive for Philadelphia chromosome or BCR-ABL gene</td>
<td>Discuss treatment options</td>
</tr>
<tr>
<td>Blood chemistry profile</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HLA testing if considering HSCT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone marrow aspiration and biopsy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assesment of cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Percent of blasts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Percent of basophils</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone marrow cytogenetics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FISH (if bone marrow can’t be collected)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>QPCR using the International Scale</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Determine risk score</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Part 5.1 describes the initial tests that are recommended when your doctor thinks you may have CML. These tests help your doctor confirm if you have CML, assess for symptoms, and determine the phase of CML. The three phases of CML are described in Part 3 on page 21.

The medical history and physical exam give your doctor an idea about your general health. During the physical exam, your doctor will feel parts of your body to assess if organs are of normal size. This includes feeling the upper, left part of your belly area underneath your ribs to check if your spleen is enlarged. An enlarged spleen may be a sign of CML.

A CBC with differential will show if blood counts are abnormal. A high white blood cell count and low red blood cell count may be signs of CML. A blood chemistry profile measures chemicals in the blood to assess if organs are working well. HLA testing finds the unique

Definitions:

- See Part 2 on page 11 for more test definitions.

Red blood cell: Blood cell that carries oxygen from the lungs to all body parts

Spleen: Organ to the left of the stomach that helps protect against disease

White blood cell: Cell that helps fight infections

Acronyms:

- CBC = Complete blood count
- FISH = Fluorescence in situ hybridization
- HLA = Human leukocyte antigen
- HSCT = Hematopoietic stem cell transplant
- QPCR = Quantitative reverse transcriptase polymerase chain reaction
5.1 Initial testing

set of proteins on white blood cells that help your body identify its own cells from foreign cells. This test is only needed if your doctor is considering treatment with an allogeneic HSCT (described on page 37).

To confirm if you have CML, a sample of peripheral blood and/or bone marrow must be removed from your body to test for CML cells with a microscope. A biopsy is the removal of tissue from your body for testing. A bone marrow biopsy removes a small piece of solid bone along with the marrow inside the bone. A bone marrow aspiration removes a small amount of liquid marrow from inside the bone.

A number of lab tests will be performed on the bone marrow and peripheral blood samples. Assessment of cells in the marrow sample is important because CML may cause increased numbers of blasts (immature blood cells) and basophils (a type of white blood cell).

Bone marrow cytogenetics is used to detect the Philadelphia chromosome and measure the number of cells that have it. It involves examining the bone marrow sample with a microscope to look for changes in the cells’ chromosomes. This is the preferred test for confirming CML. However, sometimes a bone marrow sample can’t be collected. In this case, FISH analysis of a peripheral blood sample may be used to detect the Philadelphia chromosome and the BCR-ABL gene. QPCR is a very sensitive test that detects the BCR-ABL gene and measures the number of cells that have it. QPCR should be done at a lab that uses the International Scale, which is described on page 53. This test can be done on a bone marrow or peripheral blood sample.

Risk scores help predict the likely outcome of treatment. They are based on many factors, such as your age and the phase of CML. (See page 25 for details.)

Based on the results of these tests, specifically bone marrow cytogenetics and QPCR, your doctor will confirm if you have CML. A positive test result means that you do have the Philadelphia chromosome or the BCR-ABL gene. A negative test result means that you don’t have them. If you do not have the Philadelphia chromosome or the BCR-ABL gene, then you do not have CML.

5.1 Next steps

For CML in the chronic phase, see Part 5.2 for treatment recommendations. For accelerated phase or blast phase, see Part 5.5 for recommendations.

Acronyms:

- FISH = Fluorescence in situ hybridization
- HSCT = Hematopoietic stem cell transplant
- mg = Milligrams
- QPCR = Quantitative reverse transcriptase polymerase chain reaction
- TKI = Tyrosine kinase inhibitor
5.2 Chronic phase primary treatment

Chronic phase primary treatment

<table>
<thead>
<tr>
<th>Before treatment</th>
<th>Primary treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment options to discuss with your doctor:</td>
<td>Imatinib 400 mg once daily,</td>
</tr>
<tr>
<td>• TKI therapy</td>
<td>Nilotinib 300 mg twice daily, or</td>
</tr>
<tr>
<td>• Role of HSCT</td>
<td>Dasatinib 100 mg once daily</td>
</tr>
</tbody>
</table>

Part 5.2 describes the recommended primary treatment for CML in the chronic phase. Primary treatment is the first or main treatment used to rid your body of cancer.

Before beginning treatment for CML, a member of your treatment team will explain the benefits and risks of each treatment option. The main treatment options for CML in the chronic phase include TKI therapy, allogeneic HSCT, and clinical trials. See Part 4 on page 27 for details about each treatment option.

Currently, TKI therapy is the preferred primary treatment option for CML in the chronic phase. TKIs are targeted therapy drugs that block the BCR-ABL protein from sending signals that cause abnormal white blood cells to grow out of control. TKIs are generally very good at controlling CML for long periods of time.

The three TKIs approved for primary treatment of chronic phase CML are imatinib, nilotinib, and dasatinib. Imatinib was the first TKI developed for CML and is therefore called a first-generation TKI. Nilotinib and dasatinib were developed later and are called second-generation TKIs. Each TKI drug works in a slightly different way. (See page 28 for details.)

5.2 Next steps

See Part 5.3 to read about follow-up testing and treatment responses. Then see Part 5.4 for follow-up treatment recommendations.

Definitions:

- **BCR-ABL gene**: Abnormal gene, formed when the BCR and ABL genes join
- **Bone marrow**: Soft tissue in the center of most bones where blood cells are made
- **Chromosome**: Strand of bundles of coded instructions in cells for making and controlling cells
- **Gene**: Set of coded instructions in cells for making and controlling cells
- **Microscope**: Tool that uses lenses to see things the eyes can’t
- **Peripheral blood**: Blood outside of the bone
- **Philadelphia chromosome**: A shorter chromosome 22 that is formed when parts of chromosome 9 and 22 switch with each other
### 5.3 Follow-up tests and treatment responses

#### 5.3.1 Treatment response and relapse criteria

<table>
<thead>
<tr>
<th></th>
<th>Hematologic response</th>
<th>Cytogenetic response</th>
<th>Molecular response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete</td>
<td>Peripheral blood counts completely returned to normal; platelet count is normal; no blasts or other immature cells in peripheral blood; and no signs or symptoms of disease, including no enlarged spleen</td>
<td>No Philadelphia chromosomes are detected with bone marrow cytogenetics</td>
<td>No (BCR-ABL) copies are detectable by QPCR using the International Scale</td>
</tr>
<tr>
<td>Partial</td>
<td>1% to 35% of cells have the Philadelphia chromosome on bone marrow cytogenetics</td>
<td>0% to 35% of cells have the Philadelphia chromosome on bone marrow cytogenetics (complete + partial response)</td>
<td>At least a 3-log reduction in (BCR-ABL) levels, or (BCR-ABL) 0.1%, found by QPCR using the International Scale</td>
</tr>
<tr>
<td>Major</td>
<td>0% to 35% of cells have the Philadelphia chromosome on bone marrow cytogenetics</td>
<td>More than 35% of cells have the Philadelphia chromosome on bone marrow cytogenetics</td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>– –</td>
<td>– –</td>
<td>– –</td>
</tr>
</tbody>
</table>

**Part 5.3 describes the tests, criteria, and milestones doctors use to assess how well treatment is working. A treatment response is an outcome or improvement related to treatment. The return or worsening of cancer after a period of improvement is called a relapse or loss of response. Many of the tests used to diagnose CML are repeated during treatment to monitor the treatment response. The types of treatment response and relapse for CML, listed in the chart above, are described next.**

**Hematologic response**

A CBC with differential is used to check for a hematologic response—when peripheral blood counts begin to go back down to a normal level. A CHR (complete hematologic response) is when the peripheral blood counts have completely returned to normal and all signs and symptoms of CML have disappeared.
5.3 Follow-up tests and treatment responses

Cytogenetic response

Bone marrow cytogenetics is used to check for a cytogenetic response—a decrease in the number of cells that have the Philadelphia chromosome. A CCyR (complete cytogenetic response) is when no Philadelphia chromosomes are detected. A PCyR (partial cytogenetic response) is when the Philadelphia chromosome is found in 1 to 35 cells out of 100. An MCyR (major cytogenetic response) is when the Philadelphia chromosome is found in 0 to 35 cells out of 100. A minor cytogenetic response is when the Philadelphia chromosome is found in more than 35 cells out of 100.

Molecular response

QPCR is used to check for a molecular response—a decrease in the number of cells that have the BCR-ABL gene. This test should be done at a lab that uses the International Scale, which is described on page 53. An MMR (major molecular response) is when you have at least a 3-log reduction in BCR-ABL levels from the standardized baseline using the International Scale. A CMR (complete molecular response) is when no BCR-ABL copies are detectable by QPCR using the International Scale with a sensitivity of at least 4.5 logs below the standardized baseline.

Relapse

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

5.3.2 Recommended follow-up testing schedule for TKI therapy

<table>
<thead>
<tr>
<th>Test</th>
<th>When test is recommended</th>
</tr>
</thead>
</table>
| Bone marrow cytogenetics      | • 3 months after starting treatment if QPCR using the International Scale is not available to assess treatment response  
                               | • 12 months after starting treatment if you haven’t had either a complete cytogenetic response or a major molecular response  
                               | • 18 months after starting treatment if you haven’t had either a major molecular response or a complete cytogenetic response so far  
                               | • If BCR-ABL levels increase by 1 log without a major molecular response  
                               | • At any scheduled follow-up after starting treatment if QPCR using the International Scale is not available to assess treatment response |
| QPCR using the International Scale | • Every 3 months when you are responding to treatment  
                               | • After a complete cytogenetic response has been achieved, every 3 months for 3 years, then every 3 to 6 months  
                               | • Repeat in 1 to 3 months if BCR-ABL levels increase by 1 log with a major molecular response |
| BCR-ABL gene mutation analysis | Chronic phase:  
                               | • If initial response is below goal—didn’t have either a partial cytogenetic response or BCR-ABL ≤10% (using International Scale) at 3 months, or  
                               | didn’t have a complete cytogenetic response at 12 and 18 months  
                               | • If there’s any sign of loss of response (hematologic or cytogenetic relapse), or a 1-log increase in BCR-ABL levels with loss of major molecular response  
                               | • If disease progresses to accelerated phase or blast phase |

The chart above describes the recommended schedule of follow-up tests after beginning TKI therapy. These tests are used to check how well TKI therapy is working or to assess why it isn’t working. A treatment response is an outcome or improvement related to treatment. Which tests are recommended at each follow-up visit depends on your treatment response so far. This includes whether or not you’ve reached the response goal or milestone for a particular follow-up period. (See page 48 for definitions of each type of treatment response.)
5.3 Follow-up tests and treatment responses

The goal of TKI therapy is to achieve a complete cytogenetic response within 12 months of beginning treatment, to eventually achieve a major molecular response, and to prevent disease progression to accelerated phase or blast phase. Most patients on TKI therapy will have a complete hematologic response within 3 months of beginning treatment, and will have a complete cytogenetic response within 6, 12, or 18 months of beginning treatment. Then, BCR-ABL levels usually fall slowly after a complete cytogenetic response is achieved. Absence of a major molecular response in the presence of a complete cytogenetic response is not considered a treatment failure. Loss of a major molecular response is a reason for close, frequent monitoring, but alone should not prompt a treatment change.

Bone marrow cytogenetics detects and measures the number of cells in a sample of bone marrow that have the Philadelphia chromosome. This test is recommended at the 3-month follow-up if QPCR using the International Scale isn’t available. It is recommended at the 12-month follow-up if you haven’t had at least one of the following so far: a complete cytogenetic response (no Philadelphia chromosomes detected) or a major molecular response (at least a 3-log reduction in BCR-ABL levels from the standardized baseline). Bone marrow cytogenetics is recommended at the 18-month follow-up if you haven’t had either a major molecular response or a complete cytogenetic response at any follow-up point so far. This test is also recommended any time QPCR using the International Scale shows a 1-log increase in BCR-ABL levels without a major molecular response—whether you previously had a major molecular response and lost it or never had it at all. (Read page 53 for details on the International Scale.) Bone marrow cytogenetics is the recommended alternative option at any scheduled follow-up if QPCR using the International Scale is not available.

QPCR using the International Scale is a very sensitive test that measures the number of cells that have the BCR-ABL gene. This test is recommended every 3 months as long as the CML is still responding to treatment. Once no copies of the Philadelphia chromosome are detected on bone marrow cytogenetics, QPCR is recommended every 3 months for 3 years. After 3 years, the test can be done every 3

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**Definitions:**

- **BCR-ABL gene:** Abnormal set of instructions in cells, formed when the BCR and ABL genes join (fuse) on the Philadelphia chromosome.
- **Bone marrow:** Soft tissue in the center of most bones where blood cells are made.
- **Chromosome:** Strand of bundled instructions in cells to make and control cells.
- **Standardized baseline:** A standardized starting point for measuring changes in the number of cells that have the BCR-ABL gene.

**Acronyms:**

- **QPCR** = Quantitative reverse transcriptase polymerase chain reaction.
- **TKI** = Tyrosine kinase inhibitor.
Follow-up tests and treatment responses

5.3 Follow-up tests and treatment responses

to 6 months. If \( BCR-ABL \) levels increase by 1 log with a major molecular response—meaning response is maintained despite the log increase—then QPCR should be repeated in 1 to 3 months. (See page 53 for details on the International Scale.)

**BCR-ABL gene mutation analysis** is a test that checks for changes (mutations) in the \( BCR-ABL \) gene, which change the shape of the \( BCR-ABL \) protein and can affect how well certain TKIs work. This test is recommended if your initial treatment response is less than the response goal or milestone for a particular follow-up period. The treatment response milestone at the 3-month follow-up is to have a partial cytogenetic response (1 to 35 out of 100 cells have the Philadelphia chromosome) or \( BCR-ABL \leq 10\% \) (no more than 10 out of 100 cells have the \( BCR-ABL \) gene) by QPCR using the International Scale. The response milestone for the 12- and 18-month follow-ups is to have a complete cytogenetic response (no copies of the Philadelphia chromosome detected by bone marrow cytogenetics).

\( BCR-ABL \) mutation analysis is also recommended any time there are signs of a loss of treatment response such as a hematologic or cytogenetic relapse. A hematologic relapse—loss of complete hematologic response—is when blood counts are increasing and are no longer normal. A cytogenetic relapse—loss of complete cytogenetic response—is when tests detect an increasing number of cells with the Philadelphia chromosome. This test is also recommended if there’s a 1-log increase in \( BCR-ABL \) levels with loss of major molecular response—\( BCR-ABL \) levels are no longer 3 logs below the standardized baseline. \( BCR-ABL \) mutation analysis is also recommended if the CML progresses to accelerated phase or blast phase.

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**5.3 Next steps**

For chronic phase CML, see Part 5.4 for follow-up recommendations. For accelerated or blast phase CML, see Part 5.5.

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**Definitions:**

- **BCR-ABL gene**: Abnormal set of instructions in cells, formed when the \( BCR \) and \( ABL \) genes join (fuse) on the Philadelphia chromosome
- **BCR-ABL protein**: Protein that causes too many white blood cells to be made
- **Philadelphia chromosome**: A shorter chromosome 22 that is formed when parts of chromosome 9 and 22 switch with each other
- **Treatment response**: An outcome or improvement related to treatment

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**Acronyms:**

- **QPCR** = Quantitative reverse transcriptase polymerase chain reaction
- **TKI** = Tyrosine kinase inhibitor
5.3 Follow-up tests and treatment responses

QPCR using the International Scale

The International Scale is a standardized scale for measuring and reporting QPCR test results using a standardized baseline level of BCR-ABL. A baseline is an initial or starting point measurement to which future test results are compared.

QPCR test results from different labs are converted to the International Scale so that all test results are consistent and can be compared between labs. The International Scale defines the standardized baseline as BCR-ABL 100%. This means that 100 out of 100 cells have the BCR-ABL gene. Changes in BCR-ABL levels are measured in logs, and the remaining number of cells with the BCR-ABL gene is measured as a percentage.

A log reduction means the BCR-ABL level has decreased by a certain amount from the standardized baseline.

1-log reduction:
BCR-ABL levels decreased to 10 times below the standardized baseline. This is also written as BCR-ABL 10%, which means that 10% of cells—10 out of 100 cells—have the BCR-ABL gene. This correlates with a major cytogenetic response.

2-log reduction:
BCR-ABL levels decreased to 100 times below the standardized baseline. This is also written as BCR-ABL 1%, which means that 1% of cells—1 out of 100 cells—have the BCR-ABL gene. This correlates with a complete cytogenetic response.

3-log reduction:
BCR-ABL levels decreased to 1,000 times below the standardized baseline. This is also written as BCR-ABL 0.1%, which means that 0.1% of cells—1 out of 1,000 cells—have the BCR-ABL gene. A 3-log reduction or greater is considered a major molecular response.

Results of QPCR using the International Scale may also be written as a percentage ratio of the number of cells that have the BCR-ABL gene compared to the number of cells that have the ABL gene. In this case, a 1-log reduction is written as BCR-ABL/ABL 10%.
5.3 Follow-up tests and treatment responses

TKI adherence

Medication adherence—in this case, TKI adherence—is the extent to which you take your TKI as prescribed and recommended by your doctor. Good adherence means that you consistently follow all of your doctor’s recommendations. This includes taking the right number of pills, at the right time, on the right day, every day. Not taking your TKI as prescribed, such as missing a dose, is considered nonadherence or poor adherence.

TKI adherence is very important and has a direct impact on the effectiveness of the treatment. This means that you must take your TKI as prescribed in order for the TKI to work as well as possible. A treatment response is an outcome or improvement related to treatment. Studies show that good TKI adherence is associated with achieving and maintaining good treatment responses. Likewise, not taking your TKI as prescribed (nonadherence) can decrease the chances of achieving 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 unless your doctor says to do so or it is part of a clinical trial.

There are many factors that may interfere with taking your TKI as prescribed. You may occasionally miss a dose due to forgetfulness. Or, you may decide to skip a dose to try to lessen the side effects. Regardless of the cause, you shouldn’t keep it to yourself. Tell your doctor or nurse right away so they can help you manage or overcome any problems you are having with taking your TKI as prescribed. This is especially important if you are experiencing side effects that make it difficult to take your TKI. These side effects can and should be managed—there are many ways your treatment team can help you.

Definitions:

Clinical trial: Research on a test or treatment to assess its safety or how well it works

Side effect: An unplanned physical or emotional response to treatment

TKI: A type of drug that targets and blocks (inhibits) certain proteins that cause too many white blood cells to be made

Acronyms:

HSCT = Hematopoietic stem cell transplant
mg = Milligrams
QPCR = Quantitative reverse transcriptase polymerase chain reaction
TKI = Tyrosine kinase inhibitor
## 5.4 Chronic phase follow-up treatment

### 5.4.1 Chronic phase 3-month follow-up treatment

<table>
<thead>
<tr>
<th>Test results</th>
<th>Follow-up treatment</th>
</tr>
</thead>
</table>
| *BCR-ABL* ≤10% by QPCR using the International Scale or Partial cytogenetic response on bone marrow cytogenetics | Continue same dose of current TKI treatment—imatinib, nilotinib, or dasatinib  
Monitor with QPCR every 3 months  
*No relapse* → Continue to monitor with QPCR every 3 months  
*Relapse* → *BCR-ABL* gene mutation analysis, and discuss TKI adherence and all of the medications you take |
| *BCR-ABL* >10% by QPCR using the International Scale or Less than a partial cytogenetic response on bone marrow cytogenetics | *BCR-ABL* gene mutation analysis, and discuss TKI adherence and all medications that you take  
If prior imatinib treatment  
Clinical trial,  
Switch to TKI other than imatinib, or  
Increase imatinib dose up to 800 mg as tolerated, if not candidate for other TKI  
Evaluate for HSCT based on response to second-line treatment  
If prior nilotinib or dasatinib treatment  
Clinical trial,  
Continue same dose of nilotinib or dasatinib, or  
Switch to alternate TKI other than imatinib  
Evaluate for HSCT based on response to second-line treatment |

Part 5.4.1 describes the follow-up tests and treatments that are recommended 3 months after starting treatment. Follow-up tests are used to check for a treatment response—an outcome or improvement related to treatment. The results of these tests help your doctor decide which follow-up treatment options are best for you.
5.4 Chronic phase follow-up treatment

Follow-up tests
At your 3-month follow-up visit, QPCR using the International Scale is recommended to assess for a treatment response. This test measures the number of cells that have the \textit{BCR-ABL} gene. (See page 53 for details on the International Scale.) If QPCR using the International Scale isn’t available, then bone marrow cytogenetics is recommended to check for a response. This test measures the number of cells that have the Philadelphia chromosome.

Follow-up treatments
If the test results show \textit{BCR-ABL} \leq 10\% or a partial cytogenetic response, then you will continue your current TKI treatment. \textit{BCR-ABL} \leq 10\% means that no more than 10 out of 100 cells have the \textit{BCR-ABL} gene. A partial cytogenetic response means that 1 to 35 out of 100 cells have the Philadelphia chromosome. TKI therapy should be continued indefinitely or until it stops working. You will also have a QPCR test every 3 months as long as the CML is responding to treatment. Continue recommended follow-up tests according to the schedule on page 50 until your 12-month follow-up visit. If QPCR monitoring tests show a relapse—any sign of loss of treatment response—then your doctor will assess for possible causes.

\textit{BCR-ABL} mutation analysis is recommended to test for changes (mutations) in the \textit{BCR-ABL} gene. These gene mutations change the shape of the \textit{BCR-ABL} protein and can affect how well TKI treatments work. In addition, treatment may not work as well if you don’t take your TKI as prescribed or if you are also taking certain other medications. For more details, read \textit{TKI adherence} on page 54 and \textit{Drug interactions} on page 34.

If test results show \textit{BCR-ABL} > 10\% (more than 10 out of 100 cells have the \textit{BCR-ABL} gene) or less than a partial cytogenetic response (more than 35 out of 100 cells have the Philadelphia chromosome), then your doctor will first assess why treatment isn’t working well. This should include mutation testing and a discussion about TKI adherence and drug interactions as described in the paragraph above. The follow-up treatment options differ slightly depending on whether you were previously treated with imatinib or with a second-generation TKI such as nilotinib or dasatinib. Joining a clinical trial—research on a test or treatment to assess its safety or how well it works—is an option regardless of previous treatment.

If you previously received imatinib, then one option is to switch to a different TKI you haven’t yet received such as dasatinib, nilotinib, or bosutinib. If you aren’t a candidate for other TKI drugs, then another option is to increase
the imatinib dose up to 800 mg unless side effects become too severe. A side effect is an unplanned or unwanted physical or emotional response to treatment. Depending on your response to the second-line treatment, your doctor may then assess if an allogeneic HSCT is a good treatment option for you. Second-line treatment is the next treatment used against a disease after the first treatment fails.

If you previously received nilotinib or dasatinib, one option is to continue treatment with the same dose of your current TKI. Another option is to switch to a different TKI you haven’t received before, other than imatinib. Depending on your response to the second-line treatment, your doctor may then assess if an allogeneic HSCT is a good treatment option for you.

### 5.4.1 Next steps

If you had $BCR-ABL \leq 10\%$ or had a partial cytogenetic response, see Part 5.4.3 for 12-month follow-up recommendations. If you had $BCR-ABL > 10\%$ or had less than a partial cytogenetic response and are on TKI therapy, see Part 5.4.2 for 6-month follow-up recommendations. If you will receive an allogeneic HSCT, see Part 5.6 for recommendations. If the CML progressed to accelerated or blast phase, see Part 5.5 for recommendations.
5.4 Chronic phase follow-up treatment

5.4.2 Chronic phase 6-month follow-up treatment

<table>
<thead>
<tr>
<th>Test results</th>
<th>Follow-up treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCR-ABL ≤10% by QPCR using the International Scale or At least a partial cytogenetic response on bone marrow cytogenetics</td>
<td>Continue same dose of current TKI treatment → Monitor with QPCR every 3 months</td>
</tr>
<tr>
<td>BCR-ABL &gt;10% by QPCR using the International Scale or Less than partial cytogenetic response on bone marrow cytogenetics</td>
<td>BCR-ABL gene mutation analysis, and discuss TKI adherence and all the medications you currently take → Clinical trial, or Switch to alternate TKI therapy other than imatinib + Evaluate for HSCT based on response to second-line therapy</td>
</tr>
</tbody>
</table>

These 6-month follow-up recommendations are only for patients who, at the 3-month follow-up, had BCR-ABL >10% or had less than a partial cytogenetic response.

Part 5.4.2 describes the 6-month follow-up tests and treatments that are recommended only if your 3-month follow-up showed BCR-ABL >10% or showed less than a partial cytogenetic response. If you had BCR-ABL <10% or at least a partial cytogenetic response, see Part 5.4.3.

Follow-up tests

The results of these follow-up tests help your doctor decide which follow-up treatment options are best for you. At the 6-month follow-up visit, QPCR using the International Scale is recommended to assess for a **treatment response**. This test measures the number of cells that have the BCR-ABL gene. (See page 53 for details on the International Scale.) If QPCR using the International Scale isn’t available, then bone marrow cytogenetics is recommended. This test measures the number of cells that have the Philadelphia chromosome.

Follow-up treatments

If 6-month follow-up tests show BCR-ABL ≤10% or at least a partial cytogenetic response, then you will continue your current TKI treatment. BCR-ABL ≤10%
5.4 Chronic phase follow-up treatment

means that no more than 10 out of 100 cells have the BCR-ABL gene. A partial cytogenetic response means that 1 to 35 out of 100 cells have the Philadelphia chromosome. TKI therapy should be continued indefinitely or until it stops working. You will also have a QPCR test every 3 months as long as the CML is responding to treatment. Follow the test schedule on page 50 until your 12-month follow-up visit.

If 6-month follow-up tests show BCR-ABL >10% (more than 10 out of 100 cells have the BCR-ABL gene) or show less than a partial cytogenetic response (more than 35 out of 100 cells have the Philadelphia chromosome), then your doctor will assess why treatment isn’t working very well. Treatment may not work as well if you don’t take your TKI as prescribed or if you are also taking certain other medications. (For details, read TKI adherence on page 54 and Drug interactions on page 34.) Your doctor may want to check for changes (mutations) in the BCR-ABL gene, which change the shape of the BCR-ABL protein and can affect how well TKI treatments work. This type of test is called BCR-ABL mutation analysis.

Based on the results of these tests and discussions with your doctor, you have a few follow-up treatment options. One option is to join a clinical trial—a type of research that studies the safety and effectiveness of a test or treatment. Another option is to switch to a TKI you haven’t received before, other than imatinib, such as dasatinib, nilotinib, or bosutinib. If you experience resistance or intolerance with 2 or more TKIs, then the chemotherapy drug omacetaxine is an option. Based on your response to the second-line treatment, your doctor may assess if an allogeneic HSCT is a good option for you.

5.4.2 Next steps

If you are on TKI therapy or another drug for chronic phase CML, see Part 5.4.3 for 12-month follow-up recommendations. If you will receive an allogeneic HSCT, see Part 5.6 for recommendations. If the CML progressed to accelerated or blast phase, see Part 5.5 for recommendations.

Definitions:

Allogeneic HSCT: A treatment that transfers blood-forming cells from a person to the patient

Intolerance: When a drug treatment must be stopped due to severe side effects

Resistance: When cancer does not respond to treatment

Second-line treatment: The next treatment used against a disease when the first treatment fails

TKI: A type of drug that targets and blocks (inhibits) certain proteins that cause too many white blood cells to be made

Treatment response: An outcome or improvement related to treatment

See pages 15–18 for test details and page 27 for treatments.
### 5.4 Chronic phase follow-up treatment

#### 5.4.3 Chronic phase 12-month follow-up treatment

<table>
<thead>
<tr>
<th>Test results</th>
<th>Follow-up treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complete cytogenetic response</strong></td>
<td>Continue same dose of current TKI treatment → Monitor with QPCR every 3 months</td>
</tr>
<tr>
<td><strong>Partial cytogenetic response</strong></td>
<td>• Possible ( BCR-ABL ) gene mutation analysis, and</td>
</tr>
<tr>
<td></td>
<td>• Talk to your doctor about:</td>
</tr>
<tr>
<td></td>
<td>– Taking your TKI as prescribed</td>
</tr>
<tr>
<td></td>
<td>– All the medications you take</td>
</tr>
<tr>
<td></td>
<td>Switch to alternate TKI therapy other than imatinib (preferred),</td>
</tr>
<tr>
<td></td>
<td>Continue same dose of TKI, or</td>
</tr>
<tr>
<td></td>
<td>Increase imatinib dose up to 800 mg unless severe side effects appear*</td>
</tr>
<tr>
<td><strong>Minor or no cytogenetic response</strong></td>
<td>Switch to alternate TKI therapy other than imatinib (preferred)</td>
</tr>
<tr>
<td></td>
<td>Evaluate for HSCT based on response to second-line treatment, or</td>
</tr>
<tr>
<td></td>
<td>Clinical trial</td>
</tr>
<tr>
<td><strong>Cytogenetic relapse</strong></td>
<td>Switch to alternate TKI therapy other than imatinib (preferred), or</td>
</tr>
<tr>
<td></td>
<td>Increase imatinib dose up to 800 mg unless severe side effects appear*</td>
</tr>
<tr>
<td></td>
<td>Evaluate for HSCT based on response to second-line treatment, or</td>
</tr>
<tr>
<td></td>
<td>Clinical trial</td>
</tr>
</tbody>
</table>

*If not candidate for alternate TKI or omacetaxine.*
5.4 Chronic phase follow-up treatment

Part 5.4.3 describes the follow-up tests and treatments that are recommended 12 months after the start of treatment. These follow-up recommendations are based on how well treatment has worked so far. Follow-up tests are used to monitor the treatment response—an outcome or improvement related to treatment—and to assess why treatment may not be working well.

Follow-up tests
At your 12-month follow-up, QPCR using the International Scale is recommended to assess for a treatment response. QPCR measures the number cells that have the BCR-ABL gene. If QPCR using the International Scale is not available, then bone marrow cytogenetics is recommended. This test measures the number of cells that have the Philadelphia chromosome. Bone marrow cytogenetics is also recommended if you haven’t had either a major molecular response or a complete cytogenetic response so far. (Read page 48 for definitions of each type of treatment response.)

Follow-up treatments
Based on the results of these tests, you have several follow-up treatment options. If tests show a complete cytogenetic response, then you will continue your current TKI treatment. A complete cytogenetic response—no Philadelphia chromosomes detected on bone marrow cytogenetics—correlates with a 2-log reduction in BCR-ABL levels found by QPCR using the International Scale. TKI therapy should be continued indefinitely or until it stops working. You will also have a QPCR test every 3 months as long as the CML is responding to treatment. Follow the test schedule on page 50 until your 18-month follow-up visit.

If tests show less than a complete cytogenetic response (cells with the Philadelphia chromosome are detected on bone marrow cytogenetics), then your doctor will first assess why treatment isn’t working very well. Treatment may not work as well if you don’t take your TKI as prescribed or if you are also taking

Definitions:

See pages 15–18 for test details and page 53 for QPCR using the International Scale.

BCR-ABL gene: Abnormal set of instructions in cells, formed when the BCR and ABL genes join (fuse) on the Philadelphia chromosome

Philadelphia chromosome: A shorter chromosome 22 that is formed when parts of chromosome 9 and 22 switch with each other

TKI: A type of drug that targets and blocks (inhibits) certain proteins that cause too many white blood cells to be made

Acronyms:

QPCR = Quantitative reverse transcriptase polymerase chain reaction

TKI = Tyrosine kinase inhibitor

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5.4 Chronic phase follow-up treatment

certain other medications. (See page 54 for details on TKI adherence and page 34 for details on drug interactions.) Your doctor may want to check for changes (mutations) on the BCR-ABL gene, which can change the shape of the BCR-ABL protein and affect how well TKI treatments work. This type of test is called BCR-ABL mutation analysis and is described on page 18.

If tests show a partial cytogenetic response (1 to 35 out of 100 cells have the Philadelphia chromosome), then you have 3 treatment options. The preferred option is to switch to a different TKI, other than imatinib, that you haven’t received before. Another option is to continue the same dose of your current TKI therapy. TKI therapy should be continued indefinitely or until it stops working. If you experience resistance or intolerance with 2 or more TKIs, then the chemotherapy drug omacetaxine is an option. Resistance is when CML doesn’t respond to a treatment. The types of resistance are described on page 34. Intolerance is when treatment with a drug must be stopped due to severe side effects. If you are not a candidate for treatment with other TKIs or omacetaxine, then another option is to increase the imatinib dose up to 800 mg unless the side effects are too severe.

If tests show a minor cytogenetic response (more than 35 out of 100 cells have the Philadelphia chromosome) or no cytogenetic response (no decrease in the number of cells with the Philadelphia chromosome), then you have 3 treatment options. The preferred option is to switch to a different TKI, other than imatinib, that you haven’t received before. If you experience resistance or intolerance with 2 or more TKIs, then omacetaxine is an option. Based on your response to the second-line treatment, your doctor may assess if an allogeneic HSCT is a good treatment option for you. Another option is to join a clinical trial—a type of research that studies the safety and effectiveness of a test or treatment.

If you had a cytogenetic relapse (loss of complete cytogenetic response due to an increase in the number of cells with the Philadelphia chromosome), then you have 4 treatment options. The preferred option is to switch to a different TKI, other than imatinib, that you haven’t received before. If you experience resistance or intolerance with 2 or more TKIs, then omacetaxine is an option. If you are not a candidate for treatment with other TKIs or omacetaxine, then another option is to increase the imatinib dose up to 800 mg unless the side effects are too severe. Based on your response to the second-line treatment, your doctor may assess if an allogeneic HSCT is a good treatment option for you. Another option is to join a clinical trial—a type of research that studies the safety and effectiveness of a test or treatment.

5.4.3 Next steps

If you are on TKI therapy or another drug for chronic phase CML, see Part 5.4.4 for 18-month follow-up recommendations. If you will receive an allogeneic HSCT, see Part 5.6 for recommendations. If the CML progressed to accelerated or blast phase, see Part 5.5.
5.4 Chronic phase follow-up treatment

5.4.4 Chronic phase 18-month follow-up treatment

<table>
<thead>
<tr>
<th>Test results</th>
<th>Follow-up treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete cytogenetic response</td>
<td>Continue same dose of current TKI treatment</td>
</tr>
<tr>
<td></td>
<td>Monitor with QPCR every 3 months</td>
</tr>
<tr>
<td>Partial cytogenetic response</td>
<td>Switch to alternate TKI therapy other than imatinib (preferred)</td>
</tr>
<tr>
<td>or Cytogenetic relapse</td>
<td>Evaluate for HSCT based on response to second-line treatment, or Clinical trial</td>
</tr>
</tbody>
</table>

Part 5.4.4 describes the follow-up tests and treatments that are recommended 18 months after the start of treatment. These recommendations are based on how well treatment has worked so far. Follow-up tests are used to monitor the treatment response—an outcome or improvement related to treatment—and to assess why treatment may not be working well.

Follow-up tests

At your 18-month follow-up visit, QPCR is recommended to assess for a treatment response. QPCR measures the number of cells that have the BCR-ABL gene. (See page 53 for details on QPCR using the International Scale.) If QPCR using the International Scale isn’t available, then bone marrow cytogenetics is the recommended alternative. This test measures the number of cells that have the Philadelphia chromosome. Bone marrow cytogenetics is also recommended if you haven’t had either a major molecular response or a complete cytogenetic response so far. Read page 48 for definitions of the types of treatment responses.

Definitions:

- **Adherence:** Extent that you take your TKI as directed by your doctor
- **Chemotherapy:** Drugs that kill fast-growing cells throughout the body
- **Second-line treatment:** Next treatment used when the first treatment fails
- **Side effect:** An unplanned physical or emotional response to treatment

Acronyms:

- **HSCT** = Hematopoietic stem cell transplant
- **mg** = Milligrams
- **QPCR** = Quantitative reverse transcriptase polymerase chain reaction
- **TKI** = Tyrosine kinase inhibitor
5.4 Chronic phase follow-up treatment

Follow-up treatment

Based on the results of the 18-month follow-up tests, you have several follow-up treatment options. If tests show a complete cytogenetic response, then you will continue your current TKI treatment. A complete cytogenetic response—no Philadelphia chromosomes detected on bone marrow cytogenetics—correlates with a 2-log reduction in BCR-ABL levels found by QPCR using the International Scale. (See page 53 for details on the International Scale.) TKI therapy should be continued indefinitely or until it stops working. You will also have a QPCR test every 3 months as long as the CML is responding to treatment. Read page 50 for the full schedule of recommended follow-up testing.

If tests show less than a complete cytogenetic response (cells with the Philadelphia chromosome are detected on bone marrow cytogenetics), then your doctor will first assess why treatment isn’t working very well. Treatment may not work as well if you don’t take your TKI as prescribed or if you are also taking certain other medications. Adherence is the extent to which you take your TKI as prescribed and directed by your doctor. For details, read TKI adherence on page 54 and Drug interactions on page 34. Your doctor may also want to check for changes (mutations) on the BCR-ABL gene, which change the shape of the BCR-ABL protein and can affect how well TKI treatments work. This type of test is called BCR-ABL mutation analysis.

If you had a partial cytogenetic response (1 to 35 cells out of 100 have the Philadelphia chromosome) or a cytogenetic relapse (loss of complete cytogenetic response due to an increase in the number of cells with the Philadelphia chromosome), then you have a few follow-up treatment options. The preferred treatment option is to switch to a different TKI therapy, other than imatinib, that you haven’t received before. If you experience resistance or intolerance with 2 or more TKIs, then omacetaxine is an option. Resistance is when CML doesn’t respond to a drug. The types of TKI resistance are described on page 34. Intolerance is when treatment with a drug must be stopped due to severe side effects. Based on your response to second-line treatment, your doctor may then assess if an allogeneic HSCT is a good treatment option for you. Another option is to receive treatment within a clinical trial—a type of research that studies the safety or effectiveness of a test or treatment.

5.4.4 Next steps

If you will receive an allogeneic HSCT, see Part 5.6 for recommendations. If the CML progressed to accelerated or blast phase, see Part 5.5 for recommendations.
5.5 Accelerated and blast phase tests and treatment

### 5.5.1 Accelerated and blast phase tests

<table>
<thead>
<tr>
<th>Phase</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Accelerated phase</td>
<td>• Bone marrow cytogenetics</td>
</tr>
<tr>
<td></td>
<td>• Flow cytometry</td>
</tr>
<tr>
<td></td>
<td>• BCR-ABL gene mutation analysis if received prior TKI therapy</td>
</tr>
<tr>
<td>Blast phase</td>
<td>• Bone marrow cytogenetics</td>
</tr>
<tr>
<td></td>
<td>• Flow cytometry</td>
</tr>
<tr>
<td></td>
<td>• Cytochemistry if available</td>
</tr>
<tr>
<td></td>
<td>‣ Myeloperoxidase and TdT</td>
</tr>
<tr>
<td></td>
<td>• BCR-ABL gene mutation analysis if received prior TKI therapy</td>
</tr>
</tbody>
</table>

Part 5.5.1 describes the recommended tests for CML in advanced phases—accelerated phase and blast phase. These phases of CML are characterized by higher numbers of immature white blood cells, called blasts, in the peripheral blood and bone marrow.

The recommended initial tests will help your doctor confirm the phase of CML and plan the best treatment for you. The CML phase is a rating or description of the progression of CML in your body. Many of the same tests are recommended for both accelerated phase and blast phase. Bone marrow cytogenetics is used to detect the Philadelphia chromosome and measure the number of cells that have it. This test involves examining the bone marrow sample with a microscope to look for changes in the cells’ chromosomes. Chromosomes are long strands that contain bundles of coded instructions in cells for making and controlling cells. Read more about this test on page 17.

Flow cytometry is a test that looks at substances on the surface of cells to identify the specific type of cells present. It is used to determine if the leukemia

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**Definitions:**

- **BCR-ABL protein:** Abnormal protein that causes too many white blood cells to be made
- **Bone marrow:** Soft tissue inside most bones where blood cells are made
- **Peripheral blood:** Blood outside of the bone
- **Second-line treatment:** The next treatment used against a disease when the first treatment fails

**Acronyms:**

- **HSCT =** Hematopoietic stem cell transplant
- **QPCR =** Quantitative reverse transcriptase polymerase chain reaction
- **TKI =** Tyrosine kinase inhibitor
cells are mostly myeloid or lymphoid cells. Cytochemistry is a test that uses chemical dyes to determine if the leukemia cells are mostly myeloid or lymphoid cells. The chemical dyes cause a color change in one type of leukemia cell and not another. Myeloperoxidase is a chemical found in myeloid cells but not in lymphoid cells. TdT is a chemical found in lymphoid cells but not in myeloid cells. Cytochemistry is only recommended for CML in blast phase.

If the CML progressed during prior treatment with a TKI, then your doctor will want to test for changes (mutations) on the BCR-ABL gene. This is called BCR-ABL mutation analysis. Mutation analysis is important because BCR-ABL gene mutations can affect how and which TKI drugs can bind to the BCR-ABL protein to stop leukemia cells from growing out of control. Read page 18 for more details about BCR-ABL mutation analysis.

5.5.1 Next steps

For CML in accelerated phase, see Part 5.5.2 for recommended treatments. For CML in blast phase, see Part 5.5.3 for recommended treatments.
5.5 Accelerated and blast phase tests and treatment

5.5.2 Accelerated phase treatment

<table>
<thead>
<tr>
<th>Initial treatment</th>
<th>Relapse treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical trial, or TKI therapy:</td>
<td>Clinical trial</td>
</tr>
<tr>
<td>Imatinib 600 mg once daily,</td>
<td></td>
</tr>
<tr>
<td>Dasatinib 140 mg once daily,</td>
<td></td>
</tr>
<tr>
<td>Nilotinib 400 mg twice daily,</td>
<td></td>
</tr>
<tr>
<td>Bosutinib 500 mg once daily,</td>
<td></td>
</tr>
<tr>
<td>Omacetaxine</td>
<td></td>
</tr>
<tr>
<td>Consider HSCT based on response to TKI therapy</td>
<td></td>
</tr>
</tbody>
</table>

It is strongly recommended that these patients are treated in specialized centers.

Part 5.5.2 describes the recommended treatments for CML in accelerated phase. In this phase, there are more blast cells in the blood and/or bone marrow and symptoms may be more severe. Your doctor will use the results of the tests described in Part 5.5.1 to decide which treatment option is best for you.

You have two main treatment options to choose from. One option is to join a clinical trial—a type of research that studies the safety and effectiveness of a test or treatment. The other treatment option is to begin TKI therapy. Which TKI is best for you depends on a number of factors.

If the CML was in accelerated phase when first diagnosed and you haven’t had a TKI before, then imatinib 600 mg once daily is an option. If the CML progressed

Definitions:

- **Blast cell**: Immature blood cell
- **Bone marrow**: Soft tissue in the center of bones where blood cells are made
- **Lymphoid**: Referring to a type of white blood cell called a lymphocyte
- **Myeloid**: Referring to a type of white blood cell called a granulocyte
- **TKI**: Drug that targets and blocks certain proteins that cause too many white blood cells to be made

Acronyms:

- mg = Milligrams
- TdT = Terminal deoxynucleotidyl transferase
- TKI = Tyrosine kinase inhibitor

See pages 15–18 for test details and page 27 for treatments.
from chronic to accelerated phase during prior TKI therapy, then options include a TKI other than imatinib that you haven't received before. These second-line treatment options are listed in the chart on page 67 and include dasatinib, nilotinib, and bosutinib. If you experience resistance or intolerance with two or more TKIs, then the chemotherapy drug omacetaxine is another treatment option. Resistance is when CML doesn't respond to a treatment. The types of TKI resistance are described on page 34. Intolerance is when treatment with a drug must be stopped due to severe side effects—unplanned physical or emotional responses to treatment.

Results of the BCR-ABL gene mutation analysis may help guide TKI therapy selection. This test detects changes (mutations) on the part of the BCR-ABL gene that makes the BCR-ABL protein. These gene mutations change the shape of the BCR-ABL protein and can affect how and which TKI drugs can bind to the BCR-ABL protein to stop leukemia cells from growing out of control.

Based on your response to second-line treatment, your doctor may then assess if an allogeneic HSCT is a good treatment option for you. If follow-up tests show that the CML is not responding to treatment or that it has relapsed, then the next option is a clinical trial. See page 48 to read about the types of treatment response and relapse.
5.5 Accelerated and blast phase tests and treatment

5.5.3 Blast phase treatment

<table>
<thead>
<tr>
<th>Cell type</th>
<th>Initial treatment</th>
<th>Relapse treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoid</td>
<td>Clinical trial, ALL-type induction chemotherapy + TKI followed by HSCT if possible, or TKI followed by HSCT if possible</td>
<td>Clinical trial</td>
</tr>
<tr>
<td>Myeloid</td>
<td>Clinical trial, AML-type induction chemotherapy + TKI followed by HSCT if possible, or TKI followed by HSCT if possible</td>
<td>Clinical trial</td>
</tr>
</tbody>
</table>

It is strongly recommended that these patients are treated in specialized centers.

Part 5.5.3 describes the recommended treatments for CML in blast phase. This phase of CML has the highest number of immature blood cells, called blasts, in the circulating (peripheral) blood and bone marrow. CML in blast phase may cause more severe symptoms and can be life-threatening. Your doctor will use the results of the tests described in Part 5.5.1 to decide which treatment option is best for you.

One important factor your doctor will consider when recommending treatment options is whether or not the leukemia cells are mostly myeloid cells or lymphoid cells. This is because CML in blast phase often acts similar to one of two types of acute leukemia. The first type, called ALL, affects lymphoid cells. The second type, called AML, affects myeloid cells. Because of this similarity, treatments that are used for acute leukemia are sometimes used to treat CML in blast phase.

Definitions:

- **Acute leukemia**: A fast-growing cancer that starts in blood-forming cells in the bone marrow
- **Bone marrow**: Soft tissue in the center of most bones where blood cells are made
- **Lymphoid**: Referring to a type of white blood cell called a lymphocyte
- **Myeloid**: Referring to a type of white blood cell called a granulocyte

Acronyms:

- **ALL** = Acute lymphoblastic leukemia
- **AML** = Acute myeloid leukemia
- **HSCT** = Hematopoietic stem cell transplant
- **TKI** = Tyrosine kinase inhibitor
5.5 Accelerated and blast phase tests and treatment

There are 3 main treatment options for CML in blast phase. The first option for both types of leukemia cells is to join a clinical trial. A clinical trial is a type of research that studies the safety and effectiveness of a test or treatment.

The second option is to receive induction chemotherapy along with a TKI and then, if possible, an allogeneic HSCT. Induction therapy is the first set of treatments given to treat a disease. If the leukemia cells are mostly lymphoid cells, then you will receive ALL-type induction chemotherapy—induction chemotherapy that is used to treat ALL. If the leukemia cells are mostly myeloid cells, then you will receive AML-type induction chemotherapy—induction chemotherapy that is used to treat AML. Which TKI you receive depends on prior TKI therapy and/or results of the BCR-ABL gene mutation analysis. This test detects changes (mutations) on the BCR-ABL gene, which change the shape of the BCR-ABL protein and can affect how well TKI treatments work. (See page 28 to read more about TKI therapy.)

The third option for both types of leukemia cells is to receive TKI therapy and then, if possible, an allogeneic HSCT. Which TKI you receive depends on prior TKI therapy and/or results of the BCR-ABL gene mutation analysis.

If follow-up tests show that the CML has not responded or that it has relapsed, then the next option is to join a clinical trial. Read page 48 for details about each type of treatment response and relapse.

5.5.3 Next steps

If you will receive an allogeneic HSCT, see Part 5.6 for recommendations.

Definitions:

- **Bone marrow**: Soft tissue in the center of most bones where blood cells are made
- **Immune system**: Body's natural defense against infection and disease
- **Chemotherapy**: Drugs that kill fast-growing cells throughout the body
- **Stem cell**: Immature cell from which other types of cells develop

Acronyms:

- **ALL** = Acute lymphoblastic leukemia
- **AML** = Acute myeloid leukemia
- **HSCT** = Hematopoietic stem cell transplant
- **TKI** = Tyrosine kinase inhibitor
### Hematopoietic stem cell transplant

**Allogeneic HSCT**

<table>
<thead>
<tr>
<th>HSCT results</th>
<th>Follow-up tests</th>
<th>Follow-up treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete cytogenetic response</td>
<td>QPCR monitoring of peripheral blood:</td>
<td><strong>Positive</strong> Discourage options with transplant team:</td>
</tr>
<tr>
<td></td>
<td>• Every 3 months for 2 years, then</td>
<td>• Imatinib, dasatinib, nilotinib, bosutinib, or omacetaxine</td>
</tr>
<tr>
<td></td>
<td>• Every 6 months for 3 years</td>
<td>• DLI (donor lymphocyte infusion)</td>
</tr>
<tr>
<td></td>
<td><strong>Negative</strong></td>
<td>• Interferon/PEG-interferon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Clinical trial</td>
</tr>
<tr>
<td>Did not have a complete cytogenetic response, or</td>
<td>Monitored withdrawal of treatments that suppress the</td>
<td><strong>Discuss options with transplant team:</strong></td>
</tr>
<tr>
<td>had a relapse</td>
<td>immune system</td>
<td>• Imatinib, dasatinib, nilotinib, bosutinib, or omacetaxine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• DLI (donor lymphocyte infusion)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Interferon/PEG-interferon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Clinical trial</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Continue scheduled follow-up tests</td>
</tr>
</tbody>
</table>

**Part 5.6 describes the tests and treatments that are recommended after an allogeneic HSCT.** An allogeneic HSCT replaces damaged or diseased bone marrow in your body with healthy stem cells taken from another person. This creates a new immune system for your body.

Follow-up recommendations after an allogeneic HSCT depend on how the CML responded. A treatment response is an outcome or improvement related to treatment. A complete cytogenetic response is when no Philadelphia chromosomes are detected with bone marrow cytogenetics. A relapse is when there are any signs of loss of treatment response. (See page 48 for more details on the types of treatment response and relapse.)
If you had a complete cytogenetic response (no copies of the Philadelphia chromosome detected), then you will begin follow-up testing with QPCR. The chart on page 71 lists the recommended schedule for follow-up QPCR testing. A positive test result means that QPCR detected copies of the \textit{BCR-ABL} gene. A negative test result means that QPCR did not detect any copies of the \textit{BCR-ABL} gene—defined as a complete molecular response. You will continue 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 follow-up QPCR tests are positive, then the next step is to discuss possible follow-up treatment options with the transplant team. One option is TKI therapy with imatinib, dasatinib, nilotinib, or bosutinib. Omacetaxine may be given if you've had resistance or intolerance to two or more TKIs. Resistance is when CML doesn't respond to a drug. The types of TKI resistance are described on page 34. Intolerance is when treatment with a drug must be stopped due to severe side effects—unplanned physical or emotional responses to treatment. Another treatment option is to receive lymphocytes from the same person who donated the blood stem cells for the HSCT. This type of treatment is called a DLI. A third option is to receive immunotherapy with interferon or PEG-interferon. Another 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 the follow-up treatment options are the same as described above. But, you cannot start follow-up treatment right away. The first step is to discontinue 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 and once it’s complete the transplant team will go over your follow-up treatment options.

\textbf{Definitions:}

- **Blood stem cell:** Immature blood-forming cells located in the bone marrow
- **Immune system:** Body's natural defense against infection and disease
- **Immunotherapy:** Treatment with drugs that use the immune system to attack cancer cells
- **Lymphocyte:** A type of white blood cell that fights infections in the body

\textbf{Acronyms:}

- **HSCT** = Hematopoietic stem cell transplant
- **QPCR** = Quantitative reverse transcriptase polymerase chain reaction
- **TKI** = Tyrosine kinase inhibitor

See pages 15–18 for test details and page 27 for treatments.
Part 6: Deciding on a treatment plan

Cancer can be very stressful. While absorbing the fact that you have cancer, you must also learn about tests and treatments. And, the time to decide on a treatment plan may feel short. Parts 1 through 5 aimed to teach you about chronic myelogenous leukemia, its treatment, and other challenges. Part 6 addresses issues related to deciding on a treatment plan.

6.1 – Benefits of a treatment plan
Explains how a treatment plan can help.

6.2 – Parts of a treatment plan
Presents the information found in a treatment plan.

6.3 – Your role in planning
Describes how you can take part in treatment planning.

6.4 – Getting a 2nd opinion
Discusses getting another treatment plan from a different doctor or treatment team.

6.5 – Tools
Lists webpages with helpful information about treatment planning.
6.1 Benefits of 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 is useful for:

- Starting and guiding talks about treatment,
- Teaching what the treatment choices are,
- Informing everyone of the decisions made,
- Reminding everyone of the decisions made,
- Pinpointing who is in charge of each part of care,
- Controlling stress,
- Knowing what to expect,
- Changing from one doctor to another,
- Improving contact among your doctors, and
- Providing care for all issues.
6.1 Benefits of a treatment plan

Becoming a “cancer patient”

Hearing “you have cancer” is likely to be life-changing. Some challenges may include managing doctor visits, figuring out how to care for your kids, missing work, and feeling a loss of control. Some people try to keep their life as normal as they can. Others change their life a lot. However, many cancer survivors will tell you that during the active treatment period, being a patient is your job. It’s a job that requires much time and energy. This can be hard.

Accept the support offered to you and reach out for more help if you need it. Maintain warm relationships with family and friends. Most people would be happy to hear what you need. Make a list for them of things that would help you. If you are a person of faith, your personal beliefs and faith community can help. There are also professionals in mental health, social work, and pastoral services who are able to assist you. You can also start attending support groups to receive help from other cancer survivors.
6.2 Parts of a treatment plan

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 cancer phase. See Part 2 to read about the tests used for CML and Part 3 to read about the phases of CML progression.

Your treatment team
Cancer care is a team effort. Who is on your team depends on the treatments you choose. A hematologist is a doctor who’s an expert in treating 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 for disease. A surgeon is an expert in operations to remove or repair a part of the body. Your primary care doctor can also be part of your team. He or she can help you express your feelings about treatment 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 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. Treatment planning takes into account many factors, such as:

- The CML phase,
- Your general health,
- Treatment side effects,
- Costs of treatment,
- Changes to your life,
- What you want from treatment, and
- Your feelings about side effects.

A guide to treatment options can be found in Part 5. The cancer 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 response. In addition, all known side effects should be listed and the time required to treat them should be noted.
6.2 Parts of a treatment plan

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 or its treatment can cause bothersome symptoms. You may also have symptoms from the stress of having cancer. Such symptoms include pain, sleep loss, anxiety, and depression. Helping you to be comfortable and stay active are key goals of the treatment plan. There are ways to treat many symptoms, so tell your treatment team about any symptoms you have so they can help make sure you receive the supportive care you need. Supportive care treats the symptoms caused by CML and side effects caused by CML treatment.

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. You may feel anxious before testing and while waiting for the results. Likewise, you may have a passing depression during a hard part of treatment. Feeling distressed may be a minor problem or it may be more serious. Serious or not, tell your treatment team so that you can get help if needed. 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.

**Definitions:**

- **Clinical trial:** Research on a test or treatment to assess its safety or how well it works.
- **Phase:** A description or rating of the progression of chronic myelogenous leukemia in the body.
- **Side effect:** An unplanned physical or emotional response to treatment.
- **Treatment response:** An outcome or improvement in disease that is related to treatment.
6.2 Parts of a treatment plan

After cancer treatment, some people dislike their looks because of side effects. Common concerns include hair loss from chemotherapy and scars from surgery. It can be difficult to adapt to these changes. You may be concerned about what your partner thinks. Likewise, your partner may act differently and feel more like a caregiver than a partner during treatment. Sharing what you need and want can help you and your partner.

Financial stress may result from being unemployed or missing 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.

Caring for caregivers

No one experiences cancer alone. Having cancer can affect your loved ones, especially those who provide care. This care can take many forms. It can range from giving emotional support to giving medical services in the home. Caregivers often take on extra duties to keep life normal for the family. They also play a central role in explaining what is happening to you to others, like friends and doctors.

It is natural for caregivers to focus on you. Don’t feel guilty. However, caregivers need to meet their own needs as well. Cancer treatment can last from months to years. Caregivers often get too tired from the physical and mental challenges related to the cancer. It isn’t easy, but caregivers need to take care of themselves. If they don’t, they won’t be able to take good care of anyone.
6.2 Parts of a treatment plan

Survivorship care
Cancer survivorship begins on the day you learn of having CML. For many CML survivors, cancer treatment is an ongoing process. Because TKI therapy only controls the CML and does not cure it, you will need to continue treatment indefinitely. You will also need to continue regular follow-up visits with your cancer care team. Your treatment plan should include a schedule of follow-up cancer 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 TKI therapy or other treatments, if at

Definitions:
Chemotherapy: Drugs that kill fast-growing cells throughout the body, including normal cells and cancer cells
Prognosis: The likely or expected course and outcome of a disease
Side effect: An unplanned physical or emotional response to treatment
TKI therapy: Treatment with drugs that target and block proteins called tyrosine kinases that cause too many white blood cells to be made

Acronyms:
TKI = Tyrosine kinase inhibitor
6.2 Parts of a treatment plan

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.
6.3 Your role in planning

The role patients want in treatment planning differs. Some patients want to be involved as little as possible. Others want to know everything and share decision-making with their doctors. These two roles are described as passive and active. Tell your treatment team which role you want or if you want a role somewhere in the middle.

**Passive role**

In a passive role, a person often doesn’t seek out information, speak up for him/herself, or think through treatment options. 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 also want a passive role because you don’t know much about cancer. You may have never heard the words used to describe CML, tests, or treatments. Likewise, you may think that your judgement isn’t any better than your doctors’.

Letting others decide your treatment may make you feel more at ease. But, whom do you want to make the decisions? 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 decision-making with your doctors. Even if others decide your treatment, you still have to agree to treatment by signing a consent form.

**Active role**

In an active role, a person often searches for all information, prepares for all outcomes, and speaks up for him/herself. He or she may take the lead or share in decision-making. Taking this role may make you feel more certain and hopeful. You’ll likely get the treatment you want, at the place you want, and by the doctors you want.
6.3 Your role in planning

There are four key steps to making a shared treatment decision. First, know what you want from treatment. Do you want a cure or symptom relief? What hardships are you willing to accept to meet your goal? Second, know your test results. This information can pinpoint what's important for you on websites and in books and brochures. It can also clarify which treatments are needed. Third, strive to have helpful talks with your doctor. Prepare questions before your visit and ask questions if your doctor isn't clear. You can also record your talks and get copies of your medical records. Fourth, accept help from others. An active role doesn’t mean going through it alone. Others can help you be active by finding information, taking notes, asking questions, and helping you talk through your options.

6.4 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 further. 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. Chronic myelogenous leukemia is a serious disease, and new information may have been published about which treatments are most effective and safe. 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. There are few cancers that are so aggressive that you can't take a few weeks to get a 2nd opinion and select the best treatment for you.
6.5 Tools

Webpages
American Cancer Society
www.cancer.org/Treatment/FindingandPayingforTreatment/index

National Cancer Institute
www.cancer.gov/cancertopics/factsheet/Therapy/doctor-facility

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

Review of Part 6

- A treatment plan can help you through treatment and beyond.
- It 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.
**Part 7: 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 in the bone marrow (soft tissue in the center of bones where blood cells are made).

**Acute myeloid leukemia (AML)**
A fast-growing cancer that causes too many immature white blood cells called myeloblasts to be made in the bone marrow (the soft tissue in the center of bones where blood cells are made).

**Advance directive**
Written statements about your wishes for health care should you become unable to make these wishes known at a later time.

**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 stem cell transplant (HSCT)**
A treatment in which the patient receives healthy, immature blood-forming cells (blood stem cells) from another person.

**Alternative medicine**
Treatments used in place of ones usually given by doctors.

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

**Anesthesia**
Loss of feeling with or without loss of wakefulness caused by drugs.

**Antibiotic**
A drug used to treat infections caused by bacteria.

**Anti-fungal**
A drug that treats infections caused by fungus.

**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 instructions in cells for making and controlling cells—formed when the BCR gene and the ABL gene join (fuse) together on the Philadelphia chromosome.

**BCR-ABL gene mutation analysis**
A test that looks for abnormal changes in the BCR-ABL gene (set of instructions in cells for making and controlling cells) that affect the BCR-ABL protein.
Part 7: Dictionary

**BCR-ABL protein**
A protein that is made by an abnormal gene (set of instructions in cells for controlling cells) called the *BCR-ABL* gene and that causes too many white blood cells to be made.

**BCR-ABL transcript**
A copy of the abnormal gene (set of instructions in cells for making and controlling cells) called the *BCR-ABL* gene.

**Biopsy**
Removal of small amounts of tissue from the body to be tested for disease.

**Blast cell**
An immature blood cell.

**Blast crisis**
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 phase.

**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.

**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). Also called conventional cytogenetics.

**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 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.

**Blood chemistry profile**
A test to show unusual amounts of chemicals in the blood.

**Blood stem cells**
Immature blood-forming cells located in the bone marrow (the soft, sponge-like tissue in the center of most bones where blood cells are made).

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

**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). Also called conventional cytogenetics.

**Cardiotoxicity**
Having a harmful effect on the heart.

**Cell assessment**
Use of a microscope and special dyes to examine the features—size, shape, type, maturity—of cells in a tissue sample removed from your body.

**Chemotherapy**
Drugs that kill fast-growing cells throughout the body, including normal cells and cancer cells.
Part 7: Dictionary

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

**Chronic leukemia**
A slow-growing type of cancer that starts in blood-forming cells of the bone marrow (the soft, sponge-like tissue in the center of most bones where blood cells are made).

**Chronic myelogenous leukemia**
A slow-growing type of leukemia (cancer that starts in blood-forming tissue called bone marrow) that 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.

**Complementary medicine**
Treatment given along with standard treatment.

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

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

**Complete cytogenetic response (CCyR)**
When tests don’t detect any copies of the Philadelphia chromosome—the abnormal chromosome (strand of bundled instructions in cells for making and controlling cells) that contains the *BCR-ABL* gene.

**Complete hematologic response (CHR)**
When blood cell counts in circulating (peripheral) blood have completely returned to normal—there are no immature cells in peripheral blood and there are no signs or symptoms of disease.

**Complete molecular response (CMR)**
No copies of the abnormal *BCR-ABL* gene are detectable using a very sensitive test.

**Conventional 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). Also called bone marrow cytogenetics.

**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 detect an increase in the number of cells with the Philadelphia chromosome—the abnormal chromosome (strand of bundled instructions for making and controlling cells) that contains the *BCR-ABL* gene—after a period of improvement when no cells with the Philadelphia chromosome were detected.

**Cytogenetic response**
A decrease in the number of cells that have the Philadelphia chromosome—the abnormal strand of bundled genetic information (instructions for controlling cells) that contains the *BCR-ABL* gene.

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

**Cytopenia**
A health condition in which the number of blood cells in general is low.

**Deoxyribonucleic acid (DNA)**
Molecules that contain a cell’s genes (coded instructions for making and controlling cells) and are bundled together into long strands called chromosomes.

**Diagnose**
To identify a disease or health condition.

**Differential**
Measurement of the different types of white blood cells present in a blood sample.

**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 (blood stem 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 intolerance**
When treatment with a drug must be stopped due to its severe side effects.

**Drug resistance**
When cancer does not respond to 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.

**First-line treatment**
The first set of treatments given to treat a disease.

**Flow cytometry**
A test that assesses substances on the outside surface of cells to identify the specific type of cells present.
**Fluorescence in situ hybridization (FISH)**  
A lab test used to assess the genes (coded instructions for controlling cells) and chromosomes (long strands containing bundles of genes) in cells.

**Follow-up test**  
Tests done after the start of treatment to check how well treatment is working or why it isn’t working.

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

**Fusion gene**  
A gene—set of instructions for making and controlling cells—that is made by joining parts of two separate genes.

**Gene**  
A set of coded instructions in cells needed to make new cells and control how cells behave.

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

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

**Graft-versus-tumor (GVT) effect**  
An attack on cancer cells by transplanted stem cells (immature blood-forming cells).

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

**Hematologic relapse**  
Tests detect increasingly abnormal blood cell counts in the circulating (peripheral) blood after a period of improvement when blood cell counts were completely normal.

**Hematologic response**  
The numbers of different blood cells in the circulating (peripheral) blood are returning to a normal level.

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

**Hematopoietic stem cell**  
Immature blood-forming cell located in the bone marrow—the soft, sponge-like tissue in the center of most bones where blood cells are made.

**Hematopoietic stem cell transplant**  
A treatment that replaces damaged or diseased bone marrow—sponge-like tissue in the center of bones where blood cells are made—with healthy blood-forming cells called blood stem cells.

**Hospice**  
Physical and emotional care for people who are close to the end of life.

**Human leukocyte antigen (HLA)**  
Proteins on the edge of white blood cells that help the body to identify its own cells from foreign cells.

**Human leukocyte antigen (HLA) testing**  
A test that helps to identify a person’s unique set of proteins on the edge of white blood cells.
Human leukocyte antigen (HLA) type
The unique set of proteins on the edge of white blood cells that help the body to identify its own cells 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.

Induction chemotherapy
The first set of chemotherapy—drugs that kill fast-growing cells, including cancer cells and normal cells—given to treat cancer.

Induction therapy
The first set of treatments given to treat a disease. Also called first-line treatment or primary treatment.

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

International Scale
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.

Intestines
The organs that food travels through after leaving the stomach.

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

Kidneys
A pair of organs that filter blood and remove waste from the body through urine.

Leukemia
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.

Liver
An organ that removes waste from the blood.

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 blood cell that develops into a mature white blood cell called a lymphocyte.

Lymphocyte
A type of cell that fights infections—called white blood cells.

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.
Part 7: Dictionary

**Major cytogenetic response (MCyR)**
An improvement related to treatment, when tests detect the Philadelphia chromosome in 0 to 35 cells out of 100.

**Major molecular response (MMR)**
An improvement related to treatment, when tests detect a 3-log reduction in $BCR-ABL$ levels—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.

**Medical oncologist**
A doctor who’s an expert in treating cancer with drugs.

**Medication adherence**
The extent to which you take your medication as prescribed and directed by your doctor.

**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.

**Monocyte**
A type of cell that fights infections—called white blood cells.

**Mutation**
An abnormal change in the 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.

**Myeloperoxidase**
A chemical found in a type of white blood cell called a granulocyte or a myeloid cell.

**Myelosuppression**
A condition in which the bone marrow (soft tissue in the center of bones where blood cells are made) is weakened and makes fewer blood cells.

**Neutropenia**
A condition in which the number of white blood cells called neutrophils is low.

**Neutrophil**
A type of white blood cell that helps fight infections and has small particles (granules).
Part 7: Dictionary

Nonadherence
Not taking your medication as prescribed or directed by your doctor.

Pancreas
An organ that makes digestive fluids and chemicals to control blood sugar.

Partial cytogenetic response (PCyR)
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.

Peripheral blood
Blood outside of the bone that circulates throughout the body.

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 chromosome 9 and 22 switch with each other. It is the hallmark of chronic myelogenous leukemia and contains the BCR-ABL gene.

Phosphorus
A substance found in the blood, muscles, nerves, bones, and teeth.

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

Platelets
A type of blood cell that helps control bleeding.

Pleural effusion
Excess fluid between the two layers of tissue lining around the lungs.

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 or 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 a number of different factors.

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

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 detects the BCR-ABL gene and measures the number of cells that have it.
**Part 7: Dictionary**

**Radiation therapy**  
Use of high-energy rays to destroy cancer cells.

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

**Relapse**  
Any sign of loss of treatment response—signs of the return or worsening of cancer after a period of improvement.

**Resistance**  
When cancer does not respond to treatment.

**Risk group**  
Grouping of patients who will likely have a similar response to treatment.

**Risk score**  
A calculation of the likely chance of a good response to treatment.

**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)**  
TKI drugs that were developed after imatinib, the first TKI approved for chronic myelogenous leukemia.

**Second-line treatment**  
The next treatment used against a disease when the first treatment fails.

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

**Side effect**  
An unplanned physical or emotional response to 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.

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

**Stem cell**  
An immature cell from which other types of cells develop.

**Steroid**  
A drug used to reduce swelling, pain, and redness.

**Supplement**  
A product that is added to the diet, such as a vitamin, mineral, or herb.

**Supportive care**  
Treatment for symptoms of cancer or side effects of cancer treatment.

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

**Terminal deoxynucleotidyl transferase (TdT)**  
A chemical found in a type of white blood cell called a lymphocyte or a lymphoid cell.

**Thrombocytopenia**  
A health condition in which the number of platelets (blood cells that stop bleeding) is below normal.
**Part 7: Dictionary**

**Transcript level**  
The number of copies of the *BCR-ABL* gene in your body detected by a very sensitive test.

**Transfusion**  
Replacing lost blood with new blood.

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

**Treatment plan**  
A written course of action through cancer treatment and beyond.

**Treatment response**  
An outcome or improvement in disease that is related to treatment.

**Treatment response milestone**  
An optimal degree of improvement in disease (response) to be reached by a certain time point or time period after beginning treatment.

**Tyrosine kinase**  
A type of protein that is located on or near the surface of cells and sends signals telling cells when to grow and divide.

**Tyrosine kinase inhibitor (TKI)**  
A type of drug that specifically targets and blocks (inhibits) proteins called tyrosine kinases so the proteins cannot tell cells to grow and make more cells.

**Tyrosine kinase inhibitor (TKI) adherence**  
The extent to which you take your TKI medication as prescribed and directed by your doctor.

**White blood cell**  
A type of cell that helps fight infections in the body.
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 booklets for patients called the NCCN Patient Guidelines. Each booklet presents the standard of care for a type of cancer.

The patient booklets are based on guidelines written for doctors. These guidelines are called the NCCN Guidelines. They give a step-by-step course of care that many cancer doctors follow. Panels of experts create the NCCN Guidelines. Most of the experts are from the 23 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. The patient booklets are updated as often as possible on an ongoing basis, with the goal of reflecting the most recent version of the NCCN Guidelines for doctors. For additional information about the NCCN Guidelines and how they are developed, visit NCCN.org/clinical.asp.

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**NCCN abbreviations and acronyms**

NCCN® - National Comprehensive Cancer Network®

NCCN Patient Guidelines® - NCCN Guidelines for Patients®

NCCN Guidelines® - NCCN Clinical Practice Guidelines in Oncology®
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<table>
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<th>Institution</th>
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<th>Phone</th>
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<tbody>
<tr>
<td>Fred &amp; Pamela Buffett Cancer Center at The Nebraska Medical Center</td>
<td>Omaha, Nebraska</td>
<td>800.999.5465</td>
<td><a href="http://unmc.edu/cancercenter">unmc.edu/cancercenter</a></td>
</tr>
<tr>
<td>City of Hope Comprehensive Cancer Center</td>
<td>Los Angeles, California</td>
<td>800.826.4673</td>
<td><a href="http://cityofhope.org">cityofhope.org</a></td>
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<tr>
<td>Dana-Farber/Brigham and Women’s Cancer Center Massachusetts General Hospital Cancer Center</td>
<td>Boston, Massachusetts</td>
<td>800.320.0022</td>
<td><a href="http://dfbwcc.org">dfbwcc.org</a></td>
</tr>
<tr>
<td>Duke Cancer Institute</td>
<td>Durham, North Carolina</td>
<td>888.275.3853</td>
<td><a href="http://dukecancerinstitute.org">dukecancerinstitute.org</a></td>
</tr>
<tr>
<td>Fox Chase Cancer Center</td>
<td>Philadelphia, Pennsylvania</td>
<td>888.369.2427</td>
<td><a href="http://foxchase.org">foxchase.org</a></td>
</tr>
<tr>
<td>Huntsman Cancer Institute at the University of Utah</td>
<td>Salt Lake City, Utah</td>
<td>877.585.0303</td>
<td><a href="http://huntsmancancer.org">huntsmancancer.org</a></td>
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<td>Fred Hutchinson Cancer Research Center/Seattle Cancer Care Alliance</td>
<td>Seattle, Washington</td>
<td>206.288.7222 • <a href="http://seattlecca.org">seattlecca.org</a></td>
<td>206.667.5000 • <a href="http://fhcrc.org">fhcrc.org</a></td>
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<td>The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins</td>
<td>Baltimore, Maryland</td>
<td>410.955.8964</td>
<td><a href="http://hopkinskimmelcancercenter.org">hopkinskimmelcancercenter.org</a></td>
</tr>
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<td>Robert H. Lurie Comprehensive Cancer Center of Northwestern University</td>
<td>Chicago, Illinois</td>
<td>866.587.4322</td>
<td><a href="http://cancer.northwestern.edu">cancer.northwestern.edu</a></td>
</tr>
<tr>
<td>Moffitt Cancer Center</td>
<td>Tampa, Florida</td>
<td>800.456.3434</td>
<td><a href="http://moffitt.org">moffitt.org</a></td>
</tr>
<tr>
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<td>Columbus, Ohio</td>
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<td><a href="http://cancer.osu.edu">cancer.osu.edu</a></td>
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<td>Roswell Park Cancer Institute</td>
<td>Buffalo, New York</td>
<td>877.275.7724</td>
<td><a href="http://roswellpark.org">roswellpark.org</a></td>
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<tr>
<td>Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine</td>
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<td>800.600.3606</td>
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888.226.4343 • stjude.org
877.988.3627 • utcancer.org

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Stanford, California
877.668.7535
cancer.stanfordhospital.com

University of Alabama at Birmingham Comprehensive Cancer Center
Birmingham, Alabama
800.822.0933
ccc.uab.edu

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

UCSF Helen Diller Family Comprehensive Cancer Center
San Francisco, California
800.888.8664
cancer.ucsf.edu

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

University of Michigan Comprehensive Cancer Center
Ann Arbor, Michigan
800.865.1125
mcancer.org

The University of Texas MD Anderson Cancer Center
Houston, Texas
877.632.6789
mdanderson.org

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
800.811.8480
vicc.org
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The NCCN Foundation® gratefully acknowledges Pfizer for its support for the availability of these NCCN Guidelines for Patients®