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LEUKEMIA &  
LYMPHOMA  
SOCIETY®

fighting blood cancers

# The CML Guide

## Information for Patients and Caregivers

### Chronic Myeloid Leukemia



**Matthew, CML survivor**



## A Message from Louis J. DeGennaro, PhD

President and CEO of The Leukemia & Lymphoma Society

The Leukemia & Lymphoma Society (LLS) is the world's largest voluntary health organization dedicated to finding cures for blood cancer patients. Since 1954, we have invested more than \$1 billion in research specifically targeting blood cancers to advance therapies and save lives. We will continue to invest in research for cures, programs and services to improve the quality of life for people with chronic myeloid leukemia (CML).

We know that understanding CML can be tough.

We are here to help and are committed to provide you with the most up-to-date information about CML, your treatment and your support options. We know how important it is for you to understand your health information and to use it with your healthcare team toward good health, remission and recovery.

Our vision is that one day all people with CML will be cured or be able to manage their disease with good quality of life.

Until then, we trust the information in this *Guide* will help you along your journey.

We wish you well.

A handwritten signature in black ink, appearing to read 'Louis J. DeGennaro', with a long horizontal flourish extending to the right.

**Louis J. DeGennaro, PhD**

*President and Chief Executive Officer  
The Leukemia & Lymphoma Society*

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This LLS Guide about CML is for information only. LLS does not give medical advice or provide medical services.

# Introduction

Chronic myeloid leukemia (CML) is a type of blood cancer. The number of people with CML who are living well is growing. This is due to new treatments.

Six new CML drugs have been approved since 2001. Other new treatments are being studied in clinical trials. Progress toward a cure is under way.

People who have CML need to see special blood cancer doctors, called **hematologist/oncologists** to help them.

Please use this *Guide* as a resource to help you –

- Understand CML
- Find good doctors and other healthcare providers
- Understand complicated healthcare terms
- Find and use our Information Specialists, healthcare information, publications and resources

This *Guide* includes

- Information on how to contact our Information Specialists: call (800) 955-4572
- Links to important free LLS disease and treatment information: [www.LLS.org/publications](http://www.LLS.org/publications)
- Information about CML, diagnosis, treatment and care
- List of suggested questions to ask the doctor (See page 36)
- Simplified glossary of healthcare terms (See page 32)

We are here to help.

### Want more information?



You can view, print or order the free LLS publications *Understanding Leukemia* and *Chronic Myeloid Leukemia* at [www.LLS.org/publications](http://www.LLS.org/publications) or contact our Information Specialists for copies.

## Resources and Information

LLS offers free information and services for patients and families touched by blood cancers. This section of the booklet lists various resources available to you. Use this information to learn more, to ask questions and to make the most of your healthcare team.

### For Help and Information

**Consult with an Information Specialist.** Information Specialists are master's level oncology social workers, nurses and health educators. They offer up-to-date information about disease, treatment and support. Language services are available.

For more information, please

- Call: (800) 955-4572 (Monday through Friday, 9 a.m. to 9 p.m. ET)
- Email: [infocenter@LLS.org](mailto:infocenter@LLS.org)
- Live chat: [www.LLS.org/information specialists](http://www.LLS.org/information specialists)

**Free Materials.** LLS offers free education and support publications that can either be read online or downloaded and printed. Free print versions can be ordered. For more information, please visit [www.LLS.org/publications](http://www.LLS.org/publications).

**Telephone/Web Education Programs.** LLS offers free telephone/Web education programs for patients, caregivers and healthcare professionals. For more information, please visit [www.LLS.org/programs](http://www.LLS.org/programs).

**Co-Pay Assistance Program.** LLS offers insurance premium and medication co-pay assistance for certain eligible patients.

For more information, please

- Call: (877) 557-2672
- Visit: [www.LLS.org/copay](http://www.LLS.org/copay)

## Community Resources and Networking

**Online Blood Cancer Discussion Boards and Chats.** Online discussion boards and moderated online chats can help cancer patients reach out, share information and provide and receive support. For more information, please visit [www.LLS.org/getinfo](http://www.LLS.org/getinfo).

**LLS Chapters.** LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), in-person support groups and other great resources.

For more information about these programs or to contact your chapter, please

- Call: (800) 955-4572
- Visit: [www.LLS.org/chapterfind](http://www.LLS.org/chapterfind)

**Other Helpful Organizations.** LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, locating summer camps and other needs. For more information, please visit [www.LLS.org/resourcedirectory](http://www.LLS.org/resourcedirectory).

**Clinical Trials (Research Studies).** New treatments for patients with CML are under way. Many are part of clinical trials. Patients can learn about clinical trials and how to access them.

For more information, please

- Call: (800) 955-4572 to speak with an LLS Information Specialist who can help conduct a clinical trial search
- Visit: [www.LLS.org/clinicaltrials](http://www.LLS.org/clinicaltrials).

**Advocacy.** The LLS Office of Public Policy (OPP) enlists volunteers to advocate for policies and laws to speed new treatments and improve access to quality medical care.

For more information, please

- Call: (800) 955-4572
- Visit: [www.LLS.org/advocacy](http://www.LLS.org/advocacy)

## **Additional Help for Specific Populations**

**Información en Español (LLS information in Spanish).** For more information, please visit [www.LLS.org/espanol](http://www.LLS.org/espanol).

**Language Services.** Let your doctor know if you need a language interpreter or other resource, such as a sign language interpreter. Often, these services are free.

**Children.** CML is rare in children. Families face new and unfamiliar treatments and care protocols. The child, parents and siblings may all need support.

For more information, please

- Call: (800) 955-4572
- Visit: [www.LLS.org/publications](http://www.LLS.org/publications)
  - Click on Childhood Blood Cancer and choose *Coping With Childhood Leukemia and Lymphoma*

**Information for Veterans.** Veterans with CML who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs (VA). For more information call the VA at (800) 749-8387 or visit [www.publichealth.va.gov/exposures/agentorange](http://www.publichealth.va.gov/exposures/agentorange).

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

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

For more information, please

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

**Depression.** Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time, for example, if you feel depressed every day for a two-week period.

For more information, please

- Call: National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at [www.nimh.nih.gov](http://www.nimh.nih.gov), enter “depression” in the search box

## Feedback

Like this booklet? Have suggestions? We'd love to know what you think. To tell us

- Visit: [www.LLS.org/publicationfeedback](http://www.LLS.org/publicationfeedback)
- Click on “LLS Disease & Treatment Publications—Survey for Patients, Family and Friends”

# Understanding CML

Leukemia is the general term for different types of blood cancer. CML is one of four main types of leukemia.

## About Blood

Blood is the red liquid that circulates in our bodies. It is created inside the bones, in a special spongy place called the marrow.

Blood is made up of plasma and blood cells.

**Plasma.** This is the liquid part of the blood. It is mostly water. It also has some vitamins, minerals, proteins, hormones and other natural chemicals.

**Blood cells.** Each blood cell starts as a stem cell. Then it turns into one of three types of blood cells

- Blood platelet (helps blood to clot)
- White blood cell (fights infection)
- Red blood cell (carries oxygen)

## Normal Blood Cell Count Fast Facts

The ranges of blood cell counts below are for adults. They may be a little different from lab to lab and for children and teens.

### Red blood cell (RBC) count

- Men: 4.5 to 6 million red cells per microliter of blood
- Women: 4 to 5 million red cells per microliter of blood

### Hematocrit (the part of the blood made up of red cells)

- Men: 42% to 50%
- Women: 36% to 45%

### Hemoglobin (amount of the red cell pigment that carries oxygen)

- Men: 14 to 17 grams per 100 milliliters of blood
- Women: 12 to 15 grams per 100 milliliters of blood

### Platelet count

- 150,000 to 450,000 platelets per microliter of blood

### White blood cell (WBC) count

- 4,500 to 11,000 white cells per microliter of blood

### Differential (also called diff)

- Shows the part of the blood made up of different types of white cells
- The types of white cells counted are neutrophils, lymphocytes, monocytes, eosinophils and basophils.
- Adults usually have about 60% neutrophils, 30% lymphocytes, 5% monocytes, 4% eosinophils and less than 1% basophils in the blood.

## What is CML?

CML starts in the bone marrow. Most people who have CML are adults. A small number of children have CML. CML is a cancer.

This means:

- A normal cell mutates (changes)
- Changed cells multiply into many cells (CML cells)

Without treatment, the following changes take place:

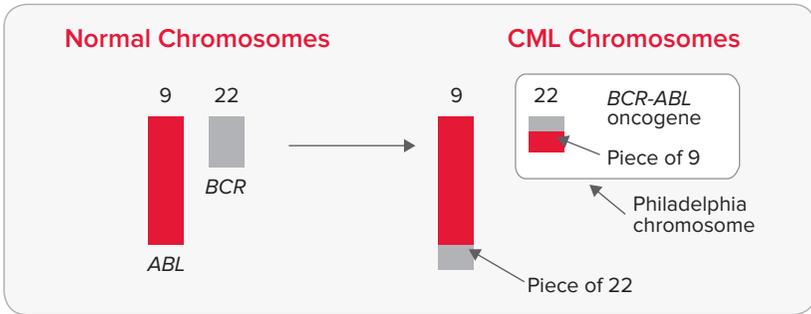
- The number of red blood cells is usually lower than normal
- The number of white blood cells is higher than normal and continues to grow

**Chromosomes and Genes.** Normal cells have pairs of chromosomes that are numbered from 1 to 22 and one pair of sex chromosomes (XX for females and XY for males). Chromosomes are structures in the cells that contain genes. The genes give instructions to the cells.

**The Philadelphia Chromosome.** In CML cells, a change takes place on chromosome 22. The changed chromosome 22 is known as the **Philadelphia chromosome**. It is also called the **Ph chromosome**. The Ph chromosome is made when a piece of chromosome 22 breaks off and attaches to the end of chromosome 9. A piece of chromosome 9 also breaks off and attaches to the end of chromosome 22.

**The *BCR-ABL* Cancer Gene.** The break on chromosome 9 involves a gene called *ABL*. The break on chromosome 22 involves a gene called *BCR*. The *BCR* and *ABL* genes combine to make the CML-causing gene called the *BCR-ABL* gene.

## How the *BCR-ABL* Cancer-Causing Gene (Oncogene) Is Created



- A piece of the *ABL* gene on chromosome 9 breaks off.
- A piece of the *BCR* gene on chromosome 22 breaks off.
- These 2 pieces switch places.
- The switch leads to the cancer gene called *BCR-ABL*.

**Causes of CML.** Doctors do not know why the *BCR-ABL* gene that leads to CML forms in some people but not in others.

People treated with high-dose radiation therapy for other cancers have a small increase in risk of CML. But most people treated for cancer with radiation do not develop CML. And most people with CML were not exposed to high-dose radiation. There is no link between dental or medical x-rays and increased risk of CML. You cannot catch CML from someone else.

## Signs and Symptoms

Healthy people often get a sign or a symptom when they get an illness or a disease.

- A sign is a change in the body that the doctor sees in an exam or a test result.
- A symptom is a change in the body that the patient can see or feel.

CML signs and symptoms tend to develop slowly. Many of the signs and symptoms of CML are also signs and symptoms of other illnesses. Most people with these signs and symptoms do not have CML.

## Some Signs and Symptoms of CML

|                            |   |
|----------------------------|---|
| <b>Tiring more easily</b>  | People may have less energy due to fewer healthy red blood cells and more CML cells.  |
| <b>Shortness of breath</b> | People may have shortness of breath when doing usual day-to-day activities because they have fewer healthy red blood cells and more CML cells.                |
| <b>Pale skin color</b>     | People may have pale skin color due to a low number of red blood cells.   |
| <b>Swollen spleen</b>      | People may have aches or a “dragging” feeling on the upper left side of the belly (in the spleen) because of swelling caused by the high number of CML cells. |
| <b>Weight loss</b>         | Some people with CML lose weight because they eat less and/or because they are using more energy.   |

People with CML sometimes have other symptoms, such as night sweats.

## Diagnosing CML

The diagnosis of CML is usually made with information from blood and bone marrow tests. These tests may be done in the doctor’s office or in a hospital.

**Blood Tests.** Testing for CML includes blood cell counts and a blood cell examination.

- Blood cell counts. The doctor orders a lab test called a **complete blood count (CBC)** to check the numbers of blood cells. With CML, the red blood cell count is lower than normal. The number of white blood cells is higher than normal and may be very high. The number of platelets may be higher or lower than normal.

- Blood cell examination. The cells are stained (dyed) and looked at with an instrument called a **light microscope**. A person with CML has a small number of developing cells called **blast cells** in his or her blood. Blast cells are not found in the blood of healthy individuals.

**Bone Marrow Tests and Cytogenetic Tests.** Some signs of CML do not show up in blood tests. The doctor has to look at a small number of cells (a sample) from the marrow. The samples of cells are obtained with tests that are known as a bone marrow aspiration and a bone marrow biopsy. These tests

- Are almost always done together
- Require a special needle

Often, patients are awake during this procedure. These patients are given medication to their hip bone to numb the site of the biopsy and aspiration. Once that area of the body is really numb, the bone marrow samples are taken. Some patients are sedated (asleep) for the procedure.

Samples of the marrow cells are examined under a microscope. This is called a **cytogenetic analysis**. The examiner looks at a “map” of the chromosomes in the cell. The map is called a **karyotype**. The Ph chromosome in a CML cell can be detected on the karyotype. The presence of the Ph chromosome is important information that—along with information about high white blood cell counts—helps the doctor diagnose a person’s CML.

## How Are the Blood and Bone Marrow Tests Done?

|                               |  |
|-------------------------------|--|
| <b>Blood Tests</b>            | Usually, a small amount of blood is taken from the person's arm with a needle. The blood is collected and sent to a lab.           |
| <b>Bone Marrow Aspiration</b> | A liquid sample of cells is taken from the marrow through a needle. The cells are then looked at under a microscope.               |
| <b>Bone Marrow Biopsy</b>     | A very small amount of bone filled with marrow cells is removed through a needle. The cells are then looked at under a microscope. |

**FISH.** A special test called **fluorescence in situ hybridization** or **FISH** can detect CML cells that may not show up on a standard cytogenetic test for the Ph chromosome.

**Polymerase Chain Reaction (PCR).** A PCR test can detect a very small number of CML cells. A PCR can be done on cells from blood or marrow. Information about follow-up tests to check a person's response to CML drug treatment begins on page 28.

## Tracking Your CML Tests

These tips may help you save time and learn more about your health.

- Ask your doctor why certain tests are being done and what to expect.
- Discuss test results with your doctor.
- Ask for and keep copies of lab reports in a file folder or three-ring binder. Organize test reports by date.
- Find out if and when follow-up tests are needed.
- Mark appointments that are coming up on your calendar.

Want more information?



You can view, print or order the free LLS publication *Understanding Lab and Imaging Tests*. Go to [www.LLS.org/publications](http://www.LLS.org/publications) or contact our Information Specialists for a copy.

## Phases of CML

There are three phases of CML:

- Chronic phase
- Accelerated phase
- Blast crisis phase

**Chronic Phase CML.** Most people have chronic phase CML when they are diagnosed. CML symptoms are milder in the chronic phase. White blood cells can still fight infection. Once people with chronic phase CML start treatment, they can go back to their usual day-to-day activities.

**Accelerated Phase CML.** People with accelerated phase CML may develop anemia (a decreased number of red cells in the blood). The number of white blood cells go up. The number of platelets may go up or drop. The number of blast cells increases. The spleen may swell. People with accelerated phase CML may feel ill.

**Blast Crisis Phase CML.** People with blast crisis phase CML have an increased number of blast cells in their marrow and blood. The numbers of red blood cells and platelets drop. The person may have infections or bleeding. He or she may be tired or have shortness of breath, stomach pain or bone pain.

# Treating CML

## Finding the Right Doctor

Patients with CML are treated by special doctors that understand cancer and the blood. These doctors are called **hematologist/oncologists**.

Finding the right doctor, one that you like and feel comfortable with, is important. Refer to these resources to help you find the right cancer specialist:

- Your primary care doctor
- The community cancer center or medical society
- Your health plan and its referral services
- Online doctor-finder resources, such as
  - The American Medical Association's (AMA) "DoctorFinder"
  - The American Society of Hematology's (ASH) "Find a Hematologist"
- LLS resources such as our Information Specialists, who can be reached from Monday to Friday 9 a.m. to 9 p.m. ET at (800) 955-4572

Your doctor will help you to understand CML and create a treatment plan. When you meet with your doctor:

- Ask questions.
  - Use the question guides in the back of this *Guide* to help.
  - Read and print LLS "What To Ask" question guides at [www.LLS.org/whattoask](http://www.LLS.org/whattoask).
- Take notes or bring an audio recorder to record your visits.
- Bring a friend or family member to help you understand and take notes.
- Make sure you understand what the doctor is saying. If you don't, ask the doctor to explain things so you can understand.
- If you need more information, consider getting another opinion (a second opinion).

### Want more information?



You can view, print or order the free LLS publication *Choosing a Blood Cancer Specialist or Treatment Center* at [www.LLS.org/publications](http://www.LLS.org/publications). For a list of questions to ask your doctor, see the question guides starting on page 36. You can also access and print Healthcare Question Guides about second opinions and other topics at [www.LLS.org/whattoask](http://www.LLS.org/whattoask). Or contact our Information Specialists for copies.

## Chronic Phase CML Treatment Goals

For people with chronic phase CML, the goals of treatment are to

- Return the levels of blood cells to normal
- Kill all cells that have the *BCR-ABL* cancer gene

Treatment for chronic phase CML usually returns the levels of blood cells to normal. Most people do not have infections or unusual bleeding. The spleen goes back to normal size.

Usually people being treated for chronic phase CML feel well. They can go about their day-to-day activities.

## Treatment

A patient's treatment plan depends on a number of factors including the phase of CML at diagnosis, test results and age.

**Leukapheresis.** Leukapheresis is a process that uses a special machine to remove extra white blood cells from the blood. Leukapheresis can be used for women diagnosed with CML in the first months of pregnancy, when drug therapy may be harmful to the unborn baby. See page 26 for more information about pregnancy and CML.

There are six drugs approved to treat CML; three are approved for newly diagnosed patients. The following five drugs (Gleevec, Sprycel, Tasisign, Bosulif and Iclusig) are known as tyrosine-kinase inhibitors (TKIs). For full prescribing information, please see *Health Terms* on page 32.

**Gleevec.** Most people with newly diagnosed CML begin treatment with imatinib mesylate (Gleevec®). Gleevec is taken by mouth (oral drug therapy). It is an FDA-approved drug (see page 33).

Gleevec controls chronic phase CML for most people as long as they continue to take it. People with CML who do not respond to the usual dose of Gleevec may respond to a higher dose.

Gleevec does not help all people with CML. Another drug may be used to treat a person with CML for one of these reasons:

- Gleevec did not control the person's CML (called **drug resistance** or **refractory CML**).
- The person has strong side effects from Gleevec (called **drug intolerance**).
- Gleevec stopped working (called a **loss of response**).

**Sprycel and Tasigna.** The drugs dasatinib (Sprycel®) and nilotinib (Tasigna®) are FDA approved for patients with newly diagnosed chronic phase CML and for patients who cannot tolerate Gleevec or who have CML that is resistant to Gleevec. These drugs are also taken by mouth (oral drug therapy).

Neither Sprycel nor Tasigna has been shown to result in longer survival than Gleevec at this time. However, for patients taking either of these drugs, the likelihood of developing accelerated or blast phase disease appears to be lower than in those being treated with Gleevec.

**Bosulif and Iclusig.** Bosutinib (Bosulif®) is FDA approved to treat all phases of CML in adults who have resistance or intolerance to prior therapy including Gleevec. Ponatinib (Iclusig®) is FDA approved for the treatment of all phases of CML in patients who have resistance or intolerance to prior therapy, including those with one particular drug-resistant mutation known as T315I. Both drugs are taken by mouth (oral drug therapy).

**Note:** Gleevec, Sprycel, Tasigna, Bosulif and Iclusig work in different ways to block the protein produced by the *BCR-ABL* cancer gene. When taking any of these drugs, it is important to:

- Take the prescribed amount of CML medication each day to keep the response to treatment.

- Follow the doctor's instructions for taking your CML medication—the instructions for taking Gleevec, Sprycel, Tasigna, Bosulif or Iclusig may be different.
- Get regular checkups for CML. Blood tests—and from time to time, bone marrow tests—are needed.

**Synribo.** Omacetaxine mepesuccinate (Synribo®) is a different type of drug from Gleevec, Sprycel, Tasigna, Bosulif and Iclusig. It is a type of drug called a protein synthesis inhibitor. It is FDA approved for patients who have chronic and accelerated phase CML and who also have resistance or intolerance to at least two prior TKIs. Synribo is given by injecting the drug under the skin.

See **Some Drugs Used to Treat CML** on page 21 for a list of CML drugs. Information about *Treatment Response* begins on page 28.

## Side Effects

The term **side effect** is used to describe the ways that treatment affects healthy cells.

Many treatment side effects go away or become less noticeable over time. Most can be handled without the need to stop the drug. Talk to your doctor about the possible side effects and long-term effects of your treatment. You can also call our Information Specialists.

**Gleevec.** Common side effects may include:

- Swelling from too much fluid in the body
- Puffiness around the eyes
- Rash
- Muscle cramps
- Diarrhea
- Nausea and vomiting

Gleevec may also cause loss of the bone mineral phosphorus. The doctor will check for these possible side effects.

**Sprycel.** Common side effects may include:

- Too few white blood cells and/or platelets
- Too much fluid in the chest
- Too much fluid in other tissues (edema)
- Diarrhea
- Headache
- Low calcium levels in the blood
- Slight changes in liver function

**Tasigna.** Common side effects may include:

- Too few white blood cells and/or platelets
- Changes in pancreatic enzymes
- Changes in liver enzymes
- Rash
- Nausea
- Constipation
- Diarrhea
- Itching

**Bosulif and Iclusig.** Common side effects may include:

- Vomiting
- Nausea
- Diarrhea

**Synribo.** Common side effects may include:

- Low red blood cell and white blood cell counts
- Low platelet counts
- Diarrhea

- Nausea
- Fatigue
- Fever
- Infection
- Reaction at the injection site

**Cardiac Effects.** Patients treated with Gleevec, Sprycel and Tasigna have sometimes, although rarely, developed:

- Severe congestive heart failure (a weakness of the heart that leads to a buildup of fluid in the lungs and surrounding body tissues)
- Left ventricular dysfunction (difficulty emptying blood from the left lower chamber of the heart)

To date, most of these patients had other health problems and risk factors, including older age and a medical history of cardiac disease. A possible side effect of Tasigna that needs to be regularly monitored is a heart rhythm condition called **QT prolongation**. Although Gleevec and Sprycel may occasionally cause QT prolongation, other medications are known to frequently cause QT prolongation, and should be avoided whenever possible. Your doctor will give you a list of medications to avoid and will monitor you for these conditions as needed.

**Other Side Effects.** Sprycel may increase the risk of a serious condition called **pulmonary arterial hypertension (PAH)**. This side effect appears to be rare, however. Tasigna may be associated with an increased risk of vascular events (disease relating to blood vessels), such as a rare but serious condition called **peripheral arterial occlusive disease (PAOD)**. Iclusig is only for patients who can't take any other TKI therapy because of an association with severe liver toxicity and serious vascular events like arterial thrombosis. Talk to your doctor for more information about these rare side effects.

**Want more information?**



You can view, print or order the free LLS publication *Understanding Side Effects of Drug Therapy* at [www.LLS.org/publications](http://www.LLS.org/publications) or contact our Information Specialists for a copy.

### **Some Drugs Used to Treat CML**

- Imatinib mesylate (Gleevec®)
- Dasatinib (Sprycel®)
- Nilotinib (Tasigna®)
- Bosutinib (Bosulif®)
- Ponatinib (Iclusig®)
- Omacetaxine mepesuccinate (Synribo®)

**CML that does not respond to the drugs above may be treated with the drugs listed below. Or a patient may want to receive treatment in a clinical trial.**

- Interferon (Intron A®, Roferon-A®)
- Peginterferon alfa-2a (Pegasys®)
- Busulfan (Myleran®)
- Cytarabine (Cytosar-U®)
- Hydroxyurea (Hydrea®)

## **Accelerated or Blast Crisis Phase CML**

In both the accelerated and blast crisis phases of CML, the goal of therapy is to kill all cells that contain the *BCR-ABL* cancer gene or to return the person's disease to chronic phase CML.

Gleevec, Sprycel, Tasigna, Bosulif, Iclusig or Synribo are effective treatments for people who have accelerated or blast crisis phase CML.

Other drugs—such as interferon (Intron A<sup>®</sup>, Roferon-A<sup>®</sup>), busulfan (Myleran<sup>®</sup>), cytarabine (Cytosar-U<sup>®</sup>) or hydroxyurea (Hydrea<sup>®</sup>)—may be used along with those CML drugs.

Some people with accelerated or blast crisis phase CML have a very high white blood cell count at the time of diagnosis. This can reduce blood flow to the brain, lungs, eyes and other parts of the body. Hydrea may be used to decrease the white blood cell count. After the white blood cell count drops, oral drug therapy can be started.

Stem cell transplantation is another important treatment option for some patients who are first diagnosed in, or progress to, advanced phases of CML. See below for more information about this treatment option.

## Stem Cell Transplantation

Your doctor will talk to you about whether stem cell transplantation is a treatment option for you. Most people with CML have a good response to drug treatment which may be able to control CML for a very long time. But in some cases, allogeneic stem cell transplantation may be used to treat CML.

**Allogeneic Stem Cell Transplantation.** This is a procedure in which stem cells from another person (a donor) are infused into your body. The donor may be a brother or sister. Or the donor can be an unrelated person with stem cells that “match” the patient’s. Stem cells may also come from a cord blood unit (the blood in the umbilical cord after a baby’s birth).

The goals of an allogeneic transplant are to:

- Cure the patient of CML by killing remaining CML cells
- Restore the body’s ability to make healthy blood cells after high-dose chemotherapy

This procedure may be done in the hospital. Before the transplant, the person receives CML drug therapy to bring the disease under control. After the person responds to this treatment, the patient is given high-dose chemotherapy and/or radiation therapy. Stem cells are collected from a donor. The donor stem cells are given to the patient through an intravenous (IV) line or central line. The donor stem cells

go from the patient's blood to the marrow. They help start a new supply of healthy red blood cells, white blood cells and platelets.

Allogeneic stem cell transplantation is most successful in younger patients. However, there is no specific age cutoff for stem cell transplantation. It may be a good treatment for a younger CML patient who does not respond well to oral drug treatment and has a matched stem cell donor.

Allogeneic stem cell transplantation is the only treatment that can cure CML. About 7 out of 10 people who have an allogeneic transplant are cured of their CML. But this procedure has a high risk of serious complications. Your doctor will explain the benefits and the risks, if a transplant is suggested for you.

**Reduced-Intensity Transplant.** Doctors are working to make allogeneic stem cell transplants safer. A type of transplant called a **reduced-intensity transplant** uses a lower dosage of chemotherapy than the dosage used with a standard allogeneic stem cell transplant. This treatment is also called a **nonmyeloablative** transplant. Older and sicker people may be helped by this treatment.

**Donor Lymphocyte Infusion.** One treatment option for patients whose disease has returned (relapsed) after an allogeneic stem cell transplant may be to treat them with a **donor lymphocyte infusion** (an infusion of white blood cells called lymphocytes that come from the original stem cell donor). Other options may be a TKI, other drugs or a second transplant.

**Want more information?**



You can view, print or order the free LLS publication *Blood and Marrow Stem Cell Transplantation* at [www.LLS.org/publications](http://www.LLS.org/publications) or contact our Information Specialists for a copy.

## Mutation Testing

Mutation testing may help find changes in a cancer gene. A patient should talk to his or her doctor about ordering a mutation test and sending a blood sample to a reference laboratory (used for specialized tests) if there is:

- A treatment milestone the patient does not meet
- Loss of **hematologic** or **cytogenetic** response despite taking an appropriate dose of TKI (see *Treatment Response* on page 28)
- Unexplained rise in CML cells as shown on a PCR test
- Concern about the medication working

The results of a mutation test may tell the doctor why one drug may work and another may not. A mutation test does not need to be done for a patient who is switching medication because of side effects.

For information about the CML mutation testing guidelines from the National Comprehensive Cancer Network (NCCN), please visit [www.nccn.org](http://www.nccn.org).

## Children and Young Adults with CML

A small percentage of patients diagnosed with CML are children and young adults. CML represents about 3 percent of newly diagnosed childhood leukemias.

CML has the same disease path in children as it does in adults. Specific guidelines for CML treatment in children have yet to be determined. However, Gleevec® is the main treatment used for young patients. More than 80 percent of children with chronic phase disease treated with Gleevec enter complete cytogenetic remission. For more information, see *Treatment Response* on page 28.

Although not a great number of studies have focused on the treatment of pediatric patients with CML, there is evidence that TKI drugs such as Gleevec may slow growth in children, particularly

for those treated before they reach puberty. Careful monitoring of the child's height and overall growth during and after treatment is recommended.

For children who have CML that does not respond well to Gleevec, other TKI drugs such as Sprycel® or Tasigna® and, possibly, stem cell transplantation are options. Complications of a transplant remain challenging, so treatment with Gleevec continues to be the first choice for younger patients in chronic phase CML.

With oral medications, it is important to follow the doctor's directions and keep taking the medication for as long as prescribed. This can be difficult for parents of children and young adults, because remembering to take the drug can be hard.

Talk to your child's doctor about the best treatment for him or her. It is important for your child to be seen by a doctor who specializes in pediatric leukemia (a pediatric hematologist/oncologist).

**Want more information?**



You can view, print or order the free LLS publications *Choosing a Blood Cancer Specialist or Treatment Center* and *Coping With Childhood Leukemia and Lymphoma* at [www.LLS.org/publications](http://www.LLS.org/publications) or contact our Information Specialists for copies.

## Pregnancy, Fertility and TKIs

Today, there are more women with CML who want information about getting pregnant.

Doctors continue to study how CML treatment affects pregnancy. For more information, speak with your doctor so that you understand the

- Need for women to stop treatment during preconception and pregnancy
- Risk of relapse, if therapy is stopped
- Risk for fetal effects from Gleevec and other TKI drugs (probably greatest during the first trimester)
- Need for women on TKI therapy to refrain from breast-feeding their babies
- Uncertainty about treatment options and getting a stable response during and after pregnancy.

Data are limited on the men who father children while taking Gleevec and other TKIs. Right now, there does not seem to be any cause for concern; however, Gleevec and other TKIs have not been proven to be safe in this setting either. Talk to your doctor if you are thinking about having a child.

## Treatment Cessation

Many patients with chronic phase CML develop deep and lasting remission with drugs such as Gleevec, Sprycel and Tasigna. At this time, however, the drugs available are not able to cure CML.

Careful clinical trials have begun to look at whether patients who have deep remissions while taking therapy are able to sustain stable remissions after they stop therapy. Talk to your doctor for more information.

## CML-Related Diseases

The name chronic myeloid leukemia is sometimes used for other types of chronic leukemia, such as chronic myelomonocytic leukemia (CMML) and chronic neutrophilic leukemia (CNL). People with these diseases do not have the *BCR-ABL* gene. They are not treated with TKI drug therapy.

**Want more information?**



You can view, print or order the free LLS publication *Chronic Myelomonocytic Leukemia (CMML) and Juvenile Myelomonocytic Leukemia (JMML)* at [www.LLS.org/publications](http://www.LLS.org/publications) or contact our Information Specialists for a copy.

## Part 3

# About Clinical Trials

Doctors may recommend that a patient joins a clinical trial. Clinical trials are careful studies done by doctors to test new drugs or treatments or new uses for approved drugs or treatments. For example, changing the amount of the drug or giving the drug along with another type of treatment might be more effective. Some clinical trials combine drugs for CML in new sequences or dosages.

There are clinical trials for

- Newly diagnosed CML patients
- Patients who do not get a good response to treatment
- Patients who relapse after treatment

A carefully conducted clinical trial may provide the best available therapy. Ask your doctor if treatment in a clinical trial is right for you. Some of the drugs listed in *Some Drugs Used to Treat CML* on page 21 are being studied in clinical trials. You can call our Information Specialists for information about clinical trials. Or, use our free clinical-trial search service at [www.LLS.org/clinicaltrials](http://www.LLS.org/clinicaltrials).

**Want more information?**



You can view, print or order the free LLS publication *Knowing All Your Treatment Options* at [www.LLS.org/publications](http://www.LLS.org/publications) or contact our Information Specialists for a copy.

# Treatment Response

Measuring treatment response is very important. Blood and marrow tests are used to track a person's level of response to treatment. The results are used to help the doctor decide if the person's CML is well controlled or if there is a need to:

- Increase the dose to try for a better response
- Decrease or stop the drug briefly because of side effects
- Change to a different drug or combination of drugs to better control the CML
- Change to a different drug or combination of drugs to manage side effects

## Treatment Response Guidelines

There are general treatment response guidelines for CML drug therapy. But keep in mind that people with CML respond to treatment in different ways. Blood tests and/or bone marrow tests may be used to determine the level of CML drug therapy response. Your doctor may use the terms hematologic, cytogenetic or **molecular response (remission)**.

A person's response is measured against his or her lab test results at the start of treatment. The numbers of red blood cells, white blood cells, platelets and CML cells are measured. After an initial diagnosis of CML, blood counts may be performed every two to four weeks. After blood counts return to normal, blood tests are generally performed every three to six months.

Bone marrow testing is recommended

- After three months for patients who do not have access to a PCR test
- At 12 months in patients who have not yet achieved either a complete cytogenetic or a major molecular response
- Infrequently after achievement of a complete cytogenetic response
- Anytime there is a change in response to CML drug therapy as measured in the blood

There are efforts to standardize PCR reporting using an International Scale so that test results are uniform.

## Hematologic Response

A complete hematologic response means that the numbers of white blood cells, red blood cells and platelets are normal or near normal.

*The Test:* A complete blood count (CBC) is done to measure the numbers of white blood cells, red blood cells and platelets, and the levels of hemoglobin (a protein in red blood cells that carries oxygen) and hematocrit (the amount of red blood cells in the total blood volume).

## Cytogenetic Response

A complete cytogenetic response means that there are no cells with the Ph chromosome and the *BCR-ABL* cancer gene that can be detected.

*The Test:* Fluorescence in situ hybridization (FISH) is done to measure the number of cells that have the Ph chromosome and the *BCR-ABL* cancer gene.

## Molecular Response

A partial molecular response means that there is a reduction in the number of cells with the *BCR-ABL* cancer gene. A major molecular response means that there is a 1,000-fold decrease in the level of cells with the *BCR-ABL* cancer gene from the level at the start of treatment. A complete molecular response means that the *BCR-ABL* cancer gene cannot be detected by polymerase chain reaction (PCR). Remaining CML cells that cannot be detected by PCR are called **minimal residual disease**.

*The Test:* A PCR measures the number of cells that have the *BCR-ABL* cancer gene. If possible, the same laboratory should be used for PCR testing each time. This is because the results may vary from lab to lab.

Most people with chronic phase CML have a complete hematologic response with TKI drugs. Many of these individuals go on to have a complete cytogenetic response. They may also have a partial, major or complete molecular response.

Information about what you can do to keep track of your CML tests is on page 13.

## Follow-up Care

CML patients will meet with their primary care doctor and oncologist for follow-up care. At these visits, the doctor will check you to see how you are doing. Additional blood tests or even marrow tests may be needed to evaluate your treatment progress and to learn if different treatment is needed. The doctor may advise longer periods of time between follow-up visits. However, follow up visits should be ongoing. For each follow-up visit:

- Track each visit and write down what was discussed.
- Ask your doctor if and why certain tests are being done and what to expect.
- Discuss test results with your doctor.
- Ask for and keep copies of lab reports in a file folder or binder.
- Organize the reports in date order
- Find out if and when follow-up tests are needed.
- Mark upcoming appointments on your calendar.

# Ongoing Care

It is very important that you take very good care of yourself. Review the following tips to keep yourself healthy and happy.

- Keep all doctors' appointments.
- Talk about how you feel with the doctor at each visit.
- Ask any questions you may have about side effects.
- People with CML may have more infections. Follow the doctor's advice for preventing infection.
- Eat healthy foods each day. It is okay to eat four or five smaller meals instead of three bigger ones.
- Contact the doctor about tiredness, fever or other symptoms.
- Do not smoke. Patients who smoke should get help to quit.
- Get enough rest.
- Exercise—but first talk with your doctor before starting an exercise program.
- Keep a healthcare file with copies of lab reports and treatment records.
- Have regular cancer screenings.
- See your primary care doctor to keep up with other healthcare needs.
- Talk with family and friends about how you feel. When family and friends know about CML and its treatment, they may worry less.
- Seek medical advice if you feel sad or depressed and your mood does not improve over time. If you feel sad or depressed every day for a two-week period, seek help. Depression is an illness. It should be treated even when a person is being treated for CML. Treatment for depression has benefits for people living with cancer.

# Health Terms

**Anemia.** A condition in which a person has fewer red blood cells, less hemoglobin, or less volume of blood than normal.

**Antibiotics.** Drugs that are used to treat infections caused by bacteria and fungi. Penicillin is one type of antibiotic.

**Antibodies.** Proteins made by plasma cells in the blood. Antibodies help fight infection in the body.

**Blast cells.** Early bone marrow cells, also known as **lymphoblasts**. About 1 to 5 percent of normal marrow cells are blast cells.

**Bone marrow aspiration.** A procedure to remove and examine marrow cells to see if they are normal. A liquid sample containing cells is taken from the marrow and the cells are looked at under a microscope.

**Bone marrow biopsy.** A procedure to remove and examine marrow cells to see if they are normal. A very small amount of bone filled with marrow cells is taken from the body and the cells are looked at under a microscope.

**Bosulif® (bosutinib).** A type of drug called a **tyrosine kinase inhibitor**. It is FDA approved for adults with chronic, accelerated or blast phase Ph positive CML who have resistance or intolerance to prior therapy.

**Chemotherapy or drug therapy.** Treatment with chemical agents for CML and other cancers.

**Chromosomes.** Any of the 23 pairs of certain basic structures in human cells. Chromosomes are made up of genes. Genes give the instructions that tell each cell what to do. The number or shape of chromosomes may be changed in blood cancer cells.

**Clinical trials.** Careful studies done by doctors to test new drugs or treatments or new uses for approved drugs or treatments. The goal of clinical trials for blood cancers is to improve treatment and quality of life and to find cures.

**Combination chemotherapy or drug therapy.** The use of two or more drugs given to one patient during the same time period to treat CML and other diseases.

**Diagnose.** To detect a disease from a person's signs, symptoms and test results. The doctor diagnoses a disease in a patient.

**FDA.** The short name for the US Food and Drug Administration. Part of the FDA's job is to assure the safety and security of drugs, medical devices and the US food supply.

**FISH.** The short name for fluorescence in situ hybridization, a test to measure the presence of a specific chromosome or gene in cells. The results of this test can be used to plan treatment and to measure the results of treatment.

**Gleevec® (imatinib mesylate).** A type of drug called a **tyrosine kinase inhibitor**. It is FDA approved for newly diagnosed adult patients with Ph positive CML in chronic phase. It is also approved for adults with Ph positive CML in blast crisis phase, accelerated phase, or in chronic phase after failure of interferon alpha therapy. Gleevec is approved for children with Ph positive CML in chronic phase who are newly diagnosed.

**Hematocrit.** The amount of red blood cells in the total blood volume.

**Hematologist.** A doctor who treats blood cell diseases.

**Hemoglobin.** The part of the red blood cell that carries oxygen.

**Immune response.** The reaction of the body to foreign material such as infection-causing microorganisms, a vaccine or the cells used for a stem cell transplant.

**Iclusig® (ponatinib).** A type of drug called a **tyrosine kinase inhibitor** that is FDA approved for adults with T315I -positive CML (chronic phase, accelerated phase, or blast phase), and adults for whom no other TKI is indicated.

**Immune system.** The system that protects the body from foreign substances, cells, and tissues by defending it against infection.

**Immunoglobulins.** Proteins in the body that fight infection.

**Immunotherapy.** The treatments that are used to boost the body's immune system.

**Karyotype.** A "map" of the chromosomes of a cell. In humans, there are 46 chromosomes, 22 matched pairs and one pair of sex chromosomes shown as XX for females and XY for males.

**Leukapheresis.** A process in which extra white blood cells in the blood are removed by a machine. Some people with CML have very high white blood cell counts at the time of diagnosis. This can reduce blood flow to the brain, lungs, eyes and other parts of the body. The drug called hydroxyurea (Hydrea®) may be used to decrease the white blood cell count. After the white blood cell count drops, oral drug therapy can be started. Leukapheresis can be used for women diagnosed with CML in the first months of pregnancy, when drug therapy may be harmful to the unborn baby.

**Leukemia.** A cancer of the blood and bone marrow.

**Lymphocyte.** A type of white blood cell that is part of the immune system and fights infection.

**Marrow.** The spongy material in the center of bones where blood cells are made.

**Oncologist.** A doctor who treats people who have cancer.

**Pathologist.** A doctor who identifies diseases by studying cells and tissues under a microscope.

**PCR.** The short name for **polymerase chain reaction**, a sensitive lab test that can measure the presence of cancer cell markers in the blood or marrow. PCR testing is used to detect remaining cancer cells that cannot be detected by other tests.

**Plasma.** The liquid part of the blood.

**Platelet.** A type of blood cell that helps prevent bleeding. Platelets cause plugs to form in the blood vessels at the site of an injury.

**Red blood cell.** The type of blood cell that carries oxygen to all parts of the body. In healthy people, red blood cells make up almost half of the blood.

**Refractory CML.** CML that has not responded to initial treatment. Refractory disease may be disease that is getting worse or staying the same (stable disease).

**Relapsed CML.** CML that responded to treatment at first, but then returned.

**Remission.** A state in which there is no sign of the disease and/or a period of time when the disease is not causing any health problems.

**Resistance.** When a drug does not work or stops working.

**Sprycel® (dasatinib).** A **tyrosine kinase inhibitor** that is FDA approved for the treatment of newly diagnosed adult patients who have Ph positive CML in chronic phase and adults in all phases of CML (chronic, accelerated, or blast phase) who have resistance or intolerance to prior therapy including Gleevec.

**Stem cell.** A type of cell found in bone marrow that makes red blood cells, white blood cells and platelets.

**Synribo® (omacetaxine mepesuccinate).** A type of drug called a **protein synthesis inhibitor** that is FDA approved for adults with chronic or accelerated phase CML who no longer respond to or who have not been able to tolerate two or more TKIs.

**Tasigna® (nilotinib).** A type of drug called a **tyrosine kinase inhibitor** that is FDA approved for the treatment of newly diagnosed adult patients with Ph positive CML in chronic phase and adults in chronic phase and accelerated phase Ph positive CML who are resistant or intolerant to prior therapy that included Gleevec.

**Tyrosine kinase inhibitor (TKI).** A drug that blocks cell growth. Gleevec, Sprycel, Tasigna, Bosulif and Iclusig are TKIs that are used to treat CML.

**White cell.** A type of blood cell that helps the body fight infection.



## Questions to Help You Choose a Specialist

Asking questions will help you take an active role in managing your (or your child's) care. If you do not understand any part of the information your healthcare provider gives you, ask him or her to explain it in another way.

Doctor's name \_\_\_\_\_

Date of appointment or call \_\_\_\_\_

- 1.** What is your board certification and licensing? Are you a member of any professional societies?

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- 2.** How much experience do you have treating patients who have my disease?

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- 3.** Is your hospital, university, center or clinic accredited and experienced in treating blood cancers?

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- 4.** How long would I usually have to wait for appointments or return of my phone calls?

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**5.** Will there be nurses, social workers and case managers available to help me with support needs and quality-of-life concerns?

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**6.** Do you know of other oncologists who specialize in treating blood cancers? Would you recommend that I speak to any of them?

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**7.** What types of things should I call you about? What types of things should I call my family doctor about?

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**8.** How should I contact you when I have questions?

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**9.** How do I contact you at night? On weekends? On holidays?

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To print additional copies of this question guide, or to print copies of question guides on other topics, go to [www.LLS.org/whattoask](http://www.LLS.org/whattoask). You may also request that copies be sent to you by contacting our Information Specialists at (800) 955-4572.



Asking your healthcare provider questions at any phase of your treatment will help you take an active role in managing your (or your child's) care. If you do not understand any part of the information your healthcare provider gives you, ask him or her to explain it in another way.

Doctor's name \_\_\_\_\_

Date of appointment or call \_\_\_\_\_

- 1.** What are my (my child's) treatment options? What is the goal of the treatment?

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- 2.** What are the FDA-approved treatments, and are there treatments being studied in clinical trials (study treatments), for my (my child's) diagnosis?\*

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- 3.** What are the benefits and risks of the treatment(s) available to me (my child)? What are the expected side effects?

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- 4.** Is there one treatment option (FDA-approved or study treatment) that you recommend over the others? Please explain.

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**5.** If I (my child) enroll(s) in a clinical trial, who will be in charge of my (my child's) treatment?

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**6.** When do you think I (my child) will need to begin treatment?

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**7.** How long will I (my child) be treated and how many treatments will be needed?

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**8.** Will I (my child) need to be hospitalized for all or part of the treatment?

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**9.** What kind of testing will be done to monitor my (my child's) disease and treatment? How often will testing be needed?

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**10.** If I am treated at an out-patient clinic or at the doctor's office, will I be able to drive/get myself home after treatments or will I need someone to assist me?

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**11.** What are the risks if I don't (my child doesn't) get treatment?

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**12.** How will I know if the treatment is effective? What options are available if the treatment is not effective?

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**13.** How do I find out if my insurance will cover the costs of my (my child's) treatment or the study treatment? Who can help answer any medical questions my insurance company or health plan asks?

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**14.** If I do not have insurance coverage, how can the healthcare team help me (my child) get treatment? Is there someone I need to speak to for assistance?

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**15.** If I'm (my child is) getting a study treatment, will I be responsible for paying any treatment-related costs, such as tests, travel or the clinical trial drug(s)?

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**16.** Will the healthcare team continue to check on me (my child) after the treatment is over? If so, for what period of time?

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**17.** I (My child) would like to continue some type of lifelong follow-up care in order to be monitored for long-term and late effects of treatment. Can I (my child) follow up with you?

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\*For definitions of an FDA-approved treatment and a clinical trial (study treatment), visit [www.LLS.org](http://www.LLS.org) or contact an Information Specialist.

To print additional copies of this question guide, or to print copies of question guides on other topics, go to [www.lls.org/whattoask](http://www.lls.org/whattoask). You may also request that copies be sent to you by contacting our Information Specialists at (800) 955-4572.

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### **Co-Pay Assistance**

LLS's Co-Pay Assistance Program helps blood cancer patients cover the costs of private and public health insurance premiums, including Medicare and Medicaid, and co-pay obligations. Support for this program is based on the availability of funds by disease.

**For more information,**  
call **877.557.2672** or  
visit **www.LLS.org/copay**.

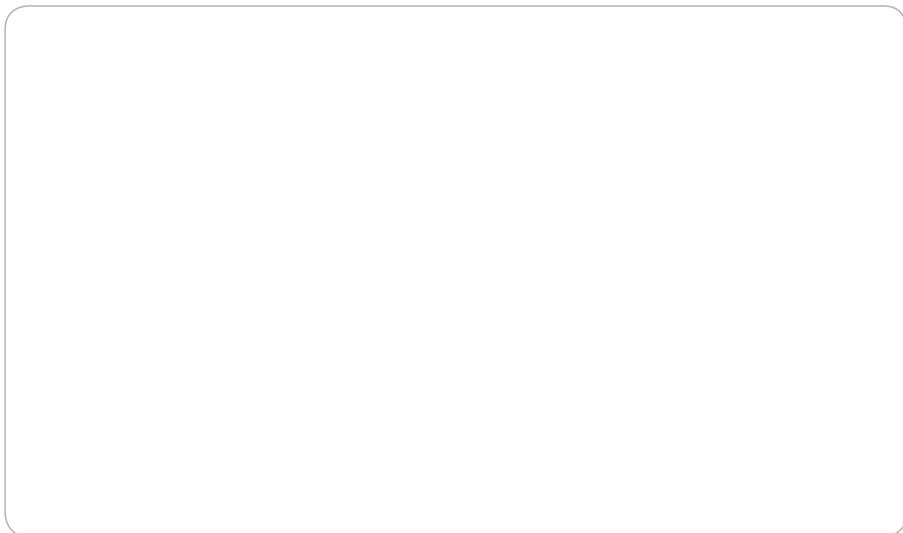


**For a complete directory of our patient services programs, contact us at**

**800.955.4572 or [www.LLS.org](http://www.LLS.org)**

*(Callers may request a language interpreter.)*

For more information, please contact:



or:

**National Office**

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Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.

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