

# Chronic Myeloid Leukemia (CML)

[www.novartis oncology.com](http://www.novartis oncology.com)

The articles in this section are provided by CancerSource, the leading provider of cancer information and patient education. Led by its world-class medical advisory board of renowned oncologists, CancerSource provides education that reflects the highest standards of editorial quality and integrity. The CancerSource mission is to enhance the efforts of its partners in the cancer community by providing information, programs and services that improve the quality of cancer care.

## What is CML?

Chronic myeloid leukemia (CML) is a slow growing cancer in which the bone marrow – the soft, spongy tissue in the center of bones – makes too many white blood cells. This type of leukemia is also called chronic myelogenous leukemia, chronic myelocytic leukemia, or chronic granulocytic leukemia.

## Statistics

CML is an uncommon type of leukemia, making up about 15% of all cases of leukemia among adults. About 4,000 to 5,000 new cases of the disease are diagnosed each year in the United States. People of any age can develop CML, but it is most common in adults 50 years of age and older.

## Risk Factors

Children of parents with CML do not have a greater risk of developing the disease. There is a question as to whether radiation used for treatment raises the risk of CML. No infectious agents are linked to the development of this leukemia.

## Screening

No standard screening process exists for detecting early stage leukemia. Doctors often find chronic leukemia during routine blood tests.

## Symptoms

During the early stages of CML most people do not have any symptoms of the disease. When symptoms do develop they include:

- Tiredness that will not go away
- Unexplained weight loss
- Fever
- Shortness of breath
- Night sweats
- Abdominal pain from a swollen spleen
- Poor appetite

People who have any of these symptoms should consult with their doctor. None of these symptoms prove that a person has cancer or leukemia and a true diagnosis can be made only by a trained oncologist or hematologist.

## Why CML Develops (Pathophysiology)

The bone marrow is where blood cells are made. There are three different types of blood cells that carry out different functions in the body:

- White blood cells, which help the body fight infection and disease
- Red blood cells, which move oxygen from the lungs throughout the body
- Platelets, which help control bleeding by forming clots

Cells in the bone marrow that mature into various types of blood cells are called blasts. Granulocytes are the type of blasts that mature into white blood cells. In CML granulocytes do not mature normally. Too many of these cells develop and they do not function correctly.

In about 95% of patients with CML, a defect in a chromosome (the genetic material) in the leukemia cells occurs. This defect is called the Philadelphia chromosome, named for the city where it was discovered. This abnormal chromosome forms when two chromosomes in the cell swap their genetic material. It is not clear what causes this to happen. Because of this event a protein that normally helps to regulate the production of new white blood cells in the bone marrow – the Abl protein – becomes stuck in the "on" position, telling the body to keep making more abnormal blood cells.

## How CML is Diagnosed (Diagnosis)

About half of all people with CML do not have symptoms at the time the disease is diagnosed. In these people the disease is found during routine blood tests.

Blood tests are done to count the different types of blood cells. A blood sample is looked at under the microscope and if an abnormally high number of mature and maturing white blood cells are noted, a bone marrow biopsy may be done.

The bone marrow sample is taken by a needle inserted into the bone. A small amount of bone marrow is taken and looked at under the microscope. A diagnosis of CML is based on the finding of the Philadelphia chromosome in cells of the bone marrow.

## The Phases of CML

CML progresses through three phases. The number of blasts in the blood and bone marrow and the severity of symptoms help doctors determine which phase of CML a patient is in.

- **Chronic phase.** In this phase there are few blasts (fewer than 5%) in the blood and bone marrow. There may be no symptoms of CML or symptoms may be mild. This phase can last for a few months to several years. Most cases of CML are diagnosed at this phase.
- **Accelerated phase.** The number of blast cells increases to about 15%. This phase can last weeks to months.
- **Blastic phase**, or blast crisis. More than 30% of cells are blasts. Sometimes blast cells will form tumors outside of the bone marrow in the bone or lymph nodes. At this point chronic leukemia has become an aggressive acute leukemia.

## How CML is Treated (Treatment)

Different treatment options are available for patients with CML. Bone marrow transplantation, drug therapy, radiation therapy, biologic therapy, or a combination of these approaches are used. Additionally, if the spleen is swollen, it may be removed.

The age of the patient, the phase of CML the patient is in, and other factors are considered in coming up with the best treatment plan for a patient.

**Stem cell transplantation (SCT).** SCT is the only treatment for CML known to bring about a cure. For this reason doctors will consider this treatment first for a newly diagnosed patient. But because SCT is a risky procedure that puts a great deal of strain on the body, not all patients can

tolerate this treatment. This method is most successful when used in patients in the chronic phase of CML and in younger patients.

The goal of SCT is to kill the patient's damaged bone marrow (the stem cells are in the bone marrow) and replace it with healthy bone marrow. If the transplanted cells take hold, they grow and produce healthy blood cells.

The first step in stem cell transplantation involves destroying the patient's existing bone marrow with high doses of one or more types of anticancer drugs. Sometimes radiation therapy is also used. Both healthy and unhealthy bone marrow cells are killed in this step.

Most often the patient's bone marrow is replaced with healthy tissue from another person (the donor). This is called an allogeneic transplant. The patient receives the donor marrow through a needle into a vein, much like a blood transfusion. The donor marrow must closely match the tissue of the patient to allow the patient's body to accept the transplant. The most suitable donor is often a brother, sister, or another family member of the patient who has the same tissue type—known as HLA type—as the patient. If there is not a family member with the same tissue type, the doctor may search for a donor whose tissue type matches the patient. There are computerized lists of volunteer donors set up for this purpose. However, it can be difficult to find a donor whose tissue is a close enough match to use successfully.

Another approach is to use bone marrow taken from the patient. This is called an autologous transplant. This approach involves taking bone marrow from the patient and treating it with anticancer drugs with or without radiation to destroy the cancer cells. The patient then receives high-dose chemotherapy to kill the remaining bone marrow. After this step, the saved and treated bone marrow is injected through a vein back into the patient.

**Interferon alpha.** Called a biological therapy because it is a substance that the body makes to fight disease, interferon-alpha is given by injection. It can help slow the growth of the leukemia cells and prolong life in about two-thirds of patients. Other patients either do not respond or cannot tolerate the drug's side effects, which include flu-like symptoms such as fever, chills and fatigue. Interferon-alpha may be given alone or in combination with the drug cytarabine (ara-C). Interferon-alpha can produce long periods where the patient is free of the signs and symptoms of CML, but it does not bring about a lasting cure as SCT can.

**Chemotherapy.** Hydroxyurea and busulfan are two oral chemotherapy drugs that are used when patients cannot receive SCT or interferon-alpha or while they are waiting for the SCT. These drugs are usually better tolerated than interferon-alpha and can lessen the symptoms of CML. As with interferon-alpha, they do not provide a lasting cure.

**Tyrosine Kinase Inhibitors (TKI's),** molecularly-targeted agents to block the bcr-abl oncogenic pathway of CML, have revolutioned treatment of this disease. Most newly diagnosed patients are now considered appropriate candidates for TKI therapy which offers excellent rates of disease control for at least 5 years.

Disclaimer: This document is intended to provide information to audiences outside the United States. Please note that not all products listed within this document may be available in all countries. Also, prescribing information and indications for products may differ from country to country, so please consult your local Novartis company for local prescribing and any other information you may be interested in.

© 2007 Novartis AG