Leukemia--Chronic Myeloid (Myelogenous)

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide into new cells, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn’t die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called benign. Benign tumors can cause problems -- they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can’t invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

What is chronic myeloid leukemia?

Chronic myeloid leukemia (CML), also known as *chronic myelogenous leukemia*, is a type of cancer that starts in the blood-forming cells of the bone marrow and invades the blood. In CML, leukemia cells tend to build up in the body over time, but in many cases people don't have any symptoms for at least a few years. In time, the cells can also invade other parts of the body, including the spleen. CML can also change into a fast-growing acute leukemia that invades almost any organ in the body.

Most cases of CML occur in adults, but very rarely it occurs in children, too. In general, their treatment is the same as for adults.

Leukemia is different from other types of cancer that start in organs such as the lungs, colon, or breast and then spread to the bone marrow. Cancers that start elsewhere and then spread to the bone marrow are not leukemia.

Normal bone marrow, blood, and lymphoid tissue

To understand the different types of leukemia, it helps to have some basic knowledge about the blood and lymph systems. The information which follows is quite complex. It may prove helpful, but you don't need to understand all of it to learn more about your leukemia.

Bone marrow

Bone marrow is the soft inner part of some bones such as the skull, shoulder blades, ribs, pelvis, and backbones. Bone marrow is made up of a small number of blood stem cells, more mature blood-forming cells, fat cells, and supporting tissues that help cells grow.

The blood-forming cells come from blood *stem cells*. These stem cells only make new blood-forming cells, not other kinds of cells. (This makes them different from embryonic stem cells, which form in a developing fetus and can develop into most other cells in the body.)

Stem cells go through a series of changes. During this process, the cells develop into cells that become *lymphocytes* (a kind of white blood cell) or into cells that form other cells found in blood. These other cells include red blood cells, white blood cells (other than lymphocytes), or platelets.

Red blood cells

Red blood cells carry oxygen from the lungs to all other tissues in the body and take carbon dioxide back to the lungs to be removed. Not having enough red blood cells in the body is called *anemia*. Symptoms of anemia include weakness, fatigue, and shortness of breath because the body tissues are not getting enough oxygen.

Platelets

Platelets aren't actually whole cells, but instead are pieces of large cells found in the bone marrow called *megakaryocytes*. Platelets are important in plugging up holes in blood vessels caused by trauma. A shortage of platelets is called *thrombocytopenia*, and can lead to problems with easy bruising and bleeding.

White blood cells

White blood cells are important in defending the body against infections. Lymphocytes are one type of white blood cell. The other types of white blood cells are granulocytes and monocytes.

Lymphocytes are the main cells that make up lymphoid tissue, a major part of the immune system. Lymphoid tissue is found in lymph nodes, the thymus gland, the spleen, the tonsils, and the adenoids. It is also scattered throughout the digestive and respiratory systems and the bone marrow.

Lymphocytes develop from cells called *lymphoblasts* to become mature, infection-fighting cells. The 2 major types of lymphocytes are known as B lymphocytes (B cells) and T lymphocytes (T cells).

- B lymphocytes protect the body from invading germs by developing (maturing) into plasma cells, which make antibodies. These antibodies attach to the germs, such as bacteria, viruses, and fungi. Once the germ has been coated in this way, it can be targeted by other parts of the immune system and be destroyed.
- T lymphocytes can recognize cells infected by viruses and directly destroy these cells.

Granulocytes develop from blood-forming cells called *myeloblasts* to become mature, infection-fighting cells. These white blood cells are called *granulocytes* because they contain granules, which can be seen as spots in the cells when they are looked at under the microscope. These granules contain enzymes and other substances that can destroy germs such as bacteria. The 3 types of granulocytes -- *neutrophils*, *basophils*, and *eosinophils* -- are distinguished by the size and color of their granules. Neutrophils are the most common type of granulocyte in the blood. They are essential in destroying bacteria that have invaded the blood.

Monocytes are related to granulocytes and are important because they protect the body against bacteria. They start in the bone marrow as blood-forming *monoblasts* and develop into mature monocytes. Monocytes circulate in the bloodstream for about a day and then they enter body tissues to become *macrophages*. These microphages can destroy some germs by surrounding and digesting them. Macrophages are also important because they help lymphocytes recognize germs and start making antibodies to fight them.

How leukemia starts

Any blood-forming or lymphoid cells can turn into a leukemia cell. Once this change takes place, the leukemia cells fail to go through their normal process of maturing. Leukemia cells may reproduce too quickly, but in most cases the problem is that they don't die when they should. They survive and build up, often crowding out normal bone marrow cells. This can lead to low counts of normal blood cells. Over time, leukemia cells spill into the bloodstream and spread to other organs, where they can prevent other cells in the body from working the way they should.

Types of leukemia

Not all leukemias are the same. Leukemias are divided into 4 main types. Knowing the specific type of leukemia can help doctors better predict each patient's prognosis (outlook) and select the best treatment.

Acute leukemia versus chronic leukemia

The first factor considered in classifying a patient's leukemia is whether most of the abnormal cells are mature (look like normal white blood cells) or immature (look more like stem cells).

Acute leukemia: In acute leukemia, the bone marrow cells cannot mature the way they should. These immature cells continue to reproduce and build up. Without treatment, most patients with acute leukemia would only live a few months. Some types of acute leukemia respond well to treatment, and many patients can be cured. Other types of acute leukemia have a less favorable outlook.

Chronic leukemia: In chronic leukemia, the cells can mature partly but not completely. These cells are not really normal, but they look more normal than the immature cells of acute leukemia. They generally do not fight infection as well as normal white blood cells do. And, of course, they survive longer, build up, and crowd out normal cells. Chronic leukemias tend to develop over a longer period of time, and most patients can live for many years. However, chronic leukemias are generally harder to cure than acute leukemias.

Myeloid leukemia versus lymphocytic leukemia

The second factor considered in classifying leukemia is the type of bone marrow cells that is affected.

Leukemias that start in early myeloid cells -- the cells that become white blood cells (other than lymphocytes), red blood cells, or platelet-making cells (megakaryocytes) -- are called *myeloid* leukemias. These are also known as *myelocytic*, *myelogenous*, or *non-lymphocytic* leukemias.

Leukemias that start in the cells that become lymphocytes are called *lymphocytic* leukemia. These are also known as *lymphoblastic* or *lymphoid* leukemias.

A doctor can look at the leukemia cells under a microscope and do certain tests to see if the leukemia is acute or chronic and whether the cells are myeloid or lymphocytic. This allows leukemias to be divided into 4 main types:

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

The rest of this document has information on chronic myeloid leukemia (CML) only. Separate American Cancer Society documents on other forms of acute and chronic leukemias are available. This document does not have information on chronic myelomonocytic leukemia (CMML), which is covered in our separate document, Leukemia: Chronic Myelomonocytic .

What are the key statistics about chronic myeloid leukemia?

The American Cancer Society's estimates for chronic myeloid leukemia (CML) in the United States for 2013 are:

- About 5,920 new cases will be diagnosed with CML (3,420 in men and 2,500 in women).
- About 610 people will die of CML (340 men and 270 women).

CML accounts for a little over 10% of all new cases of leukemia. The average person's lifetime risk of getting CML is about 1 in 625. This disease is slightly more common in men than in women. It is also more common in whites than in African-Americans.

The average age at diagnosis of CML is around 65 years. Over half of cases are diagnosed in people 65 and older. This type of leukemia mainly affects adults, and is only rarely seen in children.

Dramatic progress has been made in treatment over the past several years, so most people with CML are now surviving *at least* 5 years after diagnosis. But because the highly effective drugs are still fairly new, the average survival of people now being diagnosed with CML is not known.

What are the risk factors for chronic myeloid leukemia?

A risk factor is something that affects a person's chance of getting a disease such as cancer. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for a number of cancers. But risk factors are rarely absolute. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And many people who get the disease may not have had any known risk factors.

There are very few known risk factors for CML and for most cases, no cause is found.

High-dose radiation exposure

Being exposed to high-dose radiation (such as being a survivor of an atomic bomb blast or nuclear reactor accident) is the only known environmental risk factor for chronic myeloid leukemia.

Age and gender

The risk of getting CML increases with age. This disease is slightly more common in males than females, but it's not known why.

There are no other proven risk factors for CML. The risk of getting CML does not seem to be affected by smoking, diet, exposure to chemicals, or infections. And CML does not run in families.

Do we know what causes chronic myeloid leukemia?

Normal human cells grow and function based mainly on the information contained in each cell's chromosomes. Chromosomes are long molecules of DNA in each cell. DNA is the chemical that carries our genes, the instructions for how our cells function. We look like our parents because they are the source of our DNA. But our genes affect more than the way we look.

Each time a cell prepares to divide into 2 new cells, it must make a new copy of the DNA in its chromosomes. This process is not perfect, and errors can occur that may affect genes within the DNA.

Some genes contain instructions for controlling when our cells grow and divide. Certain genes that promote cell growth and division are called *oncogenes*. Others that slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*. Cancers can be caused by changes in DNA (mutations) that turn on oncogenes or turn off tumor suppressor genes.

During the past few years, scientists have made great progress in understanding how certain changes in DNA can cause normal bone marrow cells to become leukemia cells. In no cancer is this better understood than in chronic myeloid leukemia (CML).

Each human cell contains 23 pairs of chromosomes. Most cases of CML start when a "swapping" of chromosomal material (DNA) occurs between chromosomes 9 and 22 during cell division. Part of chromosome 9 goes to 22 and part of 22 goes to 9. This is known as a *translocation* and gives rise to a chromosome 22 that is shorter than normal. This new abnormal chromosome is known as the *Philadelphia chromosome.* The Philadelphia chromosome is found in the leukemia cells of almost all patients with CML.

The swapping of DNA between the chromosomes leads to the formation of a new gene (an oncogene) called *BCR-ABL*. This gene then produces the BCR-ABL protein, which is the type of protein called a *tyrosine kinase*. This protein causes CML cells to grow and reproduce out of control.

In a very small number of CML patients, the leukemia cells have the *BCR-ABL* oncogene but not the Philadelphia chromosome. It is thought that the *BCR-ABL* gene must form in a different way in these people. In a very small number of people who seem to have CML, neither the Philadelphia chromosome nor the *BCR-ABL* oncogene can be found. They might have other, unknown oncogenes causing their disease and are not considered to truly have CML.

Sometimes people inherit DNA mutations from a parent that greatly increase their risk of getting certain types of cancer. But inherited mutations do not cause CML. DNA changes related to CML occur during the person's lifetime, rather than having been inherited before birth.

Can chronic myeloid leukemia be prevented?

There is no known way to prevent most cases of chronic myeloid leukemia (CML). Many types of cancer can be prevented by lifestyle changes to avoid certain risk factors, but this is not true for most cases of CML. The only potentially avoidable risk factor for CML is exposure to high doses of radiation, which is seen in only a few cases.

Can chronic myeloid leukemia be found early?

The American Cancer Society recommends screening tests for certain cancers in people who have no symptoms because these cancers are easier to treat if found early. But at this time, no screening tests are routinely recommended for early detection of chronic myeloid leukemia (CML).

CML can sometimes be found on routine blood tests done for other reasons. For instance, a person's white blood cell count may be very high, even though he or she doesn't have any symptoms.

It is important to report any symptoms that could be caused by CML to the doctor right away. The symptoms of CML are discussed in the next section, "How is chronic myeloid leukemia diagnosed?"

How is chronic myeloid leukemia diagnosed?

Many people with CML do not have symptoms when it is diagnosed. The leukemia is often found when their doctor orders blood tests for an unrelated health problem or during a routine checkup. Even when symptoms are present, they are often vague and non-specific.

Signs and symptoms of chronic myeloid leukemia

Symptoms of CML can include the following:

- Weakness
- Fatigue
- Night sweats
- Weight loss
- Fever
- Bone pain
- An enlarged spleen (felt as a mass under the left side of the ribcage)
- Pain or a sense of "fullness" in the belly
- Feeling full after eating even a small amount of food

But these aren't just symptoms of CML. They can occur with other cancers, as well as many non-cancerous conditions.

Some patients have bone pain or joint pain caused by leukemia cells spreading from the marrow cavity to the surface of the bone or into the joint.

Problems caused by a shortage of blood cells

Many of the signs and symptoms of CML occur because the leukemia cells replace the bone marrow's normal blood-making cells. As a result, people with CML do not make enough red blood cells, properly functioning white blood cells, and blood platelets.

- *Anemia* is a shortage of red blood cells. It can cause weakness, tiredness, and shortness of breath.
- *Leukopenia* is a shortage of normal white blood cells. This shortage increases the risk of infections. Although patients with leukemia may have very high white blood cell counts, the leukemia cells do not protect against infection the way normal white blood cells do.
- *Neutropenia* means that the level of normal neutrophils is low. Neutrophils, a type of white blood cell, are very important in fighting infection from bacteria. People who are neutropenic have a high risk of getting very serious bacterial infections.
- *Thrombocytopenia* is a shortage of blood platelets. It can lead to excess bruising or bleeding, with frequent or severe nosebleeds and bleeding gums. Some patients with

CML actually have too many platelets (*thrombocytosis*). But since those platelets often do not function properly, these people often have problems with bleeding and bruising as well.

Types of samples used to test for chronic myeloid leukemia

If signs and symptoms suggest you may have leukemia, the doctor will need to check samples (specimens) of blood and bone marrow to be certain of this diagnosis. Other tissue and cell samples may also be taken in order to treat CML.

Blood samples

Blood samples for tests for CML are generally taken from a vein in the arm.

Bone marrow samples

Bone marrow samples are taken from a bone marrow aspiration and biopsy. These 2 tests are usually done at the same time. The samples are taken from the back of the pelvic (hip) bone, although in some cases they may be taken from the breastbone (sternum) or other bones.

For a bone marrow *aspiration*, you lie on a table (either on your side or on your belly). After the area is cleaned, the skin over the hip and the surface of the bone is numbed with local anesthetic, which may cause a brief stinging or burning sensation. A thin, hollow needle is then inserted into the bone and a syringe is used to suck out a small amount (about 1 teaspoon) of liquid bone marrow. Even with the anesthetic, most patients still feel some brief pain when the marrow is removed.

A bone marrow *biopsy* is usually done just after the aspiration. A small piece of bone and marrow (about 1/16 inch in diameter and 1/2 inch long) is removed with a slightly larger needle that is twisted as it is pushed down into the bone. The biopsy may also cause some brief pain. Once the biopsy is done, pressure will be applied to the site to help prevent bleeding.

These samples are sent to a lab, where they are looked at under a microscope for leukemia cells. These tests may also be done after treatment to see if the leukemia is responding to treatment.

Lab tests

One or more of the following lab tests may be used to diagnose CML or to help determine how advanced the disease is.

Blood cell counts and blood cell exam

The complete blood count (CBC) is a test that measures the levels of different cells, like red blood cells, white blood cells, and platelets, in the blood. The CBC often includes a differential (diff), which is a count of the different types of white blood cells in the blood sample. In a blood smear, some of the blood is put on a slide to see how the cells look under the microscope. Most patients with CML have too many white blood cells with many early (immature) cells. Sometimes CML patients have low numbers of red blood cells or blood platelets. Even though these findings may suggest leukemia, this diagnosis usually needs to be confirmed with another blood test or a test of the bone marrow.

Blood chemistry tests

These tests measure the amount of certain chemicals in the blood, but they are not used to diagnose leukemia. They can help find liver or kidney problems caused by the spread of leukemia cells or by the side effects of certain chemotherapy drugs. These tests also help determine if treatment is needed to correct low or high blood levels of certain minerals.

Routine exam under a microscope

The samples of blood and bone marrow are looked at under a microscope by a pathologist (a doctor who specializes in diagnosing diseases with lab tests) and may be looked at by a hematologist/oncologist (a doctor specializing in treating blood diseases and cancer) as well.

The doctors will look at the size and shape of the cells in the samples and whether they contain granules (small spots seen in some types of white blood cells).

An important factor is whether the cells look mature (like normal circulating blood cells) or immature (lacking features of normal circulating blood cells). The most immature cells are called myeloblasts (often called *blasts*).

An important feature of a bone marrow sample is how much of it is blood-forming cells - this is known as *cellularity*. Normal bone marrow contains both blood-forming cells and fat cells. When the bone marrow has more blood-forming cells than expected, it is said to be *hypercellular*. If too few of these cells are found, the marrow is called *hypocellular*. In people with CML, the bone marrow is often hypercellular because it is full of leukemia cells.

Genetic tests

Some sort of gene testing will be done to look for the Philadelphia chromosome and/or the *BCR-ABL* gene. This type of test is used to confirm the diagnosis of CML.

Conventional cytogenetics: This test looks at chromosomes (pieces of DNA) under a microscope to find any changes. It is also called *karyotyping*. Chromosomes in a cell can best be seen when the cell is dividing. That is why to do this test, a sample of blood or bone marrow has to be grown (in the lab) so that the cells start to grow and divide. This takes time, and is not always successful. Normal human cells have 23 pairs of chromosomes, each of which is a certain size. The leukemia cells in many CML patients contain an abnormal chromosome known as the *Philadelphia chromosome*, which looks like a short chromosome 22. It is caused by swapping pieces (translocation) between chromosomes 9 and 22 (see the section, "Do we know what causes chronic myeloid leukemia?"). Finding a Philadelphia chromosome is helpful in diagnosing CML. Even when the Philadelphia chromosome can't be seen, other tests can often find the *BCR-ABL* gene.

Fluorescent in situ hybridization: Fluorescent in situ hybridization (FISH) is another way to look at chromosomes. This test uses special fluorescent dyes that only attach to specific parts of chromosomes. FISH can be used to look for specific pieces of the *BCR-ABL* gene on chromosomes. It can be used on regular blood or bone marrow samples without culturing the cells first. FISH is very accurate, and is used in many medical centers.

Polymerase chain reaction (PCR): This is a super-sensitive test for looking for the *BCR-ABL* oncogene in leukemia cells. It can be done on blood or bone marrow samples and can detect very small amounts of *BCR-ABL*, even when doctors can't find the Philadelphia chromosome in bone marrow cells with cytogenetic testing. PCR can be used to help diagnose CML and is also useful after treatment to see if copies of the *BCR-ABL* gene are still there. If copies of this gene are still present it means that the leukemia is still present, even when the cells aren't visible under the microscope.

Imaging tests

Imaging tests produce pictures of the inside of the body. There are several imaging tests that might be done in people with leukemia. They are not needed to diagnose the leukemia, but they may be done to help find the extent of the disease.

Computed tomography scan

The computed tomography (CT) scan is a type of x-ray test that produces detailed, cross-sectional images of your body. Unlike a regular x-ray, CT scans can show the detail in soft tissues (such as internal organs). This test can help tell if any organs in your body are enlarged. It isn't usually needed to diagnose CML, but it may be done if your doctor suspects leukemia is growing in an organ, like your spleen.

Instead of taking one picture like a regular x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into detailed images of the part of your body that is being studied.

Often before any pictures are taken, you may be asked to drink 1 to 2 pints of a liquid called *oral contrast*. This helps outline the intestine more clearly. You may also receive an IV (intravenous) line through which a different kind of contrast dye (IV contrast) is injected. This helps better outline blood vessels and internal organs.

The IV injection of contrast dye can cause some flushing (redness and a feeling of warmth in the face or elsewhere). Some people are allergic to the dye and get hives. Rarely, more serious reactions like trouble breathing and low blood pressure can occur. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table moves in and out of the scanner, a ring-shaped machine that completely surrounds the table. You might feel a bit confined lying in the ring while the pictures are being taken.

Magnetic resonance imaging scan

Magnetic resonance imaging (MRI) scans are very helpful in looking at the brain and spinal cord. These scans can also be used to look at other areas of the body. MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. Not only does this create images of cross-sectional slices of the body like a CT scanner, it can also produce images of slices that are parallel with the length of your body. A contrast material might be injected, just as with CT scans, but this is done less often.

MRI scans take longer than CT scans, often up to an hour. You may have to lie inside a narrow tube, which is confining and can upset people with a fear of enclosed spaces. Special, "open" MRI machines may help with this problem. The MRI machine makes loud buzzing noises that you may find disturbing. Some places provide headphones to block this noise out.

Ultrasound

Ultrasound uses sound waves and their echoes to make a picture of internal organs or masses. For this test a small, microphone-like instrument called a *transducer* is placed on the skin (which is first lubricated with a gel). It gives off sound waves and picks up the echoes as they bounce off the organs. The echoes are converted by a computer into an image that is shown on a computer screen.

Abdominal ultrasound may be used to look for enlarged organs in your abdomen, like the liver and spleen.

This is an easy test to have done, and it doesn't use radiation. You simply lie on a table, and a technician moves the transducer over the part of your body being looked at.

Chest x-ray

A plain x-ray of your chest can be done in most outpatient settings. In patients with CML, it isn't needed for a diagnosis, but an x-ray may be used to see if you have normal lungs or if you have an infection.

How is chronic myeloid leukemia staged?

For most cancers, staging is the process of finding out how far the cancer has spread. Most types of cancer are given stages of I, II, III, or IV, based on the size of the tumor and how far from the original site in the body the cancer has spread. Stages are useful because they can help guide your treatment. They also help determine your prognosis (outlook).

Chronic myeloid leukemia (CML) is a disease of the bone marrow. It isn't staged like most cancers. The outlook for someone with CML depends on other information, such as the phase of the disease, as well as factors like the age of the patient, blood counts, and if the spleen is enlarged.

Phases of chronic myeloid leukemia

CML is divided into 3 groups that help predict outlook. Doctors call these groups *phases* instead of stages. The phases are based mainly on the number of immature white blood cells — myeloblasts (blasts) — that are seen in the blood or bone marrow. Different groups of experts have suggested slightly different cutoffs to define the phases, but a common system (proposed by the World Health Organization) is described below.

Chronic phase

Patients in this phase typically have less than 10% blasts in their blood or bone marrow samples. These patients usually have fairly mild symptoms (if any) and usually respond to standard treatments. Most patients are diagnosed in the chronic phase.

Accelerated phase

Patients are considered to be in accelerated phase if any of the following are true:

- The bone marrow or blood samples have more than 10% but fewer than 20% blasts
- High blood basophil count (basophils making up at least 20% of the white blood cells)

- High white blood cell counts that do not go down with treatment
- Very high or very low platelet counts that are not caused by treatment
- New chromosome changes in the leukemia cells

Patients whose CML is in accelerated phase may have symptoms such as fever, poor appetite, and weight loss. CML in the accelerated phase does not respond as well to treatment as CML in the chronic phase.

Blast phase (also called acute phase or blast crisis)

Bone marrow and/or blood samples from a patient in this phase have more than 20% blasts. The blast cells often spread to tissues and organs beyond the bone marrow. These patients often have fever, poor appetite, and weight loss. In this phase, the CML acts much like an aggressive acute leukemia.

Not all doctors may agree with or follow these cutoff points for the different phases. If you have questions about what phase your CML is in, be sure to have your doctor explain it to you.

Prognostic factors for chronic myeloid leukemia

Along with the phase of CML, there are other factors that may help predict the outlook for survival. These factors are sometimes helpful when choosing treatment. Factors that tend to be linked with shorter survival time are called *adverse prognostic factors*.

Adverse prognostic factors:

- Accelerated phase or blast phase
- Enlarged spleen
- Areas of bone damage from growth of leukemia
- Increased number of basophils and eosinophils (certain types of granulocytes) in blood samples
- Very high or very low platelet counts
- Age 60 years or older
- Multiple chromosome changes in the CML cells

Many of these factors are taken into account in the *Sokal system*, which develops a score used to help predict prognosis. This system considers the person's age, the percentage of blasts in the blood, the size of the spleen, and the number of platelets. These factors are

used to divide patients into low-, intermediate-, or high-risk groups. Another system, called the *Euro score*, includes the above factors, as well as the number of blood basophils and eosinophils. Having more of these cells indicates a poorer outlook.

The Sokal and Euro models were helpful in the past, before the newer, more effective drugs for CML were developed. It's not clear how helpful they are at this time in predicting a person's outlook. Newer drugs like imatinib (Gleevec®), dasatinib (Sprycel®), and nilotinib (Tasigna®) have changed the treatment of CML dramatically in recent years. These models haven't been tested in people who are being treated with these drugs.

Survival rates for chronic myeloid leukemia

New, highly effective drugs to treat most cases of CML first became available in 2001. There is no accurate information yet on how long patients treated with these drugs may live. All that is known is that most patients who have been treated with these drugs, starting in 2001 (or even before), are still alive.

One large study of CML patients treated with imatinib (Gleevec) found that about 90% of them were still alive 5 years after starting treatment. Most of these patients had normal white blood cells and chromosome studies after 5 years on the drug.

How is chronic myeloid leukemia treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

General information

This section starts with general comments about types of treatments used for chronic myeloid leukemia (CML). This is followed by a discussion of treatment options based on the phase of CML.

Targeted therapies for chronic myeloid leukemia

In the last 10 years, new drugs that target specific parts of cancer cells have become a standard treatment option for many people with cancer. Chronic myeloid leukemia

(CML) cells contain an oncogene, *BCR-ABL*, that isn't found in normal cells. This gene makes a protein, BCR-ABL, which causes CML cells to grow and reproduce out of control. BCR-ABL is a type of protein known as a *tyrosine kinase*. Drugs that target BCR-ABL, known as *tyrosine kinase inhibitors* (TKIs), have become standard treatment for CML. These drugs are less likely to affect normal cells, so their side effects are generally not as severe as those seen with standard chemotherapy drugs or with interferon (described in the “Interferon therapy for chronic myeloid leukemia” section). Still, these drugs do have side effects, some of which are discussed below. It is also important to understand that all of the TKIs can cause harm to the fetus if taken during pregnancy. These drugs seem to work best on CML that is still in the chronic phase, but some of the newer drugs also help patients with more advanced disease.

Imatinib

Imatinib (Gleevec) was the first drug to specifically target the BCR-ABL tyrosine kinase protein, and it quickly became the standard treatment for patients found to have CML. Because it was the first TKI, imatinib is known as a first generation tyrosine kinase inhibitor.

Almost all CML patients respond to treatment with imatinib, and most of these responses seem to last for many years. This drug doesn't seem to make the leukemia go away and stay away, so patients need to take it indefinitely (or until it stops working). Imatinib is taken by mouth as a pill with food, usually once a day.

The possible side effects of imatinib are usually less severe than those seen with standard chemotherapy drugs or with interferon (described in the “Interferon therapy for chronic myeloid leukemia” section). But side effects can be more serious at higher doses of the drug.

Common side effects can include diarrhea, nausea, muscle pain, and fatigue. These are generally mild. Itchy skin rashes occur in about 30% of people on the drug. Most of these symptoms can be treated effectively, if needed.

Another common side effect is fluid buildup around the eyes, feet, or abdomen. In rare cases the fluid may collect in the lungs or around the heart, which can cause trouble with breathing. Some studies have suggested that some of this fluid buildup may be caused by effects of the drug on the heart, though this is rare. It's not yet clear how serious this is or if it might go away if treatment is stopped. If you are taking this drug, tell your doctor right away if you notice sudden weight gain, trouble breathing, or fluid buildup anywhere in the body.

Many drugs can interact with imatinib, causing problems. Be sure that your doctor always has an up-to-date list of any medicines you are taking, including over-the-counter medicines, vitamins, and supplements.

Another possible side effect is a drop in a person's white blood cell and platelet counts. When this happens at the beginning of treatment, it might be because the blood-forming cells that are making these are part of the malignant process. If this is the case, normal blood-forming cells take over and the blood counts will begin to rise to normal over time. Your doctor might tell you to stop taking the drug for a short period if your blood counts get too low. This can also happen later on in treatment. In the past, low red blood cell counts were treated with a red cell growth factor, such as erythropoietin (Procrit®) or darbepoietin (Aranesp®), but these drugs are used less often now. Instead, your doctor may lower the dose of imatinib to see if counts improve.

In some patients, imatinib eventually seems to stop working. This is known as imatinib *resistance*. Resistance to imatinib seems to be caused by changes in the genes of the CML cells. Sometimes this resistance can be overcome by increasing the dose of imatinib, but some patients need to change to a different drug, such as one of the other TKIs described further on.

Dasatinib

Dasatinib (Sprycel) is another tyrosine kinase inhibitor that targets the BCR-ABL protein. Because it came after imatinib, it is called a second generation TKI. Like imatinib, this drug is taken by mouth as a pill.

Dasatinib was first used to treat CML in patients who couldn't take imatinib because of side effects or because imatinib wasn't working. Later studies showed that when it was used as the first treatment, it worked better than imatinib for many patients with CML. It has now been approved to be used as the first treatment for CML.

The dose of dasatinib that was first used was 70 mg twice a day. Later, doctors realized that giving 100 mg once a day works just as well with fewer side effects, and so this dose is used most often. The dose for patients in accelerated or blast phase is 140 mg once a day.

The possible side effects of dasatinib seem to be similar to those for imatinib, including fluid buildup, lowered blood cell counts, nausea, diarrhea, and skin rashes. A serious side effect that can occur with this drug is fluid buildup around the lung (called a *pleural effusion*). This side effect is more common in patients taking this drug twice a day. The fluid can be drained off with a needle, but it can build up again, and may require the dose of dasatinib to be decreased.

As with imatinib, there are many drugs that interact with dasatinib and should be avoided. Be sure that your doctor always has an up-to-date list of any medicines you are taking, including over-the-counter medicines.

Nilotinib

Nilotinib (Tasigna) is another second generation TKI that targets the BCR-ABL protein. Like dasatinib, this drug was initially approved for use in people who couldn't take imatinib or whose CML no longer responds to it. This includes patients in accelerated and blast phase. It has also been studied as a first treatment in a clinical trial comparing nilotinib to imatinib in patients who were newly diagnosed with CML. In this study, nilotinib was more effective than imatinib, and nilotinib is now approved as a first treatment for CML.

Side effects of nilotinib seem to be mild, but can include fluid buildup, lowered blood cell counts, nausea, diarrhea, and some lab test abnormalities. It can cause high blood sugars and pancreatitis, although this is rare. This drug can also affect the rhythm of the heart, causing something called *prolonged QT syndrome*. This usually doesn't cause any symptoms, but can be serious or even fatal. This is why patients should have an electrocardiogram (EKG) before starting nilotinib and then again while being treated.

Like other tyrosine kinase inhibitors, certain drugs can interact with nilotinib and should be avoided. This drug can cause a serious (or even fatal) heart rhythm problem, so it's especially important to be sure that your cancer doctor is aware of any medicines you take, including over the counter medicines and supplements. You also need to check with your doctor before starting any new medicine, to be sure it is safe.

Bosutinib

Bosutinib (Bosulif®) is another TKI targeting the BCR-ABL protein. At this time, this drug is only FDA approved to treat patients after they have been treated with another TKI.

Common side effects are usually mild and include diarrhea, nausea, vomiting, abdominal pain, rash, fever, fatigue, and low blood cell counts (including low platelet counts, low red blood cell counts, and low white blood cell counts). Less often, this drug can also cause problems with fluid retention, liver damage, and severe allergic reaction. Your doctor will check blood work regularly to watch for problems with your liver and low blood counts.

Like other TKIs, bosutinib can interact with a number of other drugs, so it is important to be sure that your cancer doctor is aware of any medicines you take, including over the counter medicines and supplements. You also need to check with your doctor before starting any new medicine, to be sure it is safe.

Ponatinib

Ponatinib (Iclusig™) is a new TKI targeting the BCR-ABL protein. This drug is used to treat patients with CML after they have already been treated with another TKI. This drug

often works when all of the other TKIs don’t. In some patients with CML, treatment with a TKI can cause the cancer cells to develop a particular gene change (called the T315I mutation) that makes other TKIs not work. Ponatinib is the first TKI to work against CML cells that have this mutation.

This drug is taken as a pill, once a day.

Most side effects are mild and can include abdominal (belly) pain, headache, rash or other skin problems, and fatigue. High blood pressure is also fairly common, and it may need to be treated with a blood pressure drug. Less often, more serious side effects can occur, such as blood clots affecting arteries that can cause heart attacks or stroke, liver problems, and pancreatitis (inflammation of the pancreas, which can lead to severe belly pain, nausea, and vomiting).

Interferon therapy for chronic myeloid leukemia

Interferons are a family of substances naturally made by our immune system. Interferon-alpha is the type most often used in treating chronic myeloid leukemia (CML). This substance reduces the growth and division of leukemia cells. Interferon was once considered the best treatment for CML, but imatinib (Gleevec) was shown to be better. Now, the tyrosine kinase inhibitors are the mainstay of treatment and interferon is rarely used.

To treat CML, this drug is most often given as a daily injection under the skin. It may also be injected into a muscle or vein. To treat CML, interferon is given for several years.

Interferon can cause significant side effects. These include "flu-like" symptoms like muscle aches, bone pain, fever, headaches, fatigue, nausea, and vomiting. Patients on this drug may have problems with thinking and concentration. Interferon can also lower blood cell counts. These effects continue as long as the drug is used, but can become easier to tolerate over time. They do improve after the drug is stopped. Still, some patients find it hard to deal with these side effects on a daily basis and may need to stop treatment because of them.

Chemotherapy for chronic myeloid leukemia

Chemotherapy (chemo) is the use of anti-cancer drugs that are injected into a vein or taken by mouth. These drugs enter the bloodstream and reach all areas of the body, making this type of treatment useful for cancers such as leukemia that spread throughout the body. Any drug used to treat cancer (including tyrosine kinase inhibitors) can be considered chemo, but in this document the term chemo is used to mean treatment with conventional cytotoxic drugs that mainly kill cells that are growing and dividing rapidly.

Chemo was once one of the main treatments for patients with chronic myeloid leukemia (CML), but it is used much less often now that drugs like imatinib (Gleevec) are

available. Now, chemo may be used to treat CML when the tyrosine kinase inhibitors (TKIs) have stopped working. It is also used as part of the treatment during a stem cell transplant.

The chemo drug hydroxyurea (Hydrea®) is taken as a pill, and can help lower very high white blood cell counts and shrink an enlarged spleen. Other drugs sometimes used include cytarabine (Ara-C), busulfan, cyclophosphamide (Cytoxan®), and vincristine (Oncovin®).

Omacetaxine (Synribo®) is a chemo drug that has recently been approved to treat CML that is resistant to some of the TKIs now in use. It can help some patients whose CML has developed the T315I mutation that makes most TKIs not work (discussed in the section about targeted therapy).

Side effects of chemotherapy

Chemotherapy drugs work by attacking cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to side effects.

Possible side effects depend on the type and dose of drugs given and the length of time they are taken. Some common side effects of chemotherapy include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Increased risk of infection (from low white blood cell counts)
- Easy bruising or bleeding (from low blood platelet counts)
- Fatigue (from low red blood cell counts)

Still, different drugs can have different side effects. For example, vincristine can cause nerve damage (*neuropathy*) leading to numbness, tingling, or even pain or weakness in the hands or feet. Lung damage from busulfan is rare, but can be severe. Before starting treatment, speak with your health care team about the drugs you will receive and their possible side effects. Most side effects last a short time and go away once treatment is finished, but some can be permanent.

While getting treatment, be sure to tell your cancer care team about any side effects you have because there may be ways to lessen them. For example, drugs can be given to prevent or reduce nausea and vomiting.

Drugs known as growth factors (G-CSF (Neupogen®) and GM-CSF (Leukine®), for example) are sometimes given to increase the white blood cell counts and thus reduce the chance of infection. If your white blood cell counts are very low during treatment, you can also reduce your risk of infection by avoiding exposure to germs. During this time, your doctor may advise that you:

- Wash your hands often.
- Avoid fresh flowers and plants because they can carry mold.
- Make sure other people wash their hands when they come in contact with you.
- Avoid large crowds and people who are sick (wearing a surgical mask offers some protection in these situations).

You might also be given antibiotics before there are signs of infection or at the earliest sign that an infection may be developing.

If your platelet counts are low, you may be given drugs or platelet transfusions to help protect against bleeding. Likewise, shortness of breath and extreme fatigue caused by low red blood cell counts may be treated with drugs or with red blood cell transfusions.

Radiation therapy for chronic myeloid leukemia

Radiation therapy is treatment with high-energy rays or particles to destroy cancer cells. Radiation therapy is usually not part of the main treatment for patients with chronic myeloid leukemia (CML), but it is used in certain situations.

Patients may have symptoms if swollen internal organs (such as an enlarged spleen) press on other organs. For instance, pressure against the stomach may affect appetite. If these symptoms are not helped by chemotherapy, radiation therapy to shrink the spleen may be an option.

Radiation therapy can also be useful in treating pain from bone damage caused by the growth of leukemia cells within the bone marrow.

Radiation therapy is sometimes given in low doses to the whole body, just before a stem cell transplant (see the section, "Bone marrow or peripheral blood stem cell transplant for chronic myeloid leukemia").

The main short-term side effects of radiation therapy depend on where the radiation is aimed. Sunburn-like skin changes in the treated area are possible. If the radiation is aimed at the areas of the head or neck, the inside lining of your mouth and throat may become red and irritated - this is called *mucositis*. Radiation to the stomach or intestines can cause nausea and vomiting and/or diarrhea. If large parts of the body are treated with radiation, the bone marrow may be affected, leading to low blood counts. Symptoms may include fatigue, an increased risk of infection, and easy bruising or bleeding.

Surgery for chronic myeloid leukemia

Leukemia cells spread widely throughout the bone marrow and other organs, so surgery cannot cure this type of cancer. Surgery rarely has any role even in diagnosing chronic myeloid leukemia (CML), since a blood test or bone marrow aspirate and biopsy are usually all that is needed.

If leukemia spreads to the spleen, it can lead to that organ becoming large enough to compress nearby organs and cause symptoms. If chemotherapy or radiation does not help shrink the spleen, it may be removed with surgery. This operation, called a *splenectomy*, is meant to improve the symptoms of an enlarged spleen — it has no role in curing CML.

Splenectomy may also improve blood cell counts and lower the need for blood product transfusions. One of the spleen's normal functions is to remove worn-out blood cells from the bloodstream. If leukemia or other diseases cause the spleen to become too large, it may become too active in removing blood cells, leading to a shortage of red blood cells or platelets. Taking out the spleen may improve red blood cell and platelet counts in some patients.

Most people have no problem living without a spleen. The risk for certain bacterial infections is increased, which is why doctors often recommend certain vaccines be given before the spleen is removed.

Bone marrow or peripheral blood stem cell transplant for chronic myeloid leukemia

The usual doses of chemotherapy drugs can cause serious side effects to quickly dividing tissues such as the bone marrow. Even though higher doses of these drugs might be more effective, they are not given because the severe damage to bone marrow cells would cause lethal shortages of blood cells and damage to vital organs.

A stem cell transplant (SCT) allows doctors to use higher doses of chemotherapy and, sometimes, radiation therapy. For the transplant, high doses of chemotherapy are given to kill the leukemia cells. Sometimes the whole body also is given a low dose of radiation. This treatment kills the leukemia cells, but also damages the normal bone marrow cells. Then after chemotherapy (and possibly radiation), the patient will receive a transplant of blood-forming stem cells to restore the bone marrow.

Blood-forming stem cells used for a transplant are obtained either from the blood (for a peripheral blood stem cell transplant, or PBSCT) or from the bone marrow (for a bone marrow transplant, or BMT). Bone marrow transplant was more common in the past, but it has largely been replaced by PBSCT.

There are 2 main types of stem cell transplants. They differ in the source of the blood-forming stem cells. The 2 types are:

- Allogeneic stem cell transplant
- Autologous stem cell transplant

Allogeneic stem cell transplant

In this type of transplant, the stem cells come from someone else. Usually the donor is a relative whose tissue type is almost identical to the patient's. Tissue type is based on certain substances present on the surface of cells in the body. These substances can cause the immune system to react against the cells. Therefore, the closer a tissue "match" is between the donor and the recipient, the better the chance the transplanted cells will "take" and begin making new blood cells.

Most often the donor is a brother, a sister, or another close relative. Less often, the donor is someone with the same tissue type, but who is not related by blood -- a matched unrelated donor (MUD). The stem cells from an unrelated donor can come from volunteers whose tissue type has been stored in a central list (registry) and matched with that of the patient. Sometimes umbilical cord stem cells are used. These stem cells come from blood drained from the umbilical cord and placenta after a baby is born and the umbilical cord is cut.

Allogeneic stem cell transplants (ASCT) are the main type of transplant done for patients with chronic myeloid leukemia (CML). They are the only known cure for this disease. The best candidate for this type of transplant is a young patient who has no other health problems and has a donor who is a good tissue type match. Younger patients tend to tolerate this procedure better than older ones, but age may not be as important as the overall health and fitness of the patient. Still, older patients may become very ill from this procedure and have a high chance of dying from it. However, non-myeloablative SCT can be used in some older patients.

Non-myeloablative transplant: Many older patients can't tolerate a standard allogeneic transplant that uses high doses of chemotherapy. Some may be able to have a non-myeloablative transplant (also known as a mini-transplant or reduced-intensity transplant). This is a type of allogeneic SCT that uses lower doses of chemotherapy and radiation that do not completely destroy the cells in their bone marrow. After the chemotherapy/radiation, the patient receives the allogeneic (donor) stem cells. These cells enter the body and establish a new immune system. The new immune cells see the leukemia cells as foreign and attack them. This is called a *graft-versus-leukemia* effect.

Doctors have learned that if they use small doses of certain chemotherapy drugs and low doses of total body radiation, an allogeneic transplant can still work with much less toxicity. In fact, a patient can receive a non-myeloablative transplant as an outpatient. The major complication is graft-versus-host disease.

This type of transplant isn't a standard treatment for CML, and studies are under way to determine how useful it may be against this disease.

Autologous stem cell transplant

In an autologous stem cell transplant, a patient's own stem cells are removed from his or her bone marrow or peripheral blood. They are stored while the person gets treatment (high-dose chemotherapy and/or radiation) and then are given back to the patient.

Autologous SCT is not used often to treat CML because some leukemia cells might be collected along with the stem cells and be given back to the patient after treatment. A process called *purging* can be used to try to remove the leukemia cells from the collected stem cells. Because you are given back your own cells in this type of transplant, you won't get the benefit of the graft-versus-leukemia reaction.

The transplant procedure

Blood-forming stem cells from the bone marrow or peripheral blood are collected from the donor, frozen, and stored. The patient receives high-dose chemotherapy and sometimes also radiation treatment to the entire body. (Radiation shields are used to protect the lungs, heart, and kidneys from damage during radiation therapy.)

The chemotherapy and radiation treatments are meant to destroy any remaining cancer cells. They also kill the normal cells of the bone marrow and the immune system. This prevents the stem cell transplant (graft) from being rejected. Several days after these treatments, the frozen stem cells are thawed and given as an intravenous infusion. The stem cells settle into the patient's bone marrow over the next several days and start to grow and make new blood cells.

In allogeneic SCTs, the person getting the transplant is given drugs like prednisone, methotrexate, and cyclosporine to suppress the immune system and help prevent graft-versus-host disease (see Long-term side effects). For the next few weeks the patient gets regular blood tests and supportive therapies as needed, which might include antibiotics, red blood cell or platelet transfusions, other medicines, and help with nutrition.

Usually within a couple of weeks after the stem cells have been infused, they begin making new white blood cells. This is followed by new platelet production and, several weeks later, new red blood cell production.

Patients usually stay in the hospital in protective isolation (guarding against exposure to germs) until their white blood cell count rises above 500. They may be able to leave the hospital when their white blood cell count is near 1,000. Because platelet counts take longer to return to a safe level, patients may receive platelet transfusions as an outpatient procedure.

Side effects

Side effects from SCT are generally divided into early and long-term effects.

Early side effects: The early complications and side effects are basically the same as those caused by any other type of high-dose chemotherapy (see the section called "Chemotherapy for chronic myeloid leukemia" in this document), and are caused by damage to the bone marrow and other quickly dividing tissues of the body. They can include low blood cell counts (with increased risk of infection and bleeding), nausea, vomiting, loss of appetite, mouth sores, and hair loss. Mouth and throat sores, called *mucositis*, can be severe and make it hard to eat.

One of the most common and serious short-term effects is the increased risk of infection from bacteria, viruses, or fungi. Antibiotics are often given for a time, even before there are any signs of infection, to try to keep this from happening. The risk of infection is high because the white blood cell count becomes very low for a few weeks during the transplant. During this time, patients are watched closely for fever or other signs of infection.

Other side effects, like low red blood cell and platelet counts, may require blood product transfusions or other treatments.

Long-term side effects: Some complications and side effects can last for a long time or may not happen until months or years after the transplant. These include:

- Graft-versus-host disease (GVHD), which can occur in allogeneic (donor) transplants. This happens when the donor immune system cells attack tissues of the patient's skin, liver, and digestive tract. Symptoms can include weakness, fatigue, dry mouth, rashes, nausea, diarrhea, yellowing of the skin and eyes (jaundice), and muscle aches. In severe cases, GVHD can be fatal. GVHD is often described as either acute or chronic, based on how soon after the transplant it begins. Drugs that weaken the immune system are often given to try to keep GVHD under control.
- Radiation damage to the lungs, causing shortness of breath
- Damage to the ovaries in women, causing infertility and loss of menstrual periods
- Damage to the thyroid gland that causes problems with metabolism
- Cataracts (damage to the lens of the eye that can affect vision)
- Bone damage called *aseptic necrosis* (the bone dies because of poor blood supply); if damage is severe, the patient will need to have part of the bone and the joint replaced.

Practical points

Before modern targeted therapy drugs like imatinib (Gleevec), SCT was commonly used to treat CML. That is because the drugs that were available then did not work very well. Before drugs like imatinib were available, less than half of patients survived more than 5 years after diagnosis. Now, drugs like imatinib are the standard treatment, and transplants are being used less often. Still, allogeneic SCT offers the only proven chance to cure

CML, so doctors may still recommend a transplant for younger patients, particularly children. It is more likely to be considered for those with an available matched donor, like a well-matched brother or sister. Transplant may also be recommended if the CML is not responding well to tyrosine kinase inhibitors.

Bone marrow or peripheral blood SCT is a complex treatment. If the doctors think a patient may benefit from a transplant, it should be done at a hospital where the staff has experience with the procedure and with managing the recovery phase. Some bone marrow transplant programs may not be experienced in doing certain types of transplants, especially transplants from unrelated donors.

SCT is very expensive (more than $100,000) and often requires a lengthy hospital stay. Most insurance companies will cover the cost of a standard allogeneic SCT for CML, but some view other types of SCT as experimental when they are used to treat CML and so may not pay for them. Before deciding on a transplant, it's a good idea to find out what your insurer will cover and what you might have to pay.

For more information on stem cell transplants, see our document, *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants)*.

Clinical trials for chronic myeloid leukemia

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our Web site at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art cancer treatment. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our Web site or call our toll-free number (1-800-227-2345) and have it sent to you.

Complementary and alternative therapies for chronic myeloid leukemia

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you might lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treating chronic myeloid leukemia by phase

Treatment options for people with chronic myeloid leukemia (CML) depend on the phase of their disease (chronic, accelerated, or blast phase), their age, other prognostic factors, and the availability of a stem cell donor with matching tissue type.

Chronic phase

The standard treatment for chronic phase CML is a tyrosine kinase inhibitor (TKI) such as imatinib (Gleevec), nilotinib (Tasigna), or dasatinib (Sprycel). For imatinib, the usual starting dose is 400 mg per day. If this drug stops working (or it never really worked well at all) the dose may be increased. Another option is to use one of the other TKIs, such as dasatinib or nilotinib. Dasatinib, nilotinib, bosutinib (Bosulif), and ponatinib (Iclusig) are all options if the patient can't take imatinib because of side effects.

Some people in chronic phase may be treated with an allogeneic stem cell transplant (SCT). This treatment was discussed in detail in the section, "Bone marrow or peripheral blood stem cell transplant for chronic myeloid leukemia."

Monitoring treatment results: Monitoring the patient's blood and bone marrow for a response is a very important part of treatment. It is usually done every 3 to 6 months for the first 2 years after starting a TKI. Blood counts are watched closely, and the blood and bone marrow are looked at to see if the Philadelphia chromosome is there. If the Philadelphia chromosome isn't found, the polymerase chain reaction (PCR) test, which is very sensitive, may be used to see if small amounts of the *BCR-ABL* gene are still present. Doctors look for different kinds of responses to treatment:

Hematologic response (usually happens within the first 3 months of treatment)

- When blood cell counts return to normal, there are no immature cells see in the blood, and the spleen has returned to normal size it is called a *complete hematologic response* (or CHR).
- A *partial hematologic response* is similar to this, but not all of the above conditions are met.

Cytogenetic response (may take several months or longer)

- A *complete cytogenetic response* (CCyR) occurs when no cells with the Philadelphia chromosome can be found in the blood or bone marrow.
- A *partial cytogenetic response* occurs when less than 35% of cells still have the Philadelphia chromosome.
- A *major cytogenetic response* (MCyR) includes both complete and partial responses
- A *minor cytogenetic response* occurs when 35% to 90% of cells still have the Philadelphia chromosome.

Molecular response (this is based on the results of the PCR test)

- A *complete molecular response* (CMR) means that the PCR test cannot find the *BCR-ABL* gene in the patient's blood.
- A *major molecular response* (MMR) means that the amount of *BCR-ABL* gene in the blood is very low.

Up to about 70% of people have a CCyR within 1 year of starting imatinib, and the rate of CCyR is even higher with the other TKIs (nilotinib and dasatanib); more patients have a CCyR after a year. Many of these patients also have a CMR.

But even if the *BCR-ABL* gene can't be found, these people are probably not cured. For now, doctors recommend that people stay on the drug indefinitely.

Other treatments: The goal of treatment with one of the TKIs is a complete hematologic response plus a complete cytogenetic response. If this doesn't happen, or if the leukemia gets worse, there are several options.

- Increasing the dose of the drug. This helps some people, although the higher dose often has worse side effects.
- Switching to another TKI, for example from imatinib to dasatinib, nilotinib, or bosutinib.
- For those who can't take these drugs or for whom they are not working, interferon or chemotherapy (chemo) may be tried.

- Stem cell transplant may be an option, especially for younger people who have a donor with a matching tissue type.

Treating CML after a stem cell transplant: Some people who have a stem cell transplant may not get a complete response. If they *do not* have graft-versus-host disease (GVHD), doctors may try to get their new immune system to fight the leukemia. One way to do this is by slowly lowering the doses or stopping the immune suppressing drugs they are on. This is done very carefully in order to have an anti-leukemia effect without getting too much GVHD. Patients are watched closely during this time. Another approach that helps some patients is a donor lymphocyte infusion, where the patient receives an infusion of lymphocytes taken from the person who donated the stem cells for the transplant. This can induce an immune reaction against the leukemia. Interferon may also be helpful.

In patients who *do* have GVHD after a stem cell transplant, boosting the immune system further is not likely to help. These patients are often treated with a TKI like imatinib.

Accelerated phase

When CML is in accelerated phase, leukemia cells begin to build up in the body more quickly, which causes symptoms. The leukemia cells often acquire new gene mutations, which help them grow and tend to make treatments less effective.

The treatment options for accelerated phase CML depend on what treatments the patient has already had. In general, the options are similar to those for patients with chronic phase CML, but patients with accelerated phase CML are less likely to have a long-term response to any treatment.

If the patient hasn’t had any treatment, a TKI will be used. Imatinib (often at higher doses than used for chronic phase CML) is one option for most people. Most patients in this phase can respond to treatment with imatinib, but the responses do not seem to last as long as they do in patients in the chronic phase. Still, about half these patients are still alive after 4 years. The newer drugs like dasatinib and nilotinib are often used in this phase, and other drugs are under study.

If the patient is already getting imatinib, the dose may be increased. Another option is to switch to one of the other TKIs (dasatinib, nilotinib, bosutinib, or ponatinib). Sometimes the CML cells are tested to see if they have genetic changes (mutations) that may mean that a certain TKI is more or less likely to work.

Interferon is another option, but it is also much less effective in this phase than in the chronic phase. About 20% of patients have some response to chemo, but these responses are usually shorter than 6 months.

An allogeneic stem cell transplant may be the best option for most patients who are young enough to be eligible. About 20% to 40% of patients with accelerated phase CML

are alive several years after a stem cell transplant. Most doctors prefer that the leukemia be controlled, preferably in remission, before beginning the transplant procedure. To achieve this, chemo will often be used.

In some cases, an autologous SCT may be an option to try to get the CML back into the chronic phase, but it's very unlikely to result in a cure.

Blast phase

In the blast phase of CML, the leukemia cells become more abnormal. The disease acts like an acute leukemia, with blood counts getting higher and symptoms appearing or becoming more severe.

For people with blast phase CML who haven't been treated before, high-dose imatinib may be helpful, although it works in a smaller number of people and for shorter lengths of time than when used earlier in the course of the disease. The newer agents, dasatinib and nilotinib, seem to be better in this phase, particularly if they hadn't been used earlier. Bosutinib or ponatinib is also an option for patients who had previously been on another TKI. Patients who respond to these drugs may still want to consider having a stem cell transplant, if possible.

Most often, the leukemia cells in this phase act like cells of acute myeloid leukemia (AML), but they are often resistant to the chemo drugs normally used to treat AML. Standard chemo for AML (see our document, *Leukemia: Acute Myeloid (Myelogenous)*) will bring about a remission in about 1 out of 5 patients, but this is usually short-lived. If this does occur, it may be a chance to consider some type of stem cell transplant.

A smaller number of patients have blast cells that act like cells of acute lymphoblastic leukemia (ALL). These cells are more sensitive to chemo drugs. Remissions can be induced in about half of these patients with drugs such as vincristine, prednisone, and doxorubicin, along with imatinib, if that hasn't been given yet. Like patients with ALL, these patients are at risk for having leukemia cells in the fluid that surrounds the brain and spinal cord, so they often get chemo (cytarabine or methotrexate) infused directly into that fluid (like during a spinal tap). Radiation therapy to the brain is another option but is used less often.

Allogeneic SCT is less successful for blast phase CML than for earlier phases, and the long-term survival rate is less than 10%. Still, it is the only known option that may cure the disease. It is more likely to be effective if the CML can be brought back to the chronic phase before the transplant.

Because most patients with blast phase CML can't be cured, palliative treatment (intended to relieve symptoms rather than cure the disease) is important. Radiation therapy can help shrink an enlarged spleen or reduce pain from areas of bone damaged by leukemia. Chemo (usually with drugs such as hydroxyurea) may relieve some symptoms for a time.

Clinical trials of new combinations of chemo, targeted agents, and biologic therapies are important options.

CML with the T315I mutation

As was mentioned in the section about targeted therapy, in some patients on TKI treatment, the cancer cells develop a gene change called the T315I mutation that makes most of the other TKIs not work. If your CML stops responding to treatment with a TKI, another one may be tried. Your doctor may also check to see if the cancer cells have developed the T315I mutation. If they have, you may be switched to ponatinib, which is the only TKI that works against CML with this mutation. If this doesn’t work or you can’t take it because of side effects, you may be started on chemotherapy (chemo). Omacetaxine (Synribo) is a newer chemo drug that has been shown to help sometimes in this situation, but other chemo drugs may help as well.

More treatment information for chronic myeloid leukemia

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN Web site (www.nccn.org).

The NCI also provides treatment guidelines. You can get them from its telephone information center (1-800-4-CANCER) and its Web site (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What should you ask your doctor about chronic myeloid leukemia?

As you cope with cancer and cancer treatment, you need to have honest, open discussions with your doctor. You should feel free to ask any question that's on your mind, no matter how small it might seem. Here are some questions you might want to ask. Nurses, social workers, and other members of the treatment team may also be able to answer many of your questions.

- What phase is my chronic myeloid leukemia in?
- What treatment choices do I have?
- Which treatment do you recommend, and why?

- How often will you test my blood or bone marrow to see how my therapy is working?
- What side effects are there to the treatments that you recommend?
- What can I do to be ready for treatment?
- Should I consider a stem cell transplant at this time?
- What are the chances that my leukemia will come back once I am in remission?

Be sure to write down any questions that occur to you that are not on this list. For instance, you might want information about recovery times so that you can plan your work schedule. Or you may want to ask about second opinions or about clinical trials for which you may qualify.

Taking another person and/or a tape recorder to the appointment may be helpful. Getting copies of your medical records, including pathology and radiology reports, may be useful in case you wish to seek a second opinion at a later time.

What happens after treatment for chronic myeloid leukemia?

For a few people with chronic myeloid leukemia (CML), treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about cancer coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are living full lives. Our document called *Living With Uncertainty: The Fear of Cancer Recurrence* gives more detailed information on this.

For most patients with CML, treatment doesn't end and they stay on a tyrosine kinase inhibitor (TKI) like imatinib indefinitely. Often, the TKIs keep the CML in check, but they don't seem to cure this disease. Being on long-term treatment can be difficult and very stressful. It has its own type of uncertainty. Our document, *When Cancer Doesn't Go Away,* talks more about this.

Follow-up care

Even if there are no signs of the disease, your doctors will still want to watch you closely. It is very important to go to all of your follow-up appointments. During these visits, your doctors will ask questions about any problems you may have and may do exams and lab tests to look for signs of CML and treatment side effects. Almost any cancer treatment

can have side effects. Some may last for a few weeks to months, but others can last the rest of your life. This is the time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have.

It is important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen.

Should your cancer come back, our document called *When Your Cancer Comes Back: Cancer Recurrence* can give you information on how to manage and cope with this phase of your treatment.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know anything about your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- If you had surgery, a copy of your operative report(s)
- If you were in the hospital, a copy of the discharge summary that doctors prepare when patients are sent home
- If you had radiation therapy, a copy of your treatment summary
- If you had chemotherapy or targeted therapy, a list of the drugs, drug doses, and when you took them

The doctor may want copies of this information for his records, but always keep copies for yourself.

Lifestyle changes after treatment for chronic myeloid leukemia

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life — making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Making healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on the alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society for information and support. This tobacco cessation and coaching service can help increase your chances of quitting for good.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is put healthy eating habits into place. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits.

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a "bone-weary" exhaustion that doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your

own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis twice a week. If you haven't exercised in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, you will need to balance activity with rest. It is OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more information on dealing with fatigue, please see *Fatigue in People With Cancer* and *Anemia in People With Cancer*.)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

And long term, we know that getting regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

How does having chronic myeloid leukemia affect your emotional health?

At some point, you may find yourself overcome with many different emotions. This happens to a lot of people. You may have been going through so much when you first started treatment that you could only focus on getting through each day. Now it may feel like a lot of other issues are catching up with you.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationship with those around you. Unexpected issues may also cause concern. For instance, as you feel better and have fewer doctor visits, you will see your health care

team less often and have more time on your hands. These changes can make some people anxious.

Almost everyone who has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you do not include them. Let them in, and let in anyone else who you feel may help. If you aren’t sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you.

If treatment for chronic myeloid leukemia stops working

If your leukemia keeps growing or comes back after one treatment, often another treatment will help. But when a person has tried many different treatments and the cancer has not gotten any better, the cancer tends to become resistant to all treatment. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer -- when you have been through many medical treatments and nothing's working anymore. Your doctor may offer you new options, but at some point you may need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. In many cases, your doctor can estimate how likely it is the cancer will respond to treatment you are considering. For instance, the doctor may say that more chemo or radiation might have about a 1% chance of working. Some people are still tempted to try this. But it is important to think about and understand your reasons for choosing this plan.

No matter what you decide to do, you need to feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose - the main purpose of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve bone pain caused by cancer that has spread to the bones. Or chemo might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer.

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more about hospice in our document called *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

What's new in chronic myeloid leukemia research and treatment?

Studies of chronic myeloid leukemia (CML) are being done in labs and in clinical trials around the world.

Genetics of chronic myeloid leukemia

Scientists are making great progress in understanding how changes in a person's DNA can cause normal bone marrow cells to develop into leukemia cells. Learning about changes in the genes (regions of the DNA) involved in CML is providing insight into why these cells grow too quickly, live too long, and fail to develop into normal blood cells. The explosion of knowledge in recent years is being used to develop many new drugs.

Treatment

Sorting out the targeted drugs

Imatinib (Gleevec) has now been used for several years and has been shown to be very effective, but studies have shown that the other tyrosine kinase inhibitors (TKIs), such as dasatinib (Sprycel) and nilotinib (Tasigna), work at least as well as imatinib for patients who are just starting treatment. Which drug is the best treatment to use first is still being studied. Another approach would be to combine 2 or more of these drugs to treat CML. This approach is also being studied.

Can treatment be stopped?

A recent study looked to see if patients who had a complete molecular response (CMR) for at least 2 years while on imatinib could safely stop drug treatment (patients who are in CMR have no signs of CML even with the most sensitive testing). Results showed that a little less than half of the patients who stopped were still without any signs of disease (and still in CMR) 12 months later. But, imatinib worked again for the patients whose CML came back. More research is needed to see if which patients can safely stop taking their TKI for CML.

Combining the targeted drugs with other treatments

Imatinib and other drugs that target the BCR-ABL protein have proven to be very effective, but by themselves these drugs don't help everyone. Studies are now in progress to see if combining these drugs with other treatments, such as chemotherapy, interferon, or cancer vaccines (see below) might be better than either one alone. A recent study showed that giving interferon with imatinib worked better than giving imatinib alone. The 2 drugs together had more side effects, though. It is also not clear if this combination is better than treatment with other TKIs, such as dasatinib and nilotinib. Studies are also looking at the role of different treatments combined with stem cell transplants.

New drugs for CML

Because researchers now know the main cause of CML (the *BCR-ABL* gene and its protein), they have been able to develop many new drugs that might work against it.

In some cases, CML cells develop a change in the *BCR-ABL* oncogene known as a *T315I* mutation, which makes them resistant to many of the current targeted therapies (imatinib, dasatinib, and nilotinib). Ponatinib (Iclusig) is a new drug that often works against T315I mutant cells. More drugs aimed at this mutation are now being tested.

Other drugs called *farnesyl transferase inhibitors*, such as lonafarnib and tipifarnib, seem to have some activity against CML and patients may respond when these drugs are combined with imatinib. These drugs are being studied further.

Cancer vaccines

Cancer cells are different from normal cells, so it is sometimes possible to get the body's immune system to react against them. One way to do this is to use a cancer vaccine - a substance injected into the body that boosts the immune system and causes it to attack certain cells. Several vaccines are now being studied for use against CML. For instance, in one small study, a vaccine called CMLVAX100 was given along with imatinib and seemed to increase its effectiveness. Research into this and other vaccines is continuing.

Additional resources for chronic myeloid leukemia

More information from your American Cancer Society

The following information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

After Diagnosis: A Guide for Patients and Families (also available in Spanish)

Anemia in People With Cancer

Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants)

Caring for the Patient With Cancer at Home: A Guide for Patients and Families (also available in Spanish)

Fatigue in People With Cancer

Leukemia: Acute Myeloid (Myelogenous) (also available in Spanish)

Living With Uncertainty: The Fear of Cancer Recurrence

Understanding Chemotherapy: A Guide for Patients and Families (also available in Spanish)

When Your Cancer Comes Back: Cancer Recurrence

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online at cancer.org/bookstore to find out about costs or to place an order.

National organizations and Web sites*

In addition to the American Cancer Society, other sources of patient information and support include:

Caitlin Raymond International Registry (for unrelated bone marrow transplants)
Toll-free number: 1-800-726-2824
Web site: www.crir.org

Leukemia & Lymphoma Society
Toll-free number: 1-800-955-4572
Web site: www.lls.org

National Bone Marrow Transplant Link (nbmtLINK)
Toll-free number: 1-800-LINK-BMT (1-800-546-5268)
Web site: www.nbmtlink.org

National Cancer Institute
Toll-free number: 1-800-4-CANCER (1-800-422-6237)
Web site: www.cancer.gov

Be the Match (formerly National Marrow Donor Program)
Toll-free number: 1-800-MARROW2 (1-800-627-7692)
Web site: www.bethematch.org

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are we can help, contact us any time, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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