

Chronic Myeloid Leukaemia

J A S C A P

JEET ASSOCIATION FOR SUPPORT TO CANCER PATIENTS, MUMBAI, INDIA

JASCAP
JEET ASSOCIATION FOR SUPPORT TO CANCER PATIENTS
c/o. Abhay Bhagat & Co., Office No.4, "Shilpa", 7th.Road, Prabhat Colony,
Santacruz (East), Mumbai – 400 055
Tel.: 2617 7543, 2616 0007. Fax: 91-22-2618 6162
E-mail : pkrijascap@gmail.com & abhay@abhaybhagat.com

JASCAP is a charitable trust that provides information on various aspects of cancer. This can help the patient and his family to understand the disease and its treatment and thus cope with it better.

Registered under the Societies Registration Act, 1860 No.1359 / 1996 G.B.B.S.D., Mumbai and under the Bombay Public Trusts Act, 1950 No. 18751 (Mumbai). Donations to JASCAP qualify for deduction u/s 80G (1) of the Income Tax Act, 1961 vide Certificate No. DIT (E) / BC / 80G / 1383 / 96-97 dated 28.02.97 subsequently renewed.

Contact: Mr. Prabhakar K. Rao or Mrs. Neera P. Rao

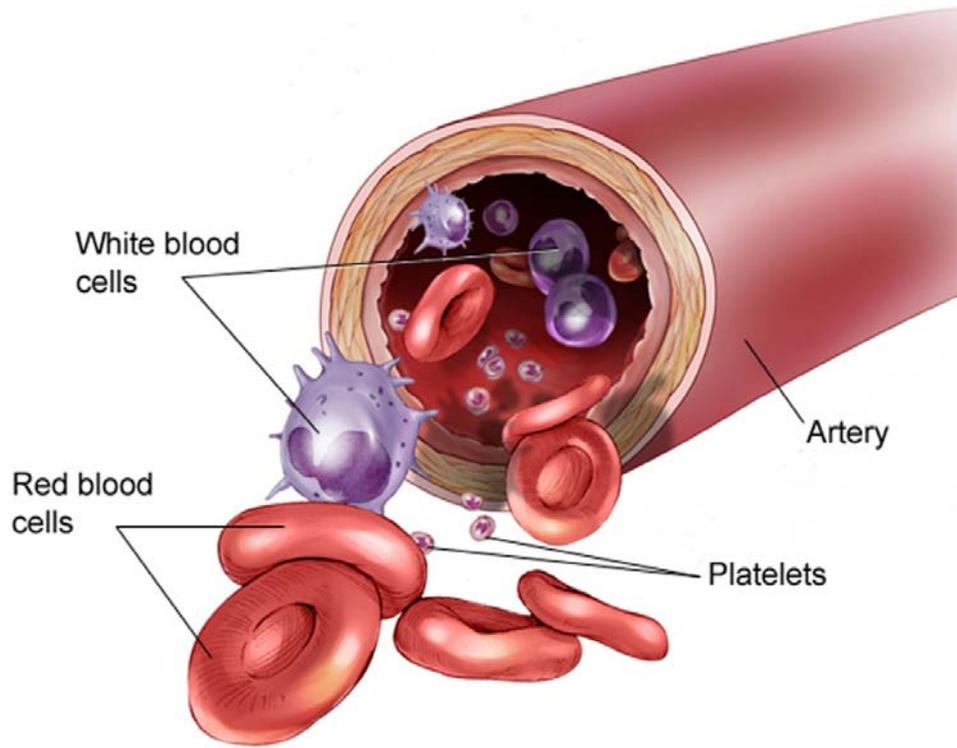
Publisher: JASCAP, Mumbai 400 055

Printer: Surekha Press, Mumbai 400 019

Edition: _____ March 2011 _____

Donation suggested ₹ 30.00

- o © Cancerbackup 01 December 2009 and Max Foundation
- o This booklet is an adaptation of "Understanding Chronic myeloid leukaemia" produced by Cancerbackup and is reproduced with their kind permission.
- o JASCAP gratefully acknowledges Cancerbackup's permission to reproduce this booklet



Contents

Chronic Myeloid Leukaemia (CML)	
• Introduction.....	
• What is cancer?	
• Types of cancers.....	
• Blood - structure and function	
• The Bone Marrow.....	
What is Leukaemia	
• What is chronic myeloid leukaemia (CML)?	
• How CML develops?	
• Risk factors and causes of CML	
• How common is Myeloid leukemia in India?	
Symptoms and Diagnosis	
• Symptoms of chronic myeloid leukemia	
• How chronic myeloid leukaemia is diagnosed?	
• Phases of chronic myeloid leukaemia.....	
Treating CML	
• Treatment overview	
• Imatinib (Glivec®) for chronic myeloid leukaemia	
• Other tyrosine kinase inhibitors, Dasatinib and Nilotinib	
• Chemotherapy for chronic myeloid leukaemia	
• High-dose treatment with stem cell support for CML	
• Interferon alpha for chronic myeloid leukaemia	
Research - Clinical trials for CML	
Glivec® International Patient Assistance Program (GIPAP)	
• What is GIPAP?	
• Qualification Requirements for GIPAP	
Tasigna® International Patient Assistance Program (TIPAP)	
Living with CML	

Chronic Myeloid Leukaemia (CML)

Introduction

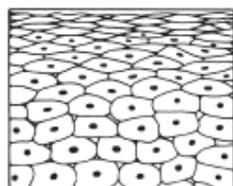
This booklet is for you if you have or someone close to you has Chronic Myeloid Leukaemia.

If you are a patient your doctor or nurse may wish to go through the booklet with you and mark sections that are particularly important for you.

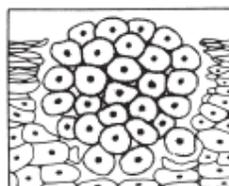
What is cancer?

The organs and tissues of the body are made up of tiny building blocks called cells. Cancer is a disease of these cells.

Cells in different parts of the body may look and work differently but most reproduce themselves in the same way. Cells are constantly becoming old and dying, and new cells are produced to replace them. Normally, cells divide in an orderly and controlled manner. If for some reason the process gets out of control, the cells carry on dividing, developing into a lump which is called a **tumour**.



Normal cells



Cells forming a tumour

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 – see below). These tumors are almost never life threatening.

Cancer is the name given to a **malignant** tumour. Doctors can tell if a tumour is benign or malignant by examining a small sample of cells under a microscope. This is called a **biopsy**.

A malignant tumour consists of cancer cells that have the ability to spread beyond the original area. If the tumour is left untreated, it may spread into and destroy surrounding tissue. Sometimes cells break away from the original (primary) cancer. They may spread to other organs in the body through the bloodstream or lymphatic system.

The lymphatic system is part of the immune system - the body's natural defence against infections and diseases. It is a complex system made up of organs, such as bone marrow, the thymus, the spleen, and lymph nodes. The lymph nodes (or glands) throughout the body are connected by a network of tiny lymphatic ducts.

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 **secondary cancer** or **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.

It is important to realise that cancer is not a single disease with a single type of treatment. There are more than 200 different kinds of cancer, each with its own name and treatment.

Types of cancers

Carcinomas

The majority of cancers, about 85% (85 in a 100), are carcinomas. They start in the epithelium, which is the covering (or lining) of organs and of the body (the skin). The common forms of breast, lung, prostate and bowel cancer are all carcinomas.

Carcinomas are named after the type of epithelial cell that they started in and the part of the body that is affected. There are four different types of epithelial cells:

- squamous cells - that line different parts of the body, such as the mouth, gullet (oesophagus), and the airways
- adeno cells - form the lining of all the glands in the body and can be found in organs such as the stomach, ovaries, kidneys and prostate
- transitional cells - are only found in the lining of the bladder and parts of the urinary system
- basal cells - that are found in one of the layers of the skin.

A cancer that starts in squamous cells is called a squamous cell carcinoma. A cancer that starts in glandular cells is called an adenocarcinoma. Cancers that start in transitional cells are transitional cell carcinomas, and those that start in basal cells are basal cell carcinomas.

Leukaemias and lymphomas

These occur in the tissues where white blood cells (which fight infection in the body) are formed, i.e. the bone marrow and lymphatic system. Leukaemia and lymphoma are quite rare and make up about 6.5% (6.5 in 100) of all cancers.

Sarcomas

Sarcomas are very rare. They are a group of cancers that form in the connective or supportive tissues of the body such as muscle, bone and fatty tissue. They account for less than 1% (1 in 100) of cancers.

Sarcomas are split into two main types:

- bone sarcomas - that are found in the bones
- soft tissue sarcomas - that develop in the other supportive tissues of the body.

Others forms of cancer

Brain tumours and other very rare forms of cancer make up the remainder of cancers.

Blood – Structure and Function

Blood is made up of blood cells suspended in liquid called plasma. There are three main types of blood cells:

- red cells, which carry oxygen around the body
- platelets, which help the blood to clot and control bleeding
- white cells, which fight infection.

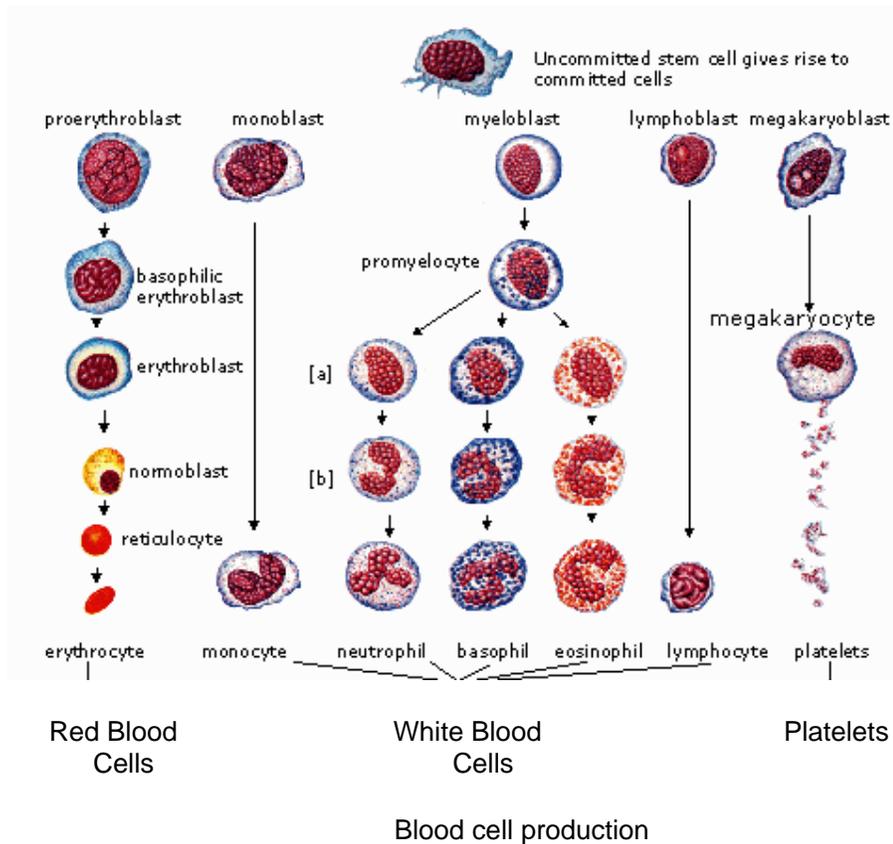
How blood cells are made?

Blood cells are made in the bone marrow, a spongy material inside the bones. Normally millions of new blood cells are made every day to replace old and worn out blood cells.

All blood cells begin as a special type of cell called a stem cell. There are two types:

- **Lymphoid stem cells** make white blood cells called lymphocytes.
- **Myeloid stem cells** make all the other types of blood cells: red cells, platelets and white cells called granulocytes.

Stem cells make new blood cells by copying themselves and then dividing to form two new cells. To begin with the new blood cells made from stem cells are immature. They don't look like red cells, white cells or platelets and they can't do the jobs in the body that they can do. These immature cells are called blast cells. Normally blast cells stay in the bone marrow until they have matured into red cells, white cells or platelets.



The bone marrow

Blood is made in the bone marrow. This is a spongy material that's found in the middle of your bones, particularly in your pelvis and backbone (spine).

All your blood cells are made from special cells called **stem cells**. The bone marrow gives the stem cells a safe place to divide and grow to form fully developed (mature) red cells, platelets and white cells.

These are then released into your blood to carry out different functions:

- Red blood cells contain **haemoglobin**, which carries oxygen from your lungs to all the cells in your body.
- White blood cells fight and prevent infection. There are several types of white cell. The two most important types are **neutrophils** and **lymphocytes**.
- Platelets are very small cells that help the blood to clot and prevent bleeding and bruising.

The levels of these cells in your blood are measured in a blood test called a **full blood count (FBC)**. The figures below are a guide to the levels usually found in a healthy person.

Type of blood cell of element	Levels found in a healthy person
Haemoglobin (Hb)	13–18g/dl (men) 11.5–16.5g/dl (women)
Platelets	150–400 x 10 ⁹ /l
White cells (WBC)	4.0–11.0 x 10 ⁹ /l
Neutrophils	2.0–7.5 x 10 ⁹ /l
Lymphocytes	1.5–4.5 x 10 ⁹ /l

These figures can vary from hospital to hospital. Your doctor or nurse will be able to tell you what levels they use. They can also be slightly different in people of African-Caribbean and Middle Eastern origin.

The figures might look complicated when they're written down, but in practice they are used in a straightforward way. For example, you'll hear doctors or nurses saying things like 'your haemoglobin is 14' or 'your neutrophils are 4'. Many people with CML soon get used to these figures and what they mean.

What is leukaemia?

Leukaemia is a cancer of the white blood cells and can start in bone marrow and lymphatic system.

There are four main types of leukaemia:

- chronic myeloid Leukemia (CML)
- acute myeloid Leukemia (AML)
- chronic lymphocytic Leukemia (CLL)
- acute lymphoblastic Leukemia (ALL).

Each type of leukemia has its own characteristics and treatment.

What is chronic myeloid leukaemia (CML)?

Chronic myeloid leukaemia (CML) is a rare cancer that causes the body to make too many white blood cells.

About 700 people in the UK are diagnosed with CML each year. It can occur at any age, but is more common in middle-aged and older people and is rare in children.

CML usually develops very slowly. This is why it's described as a 'chronic' leukaemia. It starts in the bone marrow (where our blood cells are made) in a special type of blood cell called a stem cell. To understand how CML develops, it helps to know a bit about blood and how blood cells are made.

How CML develops?

All cells have a set of instructions that tell them what to do and when to do it. These instructions are stored inside the cells as genes.

Each gene has its own distinct set of instructions that control a particular aspect of how the cell behaves. For example some genes tell a cell when to rest, others tell it when to grow. The genes are organised into structures called chromosomes.

CML develops when, by mistake, a gene gets moved from one chromosome to another one when a stem cell is dividing. The result is a joining together (fusion) of two genes that are normally completely separate. This new abnormal 'fusion' gene is then passed on to other cells. These are the leukaemia cells.

When doctors look at the leukaemia cells under a microscope, they can see a chromosome that looks different. This chromosome is called the Philadelphia chromosome.

Philadelphia chromosome

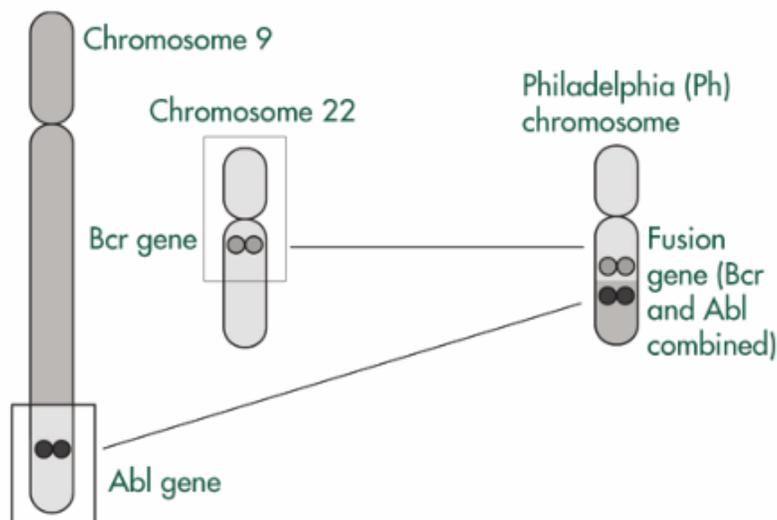
Most people with CML (more than 95 out of 100) have the Philadelphia chromosome in all their leukaemia cells. This is known as Philadelphia chromosome positive CML or Ph+CML.

The Philadelphia chromosome isn't inherited so it's not something you were born with and it can't be passed on to your children.

How the Philadelphia chromosome develops?

Most cells in the body contain 23 pairs of chromosomes. They are numbered from 1 to 22, (the 23rd pair are the sex chromosomes XX in women and XY in men).

The Philadelphia chromosome is made when the Abl gene on chromosome 9 is mistakenly transferred to chromosome 22 and attaches to the Bcr gene. This creates a new fusion gene called Bcr-Abl.



Development of the Philadelphia chromosome

The Bcr-Abl gene makes a protein called tyrosine kinase. Too much tyrosine kinase makes cells behave abnormally and causes the changes in the blood and bone marrow that are found in CML. Newer treatments for CML work by blocking the effects of tyrosine kinase.

Risk factors and causes of CML

The causes of chronic myeloid leukaemia (CML) aren't fully understood, but the ongoing research may shed more light on this issue.

CML, like other cancers, isn't infectious and can't be passed on to other people. It isn't caused by an inherited faulty gene so other members of your family can't develop CML just because you have it.

There are very few known risk factors that might increase a person's risk of developing CML. And for most people with CML, it isn't clear why it developed.

The main factor that is known to increase the risk of developing CML is radiation. Exposure to very high radiation levels (such as accidental exposure following a nuclear accident like the 1986 Chernobyl incident or the explosions in Nuclear plants in Japan due to earth quake followed by the Tsunami of March 2011) is known to increase the risk of developing CML. But very few people in the UK are exposed to radiation levels high enough to increase their risk of developing CML. For most people with CML there is no obvious link to radiation exposure.

In recent years there has been publicity about an increase in leukaemia in people living close to nuclear power plants. Research is still underway to see if there is any definite link between these factors, but as yet there is no evidence of this.

Research also hasn't found any links between exposure to electromagnetic fields, living near high-voltage electricity cables, or household radon and the risk of adults developing CML.

How common is Myeloid leukemia in India?

Leukemia is one of the common types of cancer in India. The incidence (newly diagnosed cases of Cancer in a year) of all types of leukemias together (Acute and Chronic; Lymphoid, Pro-myelocytic and Myeloid) is about 4 persons per 1,00,000 population¹.

In India, between the years 2001-2003, across five urban centers - Mumbai, Delhi, Chennai, Bhopal and Bangalore, – and one rural center - Barshi, a total of 1,173 cases of Myeloid leukemia (both Acute and Chronic combined) were registered (2.66% of all cancers) for males across all age groups; while 766 cases of Myeloid leukemia (both Acute and Chronic combined) were registered (1.72% of all cancers) for females across all age groups. Considering all men, women and children with all types of cancers together, a grand total of 1,939 cases of Myeloid leukemia (both

¹ Globocan 2008: Cancer incidence and mortality rates worldwide

Acute and Chronic combined) (2.19% of all cancers) were registered at the six centers mentioned above, between the year 2001-2003².

The TATA Memorial Hospital (T.M.H.) in Mumbai, India registered a grand-total of 19,127 cases of all types of cancer patients in the year 2006, for men, women and children combined, out of which 663 (3.5% of the total cases) were diagnosed with the Myeloid leukemia (both Acute and Chronic combined). Out of the total 663 patients diagnosed with Myeloid leukemia (both Acute and Chronic combined), mentioned above at the T.M.H., 450 (68%) were males and 213 (32%) were females³.

Twenty seven percent of all Haematopoietic cancers among men, women and children in the year 2006 at the T.M.H. were attributable to Myeloid leukemia (both Acute and Chronic combined).

Symptoms and diagnosis

Symptoms of chronic myeloid leukemia

Many people don't have symptoms when they are diagnosed. Their leukaemia is discovered by chance when a blood sample is taken for another reason.

If there are symptoms in the early stages of CML, they come on gradually and are usually mild. Symptoms may include:

- tiredness
- loss of appetite
- weight loss
- high temperatures (fever) and night sweats
- a feeling of fullness or a tenderness on the left side of the tummy area (abdomen) caused by an enlarged spleen. The spleen is an organ just below the ribs on the left side of the abdomen. It filters the blood to keep it clean and helps protect against infection.

If CML has been developing for some time, symptoms may be more noticeable and may include:

- frequent infections
- looking pale and feeling tired or breathless
- bleeding or bruising easily
- swellings in the neck, groin or armpit
- small bumps in the skin

²Population based cancer registry 2001-2003 Mumbai, Delhi, Chennai, Bhopal, Barshi and Bangalore, Indian Cancer Society.

³ TATA Memorial Hospital Registry Data for 2006

- itching.

If you have any of these symptoms, it's important to see your doctor, but remember, they are common to many illnesses other than CML.

How chronic myeloid leukaemia is diagnosed?

There are few, if any, symptoms of CML to begin with. This means that it's quite common for people with CML to be diagnosed by chance when they have a blood test for some other reason. The blood test shows a high number of white blood cells.

At the hospital

If your GP suspects you may have CML, they will refer you to a haematologist at the local hospital for specialist advice and treatment.

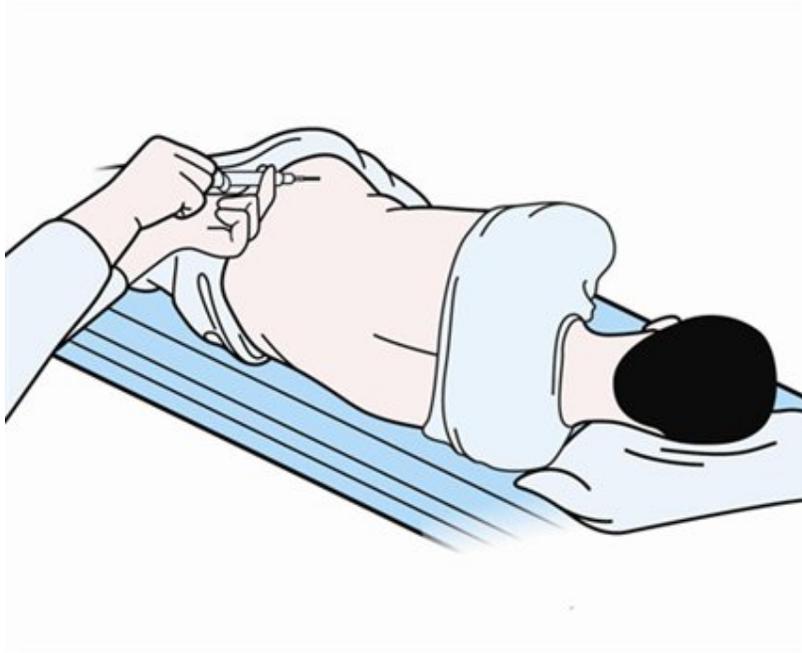
A haematologist is a doctor who specialises in the treatment of blood problems. The haematologist will examine you and ask about your general health and any illnesses you've had. They will also take blood samples to check the numbers of cells in your blood (a full blood count) and to look for leukaemia cells. If the blood test finds any leukaemia cells, the doctor will want to take a sample of your bone marrow. This will give them information to help plan your treatment.

Bone marrow sample/biopsy

In this test a small sample of bone marrow is taken from the back of the hip bone (pelvis). The sample is examined under a microscope to see if it contains any leukaemia cells.

You may be offered a sedative before the test to reduce any pain or discomfort. The bone marrow sample is normally taken under a local anaesthetic. The doctor injects some local anaesthetic into the skin and around the bone to numb it. They then pass a biopsy needle through the skin into your bone. A small sample of liquid marrow (bone marrow aspirate) is drawn into a syringe to be looked at later under a microscope. The doctor then uses a different needle to take a small core of marrow from inside your bone (a trephine biopsy).

The test can be done on the ward or in the outpatients department, and takes about 15-20 minutes. When the liquid marrow is drawn into the syringe you may feel some discomfort, but this only lasts a few seconds.



A sample of bone marrow is usually taken from the back of the hip bone

You may feel bruised and sore after the test and have an ache in your back or leg for a few days. This can be eased with mild painkillers. It can take about a week to get the results of a bone marrow biopsy.

Further tests

You may have additional tests including:

A chest x-ray: A chest x-ray which is taken to check that your heart and lungs are healthy.

A PCR (polymerase chain reaction) test: This is a blood test that measures Bcr-Abl transcripts, special molecules made by the abnormal Bcr-Abl gene usually present in CML. It's a very sensitive test and can detect tiny amounts of leukaemia that can be missed by other tests. It's used for measuring low levels of leukaemia after treatment begins.

Phases of chronic myeloid leukaemia

CML is a blood and bone marrow disease that develops slowly. There are three possible phases. The phase is determined by the number of blast cells in the blood and bone marrow and by the extent of your symptoms.

The chronic phase

Most people are diagnosed when the CML is in the chronic phase. At this time CML develops very slowly and is often stable for a long time. It's sometimes called the 'stable phase'. There may be no symptoms and most people lead a normal life.

It's rare to need to go into hospital. You can have treatment as an outpatient. This doesn't usually cause many side effects. You'll have regular blood tests to check how well you are responding to treatment.

Most people who start treatment in the chronic phase have their leukaemia well-controlled without any symptoms. And, if they keep taking their treatment, the leukaemia can be kept under control for years, perhaps even decades.

In some people CML doesn't respond as well to treatment. And, in a few people, the leukaemia may progress from the chronic phase to a more advanced phase of the disease within about five years of diagnosis.

The accelerated phase

In a small number of people, the leukaemia may gradually move into an accelerated phase. In this phase there are more immature cells (known as blasts) in the blood and bone marrow and the leukaemia develops more quickly. Sometimes this change may be picked up from your blood tests, in which blasts can be seen. Or, it may come to light because you develop new symptoms. If you feel less well or develop new symptoms, let your doctor know straight away.

The treatment for the accelerated phase is often more intensive than in the chronic phase and you may need to spend some time in hospital as an inpatient.

The blast phase

After some time, usually months, in the accelerated phase, the leukaemia 'transforms' into a blast phase, which is more like an acute leukaemia. In this phase there are many immature cells (blasts) filling much of the bone marrow. There are also many more blasts found in the blood than normal.

In some people, who have CML that doesn't respond to treatment, the leukaemia changes quickly from the chronic to the blast phase without going through the accelerated phase.

Myelofibrosis

Rarely, CML causes scar tissue to form (fibrosis) inside the bone marrow. This condition is called myelofibrosis. Areas of the bone marrow that are affected by scarring don't work properly and can't make new blood cells. Because of this, people with myelofibrosis may need regular transfusions of blood and platelets.

Remission

Remission is when the blood and bone marrow go back to normal following treatment. There are different levels of remission.

Relapse

Relapse means that leukaemia cells have reappeared after a period of remission.

Treating CML

Treatment overview

The treatment of CML depends on the phase of the illness. Your doctor will discuss the possible treatment options with you and the benefits and disadvantages of each.

Chronic phase

In the chronic phase, the aim of treatment is to control symptoms and keep you feeling well for many years, possibly for a normal lifespan.

People are usually treated with a tablet called imatinib (Glivec®). Most people manage well on this treatment and only have mild side effects.

Imatinib is one of a group of newer 'targeted' drugs called tyrosine kinase inhibitors, which have greatly improved the outlook for people with CML over the last decade. Many people have been taking imatinib for 10 years or more without any problems from their leukaemia.

Other tyrosine kinase inhibitors, such as dasatinib (Sprycel®) and nilotinib (Tasigna®), can be used if imatinib doesn't work or for people who can't take it due to problems with side effects.

Stem cell transplants (sometimes called bone marrow transplants) may be used for people who have CML that hasn't responded to tyrosine kinase inhibitor treatment.

Accelerated phase

Imatinib can be used in the accelerated phase, but only if it hasn't been used in the chronic phase. If imatinib isn't used, treatment is usually a combination of chemotherapy drugs, given by injection into a vein (intravenously). High-dose treatment with a stem cell transplant may also be used for some people.

Blast phase

In the blast phase the aim of treatment is to reduce symptoms and try to put the leukaemia back into a second chronic phase. Imatinib may be used, as long as it hasn't been given before. Blast phase CML is like an acute leukaemia, so combinations of chemotherapy drugs used to treat acute leukaemia are often given. If the leukaemia responds well to chemotherapy, the doctors may recommend high-dose chemotherapy treatment with a stem cell transplant.

Supportive treatments

Sometimes people have a very high number of white cells in their blood when they are diagnosed with CML. The cells can clog-up blood vessels and cause physical problems. Doctors may treat this by removing the excess cells from the blood using a machine called a cell separator. This process is called leukapheresis.

How your treatment is planned

Haematologists follow national guidelines for treating CML. Your treatment will be based on these guidelines but tailored to your particular situation.

In most hospitals a team of specialists will decide on the treatment that's best for you. This multidisciplinary team (MDT) may include:

- one or more haematologists
- a doctor who specialises in chemotherapy and radiotherapy (a clinical oncologist)
- specialist nurses who give information and support
- pathologists who advise on the type and extent of the leukaemia.

Other staff will be available to help you if necessary, such as:

- social workers
- dietitians
- counsellors and psychologists.

The MDT will plan your treatment by considering a number of factors, including the stage of the leukaemia and your general health.

You may be invited to take part in a clinical trial of a new treatment for CML.

If you have any questions about your treatment, don't be afraid to ask your doctor or nurse. It often helps to make a list of questions and to take a close friend or relative with you. They can remind you of questions you want to ask, and afterwards help you remember what the doctor said.

Giving your consent

Before you have any treatment, your doctor will explain its aims to you. They will usually ask you to sign a form saying that you give your permission (consent) for the hospital staff to give you the treatment. No medical treatment can be given without your consent, and before you are asked to sign the form you should be given full information about:

- the type and extent of the treatment you are advised to have
- the advantages and disadvantages of the treatment
- any other treatments that may be available
- any significant risks or side effects of the treatment.

If you don't understand what you have been told, let the staff know straight away so that they can explain again. Some cancer treatments are complex, so it's not unusual for people to need repeated explanations.

You can always ask for more time to decide about the treatment if you feel that you can't make a decision when it is first explained to you.

You're also free to choose not to have the treatment. The staff can explain what may happen if you don't have it. It's essential to tell a doctor or the nurse in charge if you

choose not to have treatment, so that they can record your decision in your medical notes. You don't have to give a reason, but it can be helpful to let the staff know your concerns so that they can give you the best advice.

The benefits and disadvantages of treatment

Sometimes people are frightened at the idea of having treatment for leukaemia because of the possible side effects. Although some of the treatments can cause side effects, these can usually be controlled or reduced with medicines.

If you've been offered treatment in the chronic phase, which aims to control the leukaemia for a long time and has few side effects, deciding whether to accept the treatment may not be difficult. However, if you are in the blast phase, and have been offered more intensive treatment, which may cause more side effects and has a lower chance of controlling the leukaemia, it may be more difficult to decide whether to go ahead.

Making decisions about treatment in these circumstances is always difficult, and you may need to discuss in detail with your doctor whether you wish to have treatment. If you choose not to have treatment, you can still be given supportive (palliative) care to help relieve any symptoms.

Second opinion

Your MDT will use national treatment guidelines to decide on the most suitable treatment for you. Even so, you may want to have another medical opinion. If you feel it will be helpful, your specialist or GP will be willing to refer you to another specialist for a second opinion. If you decide to go for a second opinion it may be a good idea to take a friend or relative with you and have a list of questions prepared, so that you can make sure your concerns are covered during the discussion.

Imatinib (Glivec®) for chronic myeloid leukaemia

Imatinib is the main treatment for CML. It's a type of treatment called a tyrosine kinase inhibitor.

It works by blocking (inhibiting) signals within the leukaemia cells that make them grow and divide. Blocking the signals makes the cells die.

The National Institute for Health and Clinical Excellence (NICE) has recommended imatinib as the first treatment to be considered in the chronic phase of CML. Imatinib can also be used in the accelerated or blast crisis phases of CML, as long as it hasn't been used before.

Imatinib comes as a tablet. You take the tablet every day for as long as it's working to control the leukaemia.

Side effects of Imatinib

The side effects are usually mild and treatable. They may be more noticeable in the first four weeks of treatment and then begin to settle after this.

Side effects generally go away when treatment is stopped, so if you have severe side effects your doctor may ask you to stop taking imatinib for a few days. After a short break, you may be able to start taking it again without having the same problems. Occasionally some people need to stop taking imatinib altogether because their side effects are too severe.

Always let your doctor know if you notice any new side effects or if your side effects get worse. **Side effects of Imatinib may include:**

Feeling sick (nausea) and indigestion: This is usually mild. It can be reduced by taking the tablet with a large glass of water after a main meal. If you continue to have problems with nausea, your doctor may prescribe anti-sickness medicine for you.

Diarrhoea: This can usually be controlled with anti-diarrhoeal medicine. It's important to drink plenty of fluids if you have diarrhoea. Let your doctor know if it's severe.

Loss of appetite: A dietitian or specialist nurse at your hospital can give advice and tips on boosting appetite, coping with eating difficulties and maintaining weight.

Headaches: Let your haematologist know if you are having headaches. They can advise you on what painkillers to take.

Muscle cramps, bone and joint pains: You may get cramps or pain in your hands, the calves of your legs and in your feet. Sometimes these lessen after a few weeks. Your haematologist can advise on what types of painkillers may help. They may also prescribe quinine, calcium or magnesium supplements to help if cramps are severe.

Build up of fluid in the tissues (oedema): This is fairly common. You may notice swelling around your eyes, especially in the morning. You may also notice swelling in other areas such as your ankles. Cutting down on the amount of salt in your diet can help. Your doctor may prescribe tablets to make you pass more urine (diuretics). It's important to contact your doctor straight away if you gain a lot of weight quickly or if you feel breathless as this can be a sign of a more serious fluid build up.

Eye changes: Your eyes may produce more tears than normal, making them watery. Some people have painful eyes or blurred vision.

Skin changes: Imatinib can cause a skin rash. Usually it's mild but sometimes it can be more severe. If the rash is itchy or your skin feels dry, antihistamine tablets and skin lotion may help. Speak to your doctor if you have a rash or other skin changes as they may prescribe additional treatments.

Some people notice changes in the colour (pigment) of their skin, with some areas becoming lighter or not tanning so well. This may be more noticeable if you have darker skin. Your skin may also become more sensitive to sunlight. It can help to use a sunscreen or cover up in the sun if you are affected.

Effects on your blood cells: Imatinib can lower the numbers of healthy blood cells that are being made in your bone marrow. This is more common if you start taking it when the CML is in accelerated or blast phase. You'll have regular blood tests while you are taking imatinib to monitor the levels of your blood cells. If your blood cell numbers are low this can cause:

Lowered resistance to infection: if your white blood cell numbers are low. Contact your doctor or the hospital straight away if your temperature goes above 38°C (100.5°F) or you suddenly feel unwell (even with a normal temperature).

Bruising or bleeding: if your platelet (cells which help the blood to clot) numbers are low. Let your doctor know if you have any unexplained bruising or bleeding.

Anaemia: (too few red blood cells) You may feel tired and breathless. You may need to have a transfusion of blood if the number of red cells in your blood is too low.

If your blood cell numbers fall too low your doctor may stop your treatment for a few days to let them recover, or you may be prescribed injections of substances called growth factors. Growth factors work by boosting the numbers of white blood cells (G-CSF) or red blood cells (erythropoietin) your bone marrow can make.

Contraception and fertility while on Imatinib

Imatinib is quite a new drug so there isn't a lot of experience of women becoming pregnant or men fathering children while taking it. But there is a slightly increased risk of damage to the developing baby if imatinib is taken during pregnancy. So, it's strongly recommended that you use contraception while taking it.

If you are taking imatinib and wish to father a child or become pregnant it's important to discuss this with your haematologist. He can discuss your treatment options with you.

Taking other medicines while on Imatinib

Some medicines can be affected by, or interact with, how imatinib works. This includes herbal medicines such as St John's Wort and some commonly used painkillers such as paracetamol. So, it's important to always check with your doctor before taking any medicines.

Monitoring response to treatment with Imatinib (Glivec®)

When you first start your treatment, you'll need to go to the clinic every week or so. This is so that your doctors can keep a close eye on how you are responding and check for any side effects.

As time goes on you won't need to go to the clinic as often and eventually you may only need a check-up about every three months.

At your follow ups your doctor will ask about your general health and if you've had any new symptoms or side effects from treatment. You'll usually have blood taken to count the numbers of blood cells in your blood (called a full blood count or FBC) and for a PCR blood test. From time to time you may also have a bone marrow sample taken. Your doctor can tell you how often this might be necessary.

The results of the tests help your doctors to judge how well your leukaemia is responding to imatinib so that they can tailor your treatment.

Remission

The aim of your treatment is to put the CML into remission. Remission means that you don't have any symptoms from CML, and that there aren't any signs of leukaemia in your blood and bone marrow tests.

There are different levels of remission that can be measured in CML, and these depend on the sensitivity of the tests that are used:

Haematological remission

This is the first level of remission. It means that no leukaemia cells can be seen in a full blood count sample and there are normal numbers of white blood cells and platelets. If your spleen was larger than normal when you were first diagnosed, this should also have gone back to its normal size.

Most people get a haematological remission within three months of starting imatinib.

Cytogenetic remission

This is the next level of remission. It means there is no sign of the Philadelphia chromosome in your blood or bone marrow sample.

A bone marrow sample contains about 20 cells for your doctor to examine. When you are first diagnosed all of these cells will have the Philadelphia chromosome (Ph+). As your treatment begins to work the number of Ph+ cells in your bone marrow will decrease. This is called a cytogenetic response.

When the bone marrow sample contains no Ph+ cells this is called a cytogenetic remission.

It takes longer (sometimes several months) to get a cytogenetic remission than a haematological remission. About 8 out of 10 people taking imatinib for CML in the chronic phase get a cytogenetic remission.

Major molecular response (MMR)

A major molecular response (MMR) is the next goal of treatment after a person gets a cytogenetic remission.

Even after someone has a cytogenetic remission there can still be leukaemia cells in his or her blood. But, because there may be only one leukaemia cell in among many thousands of normal blood cells, a very sensitive test is needed to detect the leukaemia.

The polymerase chain reaction (PCR) blood test is able to detect one leukaemia cell in up to one million (1,000,000) normal blood cells. It does this by measuring a substance (transcript) made by the Bcr-Abl gene in the leukaemia cells.

When you're first diagnosed and about every three months afterwards, you'll have blood taken for PCR testing. Because it's so sensitive the PCR test may continue to

show up signs of leukaemia for many months after your treatment starts even though you're feeling well.

If your PCR test shows that the numbers of Bcr-Abl transcripts in your blood have decreased to at least 1000 times less than when you were first diagnosed, this is called a major molecular response. In people who have a major molecular response, the risk of the CML relapsing while treatment continues seems to be very low indeed.

Complete molecular response (undetectable transcripts)

If the PCR test can't detect any Bcr-Abl transcripts this is called a complete molecular response. It's also sometimes called 'undetectable transcripts' as it's likely that there are still tiny amounts of leukaemia in your system that can't be detected by PCR.

Continuing to take imatinib

You'll usually keep taking imatinib for as long as it's working to control the leukaemia. This is important even if your PCR blood tests don't show up any signs of leukaemia after you've been taking imatinib for a while.

There is a risk that if you stop treatment or change your dose without your doctor's advice, leukaemia cells may develop again and not respond as well to treatment in future.

It can be difficult to remember to take a tablet every day. You may find it helps to build taking your imatinib into your daily routine so that it becomes a habit.

- Choose something else that you do at the same time every day, like eating lunch or dinner, and take your medicine at the same time.
- Put your tablets in a place where you'll see them every day.
- Mark off each dose of imatinib you take on a calendar or use a 7-day pill container.
- Keep a supply of tablets with you when you travel and take your medicine in your carry-on luggage when you fly.

Other tyrosine kinase inhibitors, Dasatinib and Nilotinib

In addition to imatinib there are other tyrosine kinase inhibitors called dasatinib (Sprycel®) and nilotinib (Tasigna®) that are licensed to treat Philadelphia chromosome positive CML (Ph+CML).

These drugs work in a similar way to imatinib and tend to have similar side effects. They may be helpful for people who can't take imatinib because of severe side effects or because it isn't working to control their CML.

Dasatinib and nilotinib are newer drugs, and aren't yet widely available across the UK. The National Institute for Health and Clinical Excellence (NICE), the organisation that gives guidance on what new treatments should be available on the NHS in England and Wales, is looking at both these treatments. Its guidance is expected sometime in 2010.

The Scottish Medicines Consortium (SMC), the body that makes decisions for Scotland, has said both dasatinib and nilotinib should be available in Scotland for use in people who have Ph+CML in chronic phase for whom imatinib isn't working or who have too many problems with side effects from it.

If you are prescribed one of these drugs you'll be monitored in the same way as people taking imatinib.

Chemotherapy for chronic myeloid leukaemia

Chemotherapy is the use of anti-cancer (cytotoxic) drugs, which work by destroying or damaging the leukaemia cells. The drugs circulate in the blood and can reach leukaemia cells all over the body.

Although imatinib is the standard treatment for CML, chemotherapy is occasionally used. It's most likely to be used if imatinib and closely-related drugs such as dasatinib aren't effective or cause unacceptable side effects.

Some people are given chemotherapy, usually with a tablet, when their CML is first diagnosed. This may happen when doctors are waiting for the results of tests to confirm the CML is of a type that is likely to respond to imatinib. In this situation treatment is usually changed to imatinib once the test results are available.

Often chemotherapy involves taking a tablet and this causes only mild side effects. But, sometimes more intensive chemotherapy, involving a combination of drugs given into a vein, is needed. And this causes more troublesome side effects.

People who are treated with a stem cell transplant usually have intensive chemotherapy as preparation for the transplant.

Chemotherapy tablets

When chemotherapy is used to treat CML in chronic phase it's usually given as tablets. The most commonly used tablet is hydroxycarbamide. These are often taken every day for as long as they are working. The dose of the tablets is changed depending on the results of regular blood tests.

Treatment may be interrupted for a time if the number of white blood cells falls below a certain level. For most people the side effects from the tablets are mild. The drug most commonly used is hydroxycarbamide.

Combination chemotherapy

If CML starts to behave more like an acute leukaemia, more intensive chemotherapy is the main treatment. It generally consists of a combination of three or four drugs given by injection into a vein (intravenously).

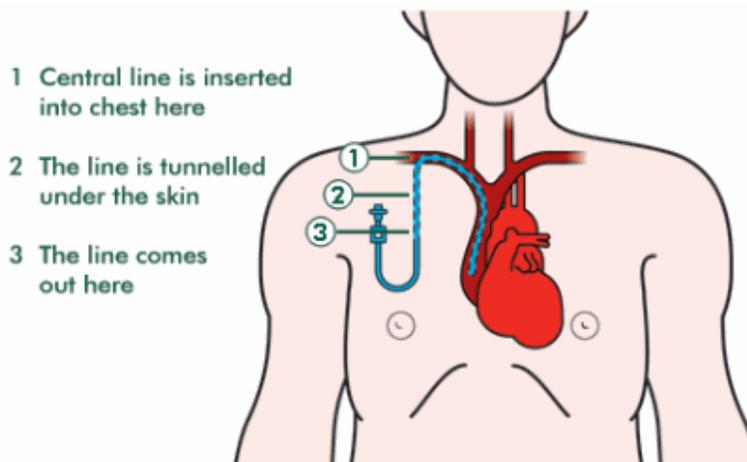
To make giving the chemotherapy easier and so that you can avoid having frequent injections, a plastic tube (called a central line) may be put into a vein in your chest. Alternatively a PICC line (peripherally inserted central venous catheter) or implantable port may be used.

Central line

The central line is put in under a general or local anaesthetic.

A small cut is made in the skin over your chest, and a thin flexible plastic tube is placed under your skin and into a large vein in your chest. The other end of the tube stays outside your body and has a screw cap at the end. The tube can be used to give drugs and fluids and collect blood samples.

It can stay in for months and the nurses will show you how to look after it to prevent blockages or infections.



A central line

PICC line

A PICC line is a long, fine tube put into a vein in the crook of your arm and threaded up into a larger vein leading to your heart.

Implantable port

An implantable port (also known as a portocath) is a thin, soft plastic tube that is put into a large vein in the chest. It has an opening (port) just under the skin on your chest or arm.

Side effects of chemotherapy

The number and degree of side effects you have will depend on the dose you're given and on whether you have just one type of chemotherapy tablet or a combination of drugs.

Side effects are generally more severe if higher doses are used or when several chemotherapy drugs are given together.

The main side effects may include:

- lowered resistance to infection due to low numbers of white blood cells
- feeling breathless or looking paler due to low numbers of red blood cells (anaemia)
- feeling very tired
- bleeding or bruising more easily due to lowered numbers of blood clotting cells (platelets)
- feeling sick (nausea) or being sick (vomiting)
- sore mouth
- hair loss (if a combination of chemotherapy drugs is used).

Although they may be hard to bear at the time, these side effects will disappear once your treatment is over.

Contraception while on chemotherapy

It's important to take effective contraceptive precautions when you're having chemotherapy, as the chemotherapy drugs might harm the baby if you or your partner becomes pregnant.

Fertility issues while on chemotherapy

Unfortunately, some chemotherapy treatments may cause infertility. Infertility is the inability to become pregnant or to father a child. This may be temporary or permanent, depending on the drugs that you have.

If you think that you may want to have children in the future, talk to your doctors about this before starting chemotherapy treatment. They will be able to tell you if your fertility is likely to be affected. You can then make an informed decision about your options.

If you have a partner it's a good idea for both of you to be there during these discussions. Don't be afraid to ask your doctor or specialist nurse any questions.

JASCAP information booklet on chemotherapy discusses the treatment and its side effects in more detail. Information about individual drugs and their particular side effects is also available.

High-dose treatment with stem cell support for CML

High-dose treatment with a stem cell transplant may benefit some people with CML.

If your doctor thinks that a transplant is necessary or possible for you, they will discuss it with you in more detail. Stem cell transplants are generally only carried out in specialist cancer treatment centres. A stem cell transplant allows you to have much higher doses of chemotherapy than usual. This can help to improve the chances of curing the leukaemia, or make a remission last longer.

Stem cells are blood cells at the very earliest stage of development in the bone marrow. They are mainly collected (harvested) from the blood, but can also be collected from the bone marrow. The stem cells can be donated by someone else (an

allogeneic transplant), or you can use your own stem cells (known as an **autologous transplant**).

The aim of this transplant is to give you a source of healthy bone marrow and to try to completely cure the leukaemia.

In an allogeneic transplant, stem cells are donated by someone else and given to you. The most suitable donor is usually a brother or a sister whose bone marrow is a close match to your own. Occasionally it's possible to use bone marrow from someone who isn't related to you, if tests have shown that their white blood cells are a good match with yours. The Anthony Nolan Trust and British Bone Marrow Registry both maintain registers of bone marrow donors in the UK.

In CML, an allogeneic transplant is usually carried out during the chronic phase, when the disease is stable.

A transplant may be used after the blast phase has been treated and you are in remission but it wouldn't usually be used as treatment for the blast phase.

High-dose treatment

The first stage of the treatment destroys your own bone marrow completely. This is done with high doses of chemotherapy, sometimes combined with radiotherapy (high-energy rays). After this treatment the donated stem cells are given to you through a drip into your central line.

The new stem cells, known as the graft, take a few weeks to settle in your bone marrow and start making the blood cells you need. Because you're very vulnerable to infections during this time, certain precautions will be taken to protect you until your white cell count has recovered. You'll be looked after in a room on your own and may be given antibiotics to help to prevent infections.

The hospital or specialist centre where you are treated will have its own policies on how to care for you during this time and your doctor or nurse will discuss this with you beforehand.

Graft versus host disease – a complication of allogeneic transplant

Your doctors and nurses will watch you carefully during the transplant and for some months afterwards, for any signs of the new marrow reacting against your own body tissue (this is called graft versus host disease – GvHD). This can occur at any time after your transplant. It doesn't mean that your transplant hasn't worked but it can cause various problems including diarrhoea, rashes and liver damage. Your doctor will prescribe drugs to help prevent the graft reacting to your body.

White blood cells from your donor (donor lymphocyte infusion)

After an allogeneic transplant, your doctors will monitor your blood closely for leukaemia cells. Having a small number of remaining leukaemia cells may be one of the reasons why CML comes back in some people after an allogeneic transplant.

One way of getting rid of these leukaemia cells is to have treatment with a type of white blood cell called lymphocytes taken from your donor. The lymphocytes help your immune system to reject the remaining leukaemic cells (known as the graft versus leukaemia effect – GvL). They can be collected from your donor especially for this reason, or they may be taken and stored when the stem cells are originally collected.

The lymphocytes are given through a drip into one of your veins (intravenously). This can be done in the outpatient department. Some people may need to have it done up to three or four times. Sometimes having a donor lymphocyte infusion can cause you to develop graft versus host disease.

Autologous Transplant - Using your own stem cells

Collecting the stem cells

The stem cells are taken while you are free of any signs of the disease (in remission). A substance called G-CSF will be given to you as an injection after a course of chemotherapy. G-CSF stimulates the stem cells to spill over from the bone marrow into the blood so that they can be collected from your blood.

High-dose treatment and recovery

You're given very high doses of chemotherapy, with or without radiotherapy (high-energy rays). Your own stem cells are then given back to you to 'rescue' you from the effects of the high-dose treatment and give you a source of healthy stem cells.

Interferon alpha for chronic myeloid leukaemia

Interferon alpha is a protein normally produced by the body during viral infections, such as flu. It may occasionally be given in the chronic phase of CML if other treatments haven't worked.

Interferon alpha is given as an injection under the skin using a very fine needle. The injections are slightly uncomfortable. You or a relative or friend can be taught how to give these injections so that they can be done at home.

Side effects of Interferon alpha

Interferon alpha can cause a range of side effects and some are similar to the symptoms of flu, including:

- chills
- fever
- depression
- weight loss
- headaches
- aching in the back, joints and muscles
- tiredness.

Some of these side effects can be reduced by taking a mild painkiller before the injection. Your doctor can prescribe these. The side effects are most noticeable with

the first one or two injections and usually wear off after that, although the tiredness often continues.

Research - clinical trials for CML

Research trials are carried out to try to find new and better treatments for leukaemia. Trials that are carried out on patients are known as clinical trials.

Clinical trials may be carried out to:

- test new treatments, such as new tyrosine kinase inhibitors, chemotherapy drugs or cancer vaccines
- look at new combinations of existing treatments, or change the way they are given, to make them more effective or to reduce side effects
- compare the effectiveness of drugs used for symptom control
- find out how cancer treatments work
- discover which treatments are the most cost-effective.

Trials are the only reliable way to find out if a different or new treatment is better than what is already available.

Taking part in a trial

You may be invited to take part in a treatment research trial. There can be many benefits in doing this. Trials help to improve knowledge about leukaemia and develop new treatments. You'll also be carefully monitored during and after the study.

Usually, several hospitals around the country take part in these trials. It's important to bear in mind that some treatments that look promising at first are often later found not to be as good as existing treatments, or to have side effects that outweigh the benefits.

If you decide not to take part in a trial, your decision will be respected and you don't have to give a reason. There will be no change in the way you're treated by the hospital staff and you'll be offered the standard treatment for your situation.

Blood and tumour samples

Many blood and bone marrow samples may be taken to make the right diagnosis. You may be asked for your permission to use some of your samples for research into cancer.

Some samples may be frozen and stored for future use when new research techniques become available.

The research may be carried out at the hospital where you are treated, or at another one. This type of research takes a long time, so you are unlikely to hear the results. The samples will be used to increase knowledge about the causes of cancer and its treatment. This research will hopefully improve the outlook for future patients.

Current research

A study called SPIRIT2 is trying to find out whether a tyrosine kinase inhibitor called dasatinib works better than the current standard treatment (imatinib) as a first treatment in chronic phase CML. People who are newly diagnosed with CML in chronic phase will be eligible to take part.

Another study is investigating a drug called omacetaxine. Tyrosine kinase inhibitors work well for most people with chronic phase CML but in some people the CML doesn't respond. Researchers are working to develop new types of drugs, such as omacetaxine, that may be effective for people in this situation.

The study is being run to find out if omacetaxine will work for people who have CML that hasn't responded to treatment with at least two tyrosine kinase inhibitors or who have CML with a very specific type of gene change called T3151 and who haven't responded to treatment with imatinib.

Glivec® International Patient Assistance Program (GIPAP)

The Glivec® International Patient Assistance Program (GIPAP) is one of the most comprehensive and far-reaching cancer access programs ever developed on a global scale.

Novartis designed GIPAP to provide Glivec (imatinib) free of cost to eligible patients in developing countries who meet specific medical and socio-economic guidelines. Through The Max Foundation, GIPAP also provides information and referral assistance to patients, their family members and caregivers.

Specifically:

- GIPAP helps patients who are properly diagnosed with Philadelphia chromosome-positive (Ph+) chronic myeloid leukemia (CML) patients and to patients with c-Kit (CD117) positive unresectable (inoperable) and/or metastatic malignant gastrointestinal stromal tumors (GISTs).
- GIPAP helps patients who are not insured, not reimbursed, cannot pay for treatment privately, and are in developing countries that have minimal reimbursement capabilities.

GIPAP is more than a drug donation program; its goal is to optimize successful Glivec treatment by providing patients with emotional support and increasing awareness within their communities.

The Max Foundation, as Novartis' main partner in the administration of GIPAP, provides socio-economic evaluation of patients, guides physicians through the patient evaluation process, and provides emotional support, information and referral assistance to patients, their family members and care givers. In addition, we monitor patients to support the highest standard of patient care, collaborate with Novartis to identify and qualify eligible medical centers and physicians worldwide, and protect confidential patient information and data received in the course of program administration.

Through The Max Foundation's partnership with Novartis, experienced physicians and local organizations, GIPAP has been able to reach patients who would otherwise not have access to Glivec for their life-threatening diseases.

What is GIPAP?

For its breakthrough cancer therapy Glivec, Novartis designed The Glivec® International Patient Assistance Program, or GIPAP, one of the most comprehensive and far-reaching cancer access programs ever developed on a global scale. The "direct-to-patient" model is designed to provide the drug directly to individual patients by their treating physicians.

Since its implementation in early 2002, GIPAP has provided Glivec to more than 19,000 patients in 80 developing countries with minimal reimbursement capabilities who would not otherwise have access to the drug to treat their life-threatening diseases. Currently, there is no other global cancer program like it in existence. Its success is due in large part to its ability to adapt program goals to local rules/regulations.

GIPAP is accessible to eligible patients who:

- are properly diagnosed with Philadelphia chromosome-positive (Ph+) chronic myeloid leukaemia (CML) patients and to patients with c-Kit (CD117) positive unresectable (inoperable) and/or metastatic malignant gastrointestinal stromal tumours (GISTs)
- cannot benefit from any reimbursement or insurance scheme
- are unable to pay for treatment privately as determined by pre-established socio-economic criteria
- are in developing countries that have minimal reimbursement capabilities
- are in developing countries where regulatory approval for Glivec has been obtained
- are in developing countries where no generic versions of imatinib are available

Unlike traditional donation programs that deliver drugs through hospitals or other third party distribution organizations, Glivec is delivered/dispensed directly to patients by their treating physician/pharmacist.

As Novartis' main partner in the administration of GIPAP, The Max Foundation is responsible for reviewing and verifying patients' eligibility according to specific medical requirements provided by Novartis and performing socio-economic evaluations. These requirements are in line with World Health Organization (WHO) guidelines, which provide global guidance on charitable donation programs. Novartis is responsible for identifying qualified medical centers and physicians, and for donating and supplying Glivec to qualified treatment centers that provide the drug to those patients approved by The Max Foundation.

To qualify to administer GIPAP, a qualified center must be able to fulfill the following conditions:

- Understand and accept the general and local conditions of the GIPAP program
- Have qualified hematology or cancer specialists that are able to provide expert opinion on the indication and the response to therapy
- Have the capacity to perform a bone marrow aspiration / biopsy and detect the Philadelphia chromosome to establish diagnosis for CML patients
- Have the capacity to stain for CD117 with antibody in GIST patients
- If a medical center doesn't have diagnostic capacities for either CML/GIST, this center can submit an application form for GIPAP to the Max Foundation provided the patient has been properly diagnosed in another qualified center.
- Provide basic diagnostic and laboratory services to ensure patient follow-up such as hematology, biochemistry, pathology and X-rays
- Provide supportive care, at a minimum blood transfusions and antibiotics
- Receive, store and keep track of the Glivec packs received and distributed according to the instructions given by Novartis
- Report Serious Adverse Events to Novartis
- Keep records of patients' data and of detailed drug accountability's data

Novartis may not qualify a Center or a physician meeting the above-mentioned criteria if the country has already enough Qualified Centers/physicians or for non-compliance reasons

In countries where Novartis Oncology does not have a local presence, Novartis partners with The Max Foundation and with Axios International to administer GIPAP.

Axios assists private and public organizations in creating and implementing practical healthcare programs in the developing world.

Qualification Requirements for GIPAP

In order to qualify for GIPAP, the patient must meet specific eligibility criteria in medical and socio-economic areas as required by Novartis. GIPAP requirements were developed in line with WHO guidelines on access to medicines.

Medical Qualifications:

- Patient has been properly diagnosed by a physician qualified to diagnose, treat and regularly monitor patients with Philadelphia chromosome-positive (Ph+) chronic myeloid leukaemia (CML) and/or c-kit (CD117) positive unresectable (inoperable) and/or metastatic malignant gastrointestinal stromal tumours (GIST).
- CML patients must fall within one of the following classifications: 1)The country in which the chronic phase Ph+ CML patient lives has approved the registration of Glivec® treatment for newly diagnosed Ph+ CML patients. 2)The patient is suffering from accelerated phase or blast crisis Ph+ CML. 3)Treatment for chronic phase Ph+ CML has been attempted first with interferon and the patient has not responded to the drug or the physician confirms that the patient cannot tolerate it.
- The patient's physician must follow treatment guidelines outlined in the Glivec® package leaflet and then supply progress information.

Socio-economic Qualifications:

- Patient cannot benefit from any reimbursement or insurance scheme
- Patient cannot afford to pay for treatment privately

Other Qualifications:

- Patients must be in developing countries that have minimal reimbursement capabilities where regulatory approval or at least an import license for Glivec for CML/GIST has been obtained; and where no generic versions of imatinib are available and reimbursement negotiations have been completed.
- The patient's physician and clinic must be qualified.
- The patient must be a country resident.

Tasigna® International Patient Assistance Program (TIPAP)

- Novartis Oncology has expanded its patient access programs to incorporate Tasigna® (nilotinib), a potent and selective inhibitor of the Bcr-Abl protein that causes production of cancer cells in the Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML)
- In countries where full donation is the only appropriate path to access to Tasigna, Novartis, in partnership with The Max Foundation, has begun to establish TIPAP to ensure that patients can receive this valuable medication.
- Full donation of Tasigna through TIPAP will be available to Glivec patients who meet both clinical and economic criteria. Leading experts in CML around the world have developed and published medical criteria to determine when it is appropriate to prescribe Tasigna for particular patients. Economic eligibility for full donation of medicine through TIPAP is consistent with criteria employed for GIPAP.
- New access models will facilitate partial donation of Tasigna to other patients in countries where full donation is not applicable.

Living with a CML

After treatment for CML

After your treatment is completed, you'll have regular check-ups and possibly blood tests. These will probably continue for several years.

If you have any problems, or notice any new symptoms in between these times, let your doctor know as soon as possible.

For people whose treatment is over apart from regular check-ups, our JASCAP booklet on **Life after cancer** gives useful advice on how to keep healthy and adjust to life after cancer treatment.

Living with and after CML

Cancer can affect many areas of your life such as your finances, work, your emotions and relationships. Find information and advice about what the effects might be, how to deal with them and how we can help.

Financial support

Find practical advice on the possible financial impact of a cancer diagnosis, including what benefits you might be entitled to.

Practical issues

Information on dealing with day-to-day problems, including work, travel, and travel insurance.

Emotional effects

Information on the emotions you might experience as a result of your cancer diagnosis, ways that you might manage them and other sources of support.

Relationships and communication

Advice on how to talk to other people, talking to children, relationships and sexuality.

How we can help

Find out about the ways in which JASCAP can offer you information and support.

Questions you might like to ask your doctor

You can fill this in before you see the doctor or surgeon, and then use it to remind yourself of the questions you want to ask, and the answers you receive.

1. _____

Answer _____

2. _____

Answer _____

3. _____

Answer _____

4. _____

Answer _____

5. _____

Answer _____

JASCAP : We need your help

We hope that you found this booklet useful.

To help other patients and their families we need and intend to extend our Patient Information Services in many ways.

Our Trust depends on voluntary donations. Please send your donation by Cheque or D/D payable in Mumbai in favour of "JASCAP".

Note for Reader

This JASCAP booklet is not designed to provide medical advice or professional services and is intended to be for educational use only. The information provided through JASCAP is not a substitute for professional care and should not be used for diagnosing or treating a health problem or a disease. If you have, or suspect you may have, a health problem you should consult your doctor.

JASCAP

JEET ASSOCIATION FOR SUPPORT TO CANCER PATIENTS,
C/O ABHAY BHAGAT & CO., OFFICE NO.4, "SHILPA",
7TH. ROAD, PRABHAT COLONY,
SANTACRUZ (East),
MUMBAI - 400 055.
PHONE: 91-22-2617 7543 & 91-22-2616 0007
FAX: 91-22-2618 6162,
e-mail: pkrajascap@gmail.com, abhay@abhaybhagat.com

AHMEDABAD: MR. D.K.GOSWAMY,
1002, LABH, SHUKAN TOWER,
NEAR JUDGES' BUNGALOWS,
AHMEDABAD - 380 015.
PHONE : 91-79-6522 4287. Mob : 93270 10529
e-mail : dkgoswamy@sify.com

BANGALORE: MS. SUPRIYA GOPI,
455, I CROSS,
HAL III STAGE,
BANGALORE – 560 075
PHONE : 91-80-2528 0309 .
e-mail : supriyagopi@yahoo.co.in

HYDERABAD: MS. SUCHITA DINAHER & DR. M. DINAHER, M.D.,
FLAT NO. G4, 1ST. FLOOR, "STERLING ELEGANZA",
STREET NO.5, NEHRUNAGAR,
SECUNDERABAD – 500 026.
PHONE : 91-40-2780 7295.
e-mail : suchitadinaker@yahoo.co.in