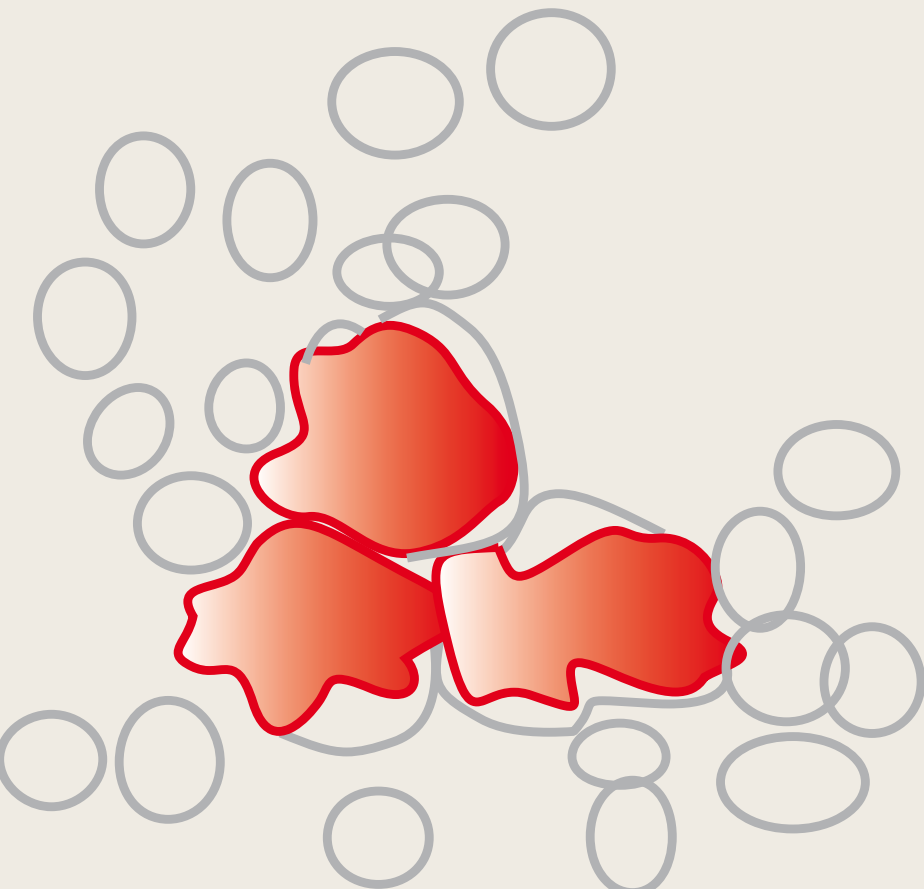


Chronic Myeloid Leukaemia (CML)



The diagnosis of a blood cancer can be a devastating event for patients, families and friends. It is therefore vital for everyone to have access to reputable and understandable information to help cope with the illness. Whenever possible our booklets are written in line with national guidelines for the treatment of patients with a blood cancer. The information in our booklets is more detailed than in many others but is written in a clear style with all scientific terms explained for the general reader.

We recognise that the amount and level of information needed is a personal decision and can change over time. Particularly at the time of diagnosis, patients may prefer less detailed information. A number of alternative sources of information are available which complement our publications.

The booklets in this series are intended to provide general information about the topics they describe. In many cases the treatment of individual patients will differ from that described in the booklets.

At all times patients should rely on the advice of their specialist who is the only person with full information about their diagnosis and medical history.

For further advice contact the clinical information team on 020 7269 9060.

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Introduction

In 1998 a new drug called imatinib (Glivec™ in the UK or Gleevec™ in the US) was introduced for treatment of chronic myeloid leukaemia (CML). This has dramatically changed the management of the disease and greatly improved the prospects for newly diagnosed patients. Most patients who have been treated with imatinib, although not cured, have had their disease stabilised and it is hoped that this will last for many years or possibly decades.

A remarkable feature is that, unlike most anti-cancer drugs, it seems that the longer a patient remains on imatinib the less likely it is that their disease will become resistant to the drug. Because the outlook for patients has changed so strikingly many doctors now refer to the older treatment as the pre-imatinib era. This booklet describes the treatment of adult patients. Children with CML will be treated in paediatric centres and their specialists will discuss treatment options in detail.



What is chronic myeloid leukaemia?

Chronic myeloid leukaemia is a cancer that starts in bone marrow stem cells, which are the cells that produce all blood cells. Blood cells can be divided into two main types. These are:

- lymphoid cells, which include lymphocytes and related cells and are key components of the immune system
- myeloid cells, which are red blood cells, platelets and all other white cells – neutrophils, monocytes, eosinophils and basophils.

The disease is known as chronic myeloid leukaemia because the leukaemic cells in both the bone marrow and the circulating blood look like myeloid cells. It is now thought that the cell first affected is actually a stem cell. This is because both the lymphoid and myeloid cells present in the blood and marrow in the later stages of the disease may be leukaemic.

Prior to the introduction of imatinib, CML was a life-threatening disease with a median life expectancy of around six to seven years, the only exception being the minority of patients who could receive a stem cell transplant. In most cases, it is now a chronic condition with good quality of life and it is expected that at least three out of four patients will be alive at ten years and overall survival may be even higher than this.

Prior to imatinib, CML used to progress slowly during the chronic phase of the disease. This phase lasted four to six years on average and then underwent a transformation to a more rapidly progressing state. In about two-thirds of patients this change was to an accelerated phase, which lasted about three to nine months. This then proceeded to a final or blast phase. In some patients the disease proceeded directly from chronic phase to blast phase. The term “advanced phase” is sometimes used to describe both the accelerated phase

and blast phase. There are two distinct types of blast phases defined by the types of blast cells present. In most patients the blast cells (immature white cells) resemble those seen in acute myeloid leukaemia (AML)¹, whereas in about a quarter of patients, the blast cells look more like those seen in acute lymphoblastic leukaemia (ALL)². This latter form of the disease is known as lymphoid blast crisis and tends to have a poorer response to treatment.

The above phases of disease progression have changed dramatically in the imatinib era. For most patients the chronic phase lasts at least ten years, possibly much longer, and only a minority of patients who start treatment in the chronic phase fail to respond well to imatinib.

^{1,2}There are separate booklets on Acute Myeloid Leukaemia and Acute Lymphoblastic Leukaemia available from Leukaemia Research.

Who gets chronic myeloid leukaemia?

Chronic myeloid leukaemia occurs at all ages, though very rarely in children below the age of 15.

The incidence increases with age. The average age at diagnosis is about 50 years and roughly a third of cases affect people over the age of 60 years. The incidence is slightly higher in males than in females. There are about 750 new cases each year in the UK.



What causes chronic myeloid leukaemia?

For most patients diagnosed in the UK there are no identifiable risk factors that might have caused their illness. There is no evidence that family members of a patient with CML are at a higher risk of developing the condition than anyone else.

The only clearly defined risk factor for chronic myeloid leukaemia is exposure to high levels of ionizing radiation. This was shown by a marked excess of CML cases in survivors of the Hiroshima and Nagasaki atomic bomb explosions. There have been reports of people who develop CML following high-dose radiotherapy as part of cancer treatment. It is now extremely unlikely that anyone in the UK would be accidentally exposed to levels of radiation high enough to increase the risk of developing CML.

What are the types of chronic myeloid leukaemia?

CML is thought to begin when a small part of chromosome 9 in a single stem cell is exchanged with a small part of chromosome 22. This event is called a chromosomal translocation. As a result chromosome 22 is shortened but gains a small section of material from chromosome 9. This smaller than normal chromosome 22 is called the Philadelphia chromosome. The translocation is written as t(9;22) in clinical notes. The result of this translocation is that part of a gene called *BCR* is linked to part of a gene called *ABL* to produce a fusion gene referred to as *BCR-ABL* on the Philadelphia chromosome. In about 90 per cent of cases it is straightforward to demonstrate the presence of the Philadelphia chromosome.

The Philadelphia chromosome and the *BCR-ABL* fusion gene are key to the diagnosis of CML and their formation is probably the event that triggers the disease. The protein produced by the *BCR-ABL* gene is the main target of imatinib and related drugs – this is described further in the treatment section. In about 5 per cent of cases very sensitive methods are needed to demonstrate the presence of the *BCR-ABL* gene in the leukaemic cells because (unusually) there is no evidence of the abnormal Philadelphia chromosome by conventional cytogenetics (examination of the chromosomes). The remaining 5 per cent of patients have the clinical picture of CML but the leukaemia cells lack the Philadelphia chromosome and the *BCR-ABL* gene. This presentation is known as atypical CML.

An extremely rare condition, which resembles CML but shows significant clinical and laboratory differences, is called chronic neutrophilic leukaemia (CNL). The leukaemic cells lack the Philadelphia chromosome and the *BCR-ABL* fusion gene. The blood count and blood film are characterised by very high numbers of neutrophils with a mature appearance.

What are the signs and symptoms of chronic myeloid leukaemia?

Most patients with CML are diagnosed during the chronic phase of the disease. Many patients will not be aware of any symptoms and are diagnosed by chance as a result of routine blood tests.

When symptoms are present they are usually non-specific and gradual in onset. They include fatigue, loss of appetite, weight loss, increased sweating and unusual or excessive bleeding from various sites. If the spleen is enlarged there may be abdominal discomfort and a feeling of fullness when eating. An enlarged spleen is a common finding on physical examination of patients with CML. This has become less common because of earlier diagnosis but is still seen in about 50-60 per cent of cases. The liver is enlarged in 10-30 per cent of patients at the time of diagnosis.

The accelerated phase, which affects about two-thirds of the patients who progress to the advanced phase, is not usually marked by any change in symptoms. It is detected on the basis of changes in the blood and bone marrow. In some cases there may be fever, night sweats and enlargement of the spleen.

The blast crisis, now increasingly rare but still encountered, is usually associated with significant symptoms. These include weight loss, fever and bone pain. Patients may become anaemic (low haemoglobin levels) and may suffer bruising/bleeding problems and repeated infections because the bone marrow is failing to produce normal blood cells. In blast crisis it is possible that leukaemia cells will invade other tissues. In the skin it may lead to the production of small nodules or painful haemorrhages. Lymph nodes may become enlarged and blast cells may be present in the fluid which surrounds the brain and spinal cord.

How is chronic myeloid leukaemia diagnosed?

About 95 per cent of patients are in chronic phase at the time of diagnosis, with the remainder being in accelerated phase or blast crisis. There is no formal definition of accelerated phase CML. It is a matter of medical judgement, which takes into account the clinical features present, the laboratory findings on blood and bone marrow samples and the changes in the cytogenetic characteristics of the leukaemia cells. In about one-third of the cases that do progress the disease appears to progress directly from chronic phase to blast crisis without an intervening stage.

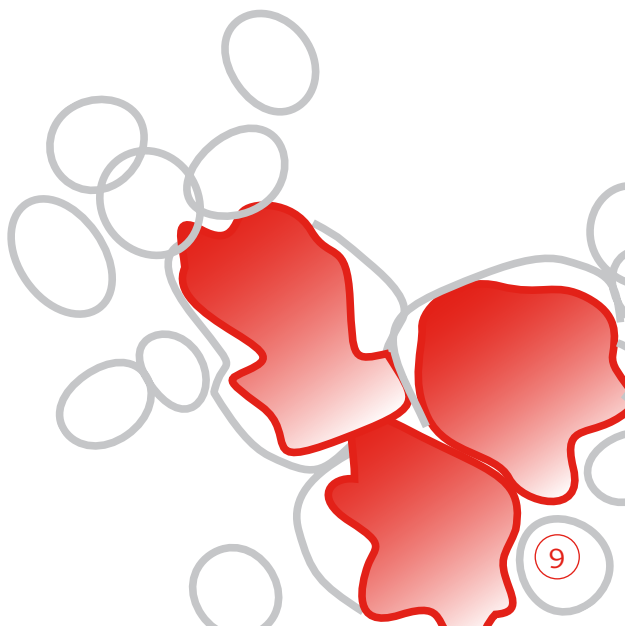
It is becoming increasingly common for CML to be diagnosed by chance in patients who have no specific symptoms. Patients typically have a raised white cell count with higher than normal numbers of immature white blood cells. The count is characteristically well above normal limits and may be very high. The cells appear normal when viewed through the microscope, unlike acute leukaemia, but there are forms of blood cells present that are not normally seen except in the bone marrow.

The blood count and the appearances of the cells under the microscope are quite distinctive and the diagnosis is usually definite at this stage. A feature that tends to confirm the diagnosis is the presence of increased numbers of basophils and to a lesser extent, eosinophils both of which are types of white blood cell. The number of lymphocytes may be slightly elevated.

In most patients there is some degree of anaemia at the time of diagnosis, which is usually mild, but this may be severe in those patients who have been diagnosed at a relatively late stage. The platelet count is often significantly raised in chronic phase CML and may be very high in a few patients.

It is usual for patients with CML to have a bone marrow sample taken soon after diagnosis. This confirms the diagnosis and provides important additional information. Normal bone marrow contains large numbers of fat cells with areas of blood cell production spaced between them. In CML there is very little fat present in the bone marrow which is entirely filled with large numbers of leukaemia cells.

Cytogenetic studies (i.e. examination of chromosomes in dividing cells from the bone marrow) are of great importance both in confirming the diagnosis of CML and in monitoring the response to treatment. The diagnosis of typical CML is confirmed in the 95 per cent of patients who have the *BCR-ABL* gene present (with or sometimes without the Philadelphia chromosome). For patients treated by stem cell transplantation the level of the BCR-ABL protein is of great value in determining whether the transplant has been successful.



How is chronic myeloid leukaemia staged?

In most forms of cancer some form of staging is used to assist in treatment planning and in making a likely prognosis. In solid tumours, staging refers primarily to the spread of the cancer from its original site. However this form of staging is not used in CML because the disease is typically widespread at the time of diagnosis.

Most patients are diagnosed in chronic phase and when they are treated with imatinib they will usually remain in this phase for a long period. When blast crisis occurs, it is characterised by the presence of at least 30 per cent blast cells in the bone marrow or circulating blood. About half of all blast crises are of the myeloid type, a quarter are of the lymphoid type and the remainder are a mixture of the two. The distinction is important because it can predict the likely response to treatment and eventual outcome i.e. prognosis. Some patients will develop localised collections of leukaemia cells outside the bone marrow. Although this is uncommon, it is usually followed by typical blast crisis within a few months.

The Sokal and Hasford scores have been devised to help doctors predict which patients are more likely to have progressive disease. The scores separate patients into good and poor-risk groups using formulas based on the following features:

- patient's age
- size of spleen
- percentage of blast cells in the blood
- number of platelets
- numbers of basophils
- numbers of eosinophils.

Before the introduction of imatinib, patients with low scores had an average survival of around eight years whilst patients with high scores had an average survival of three to four years.

The use of imatinib is expected to greatly extend these survival periods but the evidence to date suggests that the two scoring systems can still be useful for patients. However, it is too early to accurately assess the average survival for the good and poor risk groups. New techniques to predict the response to treatment are being developed and will eventually replace these older scoring systems.



How is chronic myeloid leukaemia treated?

Principles of treatment

It is possible that imatinib may offer the chance of cure to an as yet unknown proportion of patients but it will take several years to assess whether this is true in practice. Certainly the majority of patients with CML have been able to continue a normal or near-normal lifestyle. In many cases this includes the ability to continue in work or an early return to work. Because imatinib is targeted at a specific abnormality found in CML cells most patients experience much less severe side effects compared with previous treatments. In a clinical study which compared imatinib with interferon, the most effective previous treatment, many patients who started on interferon chose to switch to imatinib because they found the side effects of interferon to be unacceptable. A further benefit of imatinib is that it is taken by mouth, whereas interferon had to be injected under the skin.

For some patients with CML the disease either does not respond to imatinib or it initially responds to the drug but then becomes resistant. A second generation of imatinib-like drugs are expected to be effective against most types of resistance. In the UK there are two such drugs that are currently available or in clinical studies – these are called nilotinib (trade name Tasigna) and dasatinib (trade name Sprycel). Like imatinib, these drugs are taken by mouth, not by injection. A drug called bosutinib is not yet available in the UK but is showing promise in US studies. There are some kinds of resistant diseases that are not affected by any imatinib-type drug; newer drugs are being developed which work in a completely different way and may be effective in this situation.

Experience to date has shown that within five years of starting imatinib, 20 per cent or fewer of patients will progress to advanced phase. With earlier drugs the risk of progression was constant year after year and eventually most or all patients would enter advanced phase. It presently appears that the 80 per cent of patients who reach five years without progressive disease are likely to be able to continue indefinitely on treatment with imatinib.

Treatment recommendations

The British Committee for Standards in Haematology (BCSH) has published “Recommendations for the Management of *BCR-ABL*-positive Chronic Myeloid Leukaemia”³ which is available to download from the BCSH website at http://www.bcsHguidelines.com/pdf/CML_guidelines_270707.pdf

Almost all newly diagnosed patients with chronic phase CML are now treated initially with imatinib – usually at a dose of 400mg daily. For most patients imatinib reduces the number of leukaemia cells in the blood and bone marrow to a level that cannot be detected under the microscope. It is therefore necessary to use more sensitive techniques to measure the very small numbers of leukaemia cells still present in the body.

Present advice is that patients who are responding well to imatinib should continue to take the drug indefinitely. This is because there is no evidence, at present, that imatinib can eradicate CML and thus patients should never stop taking imatinib without discussing this with their specialist.

Imatinib has allowed many patients to return to a virtually normal lifestyle, even when they have had a poor quality of life on previous treatment. Present evidence indicates that treatment with imatinib and related drugs is likely to continue to be well tolerated. Although there are a few reports of patients stopping imatinib and remaining well, there are other reports of patients

³Cancer treatment is now preferentially based on guidelines produced by expert advisors and based on published evidence. Presently there are no evidence-based guidelines for the treatment of CML (mainly because the introduction of several new drugs makes this a fast-developing area of medicine).

experiencing relapses and it is very strongly advised that no patient should stop taking imatinib unless their doctor advises this.

All women taking imatinib (or similar drugs) should use reliable forms of contraception. This is because there have been reports of abnormalities in babies whose mothers have been taking imatinib during pregnancy. Although a number of apparently normal babies have been born to mothers taking imatinib, the risk of an abnormality is sufficiently high that doctors have strongly recommended that women taking imatinib should avoid pregnancy. It has been very clearly shown that imatinib is present in breast milk and therefore women taking imatinib should definitely not breastfeed.

There is no evidence whether the foetus could be affected when the father was taking imatinib at the time of conception. However, it is still strongly advised that men taking imatinib should also use contraception to prevent pregnancy because it is impossible to rule out a risk of harm to the baby.

> Measuring treatment response to imatinib and similar drugs

There are very specific criteria used to assess whether CML is responding to treatment with imatinib. These will be used to regularly monitor patients for their response and this will determine their future treatment. Remission is the term used when leukaemia cells cannot be detected and patients are clinically well. There are several definitions of remission recognised in CML which vary according to the sensitivity of the tests being used.

Haematological remission

When no leukaemia cells are seen on examination of a blood or bone marrow sample under the microscope it is defined as a haematological remission. This is an insensitive test, which cannot detect leukaemia cells unless they make up at least 1 per cent of the total white cell numbers. This means that there may still be large numbers of leukaemia cells remaining in the patient.

Cytogenetic remission

A more sensitive test is detection in a bone marrow sample of the characteristic Philadelphia chromosome, which is the hallmark of CML. This test can detect one leukaemia cell carrying the Philadelphia chromosome amongst 1,000 normal marrow cells. If the Philadelphia chromosome cannot be detected, it is termed a cytogenetic remission. It is recommended that patients should be monitored at three monthly intervals until they achieve complete cytogenetic remission. There is a case for continuing to examine bone marrow samples annually to detect other genetic changes that may develop. The value of this is not yet proven and practice may vary from hospital to hospital.

Molecular remission (PCR negativity)

The polymerase chain reaction (PCR) is a technique that can be used to detect minute amounts of the gene product (called a transcript) which is produced by the abnormal *BCR-ABL* fusion gene. PCR works by making large numbers of copies of the transcript – it has been referred to as “molecular photocopying”. The test is so sensitive that it can detect transcripts from one leukaemia cell in 100,000 normal blood cells. This test is now the recommended standard for monitoring the progress of patients who are responding to treatment for CML.

If the level of the *BCR-ABL* transcripts is reduced by at least 1,000-fold then it is termed a “major molecular response”. When no *BCR-ABL* transcripts can be detected it is recommended that this should be referred to as “undetectable transcripts”, rather than “complete molecular remission”, which is the term formerly used. This emphasises the fact that there could still be leukaemia cells present somewhere in the patient’s body, even when the test is negative.

Treatment options

The advice in this section is organised according to the patient’s disease stage, their risk factors and their response to treatment. The BCSH guidelines do not

treat accelerated phase and blast crisis separately; they are grouped together as advanced phase because the treatment does not differ.

The initial treatment is usually referred to as first-line therapy. If the disease no longer responds well to first-line therapy, other treatments are needed and these are called second-line, third-line and so on.

> Newly diagnosed patients

Chronic phase at diagnosis

The excellent results reported to date for imatinib mean that for almost all patients who are diagnosed in chronic phase, their initial treatment will be 400mg of imatinib per day⁴.

Before the introduction of imatinib, newly diagnosed patients who were thought unlikely to respond to drug treatment would be considered for a stem cell transplant, which is potentially curative. Patients with a poor chance of responding to drug treatment and a good chance of surviving a transplant would be offered this option. Doctors are now likely to suggest an initial trial of imatinib, as there is no evidence that this will reduce the chances of a successful transplant. Stem cell transplants are now only recommended for patients whose disease has not responded to imatinib or second-line drugs.

Advanced phase

For patients who are in advanced phase at diagnosis a dose of 600 or 800mg of imatinib per day is the recommended first-line treatment.

Very few patients are in blast crisis when diagnosed – those who are, may respond to imatinib but this response is likely to be short lasting. In this situation treatment options will be discussed in detail with the specialist.

⁴Lower starting doses will rarely be effective and may increase the risk of resistance developing – they should not be used.

Failure of initial treatment with imatinib

If the disease is not fully controlled by treatment with imatinib it will be described as warnings, sub-optimal response or failure which are defined and managed as follows:

Warnings

This means that there are features present at diagnosis or which develop on treatment which suggest that the disease may become resistant to imatinib and/or progress to advanced phase.

Recommendation: More frequent monitoring.

Sub-optimal response

This means that there is evidence of a response to treatment but this falls short of a full response.

Recommendation: Treatment with imatinib should be re-assessed and may need to be changed immediately or in the foreseeable future.

Failure

This means that there is little or no response to treatment.

Recommendation: In this case imatinib should be discontinued and another treatment initiated.

The BCSH lists several options, in order of preference, that may be considered for patients deemed to have failed initial treatment with imatinib. These are:

- increasing the dose of imatinib
- changing to a second-line drug such as dasatinib, nilotinib or, if available, entry into a clinical study of a novel drug
- a stem cell transplant from a normal donor
- treatment with drugs used before imatinib was available such as cytarabine, hydroxyurea, busulphan, homoharringtonine, decitabine, arsenic compounds or interferon

- experimental drugs, i.e. drugs which are not yet licensed for routine use
- treatments designed to stimulate the patient's immune system to attack the leukaemia cells.

> Progression to advanced phase while receiving imatinib

When the disease progresses to advanced phase, there is no basis for continuing treatment with imatinib. However, it may be possible to achieve a remission with a second-line drug, such as dasatinib or nilotinib, as these have been shown to be effective against most types of imatinib resistance.

> T315I-related resistance

One form of resistance develops when a specific mutation (known as T315I) changes the shape of the *BCR-ABL* protein so that imatinib can no longer bind to it. Nilotinib and dasatinib are not effective against this type of resistance. There are several new drugs under trial that appear to be effective against CML which tests positive for the T315I mutation and specialists will discuss available treatment options with patients affected by this mutation.

If a patient acquires the T315I mutation, or does not respond to second-line therapy, it may be reasonable to consider a stem cell transplant. The preferred donor is a tissue-matched sibling; in this situation a transplant using stem cells from a matched unrelated donor may be a reasonable alternative.

> Long-term effects of treatment

There is very good evidence that treatment with imatinib, and related drugs, will lead to prolonged survival for the majority of patients with CML. The effects of continuous life-long treatment are not yet known. There may possibly be late-effects as a consequence of prolonged treatment which will only become apparent after many years of follow-up of patients on this treatment. Present evidence indicates that patients treated with imatinib and related drugs are likely to continue to enjoy a good quality of life. Although there are a few reports of patients who stop taking imatinib and remain well,

there are other reports of patients experiencing relapses and it is very strongly advised that no patient should stop taking imatinib unless their doctor advises this.

There is some evidence that imatinib in combination with other treatments may cause more side effects than when used alone; clinical trials are being carried out to assess whether any benefit of adding other drugs to imatinib outweigh any ill effects.

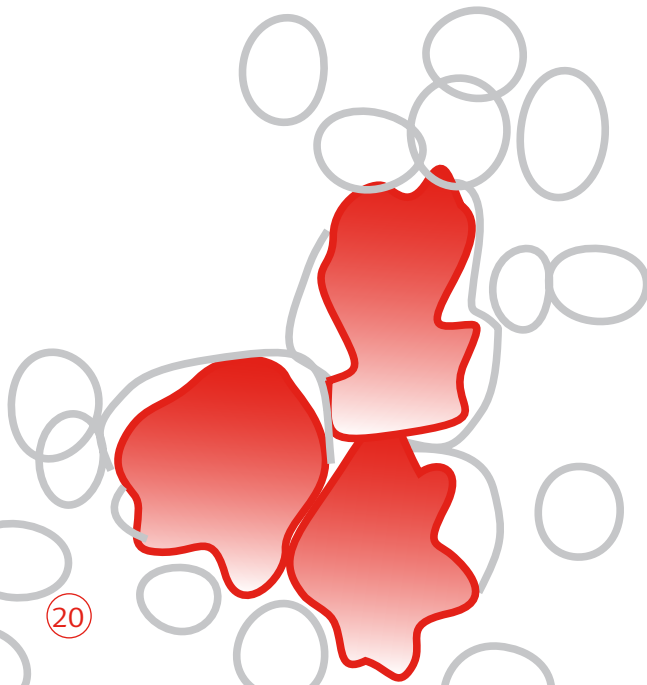


Prognosis

With ten years' experience of using imatinib to treat CML, there is a general agreement that this drug will prevent progression of disease in the majority of patients. The use of imatinib and other drugs has also led to a very significant improvement in survival and in quality of life.

For patients who do not achieve a good response to imatinib, the outlook will depend on their response to alternative treatments. They will need to discuss treatment options and likely prognosis with their specialist.

The minority of patients who are diagnosed in blast crisis, on the other hand, have gained much less benefit from the introduction of imatinib and related drugs. Such patients will have treatment options discussed in detail by their specialist; they may well be invited to take part in a clinical trial.



Summary

Chronic myeloid leukaemia is a form of leukaemia that starts at the level of a primitive stem cell. The disease is characterised by the presence of an abnormal chromosome derived from the exchange of genetic material between chromosomes 9 and 22. The abnormal chromosome is called the Philadelphia chromosome and contains a fusion gene called *BCR-ABL* which is important for the development of CML. Detection of *BCR-ABL* gene products is of great value in diagnosing and monitoring the response to treatment. The *BCR-ABL* protein has been the focus of targeted drug development.

If CML progresses it shows three, although occasionally only two, consecutive phases. The great majority of patients are diagnosed in the early chronic phase of the disease. Treatment with imatinib or related drugs leads to a prolonged chronic phase for most patients. It is not yet known how many patients will progress to advanced disease – many doctors think this will only happen for a small minority.

The preferred drug for first-line treatment is now imatinib used at a starting dose of 400mg per day. Imatinib induces very good responses compared with the drugs used previously. Additionally, the side effects are rarely severe which means that very few patients elect to discontinue treatment.

The need for a stem cell transplant to treat CML has been substantially reduced since the introduction of imatinib. Today no adult patient with newly diagnosed CML would be advised to consider a stem cell transplant as first choice of treatment. Even where the scoring system for transplants predicts a favourable outcome it is likely that an initial treatment with imatinib would be recommended.

Although the position may change in the future, as more data becomes available, it is currently expected that patients treated with imatinib and related drugs will need to take them for the rest of their lives. This has been compared to patients with diabetes whose disease can be controlled long term with insulin; in neither diabetes nor CML is the underlying disease 'cured' but appropriate drug treatment offers long-term survival with a good quality of life.

A small minority of patients will experience disease progression even when treated with the newest drugs. In about two-thirds of such cases the initial transformation is to the accelerated phase, which lasts for about three to nine months before further progressing into blast crisis. The remaining third of patients enter blast crisis directly from chronic phase. Blast crisis resembles acute leukaemia and has an average survival of about three to six months. However, some patients will respond to intensive therapy by entering into a second chronic phase that may extend survival.



Notes

Notes

Typical normal values for blood test results

	WBC x 10 ⁹ /l	RBC x 10 ¹² /l	Hb g/dl	ANC x 10 ⁹ /l	Platelets x 10 ⁹ /l
Adult male	3.7 to 9.5	4.3 to 5.7	13.3 to 16.7	1.7 to 6.1	143 to 332
Adult female	3.9 to 11.1	3.9 to 5.0	11.8 to 14.8	1.7 to 6.1	143 to 332
West Indian	2.8 to 9.8			1.0 to 6.5	122 to 374
African	2.8 to 7.8			0.9 to 4.2	115 to 342
Child 2-5 yrs	5 to 13	4.2 to 5.0	11 to 14	1.5 to 8.5	143 to 332
Child 6-9 yrs	4 to 10	4.3 to 5.1	11 to 14	1.5 to 6.0	143 to 332
Child 9-12 yrs	4 to 10	4.3 to 5.1	11.5 to 15.5	1.5 to 6.0	143 to 332

Normal ranges vary slightly between laboratories so you may wish to ask your doctor to enter your normal values below:

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WBC	White blood cell count
RBC	Red blood cell count
Hb	Haemoglobin concentration
ANC	Absolute neutrophil count

Separate ranges are quoted for West Indian and African populations as these groups have different normal ranges for white cell counts, absolute neutrophil counts and platelet counts.

This information is adapted, with permission, from *A Beginner's Guide to Blood Cells*, Dr Barbara Bain. Pub. Blackwell, Oxford, 1996.



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