Chronic Myeloid Leukaemia (CML)

A Guide for Patients

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

Being diagnosed with chronic myeloid leukaemia (CML) can be a shock, particularly when you may never have heard of it before and may even not have had obvious symptoms. If you have questions about CML – what causes it, who it affects, how it affects your body, what symptoms to expect and likely treatments – this booklet covers the basics for you.

For more information, talk to your haematologist, clinical nurse specialist or hospital pharmacist.

Booklet compiled by Ken Campbell, MSc (Clinical Oncology) and peer reviewed by Mark Crowther, Consultant Haematologist at Worcestershire Acute Hospitals NHS Trust. We are also grateful to Marie Denny and Paul Carless, CML patient reviewers, for their valuable contribution. The booklet review was completed by Lisa Lovelidge and peer reviewed by Professor Mary Frances McMullin, Dr Donal McLornan and Dr Dragana Milojkovic. It was patient reviewed by Tracey Littlebury, Steven Davies, Colin Heyes, Joanna Burridge and Fran Woodcock.

Throughout this booklet you will see a number of quotations. These are the real experiences and words of CML patients which will hopefully help you to understand your disease and situation a bit better.

If you would like any information on the sources used for this booklet, please email **communications@leukaemiacare.org.uk** for a list of references.

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In this booklet

About Leukaemia Care

Leukaemia Care is a national charity dedicated to ensuring that people affected by blood cancer have access to the right information, advice and support.

Our services

Helpline

Our helpline is available 9.00am - 10.00pm on weekdays and 9.00am - 12.30pm on Saturdays. If you need someone to talk to, call **08088 010 444**

Nurse service

We have two trained nurses on hand to answer your questions and offer advice and support, whether it be through emailing **nurse@leukaemiacare.org.uk**, over the phone on **08088 010 444** or via LiveChat.

Patient Information Booklets

We have a number of patient information booklets like this available to anyone who has been affected by a blood cancer. A full list of titles – both disease specific and general information titles – can be found on our website at **www.leukaemiacare.org.uk/support-and-information/help-and-resources/information-booklets/**

Support Groups

Our nationwide support groups are a chance to meet and talk to other people who are going through a similar experience. For more information about a support group local to your area, go to **www.leukaemiacare.org.uk/support-and-information/support-for-you/find-a-support-group/**

Buddy Support

We offer one-to-one phone support with volunteers who have had blood cancer themselves or been affected by it in some way. You can speak to someone who knows what you are going through. For more information on how to get a buddy call

08088 010 444 or email **support@leukaemiacare.org.uk**

Online Forum

Our online forum, **www.healthunlocked.com/leukaemia-care**, is a place for people to ask questions anonymously or to join in the discussion with other people in a similar situation.

Patient and carer conferences

Our nationwide conferences provide an opportunity to ask questions and listen to patient speakers and medical professionals who can provide valuable information and support.

Website

You can access up-to-date information on our website, **www.leukaemiacare.org.uk**, as well as speak to one of our care advisers on our online support service, LiveChat (9am-5pm weekdays).

Campaigning and Advocacy

Leukaemia Care is involved in campaigning for patient well-being, NHS funding and drug and treatment availability. If you would like an update on any of the work we are currently doing or want to know how to get involved, email **advocacy@leukaemiacare.org.uk**

Patient magazine

Our quarterly magazine includes inspirational patient and carer stories as well as informative articles by medical professionals. To subscribe go to **www.leukaemiacare.org.uk/communication-preferences/**

What is CML?

Chronic myeloid leukaemia (CML) is a blood cancer that affects the white blood cells known as myeloid cells.

To understand CML, it is helpful to understand how blood cells are normally produced. Blood cells are produced in the bone marrow, which is spongy tissue found inside bones. Each day the bone marrow produces more than a trillion new blood cells to replace those that are 'worn out'. Blood stem cells divide to produce either mature blood cells or more stem cells. Only about one in 5,000 of the cells in the bone marrow is a 'stem cell'. Stem cells, also called haematopoietic stem cells, have the ability to differentiate and may become a myeloid stem cell or a lymphoid stem cell.

A myeloid stem cell becomes one of three types of mature blood cells:

1. Red blood cells that carry oxygen to all tissues of the body
2. Platelets that form blood clots to stop bleeding
3. White blood cells (granulocytes) that fight infection and disease. These include neutrophils, monocytes, eosinophils and basophils

A lymphoid stem cell can become one of three types of lymphocytes, which are also white blood cells:

1. B lymphocytes that make antibodies to help fight infection
2. T lymphocytes that help B lymphocytes make the antibodies that help fight infection
3. Natural killer cells that attack cancer cells and viruses

People with CML produce too many granulocytes which is why CML used to be referred to as chronic granulocytic leukaemia (CGL). In the early stages of the disease, too many mature granulocytes are produced. If left untreated, more immature cells (so-called blast cells) are

produced and populate the blood and bone marrow. Over time, these abnormal cells will accumulate and begin to fill up the bone marrow, preventing it from producing healthy blood cells. The granulocytes may be immature, poorly functioning and not fully developed.

Stages of CML

CML typically has three stages – chronic, accelerated and blast phase.

1. **Chronic phase** - Many patients are diagnosed in this stage and it is when your body produces too many mature white blood cells called granulocytes. This is when you may start to notice some symptoms, such as weight loss, sweats and abdominal swelling from an enlarged spleen.
2. **Accelerated phase** - If left untreated, CML will progress to the accelerated phase, where the number of leukaemic cells increases. Symptoms will be more noticeable, and you may experience increased fatigue and further weight loss.
3. **Blast phase** - In the blast phase, immature white blood cells (blasts) appear and develop quicker than normal. These impair the normal functioning of the bone marrow. Additional symptoms can include spontaneous bruising and bone pain.

The Philadelphia chromosome

In almost all cases, CML cells have an identifiable abnormality called the 'Philadelphia chromosome'. This is something that has developed in your bone marrow by chance. You cannot inherit this chromosome or pass it onto your children.

There are 23 pairs of chromosomes in each cell in your body. All of the chromosomes in the body are made up of a protein called DNA, which is arranged in sections called genes.

What is CML? (cont.)

The Philadelphia chromosome is formed when the ABL gene on chromosome 9 and the BCR gene on chromosome 22 swap part of their DNA. The swap-over, so-called translocation, forms an abnormal 'fusion' gene called BCR-ABL. The BCR-ABL gene produces a new enzyme called a tyrosine kinase, which means the body's normal signals to the bone marrow to stop producing white blood cells are ignored by the bone marrow, leading to the production of too many white blood cells.

Only about 1 in 20 CML patients do not have the BCR-ABL gene – this is called atypical CML and is a different condition. The information in this booklet is about CML with the BCR-ABL gene present. If you have atypical CML, then your specialist will explain what this means and discuss treatment options with you.

Almost all patients who are diagnosed with CML will be treated with a type of drug called a tyrosine kinase inhibitor (TKI). These drugs block the harmful effect of BCR-ABL and stop CML from progressing. You can find out more about treatments further on in the booklet.

How common is CML?

Approximately 750 people are diagnosed with CML every year in the UK and CML makes up about 15 out of every 100 cases of leukaemia. CML can develop at any age, but it is very rare in children and very uncommon in young adults. The average age at diagnosis is between 60 and 65 years. CML is slightly more common in men than in women.

What causes CML?

In most cases, there is no obvious cause for CML but there are certain things that are known to be linked to a higher chance of developing CML:

- Exposure to radiation – This is the only clearly established risk factor.
- Smoking – This is not a definite risk factor, but some studies suggest a weak link.

Studies have shown no increased risk of CML in relatives of patients, so it is not hereditary and cannot

be passed onto your children.

Some patients blame themselves, or someone else, for their diagnosis. However, it is very important to remember that it is not likely that anything you have done, or not done, has caused your CML.

Our booklet on the emotional impact provides some tips on dealing with feelings of guilt and blame if you are struggling to come to terms with your diagnosis. To request your copy, visit **www.leukaemiacare.org.uk** or call us on **08088 010 444**.

Symptoms and diagnosis

Before we discuss the symptoms of CML, it is important to understand how CML affects the body compared to someone who does not have CML.

In someone without CML, bone marrow (the soft, fatty tissue inside your bones) contains blood stem cells that in time develop into mature blood cells – red blood cells, white blood cells, or platelets.

Production of new blood cells is very closely controlled to balance the loss of worn-out cells or cells lost by bleeding or damage. The healthy number of different types of blood cells varies between people but is usually kept within fairly narrow limits by tight regulation.

In someone with CML, abnormal white blood cells build up and can eventually 'take over' the bone marrow; the result is that the marrow is not able to make enough normal blood cells. The spleen may become very large due to the abnormal cells collecting there and this may cause discomfort or even pain; the spleen usually returns to its normal size with treatment.

In CML, the blood usually contains high numbers of immature white blood cells. You may also have low numbers of red blood cells, too, as that part of the bone marrow factory becomes under stress, and the platelet count can be low, normal or high.

What are the most common symptoms of CML?

Many patients with CML have no symptoms at the time when they are diagnosed. Typically, these patients are identified following abnormal results from a routine full blood test for something else.

Not everyone will get all of the symptoms and some symptoms may appear within different phases of the disease.

Many patients are diagnosed in the chronic phase and stay there. Others are diagnosed at more advanced, aggressive stages of the disease when symptoms may be similar or even worse.

Symptoms in the chronic phase are quite vague or non-specific and can often be caused by other things, not just CML. They can

include:

- Fatigue (may be caused by anaemia, which is a reduction in the number of red blood cells)
- Unexplained weight loss
- Night sweats
- Bloating or discomfort of the abdomen due to an enlarged spleen which can lead to feelings of fullness after eating
- Unusual bleeding e.g. from gums
- Frequent bruising
- Infections
- Bone pain

"I had recently started a new job which involved a longer commute and I was experiencing some pains in my back. I was also having night sweats and had lost a little weight."

Symptoms in the accelerated phase are not much different from the chronic phase, but you may experience more bone pain, caused by more leukaemia cells building up in the bone marrow and more profound symptoms.

The blast phase is when the leukaemia has become more aggressive and patients in this phase may experience much more noticeable and extreme symptoms. It is actually quite rare for people to be diagnosed at this stage, and it is equally rare, with current treatments and current monitoring, for patients to progress to the blast phase from the chronic phase, although it will happen to some.

Diagnosis of CML

If CML is suspected, you will have tests to confirm the diagnosis. If you are diagnosed with CML, you will have further tests to determine the right treatment for your bone marrow disorder. Tests to confirm the diagnosis of CML may include:

1. **Full Blood Count (FBC)** – This is a simple blood test that measures the number of red cells, white cells and platelets in the blood. In CML, you will have more white cells than normal, and your platelets may be higher too.
2. **Cytogenetics** – Cytogenetics is the study of chromosome changes and investigates the

Symptoms and diagnosis (cont.)

differences between CML cells and normal cells. This blood test is important because it identifies the Philadelphia chromosome and confirms a CML diagnosis, like the PCR test.

3. **Polymerase chain reaction (PCR) test** – The PCR test is an important test in the diagnosis of CML that measures the amount of BCR-ABL in the blood. The PCR test will be done throughout your treatment to monitor your response and to find out whether treatment needs to be changed. It is performed by doing a regular blood test.

4. **Bone marrow samples** – Some patients will have a small amount of bone marrow taken from the hip bone using a fine needle (an aspirate), to look at the cells. You may also have a sample of bone marrow using a larger needle (a trephine) to look at the structure of the bone marrow. This is often performed under local anaesthetic.

Many of these tests will be repeated throughout your treatment to check your response and any complications, while some may only be done at diagnosis.

If you want to know more about your tests and their results, you can ask your doctor or your specialist nurse.

"When I was diagnosed, it was like I had been hit by a truck. I had been so well, in fact I had felt better than I had in a long time. I had no symptoms at all, except for some night flushing, which I had put up with for ages as I thought it was the menopause. To be told, instead, that I had leukaemia was like I had been handed a death sentence overnight and from nowhere. The shock was phenomenal. But six months in I am living a new kind of normal and I am no longer scared. I believe I'm going to be okay!"

Staging and classification of CML

Following a diagnosis of CML, your doctor will do some tests to stage your cancer which will help them to determine the best

treatment option. Your doctor will want to find out if your CML is in either the chronic, accelerated or blast phase (or blast crisis). The stage of your CML will also be able to better predict your prognosis (outlook).

Most patients are diagnosed at the chronic phase and, with the revolutionary treatments available now, a very high proportion of patients do not progress beyond that phase and their CML does not affect their overall life expectancy. A small number of patients are at accelerated or blast phase CML when they are diagnosed. The phase is defined on the basis of signs and symptoms and on the results of blood and bone marrow tests.

There are three risk score systems used in classifying CML called the Sokal, Hasford and EUTOS systems. These look at your age, size of your spleen and your blood count. Risk scores are much less important with modern treatments as most patients will have a good response to treatment, regardless of risk score.

What happens next?

As with all cancers, the treatment of choice for CML will depend on your general health, your age, level of fitness and the CML phase.

Almost all patients with CML start treatment soon after diagnosis. The main exceptions would be very elderly or frail patients who may be too unfit to tolerate treatment.

You can refuse treatment at any time, but it is important that you clearly understand what might happen in this case. However, you cannot start treatment if your haematologist does not think you need to, but this is rare in CML. If you do not agree with them, you can ask for a second opinion at any time. As far as possible, all decisions about treatment will take your wishes into account.

Treating CML

CML is not a conventionally curable disease. However, a class of drugs called tyrosine kinase inhibitors (TKI) has transformed the treatment of CML to achieve an 'operational cure'. Many patients will have a normal life span with a good quality of life. Without treatment, CML is fatal.

A stem cell transplant remains a cure for the disease in a small number of patients. However, with TKIs having a good success rate, bone marrow or stem cell transplants to treat CML are fairly rare.

You can find more information about the drugs used to treat your CML (and any other medicines you are taking) at the eMC Medicine Guides website **www.medicines.org.uk/guides**

Treatment options for CML

Once your diagnosis is confirmed, you will be given the chance to discuss treatment options and detailed information on your treatment plan before it starts. The side effects of treatment vary between different types of treatment and different patients.

The aim of treatment for CML is to:

- Reduce the amount of leukaemia in the blood to a level where it causes fewer symptoms
- Achieve normal levels of blood cells
- Reduce the risk of it progressing to a more aggressive form

The three main ways in which CML is treated are:

1. **Targeted therapy** – Treatments that target the abnormal protein (tyrosine kinase) produced by the BCR-ABL gene. Targeted therapy using tyrosine kinase inhibitors (TKIs) is the usual first choice of treatment for CML.

2. **Chemotherapy** – The use of anti-cancer (cytotoxic) drugs to destroy or damage leukaemia cells. Chemotherapy is most likely to be used if the TKIs are not effective or they cause severe side effects. The chemotherapy drug most frequently used is called hydroxycarbamide and comes in a tablet form, and is often used first to reduce the very high number of leukaemic cells in the blood. Intravenous chemotherapy is not currently widely used in treatment of CML in the chronic phase and is usually reserved for blast phase patients.

3. **Stem cell transplant** – A stem cell transplant involves the use of high dose chemotherapy and/or total body irradiation to kill as many leukaemia cells as possible followed by an infusion of stem cells, from a donor who is well matched to you, to take their place. This option is only suitable for a small number of CML patients who are fit enough and have a very well-matched donor. Stem cell transplants are rarely performed for CML patients and normally only done if a patient has not responded to TKIs or is in the blast phase.

If a stem cell transplant is an option for you, then your haematologist will discuss it with you and give you a chance to ask questions. This is generally considered the only potential cure for CML, but for most patients, the risk of a transplant may be greater than the benefit. This is especially true given the very good results of treatment with TKIs.

Targeted therapy

Targeted therapy using tyrosine kinase inhibitors (TKIs) is now the most widely used treatment for CML. This treatment has transformed the outlook for CML patients. Before TKIs were introduced, the average survival after diagnosis was about seven years. Now, it is expected that many, probably most, CML patients will have a good quality of life and a normal or near-normal life expectancy. All of the currently available TKIs are taken by mouth (orally), which most patients prefer to any type of injection.

Treating CML (cont.)

There are five TKIs licensed for use in the UK, and are all NICE approved:

- First generation (first developed) - imatinib (Glivec™)
- Second generation - nilotinib (Tasigna™), dasatinib (Sprycel™) and bosutinib (Bosulif™)
- Third generation - ponatinib (Iclusig™)

The decision about which TKI is suitable depends on the effectiveness of the drug in certain situations, likely side effects and personal preference on how the drug is taken. You should discuss this with your specialist when considering your treatment options.

Imatinib is called a first generation TKI because it was the first BCR-ABL TKI to be used in the treatment of CML. It is taken orally, once a day, after eating. Although imatinib works well for most patients, and is still the most popular first choice, some patients either do not have good response or their response does not last. Others cannot tolerate the side effects. For these reasons, similar drugs were developed, which are referred to as either second or third generation TKIs.

Two of the second generation TKIs, nilotinib and dasatinib, are licensed for use in the UK for treatment of newly diagnosed CML and for patients that have tried another TKI that either was not tolerated or did not work. Bosutinib has been licensed in the UK for patients previously treated with one or more of the other TKIs and for whom imatinib, nilotinib and dasatinib are not considered appropriate treatment options.

Ponatinib is currently used in England, Scotland, Wales and Northern Ireland for the treatment of the T315i mutation (a change) in the BCR-ABL gene. In addition to this, it is also available as an additional treatment option for patients who are resistant or intolerant to nilotinib and dasatinib and for whom subsequent treatment with imatinib is not clinically appropriate.

The main reasons that the older drug, imatinib, remains the most

popular for initial treatment are the extensive experience in using it and the fact that in more than 14 years of use, no severe or unexpected side effects have been seen.

Fortunately, it is usually clear within three to six months of starting treatment if a TKI is going to be successful and, if not, patients can switch to another TKI which is usually effective. The choice of which of the three second generation TKIs to use is based on testing for changes (mutations) in the BCR-ABL protein and on the known side effects of the different drugs. Certain mutations are known to respond better to some drugs than others and, if a patient has been troubled by side effects, it is possible to choose another TKI that is unlikely to cause the same side effects.

There is evidence that some patients may be able to stop taking TKIs, or at least reduce the amount of TKI they are taking, without their CML returning. Patients who do stop treatment under medical advice and whose CML does return, usually respond well to re-treatment. At present there is not enough evidence to know which patients can safely stop treatment and you should never stop or reduce your treatment unless your doctor has advised it. Sticking to your therapy is essential for the best response and also to prevent you losing your response. Your doctor may discuss stopping your TKI if it is appropriate for you.

The CML Advocates Network has designed a mobile app, available on iPhone and Android devices, called CML Today. It has been designed for CML patients to help you track the regular intake of your medicine, remind you to take your medication and facilitate contact with other organisations.

Treating CML (cont.)

Side effects of TKIs

All treatments can cause side effects; however, because TKIs are much more targeted, unlike other cancer treatments such as chemotherapy, the side effects are much less severe.

You may notice some side effects that may be connected to the TKI you are taking. Some side effects are common to all TKIs, others are more specific to a particular type.

"Some of the side effects weren't nice; upset stomach, bone pains and tiredness. But as this drug was going to keep me alive, I was going to stick with it."

Remember to mention any side effects you are experiencing to your healthcare team as they will be able to help manage them.

Imatinib

- Side effects (for more than half of all patients) include: fatigue, headaches, diarrhoea, nausea and vomiting, odema (fluid retention), adnormal liver function.
- Less common side effects (more than one in ten patients) include: muscle and joint pain, anaemia, neutropenia, low platelets.

Dasatinib

- Side effects include: headaches, muscle and joint pain, diarrhoea, odema, pleural effusion (fluid around the lungs).
- Less common side effects: anaemia, neutropenia, low platelets.

Nilotinib

- Side effects include: fatigue, headaches, bone pain, nausea and vomiting, raised glucose levels, neutropenia.
- Less common side effects: abnormal liver function.

Bosutinib

- Side effects include: headaches, nausea and vomiting, abdominal pain, neutropenia, low platelets.
- Less common side effects include: diarrhoea, abnormal liver function, anaemia.

Ponatinib

- Side effects include: fatigue, headaches, muscle and joint pain, nausea and vomiting, abdominal pain, blocked arteries, high blood pressure, low platelets, abnormal liver function, neutropenia.

Food and drug interactions

There are a variety of foods that have the potential to affect the absorption of the CML drug and/or its levels in the blood, as indicated by the National CML Society:

- Citrus fruits: Citrus fruits, particularly grapefruit and Seville oranges, can increase drug levels in the blood. This can result in too much of the drug circulating in your system and more side effects. TKIs are particularly susceptible to the effects from citrus fruits especially grapefruit, so do not drink or eat grapefruit while you are taking these drugs.
- Pomegranate and star fruit: These also interact with TKIs and should be avoided.
- Lactose intolerance: If you are lactose intolerant, dasatinib and nilotinib contain lactose and you should therefore discuss this with your doctor before taking the drugs.
- Herbs and botanicals: As some herbal products, such as St John's wort, black cohosh, ginseng and ginko biloba, can increase the concentration of TKIs in the blood, you should discuss using them with your doctor.
- Garlic can interact with TKIs, so it is advised that you should refrain from using it.
- Teas, such as green tea, peppermint and chamomile teas, may interact with TKIs and should be discussed with your doctor.
- Liquorice can also affect the concentration of a drug in your blood and should be discussed with your doctor.

Nilotinib should be taken on an empty stomach with a large glass of water, so fasting is important.

Treating CML (cont.)

You should not eat for two hours before or for one hour after taking nilotinib, as this affects the absorption rate of the drug and may increase the side effects.

Response to treatment

It is really important that you attend appointments with your consultant as they will be measuring your response to your treatment. When you first start treatment with a TKI you will have regular blood tests to make sure that the CML is improving fast enough. Once you are settled on the treatment, you only need to have your blood monitored every three to six months. If the CML gets worse then you may need to change to another one of the TKIs. The important thing to remember is that the majority of people respond well to the first TKI and never need it changed.

The response of CML to treatment is usually measured with blood tests but occasionally requires bone marrow tests if the blood tests are difficult to interpret. There is no reason to have routine bone marrow monitoring.

There are three different types of response that can be measured:

Complete haematological response (CHR)

- This means that the blood count has become normal.
- If treatment is stopped, it is likely the white cell count would increase and the CML will soon return.
- This is usually the first improvement that is seen during treatment and the easiest to measure as it only requires a full blood count.

Cytogenetic response

- This involves a test to measure the number of cells that contain the Philadelphia chromosome.
- Fewer than 35% of cells with the Philadelphia chromosome is called a partial cytogenetic response (PCyR). Ideally this should happen by three months of treatment.
- No Philadelphia chromosome detected is a complete cytogenetic response (CCyR), ideally this should happen by six months of treatment.

Molecular response

- The next aim of treatment after a cytogenetic response is to see the levels of the BCR-ABL gene fall even further. This requires a polymerase chain reaction (PCR) test, which is a very sensitive test that is able to detect one leukaemia cell in up to one million normal blood cells. This test measures the percentage of cells in the blood which are abnormal due to CML.
- Major molecular response is where less than 0.1% on a standardised scale, called the International Scale of the quantification of the BCR-ABL protein, is detected. This is currently the aim of treatment; ideally, this should be achieved by 12 months.
- Complete molecular response is where no BCR-ABL is detectable in the PCR test.

A log reduction score has been developed to determine how far the level of CML has fallen since the start of treatment from a standardised baseline value of 100%. Log reduction is a mathematical term used to show the relative number of cells reduced 'on' something. When the term log reduction is used in CML, it refers to the reduction in the amount of BCR-ABL detected by a PCR test.

A 1-log reduction means the number of CML cells is 10 times smaller (since start of treatment); a 2-log reduction means the number of CML cells is 100 times smaller and a 3-log reduction means the number of CML cells is 1000 times smaller.

This will hopefully make it easier to compare results between different laboratories.

Treating CML (cont.)

Log reduction	Percentage of white cells due to CML	Response to treatment
0	100%	At start of treatment
1	10%	Optimal if achieved by 3 months Warning if achieved between 3 to 6 months Failure if not achieved by 6 months
2	1% (CCyR)	Optimal if achieved by six months Warning if achieved between 6 to 12 months Failure if not achieved by 12 months
3	0.1% (MMR)	Optimal if achieved by 12 months Warning if achieved >12 months
4	0.01%	
5	0.001%	

The response to treatment is defined as 'Optimal' when no change to treatment is required, 'Warning' where close monitoring is required, but no change of treatment is required, and 'Failure' where a different TKI or treatment should be considered.

If the numbers of CML cells starts to rise, then it is described as 'loss of response'.

New treatments and treatments on the horizon

The main options being considered for new approaches to CML involve new ways of using older drugs:

- Interferon alpha (Interferon)
- Re-use of older drugs
- Novel therapies
- Different sequencing of these drugs

Interferon alpha

Interferons are proteins that occur naturally in our bodies and help us fight infection. Interferon alpha was one drug used for CML before TKIs were developed. The

main disadvantages of interferon alpha were that it was given as an injection under the skin and came with unpleasant side effects. One key use of interferon alpha is in women who have CML and are in the second and third trimesters of pregnancy (there is evidence that TKIs can cause harm to the developing baby if given to a pregnant woman in the first trimester).

Re-use of older drugs

A number of drugs, which were used to treat CML before the introduction of TKIs, may offer benefit in treating patients who do not respond to TKI treatment, or who have problems with the side effects of TKIs.

At present it is not clear which, if any, of these drugs will enter routine use for treatment of CML. If any are re-introduced, they are likely to be used only for selected patients. The response to TKI treatment is so good that it is very unlikely these will ever be replaced in treatment of CML.

Novel therapies

Newer TKIs have been developed and other targeted therapies are being proposed.

One of the future treatments for CML includes ABL001 (asciminib). For more information on this, read our Chronic Myeloid Leukaemia - TKIs and TFR booklet. You can find this on our website at **www.leukaemiacare.org.uk**

Living with CML

After a diagnosis of CML, you may find that it affects you both physically and emotionally. This chapter will talk about both of these aspects.

Emotional impact of CML

Being told you have cancer can be very upsetting. Although the outlook for many CML patients is a positive one, it is a blood cancer and a rare condition, and, because of this, you may need emotional, as well as practical, support. Being diagnosed with a rare disease can affect the whole of you, not just your body, and can impact you emotionally at any point of your journey. It is likely that you will experience a range of complex thoughts and emotions, some of which may feel strange or unfamiliar to you. It is important to know that these feelings are all valid and a normal response to your illness.

"There was a total overwhelming feeling of helplessness and being out of control of my normal everyday life. But I had to carry on regardless for everyone else."

It is important to remember that, with current treatments, you can expect a good response and live a long, normal life.

Our booklet on the emotional impact provides lots of useful information that could help you cope. To request your copy, call **08088 010 444** or download it through the website.

"Having CML can be a rollercoaster. Sometimes it doesn't feel like I've got cancer at all then a side effect or symptom comes along to really remind me. I am very lucky to have a good prognosis and quality of life. Coping with the mental side is perhaps the hardest as, two years after diagnosis, it is still okay to be coming to terms with it."

Looking after you

You can live a long and normal life with CML, but you may want to make changes to your lifestyle to try to stay as well as possible

after your diagnosis and during treatment. Do not try to change too much at once. Adopting a healthy way of living is about making small, manageable changes to your lifestyle.

A healthy lifestyle includes having a well-balanced diet and being physically active. With some of the side effects you may be experiencing, the idea of getting out and being active may be the last thing you want to do, but it is important to try and stay as active as possible to make you feel better and reduce some of the symptoms or side effects you may be experiencing.

One of the most commonly reported side effects of the treatment of CML is fatigue. This is not normal tiredness and does not improve with sleep.

Some general tips on how to deal with fatigue include:

- Have a regular lifestyle – try going to bed and waking up approximately the same time every day and try to avoid lying in.
- Take part in regular, gentle exercise to maintain your fitness levels as much as possible.
- Reserve your energy for what you find important and build rest periods around those times.
- Before going to bed, avoid stimulants such as alcohol, coffee, tea or chocolate, or using laptops, tablets or mobile phones.
- Keep your bedroom quiet and at a comfortable temperature.
- Talk about your worries with family, friends or your doctor or nurse, or patient support groups.
- Discuss your fatigue with your doctor or nurse.

"Don't get me wrong, it's hard living with a chronic condition. I get tired a lot and have to be careful of picking up infections, as my immune system is lower than others. But all in all, I will not let it take over my life. I don't intend on fighting it; it will have to fight me."

Living with CML (cont.)

Practical support

Work and finances

Being diagnosed with CML can sometimes lead to difficulties relating to your work life. Your diagnosis may lead to temporary sick leave or a reduction in working hours, but it can also mean that you have to stop work altogether. You may need to make an arrangement with your employer for times when you may need to go into hospital or for those times when you may not be well enough to go into work.

Your consultant or your GP can arrange letters to confirm your diagnosis and the effects it may have on your work life to your employer. It is often worth taking time to explain CML to your employer, as it is likely they will never have heard of the disease.

It is important for you to know that people with any form of cancer are covered by law by the Equality Act. This means that legally your employer cannot discriminate against you and must make reasonable arrangements and adjustments relating to your disease.

Macmillan has published a booklet about financial support following a diagnosis of cancer. They can also give you personal advice over the phone via their helpline and you can discuss the benefits for which you are eligible. Some Macmillan centres can arrange face-to-face meetings with a benefits advisor. They can also provide financial assistance in the form of grants – ask your nurse in the hospital how to apply.

As CML is a cancer, you will also be entitled to apply for a medical exemption certificate which means that you are entitled to free NHS prescriptions. Your GP or specialist nurse at the hospital can provide you with the details on how to apply.

If you would like more information, email our Advocacy Caseworker at **advocacy@leukaemiacare.org.uk** or call **08088 010 444**.

Talking about CML

Talking to your haematologist

CML is a rare condition. It is important for you to develop a good working relationship with your haematologist, so you are given the best treatment possible for you.

The following gives advice on working well with your haematologist:

- If it is an initial consultation, take along a list of your current medications and doses, and a list of any allergies you may have.
- If you have a complicated medical history, take a list of diagnoses, previous procedures and/or complications.
- Make a list of questions to take to each appointment. This will help the discussion with your haematologist.
- It can be useful to repeat back what you have heard so that you can be sure that you fully understood.
- Note information down to help you remember what was said.
- Be open when you discuss your symptoms and how you are coping. Good patient-doctor communication tends to improve outcomes for patients.

Other tips:

- Bring someone along to your appointment. They can provide support, ask questions and take notes.
- Do not be afraid to ask for a second opinion – most haematologists are happy for you to ask.

You need to tell your haematologist if...

You are having any medical treatment or taking any products such as prescribed medicines, over the counter treatments or vitamins. It is important to understand that treatments, including complementary therapies, which are perfectly safe for most people, may not be safe if you are being treated for CML. Remember, if you choose to start any form of

complementary therapy outside of your medical treatment, consult your haematology consultant or clinical nurse specialist, prior to beginning it. It is important to understand the difference between complementary therapies, used alongside standard treatment, and alternative therapies, used instead of standard treatment. There is no evidence that any form of alternative therapy can treat CML.

For help with talking to your haematologist, you can find out more information about CML at **https://www.leukaemiacare.org.uk/support-and-information/information-about-blood-cancer/blood-cancer-information/leukaemia/chronic-myeloid-leukaemia/** which features a list of questions that you may want to ask your medical team or doctor.

Talking to other people

Telling people you have a rare condition like CML can be hard to explain. You might find it useful to let your close family and friends, as well as your employer, know about your health condition. It might be easier to provide people with basic information and give them information leaflets or a booklet like this one about CML if they want to know more in-depth details.

"I made a conscious decision to be very open about my illness. Telling family was tough. But I encouraged people to ask questions."

It is probably best to focus conversations on the symptoms that you are experiencing, how the condition affects you and how you feel about it. Often people misunderstand and, unfortunately, it will mostly fall to you to educate them as best as you can.

Where possible, it is advisable to let people know what you find helpful and unhelpful, in terms of what others say and do. Often people make assumptions and do what they think helps. For example, saying you look well, recounting stories of others they know with a similar diagnosis and encouraging you to look

Talking about CML (cont.)

ahead and stay positive is not always what people really want to hear. In many ways, the more you communicate with them, the better.

These points may help you:

- Explain that you have a condition that means your bone marrow does not function properly, and this affects the number of blood cells it produces
- Explain your symptoms (maybe you are tired, or have a lot of pain)
- Explain what you need (maybe more help day-to-day, or someone to talk to)

You could also consider the following when telling people about your diagnosis:

- **Find out more** - Try to find out as much as you can about your condition, from reliable internet sources, charitable organisations or your consultant haematologist. The more you know, the more you can share.
- **Have a print-out to hand** - It may help to have a factsheet to hand to share with family and friends. This will take the pressure off you having to remember everything they may want to know.
- **Explain your needs** - Try and be clear about what your needs may be. Perhaps you need help with the weekly food shop, help with cooking dinner, or someone to drive you to and from appointments. You may find that friends and family are pleased that they can do something to help you.
- **Be open about how you feel** - Do not be afraid of opening up about how you feel, as people who care will want to help you as best they can. Talk as and when you feel comfortable, so those around you will know when you need them most.

Glossary

Anaemia

A medical condition in which the red blood cell count or haemoglobin is less than normal.

Bone marrow

The soft blood-forming tissue that fills the cavities of bones and contains fat, immature and mature blood cells, including white blood cells, red blood cells, and platelets.

Central line

A tube which is inserted into a large blood vessel either in the chest or arm so blood samples can be taken easily and drugs can be given without the use of needles.

Chemotherapy

A form of cancer treatment that uses one or more anticancer drugs as part of a standardised chemotherapy regime.

Chronic

A human health condition or disease that is persistent or otherwise long-lasting in its effects. The term chronic is usually applied when the course of the disease lasts for more than three months.

Chronic Leukaemia

A type of blood cancer that affects the white blood cells. This tends to progress over many years.

Chronic Myeloid Leukaemia (CML)

A cancer that affects the blood and bone marrow defined by the presence of BCR-ABL translocation.

Clinical trial

A medical research study involving patients with the aim of improving treatments and their side effects. You will always be informed if your treatment is part of a trial.

Fatigue

Extreme tiredness, which is not alleviated by sleep or rest. Fatigue can be acute and come on suddenly, or chronic and persist.

Full blood count or FBC

A blood test that counts the number of different blood cells.

Leukaemia

A cancer of the blood with many

different subtypes. Some forms are acute (develop quickly) and others are chronic (develop slowly). Leukaemia is the result of an excess number of abnormal cells in the blood, usually white blood cells, which stop the bone marrow working properly.

Monoclonal Antibodies

Antibodies that are made by indentical immune cells that are all clones of a unique parent cell. They therefore all bind to the same epitope (the part of an antigen that is recognised by the antibody).

Neutropenia

Low levels of neutrophils (a type of white blood cell) in the blood, leading to increased susceptibility to infection.

Pancytopenia

Deficiency of red cells, white cells, and platelets in the blood.

Philadelphia Chromosome

The Philadelphia chromosome or Philadelphia translocation is a specific genetic abnormality in which a part of chromosome 22 and chromosome 9 are switched. This is found in leukaemia cancer cells (particularly in patients with chronic myeloid leukaemia and acute lymphoblastic leukaemia).

Platelet

A disc-shaped blood cell that assists in blood clotting. During normal blood clotting, the platelets clump together (aggregate).

Relapse

The return of a disease or the signs and symptoms of a disease after a period of improvement.

Spleen

An organ that filters the blood. It removes old blood cells and helps to fight infection. It sits under the ribs on the left of the body.

Stem cells

Cells that have the potential to develop into many different or specialised cell types.

Stem Cell Transplant (SCT)

A stem cell transplant is a treatment for some types of cancer as well as other blood diseases and disorders of the immune system. A stem

Glossary (cont.)

cell transplant involves the administration of chemotherapy plus or minus radiotherapy as conditioning followed by infusion of stem cells. The stem cells then engraft and form a new immune system.

Thrombocytopenia

Deficiency of platelets in the blood.

Tyrosine Kinase

A protein or enzyme which controls cellular functions, switching them on and off. The BCR-ABL protein is an example of a tyrosine kinase.

Tyrosine Kinase Inhibitor (TKI)

A drug which blocks the action of a tyrosine kinase (a particular type of enzyme in the cell). In CML it works mainly by blocking the activity of the BCR/ABL protein.

White blood cell

One of the cells the body makes to help fight infections. There are several types of white blood cells. The two most common types are the lymphocytes and neutrophils.

Tell us what you think!

If you would like to give us some feedback about this patient information booklet, please hover over the code to the right using your phone or tablet's camera. Click the link as it appears and this will take you to a short web form to fill in.

Suitable for Android, iPhone 7 and above.

Useful contacts and further support

There are a number of helpful sources to support you during your diagnosis, treatment and beyond, including:

- Your haematologist and healthcare team
- Your family and friends
- Your psychologist (ask your haematologist or CNS for a referral)
- Reliable online sources, such as Leukaemia Care
- Charitable organisations

There are a number of organisations, including ourselves, who provide expert advice and information.

Leukaemia Care

We are a charity dedicated to supporting anyone affected by the diagnosis of any blood cancer. We provide emotional support through a range of support services including a helpline, patient and carer conferences, support group, informative website, one-to-one buddy service and high-quality patient information. We also have a nurse on our help line for any medical queries relating to your diagnosis.

Helpline: **08088 010 444**
www.leukaemiacare.org.uk
support@leukaemiacare.org.uk

Bloodwise

Bloodwise is the leading charity into the research of blood cancers. They offer support to patients, their family and friends through patient services.

020 7504 2200
www.bloodwise.org.uk

Cancer Research UK

Cancer Research UK is a leading charity dedicated to cancer research.

0808 800 4040
www.cancerresearchuk.org

Macmillan

Macmillan provides free practical, medical and financial support for people facing cancer.

0808 808 0000
www.macmillan.org.uk

Maggie's Centres

Maggie's offers free practical, emotional and social support to people with cancer and their families and friends.

0300 123 1801
www.maggiescentres.org

Citizens Advice Bureau (CAB)

Offers advice on benefits and financial assistance.

08444 111 444
www.adviceguide.org.uk

Leukaemia Care is a national charity dedicated to providing information, advice and support to anyone affected by a blood cancer.

Around 34,000 new cases of blood cancer are diagnosed in the UK each year. We are here to support you, whether you're a patient, carer or family member.

Want to talk?

Helpline: **08088 010 444**
(free from landlines and all major mobile networks)

Office Line: **01905 755977**

www.leukaemiacare.org.uk

support@leukaemiacare.org.uk

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One Birch Court,
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Registered charity
259483 and SC039207

Leukaemia Care
YOUR Blood Cancer Charity

Health & care information you can trust
The Information Standard Certified Member