
Second- and later- line treatments for Chronic Myeloid Leukaemia (CML)

A Guide for
Patients

Leukaemia Care
YOUR Blood Cancer Charity

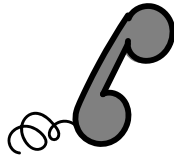
About Leukaemia Care

Leukaemia Care is the UK's leading leukaemia charity. For over 50 years, we have been dedicated to ensuring that everyone affected receives the best possible diagnosis, information, advice, treatment and support.

Our services

Helpline

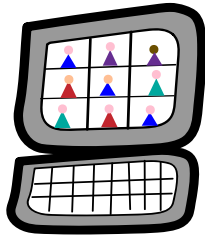
Our helpline is available 9am to 5pm Monday to Friday. If you need someone to talk to, call **08088 010 444**.



Alternatively, you can send a message via WhatsApp on **07500 068065** on weekdays 9am to 5pm.

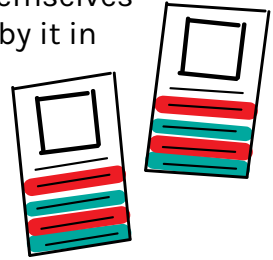
Support groups

Our nationwide support groups are a chance to meet and talk to other people who have been affected by a CML diagnosis. For more information, go to bit.ly/FindMeASupportGroup



Buddy support

We offer one-to-one phone support with volunteers who have had CML 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@leukaemicare.org.uk



Counselling service

Our counselling service helps CML patients and their loved ones access up to six sessions of counselling. To apply, go to bit.ly/LeukaemiaCounsellingFund



Advocacy and welfare

Our advocacy and welfare officers are here to help you find the support you need for many issues surrounding a CML diagnosis. These include insurance, benefits and clinical trials. If you would like support from our advocacy or welfare officer, email advocacy@leukaemiacare.org.uk or call **08088 010 444**.



Cost of living fund

This fund provides grants to patients and families affected by CML, to help with essential living costs. All applications must be made via the form which can be found at bit.ly/CostOfLivingFundLC

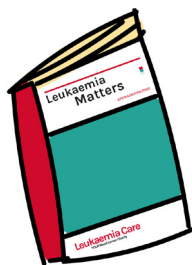


Write a free will

Using our complimentary service, you can write a simple will so you know what happens to your estate when you die. To start writing your free will today, go to bit.ly/AccessAFreeWill

Patient magazine

Our magazine includes inspirational patient and carer stories as well as informative articles by medical professionals. To subscribe to our magazine, go to bit.ly/KeepInTouchwithLC



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There is a lot of information about cancer on the internet. Some of it may not be reliable or up-to-date, and much of it will not be applicable to you. Your haematology team is best placed to give you information that is specific to you because they know your individual circumstances. If you want to search for information yourself, look for reputable organisations like the NHS or national charities. Look for a quality mark, such as the Patient Information Forum (PIF) tick.

Introduction

Chronic myeloid leukaemia (CML) is a type of blood cancer that involves the white blood cells. It develops slowly over many years.

In this booklet, we cover treatment options if your first treatment was not successful or did not suit you. This is called second-line treatment. We explain why you might need second-line treatment, when this might happen, and what options your haematology team might suggest.

This booklet is only a guide of what you might experience. Your haematology team will give you a copy of your specific treatment plan.

This booklet was reviewed by a consultant haematologist and patient reviewers, Abir, Colin and Lesley. We thank them all for their valuable contribution.

Throughout this booklet, you will see URLs that link to webpages for further support. If you are not able to access the webpages, please email information@leukaemiacare.org.uk.

Second-line and later-line treatments for CML

Summary



- First-line treatment for CML is usually a type of targeted treatment called a TKI. If first-line treatment for your CML is not successful, your haematology team will suggest a different treatment option. This is called second-line treatment.
- If your second-line treatment is not successful, the next treatment you have is called third-line treatment, and so on.
- Your team may suggest changing to a second-line treatment if:
 - Your CML did not respond to your first treatment
 - Your CML responded to the treatment at first but then stopped responding
 - You had side effects that were difficult to manage
- If your CML does not respond or stops responding to treatment, you may have symptoms similar to when you were first diagnosed. Or you may not have any symptoms and it could be picked up on blood tests.
- Second-line treatment for CML is usually a different TKI. TKIs all have slightly different ways of acting and different profiles.
- TKIs are suitable second- and third-line treatment options for most people. But if they are not suitable for you, other treatment options include a stem cell transplant or supportive care.

Second-line and later-line treatments for CML

If your first treatment for CML is not successful, your haematology team will suggest changing to a different one. This is called second-line treatment. If second-line treatment is not successful, your haematology team will try another. This is called third-line treatment, and so on.

Sometimes the term 'frontline' treatment is used instead of first-line treatment. In this booklet, we use the terms: first-, second- and later-line treatments.

Why you might need to change treatment

During treatment, your haematology team will monitor how well your CML is responding. Response means that your symptoms and test results are improving. Your team will also check how you are coping with treatment.

Your haematology team might suggest changing to a different treatment if:

- Your CML has not responded to your current treatment. This is sometimes called primary resistance. It might happen if your *BCR-ABL1* gene is not sensitive to the treatment you received.
- Your CML has come back after an initial response to treatment. This is sometimes called secondary resistance. It might happen if your *BCR-ABL1* gene changes, and becomes resistant to the treatment you have received.

- Your treatment is causing side effects that are difficult to manage, like fatigue, tummy problems, fever, rash or joint and muscle pain. This is sometimes called intolerance.

"I was placed on 400mg of imatinib, but it caused me bone pain, so after a couple of months with no improvement I was switched to 100mg of dasatinib which I stayed on for about 12 years. Ultimately, dasatinib caused me a lot of fatigue so I have recently started on asciminib. As CML patients we are very fortunate to have many treatment options available to us."

David, diagnosed with CML

When you might need to change treatment

If your CML does not respond or comes back during or after treatment, you may have symptoms similar to when you were first diagnosed. Or you may not have any symptoms and it could be picked up during your monitoring blood tests.

- Your haematology team will measure the numbers of red cells, white cells and platelets in your blood regularly.
- They will also check the level of *BCR-ABL1* gene in your blood every 3 months. This is called your 'molecular response'. It uses a very sensitive test called PCR. It can detect extremely low levels of leukaemia in your body.

Although you will be monitored throughout your treatment and afterwards, the most important time for monitoring your response is during the first year of treatment. This is when resistance is most common.

Levels of molecular response (MR)

MR1: Less than 1 in 10 white blood cells (10%) has the *BCR-ABL1* gene.



MR2: Less than 1 in 100 white blood cells (1%) has the *BCR-ABL1* gene.

MR3: Less than 1 in 1,000 white blood cells (0.1%) has the *BCR-ABL1* gene. This is sometimes called a **major molecular response (MMR)**.



MR4: Less than 1 in 10,000 white blood cells (0.01%) has the *BCR-ABL1* gene. This is sometimes called a **deep molecular response (DMR)**.

MR5: Less than 1 in 100,000 white blood cells (0.001%) has the *BCR-ABL1* gene. This is also called a **deep molecular response (DMR)**.



Your haematology team might consider changing your treatment:

- After 3 to 6 months if you have not reached MR1
- After 6 to 12 months if you have not reached MR2
- After 12 months or more if you have not reached MR3
- At any time if you reached MR3, but your *BCR-ABL1* level has started to go back up again

Response to treatment is different in every person with CML. Some people can have a slower response and may not necessarily reach MR3 after 12 months. Changing to second- or later-line treatment may allow you to reach a deeper response. It is important to discuss your *BCR-ABL1* results with your doctors.

If you reach and maintain MR3, MR4 or MR5, your haematology team are unlikely to change your treatment unless you get side effects that are hard to cope with.

Usual second-line or later-line treatment options

Around a third of people with CML do not respond to, or cannot tolerate, first-line treatment. If your CML treatment is not successful, your haematology team will suggest the next most suitable treatment for you based on:

- The reason your first-line or later-line treatment was not successful. They will do blood tests to check for any new gene changes that could affect your response to treatment. Some gene changes are more sensitive to one treatment than another.
- Whether your CML is in the blast phase or at high risk of progressing to the blast phase.
- Any other medical conditions you have. Some TKIs may not be suitable for people with heart conditions, diabetes or liver problems.
- Any side effects you've had with other treatments.

TKIs

Most people with CML have a type of targeted therapy called a TKI as first-line treatment. If this is not successful, the usual second-line treatment is a different TKI. If second-line TKI treatment is not successful, the usual next treatment is a third-line TKI.

TKIs all work in slightly different ways and have different side effects. Some are effective against particular gene changes. If one TKI is not suitable for you, a different TKI may be.

Second- and later-line TKIs include:

- Imatinib (if you did not have it as your first treatment)
- Dasatinib (if you did not have it as your first treatment)
- Nilotinib (if you did not have it as your first treatment)
- Bosutinib (if imatinib, dasatinib or nilotinib are not suitable)
- Ponatinib (if you have a change in your *BCR-ABL1* gene called *T315I*, or imatinib, dasatinib and nilotinib are not suitable)
- Asciminib (if you have had at least two previous TKIs and you do not have the *T315I* gene change)

We have separate information on each of these medicines. You can [order them in print](#) or [download them](#).

Other second-line or later-line treatment options

TKIs are effective for most people, but if they are not suitable for you, your haematology team will discuss other treatment options. This could include a stem cell transplant or supportive care.

Stem cell transplant

Your haematology team might recommend a stem cell transplant as your next treatment if:

- Treatment with at least two TKIs has been unsuccessful **OR**
- You are in the blast phase **OR**
- Your CML is at high risk of progressing to the blast phase

A stem cell transplant uses high-dose chemotherapy to kill the abnormal blood-forming stem cells in your bone marrow. These are replaced by healthy stem cells. For people with CML, these usually come from a matched donor. This is called an allogeneic stem cell transplant.

A stem cell transplant is very intensive and is only suitable for people who are fit enough to have it.

Your haematology team will let you know if a stem cell transplant is an option for you. They will discuss it with you and give you a chance to ask questions.

We have a booklet on [stem cell transplants](#). This explains what happens when you have a stem cell transplant, the benefits for people with CML and the side effects that can occur.

Supportive care

During your treatment and afterwards, you might also need medicine to prevent or treat symptoms or side effects. This is called supportive care. It does not treat your CML itself, but it helps you feel better.

Supportive care might include:

- Medicines called growth factors to help boost your blood counts
- Blood transfusions, although these can usually be avoided by having growth factors instead
- Anti-sickness medicines
- Anti-diarrhoeal medicines
- Medicines to prevent or treat infections

Supportive care is not only limited to the physical impact of your CML. It can also include:

- Psychological support
- Support with exercise or physiotherapy
- Social support
- Spiritual wellbeing

You should talk to your haematology team to find out what support they can offer you. Tell them if you have any symptoms or side effects that you are finding hard to cope with.

If all treatments are unsuccessful

Treatments for CML are usually very effective. Most people with CML can expect to live as long as people who do not have CML.

If your treatment does not work or stops working, your haematology team will talk to you about your options. They will usually suggest trying a different treatment.

If there are no suitable treatment options left, they might suggest end-of-life care. This means you will not have any more treatment that aims to control your CML. But you will still have treatment to relieve your symptoms and improve your quality of life. Your haematology team should ask you about your wishes, and your feelings about treatment. You should also have access to a palliative care team.

Our Patient Services team is here if you need support. You can email support@leukaemiacare.org.uk or call our freephone helpline on **08088 010 444**.



Glossary of medical terms

BCR-ABL1 gene

An abnormal piece of genetic code found in people with CML. It makes an abnormal version of a protein called tyrosine kinase.

Blast phase

When CML is aggressive or fast-growing.

Blood transfusion

A procedure to give you donated blood through a drip into a vein.

Chronic myeloid leukaemia (CML)

A slow-growing type of blood cancer that starts in blood-forming cells in your bone marrow called myeloid stem cells.

First-line treatment

The first treatment you have for CML.

Frontline treatment

Another name for first-line treatment.

Growth factor

A type of medicine that boosts your blood cell counts.

Intolerance

Having side effects that are hard to cope with.

Molecular response

How well your CML is responding to treatment based on the level of the *BCR-ABL1* gene in your blood. This is a very sensitive measure of how much leukaemia is left in your body.

Primary resistance

When treatment does not work from the start.

Secondary resistance

When treatment works at first but then stops working.

Second-line treatment

Treatment you have if your first treatment is unsuccessful.

Stem cell transplant

An intensive type of treatment where damaged or destroyed blood-forming cells in your bone marrow are replaced with healthy ones.

Supportive care

Treatment that does not treat the CML itself but helps with symptoms or side effects.

Tyrosine kinase inhibitor (TKI)

The most common treatment for CML, given as a tablet. TKIs block a protein called tyrosine kinase.

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

Leukaemia Care

Helpline: 08088 010 444 (Monday to Friday, 9am to 5pm)

WhatsApp: 07500 068065 (Monday to Friday, 9am to 5pm)

www.leukaemiacare.org.uk

support@leukaemiacare.org.uk

CML Support

A patient-run UK charity supporting patients with CML.

cmlsupport.org.uk

CML Advocates Network

An international network of CML patient organisations.

www.cmladvocates.net

Blood Cancer UK

Leading charity into the research of blood cancers.

0808 2080 888

www.bloodcancer.org.uk

Macmillan

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

0808 808 0000

www.macmillan.org.uk

Cancer Research UK

Leading charity dedicated to cancer research.

0808 800 4040

www.cancerresearchuk.org

Maggie's Centres

Offer free practical, emotional and social support to people with cancer and their loved ones.

0300 123 1801

www.maggiescentres.org

Citizens Advice

Offers advice on benefits and financial assistance.

0800 144 8848 (England)

0800 702 2020 (Wales)

0800 028 1456 (Scotland)

www.citizensadvice.org.uk

The Citizens Advice service does not cover Northern Ireland but their website lists contact details for local community advice agencies, depending on where you live.

How you can help us

If you've been affected by CML, sharing your story can help others going through a similar situation and help the public to better understand.

To share your story, go to bit.ly/ShareYourStoryWithLC

Alternatively, you can email our Communications team at communications@leukaemiacare.org.uk.

Tell us what you think of this booklet

We aim to provide information that's reliable, up-to-date, and covers what matters to you. We want you to feel supported and able to be involved in decisions about your care. Your feedback helps us improve our information and make sure it meets your needs. Please get in touch to let us know what we can do better. You can also contact us if you'd like a list of the references we used to compile this booklet.

- Email our Information team at information@leukaemiacare.org.uk
- Call our Head Office on **01905 755 977**
- Write to us at Leukaemia Care, One Birch Court, Blackpole East, Worcester, WR3 8SG
- Leave us a review if you've ordered a booklet online

If we've helped you - here's how you can give back

Fundraising is at the core of what we do here at Leukaemia Care, and without it we wouldn't be able to provide the support we do.

Fundraising isn't all about running a marathon, and there are plenty of ways to give thanks and show your support.

You could:

- Ask your local shop or workplace to host a collection tin
- Ask your place of work about charity of the year partnerships or grants
- Take on one of our more accessible walking challenges
- Host a quiz night or get your friends together for a catch-up and a meal
- Host a bake sale at work or school, or even a coffee morning with friends
- Share information about the activities we have going on to get friends and family joining in
- Stream online from the comfort of your own home

However, if you can run a marathon or want to do a thrilling skydive, we've got you covered!

Whatever you want to do, we can support you to raise money for Leukaemia Care. Get in touch with the fundraising team by email fundraising@leukaemicare.org.uk or calling **08088 010 444**.

You can also find out more about how to get involved online at bit.ly/BeAPartOfTeamLC

Plenty of ways to give

There are so many ways you can give in support of those affected by a leukaemia diagnosis, the possibilities are endless - find one that fits you and let's get giving!

By bank transfer

You can transfer your donation straight from your account to ours. Our bank details are:

Sort code: **20-98-61**

Account number: **80823805**

Account name: **Leukaemia Care**

By cheque

Please make your cheque payable to Leukaemia Care, and then pop it in the post to: **Leukaemia Care, One Birch Court, Blackpole East, Worcester, WR3 8SG**

Online

Simply pop onto our website at www.leukaemiacare.org.uk/donate to pay your money in. Remember to include as much information as possible to help us know it's you paying in.

By phone

You can call us to pay by debit or credit card over the phone. Simply call **01905 755977**.



Leukaemia Care is the UK's leading leukaemia charity. For over 50 years, we have been dedicated to ensuring that everyone affected receives the best possible diagnosis, information, advice, treatment and support.

Every year, 10,000 people are diagnosed with leukaemia in the UK. 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)

WhatsApp: **07500 068065**

Office Line: **01905 755977**

www.leukaemiacare.org.uk

support@leukaemiacare.org.uk

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Leukaemia Care is registered as a charity in England and Wales (no. 1183890) and Scotland (no. SCO49802).

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Leukaemia Care
YOUR Blood Cancer Charity



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