Leukaemia Care
YOUR Blood Cancer Charity

Treatment-free remission (TFR) in chronic myeloid leukaemia (CML)

Chronic myeloid leukaemia (CML) is a type of blood cancer that involves the white blood cells in the bone marrow. It can develop slowly over many years. The most common treatment is a type of targeted therapy called a tyrosine kinase inhibitor (TKI). Some people who have a deep, long-term response to TKIs may be able to reduce the dose or stop treatment completely. This is called treatment-free remission (TFR).

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

Summary

Do not stop taking your CML treatment without discussing it with your haematology team.

- Treatment-free remission (TFR) is when your CML stays under control without the need to keep taking medicines.
- It might be an option for people who have been taking TKIs for 3 to 5 years or more and have been in a deep molecular response for at least 2 years.
- If TFR is an option for you, your haematology team should talk to you about the benefits and risks. You should decide together whether it's something you'd like to try.
- If you try TFR, you have regular check-ups to monitor your response.
- Around 50 or more in every 100 people who try TFR keep their response to treatment. But up to 50 in every 100 people may lose their response.
- If your CML does not stay in remission, restarting TKI treatment is usually very effective.
- Around 20 to 30 in every 100 people who stop TKIs get muscle pain and joint stiffness. This usually goes away on its own, but some people might need a short course of treatment.

About treatment-free remission

The most common treatment for chronic myeloid leukaemia (CML) is a type of medicine called tyrosine kinase inhibitors (TKIs). They include imatinib, nilotinib, dasatinib, bosutinib, ponatinib and asciminib.

Treatment-free remission (TFR) is when your CML stays under control without the need to keep taking medicines. It may be possible for some people with CML who have had a deep, long-lasting response to TKI treatment.

> **"My hope is that at some stage, I will be able to try treatment-free remission (TFR) or at least reduce my dose level to give me a little relief from the side effects, which have been quite challenging at times."**
>
> **Helen, diagnosed with CML at 59**

For other people, it might be possible to reduce your dose of TKIs but still keep your response to treatment. This is called dose reduction. It aims to find the lowest dose of treatment that keeps your CML under control. This keeps your risk of side effects as low as possible. Many patients reduce their medication dose (usually for a year) in advance of attempting TFR.

Who might be able to try TFR?

Do not stop taking your CML treatment without discussing it with your haematology team.

TFR is not possible for everyone. But it might be an option if:

- Your CML is in the chronic phase and has never been in the blast phase.
- You've been on TKI treatment for at least 3 years (ideally at least 5 years).
- You've been in a **deep molecular response** (MR4 or MR5) for at least 2 years.
- You've never had to stop taking a TKI because it didn't work well. (You might still be able to try TFR if you had to stop a TKI because of side effects.)
- You do not have a genetic change in your *BCR-ABL1* gene that makes it resistant to treatment.
- Your hospital has quick access to accurate molecular testing (PCR) to monitor your CML.

Molecular response

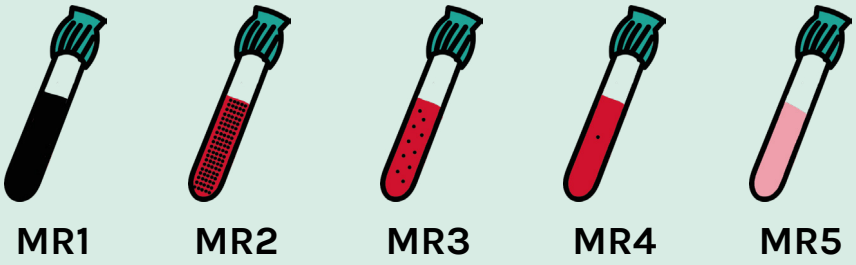
Your molecular response is based on the level of the *BCR-ABL1* gene in your blood. This gene is found in your leukaemia cells. It is measured using a test called PCR. The test is very sensitive so it can detect extremely low levels of leukaemia in your body. The results are given as your molecular response (MR) level.

There are different 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.
- MR4: Less than 1 in 10,000 white blood cells (0.01%) has the *BCR-ABL1* gene.
- MR5: Less than 1 in 100,000 white blood cells (0.001%) has the *BCR-ABL1* gene.

MR3 is classed as a **major molecular response (MMR)**.

MR4 and MR5 are classed as a **deep molecular response (DMR)**.



If you have not achieved a deep molecular response and you're keen to try TFR, talk to your haematology team. Depending on your circumstances, they might suggest changing to a different TKI to try to improve your molecular response.

Benefits and drawbacks of TFR

If TFR is an option, your haematology team should talk to you about the benefits and risks. You should decide together whether it's something you'd like to try.

"If you want to come off any medication, sit with your family, friends, Leukaemia Care, or doctor and really talk about it. Ask any questions you have, no matter how silly you think they are, and they will always be answered, and you will be supported. If you are not ready to make a big change, don't do it. The medical professionals are there for you and any decisions you make. But I will tell you, it's very scary making a massive decision like this."

Vickie, diagnosed with CML

Benefits of trying TFR

- Your CML might stay under control without having to take any medicines.
  - Around 50 or more in every 100 people who try TFR keep their molecular response. The chance of your CML staying under control is higher the longer you have been in deep molecular response.
- You do not have to remember to take medicines every day.
- You are not at risk of getting any side effects.
- If you are hoping to get pregnant, TFR might give you the chance to do this safely and stay off TKI treatment during your pregnancy.

Drawbacks of trying TFR

- Your CML might not stay under control.
  - If you try TFR, your molecular response will be monitored more closely. If you lose your response, you will need to start treatment again.
  - This may happen in up to 50 in every 100 people who try TFR. It usually happens within 6 to 9 months of stopping treatment, although it can happen much later.
- You have more frequent blood tests and appointments to check if your CML is staying under control.
- You may get treatment discontinuation syndrome (page 6).
- You may feel anxious about your CML coming back.
  - If you try TFR, you are monitored closely. But the thought of your CML coming back can still be worrying, especially around the time of your blood tests.

Deciding whether or not to try TFR should be a shared decision between you and your haematology team. If you feel anxious and you are not comfortable trying it, let them know. Your haematology team shouldn't force TFR on you if you are not comfortable with it.

If you're not keen to stop treatment completely, you could ask if trying a lower dose might be an option instead.

Treatment discontinuation syndrome

Treatment discontinuation syndrome is symptoms of muscle pain and stiffness that can develop after you stop treatment with TKIs. Around 20 to 30 in every 100 people who stop TKIs get it. Doctors do not know exactly why it happens. It usually starts within days or weeks of stopping your TKI.

Treatment discontinuation syndrome is usually mild and goes away on its own. But some people may need a short course of treatment with paracetamol, non-steroidal anti-inflammatory medicines like ibuprofen or diclofenac, or sometimes steroids (prednisolone).

What does TFR involve?

If you and your haematology team agree that TFR is right for you, they will explain what the process will involve.

- You might stop your TKI treatment straightaway, or you might take a half-dose for a year before stopping treatment. This may increase the chance of your CML staying under control once you stop treatment.
    - If you reduce your dose, you'll have blood tests every 1 to 2 months while you are taking a lower dose.
- You will have frequent blood tests to check your molecular response. You will also have check-ups to look for any symptoms of treatment discontinuation syndrome. Your haematology team are likely to monitor you:
    - Every month for the first 6 months after stopping treatment
    - Every 6 weeks from 7 to 12 months after stopping treatment
    - Every 2 months from 12 to 36 months after stopping treatment
    - Every 3 months from 3 years onwards

Your haematology team may alter your monitoring schedule based on your individual situation and results.

If your CML does not stay under control

It can be very worrying if your CML does not stay under control, but restarting TKI treatment is usually very effective.

"I was scared. Scared that my CML would get worse, like from the very beginning. My doctor assured me that as I am having close and regular monitoring, that would not happen. If my CML was to rise again, I could either take my imatinib or maybe try another TKI, due to the imatinib giving me so many side effects."

Vickie, diagnosed with CML

Up to 50 in 100 people who try TFR may not stay in major molecular response. This usually happens within 6 to 9 months of stopping treatment. It is uncommon to lose your response after a year or more, but it can happen. This is why your haematology team continue to monitor you closely.

- If you lose a major molecular response (MR3 or *BCR-ABL1* less than 0.1%), you will usually need to restart TKI treatment. This should happen within 4 weeks of losing your response.
- Your haematology team may recommend that you restart a TKI before you lose your MR3 response if your results suggest you are likely to do so soon.
- Most people restart the same TKI they were on before, but your haematologist might suggest a different one. Restarting TKI treatment is usually very effective at getting your CML back into deep molecular response.
- Once you've restarted treatment, you should have a PCR test every 4 weeks until you have achieved a major molecular response again (MR3 or *BCR-ABL1* less than 0.1%).
- If you do not achieve MR3 after 6 months, your doctor is likely to check for any changes in your *BCR-ABL1* gene that might affect how well it responds to treatment. They might suggest a different treatment option.

Further information

We have more information about CML, including booklets and factsheets to download. Follow the link, search 'CML' at leukaemiacare.org.uk or scan the QR code:

We also have booklets you can order in print free of charge. Follow the link, search 'CML' at shop.leukaemiacare.org.uk or scan the QR code:

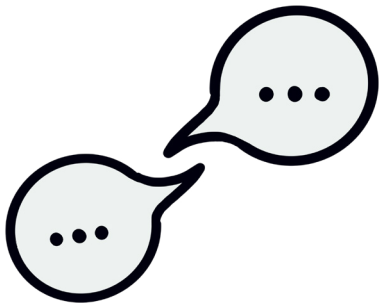
We are grateful to Guy Hannah, consultant haematologist, and Abir, Colin, Graham and Lesley, patient reviewers, for reviewing this information.

If you have any feedback on this information, or you'd like a list of the references we used to develop it:

- Email information@leukaemiacare.org.uk
- Call **01905 755 977**
- Write to **Leukaemia Care, One Birch Court, Blackpole East, Worcester, WR3 8SG**

If you need support

We're here for you if you need support. Follow the link or search 'support for you' at leukaemiacare.org.uk to find out how we can help you.



If you'd like to talk to someone who understands what you're going through:

- Call our freephone helpline on **08088 010 444**
- Message us through WhatsApp on **07500 068065**

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