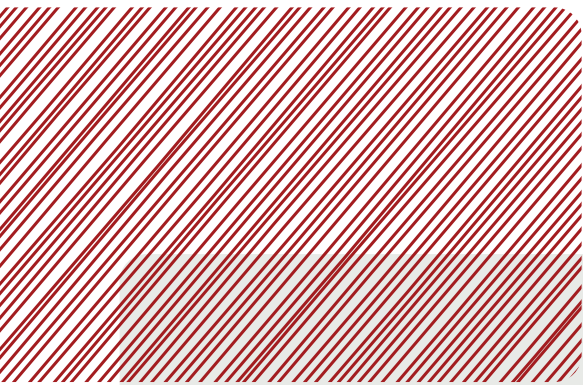




Understanding and managing
**chronic myeloid
leukemia (CML)**





What is this booklet for?

This booklet was designed to answer some questions you may have about CML. It summarizes the treatment options that are available in Canada. It can also serve as a starting point for discussions with your doctor, so that you can decide together what is best for you.

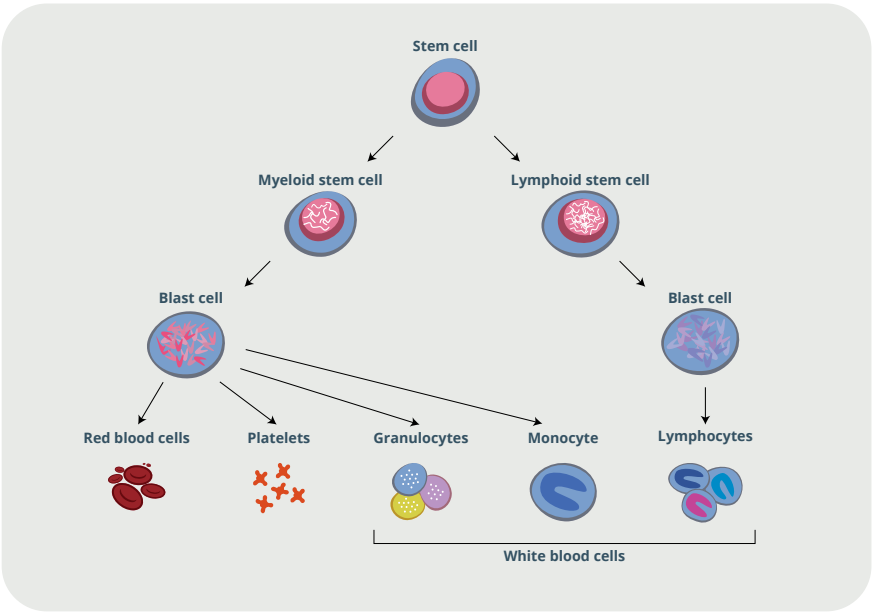
Once you have a better understanding of each treatment option, you can stay informed and take an active role in your CML treatment process.



What is CML?

CML is a cancer that starts in **blood stem cells**, which are basic cells that become either **myeloid stem cells** or **lymphoid stem cells**.

Development of blood cells



Normally, as these stem cells develop, they go on to become immature blood cells known as blast cells.

In CML, there is an overproduction of these blast cells, which become abnormal and do not develop into mature blood cells. Over time, the blast cells crowd out normal blood cells and prevent them from doing their jobs.

CML starts in abnormal myeloid stem cells and develops slowly.

Myeloid stem cells normally develop into red blood cells, granulocytes, monocytes or platelets.

- Red blood cells carry oxygen to all tissues of your body.
- Granulocytes and monocytes are types of white blood cells that destroy bacteria and help fight infection.
- Platelets form clots in blood to stop bleeding.

Usually in CML, there are too many granulocytes.

CML is the third most common type of leukemia diagnosed in adults in Canada.

What are the different phases of CML?

CML is not staged in the same way as other types of cancer because it does not form a solid tumour. Instead of stages, **CML is given a phase based on blood cell counts and symptoms.**

The phase of your disease is based mostly on the number of blast cells in your blood and bone marrow. Knowing the phase of your disease helps your doctor plan your treatment and predict how your disease will progress. CML is divided into **three phases:**

| | |
|---|---|
| Chronic phase | <ul style="list-style-type: none">• Most people are diagnosed at this phase.• You may or may not have symptoms.• People often have an increased number of white blood cells in the blood, bone marrow, or both.• Compared to other phases, chronic phase CML tends to respond better to treatment.• Without treatment, CML will progress to one of the next two phases. |
| Accelerated phase | <ul style="list-style-type: none">• The number of cancer cells increases more quickly.• Symptoms appear, such as tiredness, fever, weight loss, and enlarged spleen.• Without treatment, accelerated CML will progress to the blast phase. |
| Blast phase (also called "blast crisis" phase) | <ul style="list-style-type: none">• Blast cells may have spread outside the blood and/or bone marrow to other parts of the body.• CML cells show new, abnormal changes. |

What are the signs and symptoms of CML?

CML is often discovered when you have a blood test for another reason as there may be no obvious signs or symptoms. **The blood test usually shows that you have an abnormally high white blood cell count.** Some of the signs and symptoms that you may experience are listed below:



Weakness, tiredness, and feeling out of breath during normal activity

- May happen when you have low red blood cell counts



Fevers and night sweats

- Possibly a response from your immune system



Bone pain

- May happen when your white blood cells accumulate, causing your bone marrow to expand



Weight loss

- May happen when you are eating less or using more energy



Pain or a feeling of fullness below the ribs on the left side

- May arise when your CML cells build up in your liver or spleen, causing your abdomen to swell

What are the possible tests for CML?



Complete blood count (CBC)

A CBC measures the components of the blood, including counts of white blood cells, red blood cells, and platelets. CML often causes a high white blood cell count and/or platelet count, but can sometimes cause low counts of other blood cells.



Bone marrow tests


To diagnose CML and determine the CML phase, samples of bone marrow must be removed and tested before starting any treatment. Usually, this test is only done once at the time of diagnosis. However, you might have another during or after treatment, if needed. There are two types of bone marrow tests which may be done at the same time: bone marrow aspirate and bone marrow biopsy. These two tests look at bone marrow cells for anything unusual with your chromosomes. Keep reading to learn more about chromosomes.



Molecular tests

CML can cause changes in the genes and chromosomes of blood cells. In particular, it is caused by a mutation created when a piece of chromosome 9 and a piece of chromosome 22 break off and trade places. The result is a fused gene called *BCR-ABL1* and the abnormal chromosome 22 called the “Philadelphia chromosome.”

Molecular tests look for these changes or abnormalities. They are used to learn more about your type of CML, to target treatment, and to determine the likely path your cancer will take (prognosis). Results of molecular genetic testing can also predict how quickly the disease will progress and can help determine your best available treatment options.



DNA is the material that carries all the information about how our bodies look and function. Each piece of information is carried on a different section of the DNA and these sections are called “genes.” Genes tell a cell how to make a specific protein, which is used by the cell to grow and survive. DNA is organized into tightly coiled thread-like bundles called “chromosomes” that contain thousands of genes. Some changes, called “mutations,” can happen in your genes.

Karyotype

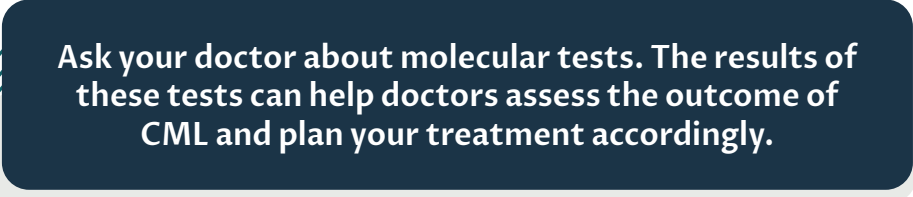
A karyotype is a picture of chromosomes. Doctors look for whether 46 chromosomes or 23 pairs are present. They also look for extra, missing, or abnormal pieces of chromosomes, such as the *BCR-ABL1* gene. Since a karyotype usually requires growing cells, a sample of bone marrow is needed. Sometimes (especially with newly diagnosed CML), enough growing cells can be found in the blood to allow a karyotype.

Fluorescence *in situ* hybridization (FISH) test

Your doctor may use this molecular genetic test to identify chromosomal abnormalities and other genetic changes in the blast cells. FISH test uses special DNA probes labelled with fluorescent dyes. It is used to tell apart leukemias that look the same but that have different genetic abnormalities and may need to be treated differently. In the case of CML, the probes attach to the *BCR* gene and the *ABL1* gene. The *BCR-ABL1* gene is detected when the colors of the probes overlap. Since this test doesn't need growing cells, it can be performed on either a bone marrow or blood sample. Sometimes, a bone marrow sample is needed to get all the information your doctor needs to help plan your treatment and care.

Quantitative reverse transcriptase polymerase chain reaction (qPCR)

A qPCR test measures the number of cells with the *BCR-ABL1* gene and can be done on cells taken from the blood or bone marrow. The qPCR test may also be used to monitor how well treatment is working.



Ask your doctor about molecular tests. The results of these tests can help doctors assess the outcome of CML and plan your treatment accordingly.

How is CML treated?

Factors affecting treatment choice for CML

Each phase of CML has a different type of treatment. Your doctor will determine the best course of treatment for you based on the CML phase and these factors:

- Age
- Size of the spleen
- Platelet counts
- Blast count (concentration of immature blood cells in your blood)
- Concentration of white blood cells in your blood
- Your overall health

Goals of CML treatment

Treating CML by phase

| | |
|------------------------------------|---|
| Chronic phase treatment | <ul style="list-style-type: none">• To keep the CML cells that contain the <i>BCR-ABL1</i> gene at a very low level.• Return blood cell counts (red blood cells, white blood cells, and platelets) to normal levels. |
| Accelerated phase treatment | <ul style="list-style-type: none">• To kill all cells that contain the <i>BCR-ABL1</i> gene.• If this is not possible, the goal is to return the disease back to the chronic phase. |
| Blast phase treatment | <ul style="list-style-type: none">• People with blast phase CML have higher blood counts and more severe symptoms.• Treatment at a specialized center with doctors who have expertise in CML is recommended to help manage symptoms. |

After considering the above factors and assessing the CML phase, your doctor will recommend one or more of the treatment options listed on pages 12–14.



Treatment options for CML phases

Chronic phase

Targeted therapy

- Tyrosine kinase inhibitor (TKI) therapy is the standard treatment.
- A TKI is a type of targeted therapy that blocks the signals that cause cancer to grow and spread.
- TKIs are taken in pill form.
- Many people are able to manage their CML for long periods of time with TKIs.
- There are several versions of TKIs, so if one kind does not work or is difficult to tolerate, other types are available.

Chemotherapy

- Chemotherapy may be offered if someone cannot cope with the side effects from targeted therapy, or the CML is resistant to targeted therapy.
- Chemotherapy kills fast-growing cells throughout the body, including cancer cells and normal cells.

Biological therapy

- Biological therapy may be offered to people who cannot cope with the side effects from, or if the CML is resistant to, targeted therapy.
- It can be used alone, or in combination with chemotherapy.
- The most common biological therapy used is interferon alfa.
 - This drug is most often given as a daily injection (shot) under the skin.
 - It may also be injected into a muscle or vein.



Accelerated phase

Targeted therapy

- If you are in the accelerated phase when you are diagnosed with CML, the first treatment option is TKIs.
- If you move from chronic to accelerated CML while taking TKIs, your doctor may give you a higher dose or a different medication.

Stem cell transplantation (SCT)

- An allogeneic stem cell transplant may be offered.
- This is a procedure in which stem cells from another person (a donor) are infused into your body. The donor may be a sibling or an unrelated person with stem cells that “match” those of the person receiving the transplant.
- Doctors will usually try to get CML to return to the chronic phase or improve the blood cell counts before the transplant.

Chemotherapy

- Chemotherapy may be offered if someone cannot cope with the side effects from targeted therapy, or the CML is resistant to targeted therapy.
- Chemotherapy is also used in preparation for a stem cell transplant.



Treatment options for CML phases

| Blast phase | |
|--|---|
| Targeted therapy with or without chemotherapy | <ul style="list-style-type: none">• Targeted therapy with a TKI may be offered.• If you are already taking targeted therapy, your doctors may increase the dose or try a different drug. |
| Radiation therapy | <ul style="list-style-type: none">• External beam radiation therapy may be offered to:<ul style="list-style-type: none">- shrink the spleen if it is larger than normal- relieve bone pain |
| Clinical trial | <ul style="list-style-type: none">• One option for people with blast phase CML is to receive treatment within a clinical trial. |

Joining a clinical trial can be a good option for you. A clinical trial is a type of research that studies a test or treatment in people. It gives people access to healthcare options that otherwise wouldn't be available. Ask your medical team if there is an open clinical trial that is right for you.

What else should you know about your CML treatment?

Treatment side effects

- When you begin CML treatment, you may experience mild to severe side effects, depending on your age, overall health, and treatment plan.
- Most side effects decrease once your body adjusts to treatment or when your treatment ends.
- New drugs and therapies can help control side effects, such as nausea and vomiting.

Speak to your doctor if you are experiencing side effects.

Remission without further treatment

- Treatment of CML has improved significantly over the past 20 years.
- Many people with CML go into remission, which happens when the number of CML cells is controlled to a low, nearly undetectable level.
- New treatments for CML mean that you may go into remission and show no signs of the disease for a long time.

If your CML has been under control for several years, you may even be able to stop taking medication for CML. This is an option that you can discuss with your doctor.



What questions should you ask your doctor?



Being an active participant in your cancer care can give you and your family a greater sense of control. One way to achieve this is by building a relationship with your medical team based on open communication.

Consider bringing this list of questions to your next doctor's appointment.

Diagnosis

- What type of cancer do I have? From what type of cell did it form? Is this cancer common?
- Will I need to have other tests before we can decide on treatment?
- What tests do you recommend for me?
- Where will the tests take place? How long will the tests take?
- How do I prepare for testing? How will the test be done? What can I expect?

General treatment

- Should I start treatment now? Why or why not?
- What should I do to be ready for treatment?
- What are my treatment options?
- Which one do you recommend for me? Why?
- What is the treatment frequency?
- How often will you test my blood or bone marrow to see how treatment is working?
- What should be avoided or taken with caution while receiving treatment?






Side effects of treatment


- What are the possible risks or side effects of my treatment? How serious are they and what should I report right away?
- How can I manage the side effects?

Other considerations

- Can treatments be taken at home?
- How will treatment affect my daily activities?
- What if I miss a treatment?
- Are there any limits on what I can do?
- Should I still take the other medications I am on?
- Is it okay to continue with the supplements I am currently taking?
- What costs will I encounter?
- In cases of emergency, how can I reach your office on nights, holidays, or weekends?



Be sure to write down any questions you have that are not on this list. For instance, you may want to ask about how you'll feel so that you can plan your work schedule. Or you may want to ask about qualifying for clinical trials.



What resource is available to you?



LEUKEMIA &
LYMPHOMA
SOCIETY
OF CANADA®

Visit our website to learn more about CML and its treatment.

bloodcancers.ca

For more information,
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You can use this app to note
down any questions that you may
have to bring to your next
doctor's appointment.



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