CONDITION

Chronic myeloid leukemia

Learn how chronic myelogenous leukemia develops, how BCR::ABL1 testing confirms it, and how targeted medicines and regular monitoring help manage CML.

WHAT IT IS
Cancer of blood-forming bone marrow cells

BODY SYSTEM
Blood and bone marrow

MAIN SYMPTOMS
Tiredness, weight loss, night sweats, easy bruising

WHAT CAUSES IT
Acquired chromosome change, usually unknown

HOW IT IS DIAGNOSED
BCR::ABL1 or Philadelphia chromosome testing

MAIN TREATMENT
Targeted medicines

CAN IT BE CURED?
Sometimes, donor stem cell transplant

IS IT AN EMERGENCY?
Sometimes, severe trouble breathing

LONG-TERM OUTLOOK
Often controlled for years but can progress

Overview

Chronic myelogenous leukemia, also called chronic myeloid leukemia or CML, is a cancer of the blood-forming cells in the bone marrow. Bone marrow is the soft tissue inside bones where blood cells are made.

CML causes the marrow to produce too many abnormal white blood cells. These cells can build up in the blood, bone marrow, and spleen. Unlike many acute leukemias, CML often develops slowly at first.

Nearly all cases involve an abnormal gene called BCR::ABL1 . It forms when pieces of chromosomes 9 and 22 switch places. The altered chromosome 22 is known as the Philadelphia chromosome . The BCR::ABL1 gene makes an overactive protein called a tyrosine kinase, which tells leukemia cells to keep growing.

Medicines called tyrosine kinase inhibitors , or TKIs, block this signal. These targeted treatments have greatly improved control of CML. Many people remain in the chronic phase for years while taking a daily oral medicine.

CML is commonly described in three phases:

The phase, test results, other health conditions, and response to treatment all affect the care plan.

- Chronic phase: Leukemia cells are present, but blood production still works relatively well. Most people are diagnosed in this phase.
- Accelerated phase: The disease shows signs of becoming less stable. Exact definitions differ among classification systems.
- Blast phase: Large numbers of very immature cells, called blasts, appear. This phase behaves more like acute leukemia and needs prompt treatment.

Symptoms

CML may not cause symptoms at first. It is sometimes found when a complete blood count done for another reason shows an unusually high white blood cell count.

When symptoms occur, they can develop gradually. They may include:

Fullness under the left ribs can occur when the spleen becomes enlarged. The spleen helps filter blood and support immune function.

These symptoms have many possible causes and do not confirm CML. A blood test and specialized testing are needed to identify the condition.

Contact the cancer care team promptly for a new fever, worsening shortness of breath, unusual bleeding, rapidly increasing abdominal fullness, or side effects that make it difficult to take treatment. Seek emergency care for severe trouble breathing, chest pain, fainting, confusion, sudden weakness on one side, uncontrolled bleeding, or other severe symptoms.

- Tiredness, weakness, or reduced exercise tolerance
- Unexplained weight loss or reduced appetite
- Night sweats
- Fever without a clear infection
- Fullness or discomfort under the ribs on the left side
- Feeling full after eating a small amount

- Easy bruising or bleeding
- Bone discomfort
- Pale skin, shortness of breath, or dizziness related to anemia

Causes and risk factors

CML begins when a blood-forming stem cell develops the chromosome change that creates BCR::ABL1. This is an acquired change, meaning it develops during a person's life. It is not usually inherited from a parent or passed directly to children.

The exact reason this chromosome change occurs is usually unknown. It is not caused by everyday activities, diet, stress, or something a person did wrong.

CML is more common in older adults, although it can occur at any age. Exposure to high levels of ionizing radiation is an established risk factor. This refers to substantial radiation exposure, not ordinary household electronics.

Most people diagnosed with CML have no known preventable risk factor. There is no routine screening test recommended for people without symptoms or abnormal blood counts.

Diagnosis

Evaluation usually begins with a complete blood count , or CBC. This test measures white blood cells, red blood cells, and platelets. CML often causes a high white blood cell count and may also affect hemoglobin or platelet levels.

A blood smear allows a laboratory professional to examine the cells under a microscope. In CML, white blood cells may appear at several stages of development. The number of basophils, a type of white blood cell, may also be increased.

Confirming CML requires evidence of BCR::ABL1 or the Philadelphia chromosome. Testing may include:

A bone marrow aspiration and biopsy may be performed at diagnosis. During this procedure, a clinician removes liquid marrow and a small core of tissue, usually from the back of the hip. The samples help assess the number and appearance of cells, the disease phase, and chromosome findings.

The care team also reviews the percentage of blast cells, spleen size, blood counts, and other chromosome changes. Blood chemistry tests help evaluate kidney and liver function before treatment.

If treatment is not working as expected, testing may look for changes in BCR::ABL1 called kinase-domain mutations. Certain mutations can make particular medicines less effective and help guide the next treatment choice.

- Chromosome analysis, or cytogenetics: Examines cells for the Philadelphia chromosome.
- Fluorescence in situ hybridization, or FISH: Uses fluorescent probes to detect the BCR::ABL1 rearrangement.
- Reverse-transcription quantitative PCR: Measures the amount of BCR::ABL1 genetic material. This highly sensitive test is also used to monitor treatment.

Treatment and management

Treatment is usually coordinated by a hematologist-oncologist, a doctor who treats blood cancers. The main treatment for chronic-phase CML is a TKI taken by mouth.

TKIs used for CML include imatinib, dasatinib, nilotinib, bosutinib, asciminib, and ponatinib. They do not all have the same approved uses or safety concerns. Some are commonly used for newly diagnosed chronic-phase disease, while others may be selected after resistance, intolerance, or a specific mutation.

Choosing a medicine involves more than comparing its effect on CML. The clinician considers heart and blood vessel health, lung disease, diabetes, liver function, other medicines, pregnancy plans, likely side effects, and the ability to take treatment consistently.

TKIs can interact with prescription medicines, over-the-counter products, supplements, and some foods. Acid-reducing medicines like omeprazole or lansoprazole can affect the absorption of certain TKIs. A pharmacist or clinician should review everything a person takes. Treatment should not be stopped, skipped, or changed without discussing it with the care team.

Possible side effects depend on the specific medicine. They can include nausea, diarrhea, rash, swelling, muscle cramps, headache, fatigue, low blood counts, or changes in liver test results. Some TKIs have more specific concerns, such as fluid around the lungs, abnormal heart rhythms, inflammation of the pancreas, or problems involving arteries and blood flow. Monitoring is tailored to the medicine and the person's health risks.

The response to treatment is measured mainly by changes in BCR::ABL1 levels. A molecular response means the amount of BCR::ABL1 has fallen. A very low level is called a deep molecular response. These terms describe laboratory findings and help the team judge whether treatment is working.

If the response is slower than expected, BCR::ABL1 rises, or side effects are difficult to manage, the team may check adherence, interactions, test accuracy, and possible resistance. Switching to another TKI may be appropriate.

A stem cell transplant uses blood-forming cells from a donor. It can potentially cure CML, but it carries significant risks. It is generally considered for selected people with advanced disease or CML that does not respond adequately to available medicines.

Blast-phase CML usually requires urgent specialist treatment. Care may combine a TKI with therapies used for acute leukemia, followed by consideration of a donor stem cell transplant when appropriate.

Some people with a long-lasting deep molecular response may be able to try treatment-free remission . This means stopping the TKI under close specialist supervision while continuing frequent PCR tests. It is not suitable for everyone. A rising BCR::ABL1 level may require treatment to restart.

TKIs can affect pregnancy and fetal development. Anyone who is pregnant, could become pregnant, or plans to have a child should discuss contraception, fertility, and pregnancy planning with the CML team. A person should not stop a TKI on their own after learning about a pregnancy.

Complications

Without effective control, CML can progress from chronic phase to blast phase. Regular testing helps identify loss of response before symptoms appear.

CML itself can cause anemia, abnormal platelet counts, bleeding, infections, bone discomfort, or an enlarged spleen. Very high white blood cell counts can rarely interfere with blood flow and organ function.

Treatment can also cause complications. Low blood cell counts may increase the risk of infection, fatigue, or bleeding. Other risks vary among TKIs and may involve the lungs, heart, blood vessels, liver, pancreas, or fluid balance.

A new symptom does not necessarily mean the leukemia is progressing. It may be related to treatment, another medical condition, or a temporary illness. Reporting changes early allows the care team to evaluate the cause and adjust supportive care when needed.

Follow up

CML requires long-term follow-up, even when a person feels well. Early in treatment, blood counts and quantitative PCR testing are usually performed at regular intervals, often about every three months. Testing may become less frequent after a stable response, but the schedule depends on the response and treatment plan.

PCR results are commonly reported on the International Scale , which helps clinicians compare results over time. Trends are more useful than a single small change. Testing through the same laboratory can make comparison easier when that is practical.

Routine visits may include a review of:

Call the care team between routine visits for fever, new shortness of breath, unusual swelling, worsening fatigue, significant diarrhea or vomiting, new abdominal fullness, unexplained bruising, or difficulty taking the medicine.

Emergency evaluation is appropriate for severe breathing difficulty, chest pain, fainting, sudden neurological symptoms, uncontrolled bleeding, or a severe allergic reaction.

- BCR::ABL1 results and blood counts
- Whether doses have been missed
- Side effects and quality of life
- New medicines, supplements, or possible interactions
- Blood pressure and heart, lung, liver, or metabolic risks
- Pregnancy or fertility plans
- Vaccination and general preventive care

Sources

- National Cancer Institute. Chronic Myelogenous Leukemia Treatment (PDQ®)-Health Professional Version . PDQ Cancer Information Summaries.
- Hochhaus A, Baccarani M, Silver RT, et al. European LeukemiaNet 2020 recommendations for treating chronic myeloid leukemia. Leukemia . 2020;34:966-984.
- Khoury JD, Solary E, Abla O, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and histiocytic/dendritic neoplasms. Leukemia . 2022;36:1703-1719.
- U.S. Food and Drug Administration. SCEMBLIX (asciminib) Prescribing Information . Revised October 2024.



- Leukemia & Lymphoma Society. Chronic Myeloid Leukemia . Patient education resource.
- American Cancer Society. Chronic Myeloid Leukemia: Early Detection, Diagnosis, and Treatment . Patient information resource.