

Understanding chronic myeloid leukaemia (CML)

CML is a type of cancer that starts in the blood-forming cells of the bone marrow and invades the blood.¹

There are three phases of CML: chronic-phase, accelerated-phase, and blast-phase.² In most patients, CML is diagnosed in the early, chronic phase, and if properly treated may remain in this phase without progressing to a more advanced phase.²⁻⁴

CML statistics



1.2 to 1.5 million people are currently living with **CML** worldwide⁵



About **15%** of all new leukaemia cases are **CML**⁶



The average age at diagnosis for **CML** is **64** years; it is rarely seen in children⁶



CML is slightly more common in men⁷

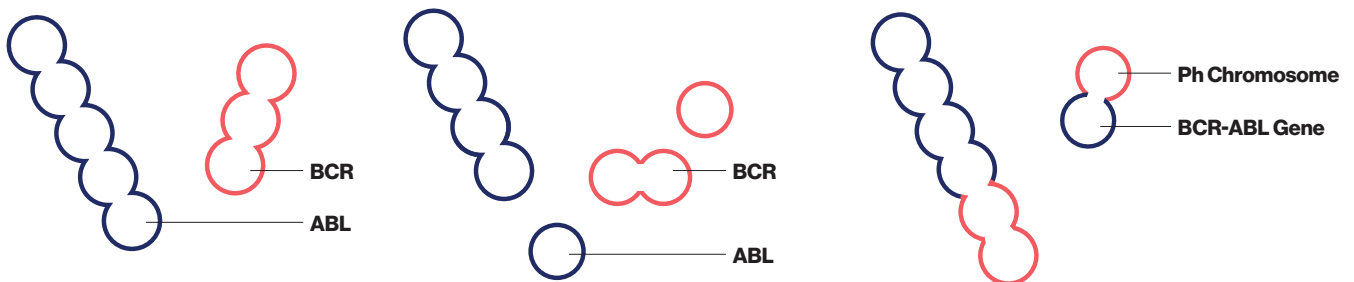
The Ph chromosome

CML is caused by a genetic mutation called the Philadelphia (Ph) chromosome – a rearrangement in the genetic material between chromosomes 9 and 22.⁸

The Ph chromosome carries a defective gene called *BCR-ABL*, which produces a protein of the same name. The protein triggers bone marrow to keep making abnormal white blood cells. When the Ph chromosome is present, CML is classified as Philadelphia chromosome-positive (Ph+).^{3,8}

95% of CML cases are classified as **Ph+ CML**.^{8,9}

Chromosomal rearrangement^{3,8}



Symptoms of CML

Many patients with CML do not show symptoms when diagnosed, and the disease is often found when a doctor orders a blood test for unrelated health problems, or during a routine checkup.¹⁰

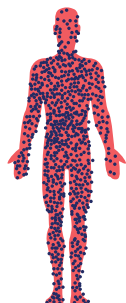
When symptoms of CML do develop, they may include:^{3,11}

- Fatigue
- Weight loss
- Bone pain
- Fever
- Pain below the ribs from an enlarged spleen
- Night sweats

Monitoring, management, and milestones

Routine monitoring of BCR-ABL levels through a sensitive blood polymerase chain reaction (PCR) test can detect early and deep response to treatment and is fundamental to the management of Ph+ CML.^{3,10,12}

This is a simplified way to understand CML treatment milestones. Think of the dots shown in the body as the amount of leukaemic cells in the blood. With each treatment milestone, the amount of leukaemia in the body is reduced.^{3,13}



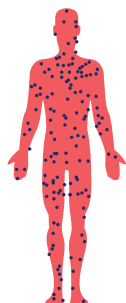
AT DIAGNOSIS

The level of *BCR-ABL* in the body is different for every patient at diagnosis, as measured on the International Scale (IS)^{3,13}



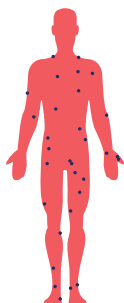
EARLY MOLECULAR RESPONSE (EMR)

The level of *BCR-ABL* in the body is $\leq 10\%$ on the IS^{3,13}



COMPLETE CYTOGENETIC RESPONSE (CCYR)

The level of *BCR-ABL* in the body is expected to correspond with $\leq 1\%$ on the IS^{3,13}



MAJOR MOLECULAR RESPONSE (MMR)

The level of *BCR-ABL* in the body is $\leq 0.1\%$ on the IS^{3,13}

Patients and their health care providers should work together to establish proper treatment goals; with regular monitoring and assessment of tolerability, treatment may need to be adjusted.^{4,8}

Treatment and management of CML

The introduction of tyrosine kinase inhibitor (TKI) therapy more than 20 years ago helped transform CML into a chronic disease for many patients, opening possibilities to achieve deeper and stable responses.^{3,14,15}

Most TKIs target the ATP binding site of the *BCR-ABL* gene, blocking this gene's ability to send signals to produce the leukemic cells.^{3,16}



Need for additional advances

Despite the significant advancements in CML care over the last few decades, many patients remain at risk of disease progression, and the sequential use of currently available TKIs is associated with treatment resistance and/or intolerance, resulting in increased failure rates in later lines.^{3,16-18}

Some patients with CML develop mutations that cause resistance to TKI therapy, including the T315I mutation, which confers resistance to most available TKIs. As a result, patients harboring this mutation have limited treatment options.¹⁷⁻¹⁹



In patients with later-line (\geq third-line) CML, approximately 55% reported intolerance to a previous TKI.^{20*}

There remains a significant unmet need for novel treatment options for patients with Ph+ CML who do not respond adequately to available therapies.^{4,21}

*Data from an analysis of studies where patients were treated with 2 prior TKIs.

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