

# Defining IS RT-Q-PCR Testing & Its Role in CML Disease Management

## About Chronic Myeloid Leukemia (CML)

CML is a cancer of the blood and bone marrow in which the body produces too many white blood cells.

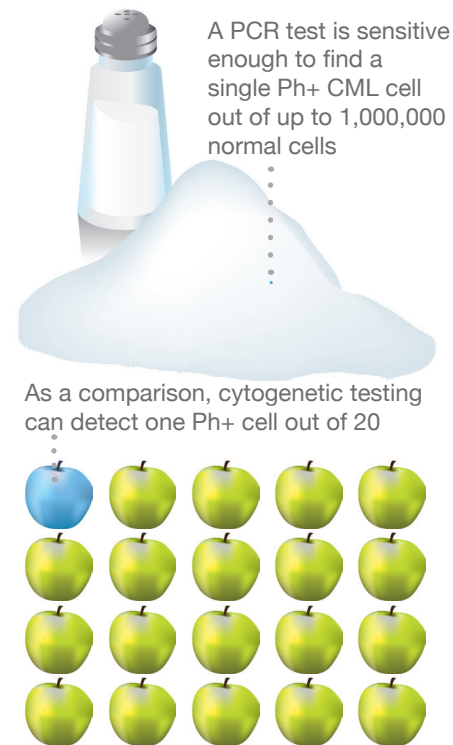
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 Almost all patients with CML have a chromosomal abnormality known as the Philadelphia chromosome. The Philadelphia chromosome produces a protein called BCR-ABL that signals the bone marrow to keep making abnormal white blood cells.

CML treatments have been developed to block the BCR-ABL protein, which helps to inhibit the reproduction of abnormal white blood cells.

## IS RT-Q-PCR Testing in CML

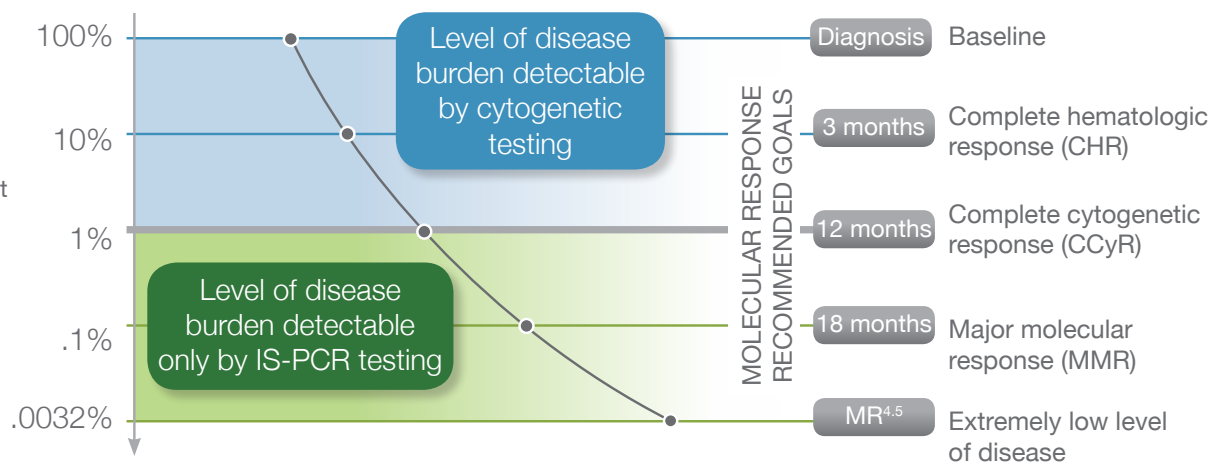
The achievement of a deeper response to treatment is associated with reduction of risk of progression to the advanced stages of the disease and overall survival. Patients who have CML need to get their blood tested frequently via a IS RT-Q-PCR test, which stands for "International Scale – Real-Time Quantitative Polymerase Chain Reaction." This test helps to ensure that a patient's level of disease is continuing to decrease, and the International Scale (IS) is a means of standardizing and validating a patient's test results. The RT-Q-PCR, also known as PCR, is a simple and convenient blood test that measures the amount of leukemia in the body. Facts about the IS RT-Q-PCR test, also known as a PCR test, include:

- The test measures BCR-ABL levels, the key cause of Ph+ CML, which can enable a more precise assessment of response to treatment
- International Scale, or IS, is a means for standardizing a patient's test results and expresses how much BCR-ABL is detected in a patient's blood as a percentage
- It is the only test that can detect early signs of resistance, allowing timely intervention before loss of cytogenetic or hematologic response
- Monitoring the trend in PCR response values over time allows for the detection of earlier trends in BCR-ABL levels and may drive clinical decisions
- Current guidelines recommend getting IS RT-Q-PCR testing every three months, with a checkpoint for major molecular response (MMR) after 18 months of treatment. Once MMR is achieved, a PCR test should be conducted at least every three to six months.



## What is Molecular Response?

Over the past 15 years, researchers have developed increasingly sensitive tests to detect ever-diminishing traces of leukemic cells in Ph+ CML patients. The RT-Q-PCR test is currently the most sensitive test available in the management of CML and it tests for the presence of leukemic cells at the molecular level. Therefore, tracking the PCR test results of their patients helps doctors to determine their degree of molecular response and evaluate how they are responding to treatment.



**MR4.5** MR4.5 is a deep level of molecular response at which patients have a disease burden equivalent to 0.0032% BCR-ABL remaining. MR4.5 is an important milestone for patients with Ph+ CML as clinical evidence demonstrates that disease does not progress or worsen in patients who achieve and maintain this milestone. Recent data correlates early molecular response at 3 months with future MMR and MR4.5, as well as increased probability of progression-free survival and overall survival. Sustaining MR4.5 is a prerequisite for enrollment in most treatment-free remission trials which evaluate the next treatment goal in CML therapy.

