

Measuring the Effect of Therapy for Chronic Myeloid Leukemia

About Chronic Myeloid Leukemia

Chronic myeloid leukemia (CML) is a hematologic stem cell disorder characterized by the presence of an abnormality called the Philadelphia (Ph) chromosome. The Ph chromosome is created by an exchange of parts between two chromosomes. A detached portion of chromosome 9 shifts to chromosome 22, and a section of chromosome 22 shifts to chromosome 9 in a phenomenon known as "translocation." The shortened chromosome 22 is referred to as the Philadelphia chromosome.

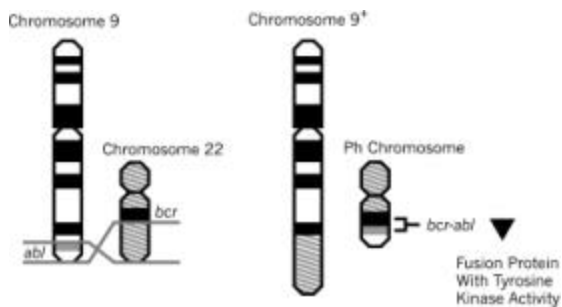


Figure 1: Formation of the Ph chromosome

The Ph chromosome produces an abnormal enzyme, known as Bcr-Abl tyrosine kinase, responsible for blocking the signal that tells the body to stop producing white blood cells.

Diagnosis of CML

The Ph chromosome is detected in approximately 95% of patients with CML and is the hallmark of the disease. At the time of diagnosis, CML patients typically have a significantly elevated white blood cell count.

A Primary Goal of Therapy: The Elimination of the Ph Chromosome

As CML is caused by a genetic abnormality, the Ph chromosome, elimination of this chromosome is a primary goal of therapy. This is considered a complete cytogenetic response (CCR). A direct association between cytogenetic response and

prolonged survival has been demonstrated for various CML therapies. Controlling the signs and symptoms of CML, reducing the number of white cells and preventing the progression of CML to the terminal phases are other important treatment objectives.

The efficacy of CML treatment is measured by two standard criteria: hematologic response and cytogenetic response.

Hematologic Response

A complete hematologic response refers to the normalization of blood counts, lasting for at least four weeks, effectively identifying the degree to which the most apparent abnormality in CML (i.e., proliferation of white blood cells) is controlled. During a hematologic response, the Ph chromosome positive (Ph+) cells may still be present.

Cytogenetic Response

A cytogenetic response, traditionally regarded by researchers as compelling evidence that a particular treatment is effective, is the disappearance or reduction of the number Ph+ cells detectable by standard lab methods. This is an indicator of the degree to which the underlying cause of the disease itself is controlled.

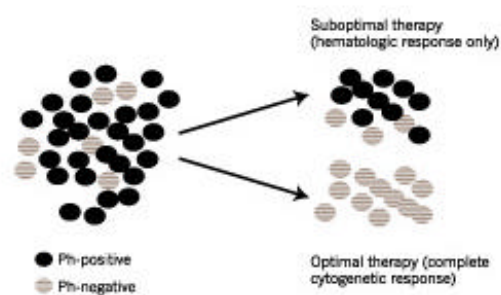


Figure 2: Hematologic vs. Cytogenetic Responses

Molecular Response

For patients who have achieved CCR, more sensitive measurement of minimal residual disease may be desired. There is a relatively new technique, called Polymerase Chain Reaction (PCR), which measures the level of Bcr-Abl transcripts at a molecular level. Achievement of a molecular response (near absence of disease by this more sensitive assay) may represent a possible new therapeutic benchmark in the future.