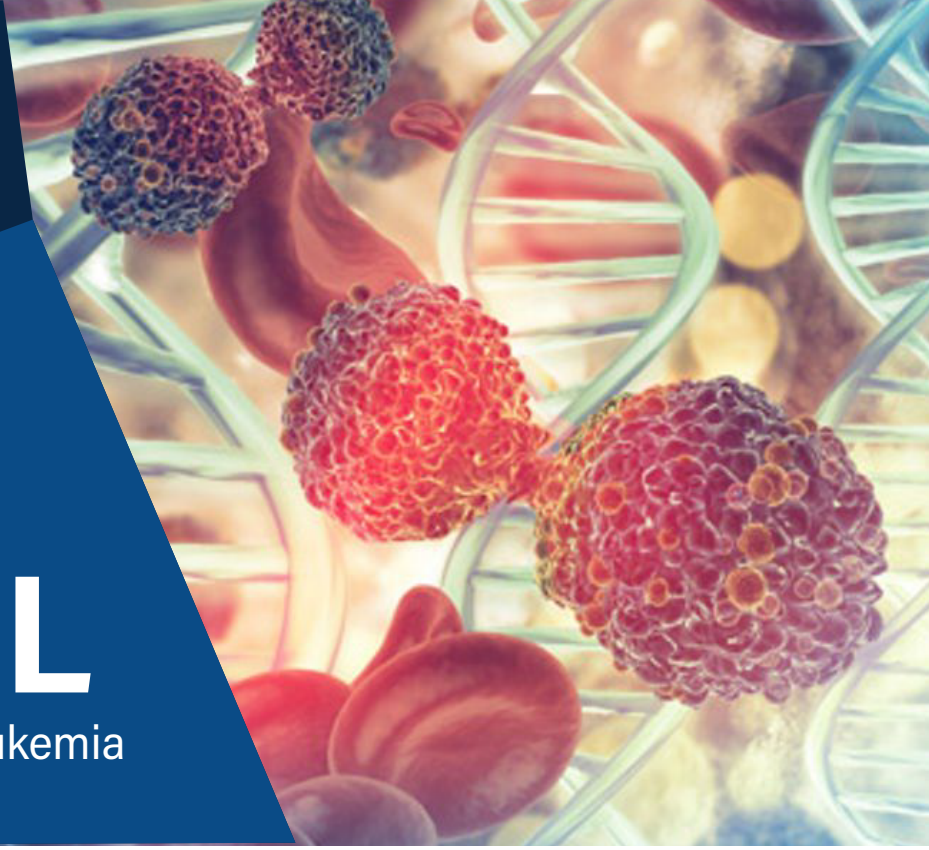
RML
MEHROTRA PATHOLOGY
Committed To Diagnostic Excellence

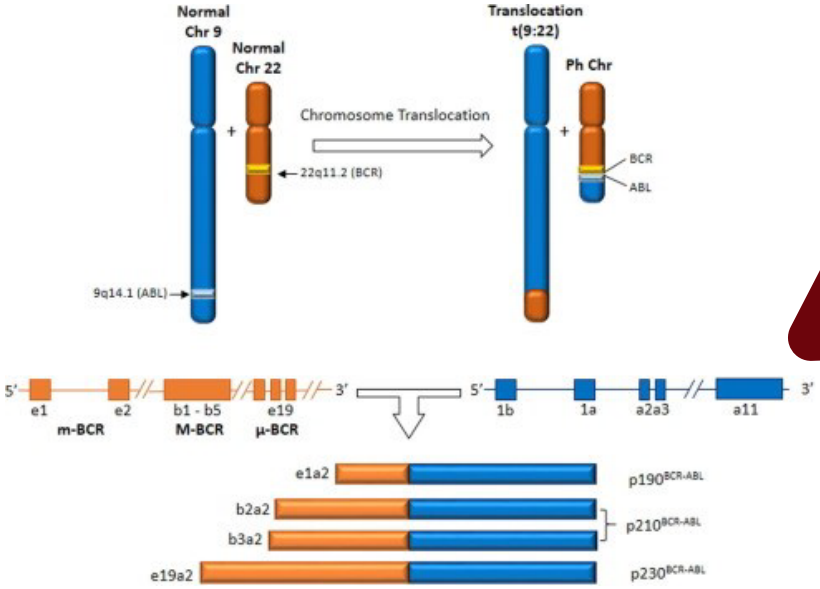


BCR-ABL

RNA PCR Quantitation for Leukemia

Background:

Chronic myeloid leukemia (CML) is a clonal hematologic stem cell malignancy associated, in greater than 90% of cases, with the Philadelphia chromosome (Ph), a reciprocal translocation between the long arms of chromosomes 9 and 22 [t(9;22)(q34;q11)].



The percentage reading on IS interpreted as follows:

- **<1% correlates with the level of complete cytogenetic response (CCgR)**
- **< 0.1% or 3 log reduction is equivalent to major molecular response (MMR) which is the therapeutic target in the CML**
- **Undetected transcript level represents a 4 log reduction or greater improvement.**

The BCR-ABL fusion gene is transcribed and translated into a 210 kD (p210) or 190 kD (p190) BCR-ABL fusion product with dysregulated (significantly enhanced) tyrosine kinase activity.

Major gene rearrangements are detected in chronic myeloid leukemia (CML) while minor gene arrangement may be detected in acute lymphoblastic leukemia (ALL).

Targeted inhibition of BCR-ABL with tyrosine kinase inhibitors (imatinib, dasatinib, nilotinib) is the standard treatment for CML (and Ph+ ALL). The efficacy of TKI therapy is routinely monitored with serial BCR-ABL RNA PCR's, which define the "molecular response". A consensus treatment goal is the achievement of "major molecular response", a 3-log drop in BCR-ABL RNA, defined as 0.1% on the BCR-ABL RNA PCR international scale (IS) of measurement.

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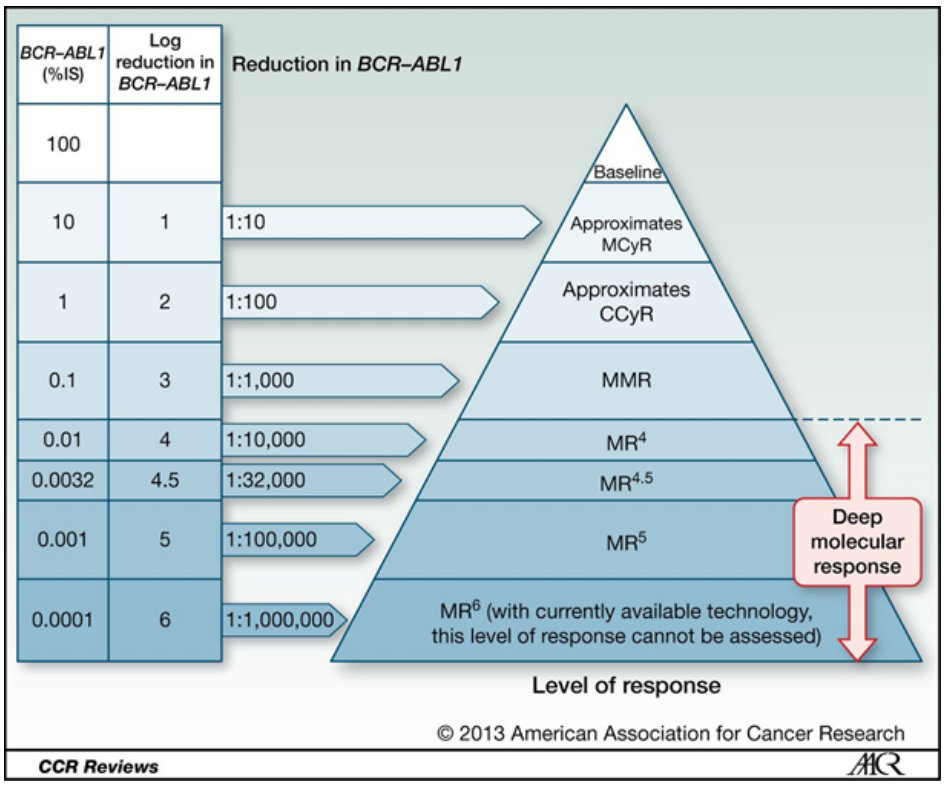
Levels of molecular response in CML. MCyR, major cytogenetic response; MR, molecular response.



ABBREVIATION	FULL FORM	INFERENCE
CHR	Complete Hematological Respose	Blood counts returning to normal values
MCyR	Major Cytogenetic Respose	Ph Chromosome 1-35% on FISH
CCyR	Complete Cytogenetic Respose	Ph Chromosome 0% on FISH
MMR	Major Molecular Respose	BCR-ABLIS <0.1
MR4	Molecular Respose	Molecular Respose with 4 Log reduction
MR4.5	Molecular Respose	Molecular Respose with 4.5 Log reduction (Deep MR)
MR5	Molecular Respose	Molecular Respose with 5 Log reduction

Clinical Utility:

The quantitative BCR-ABL RNA assay is intended to monitor the level of minimal residual disease in TKI-treated Philadelphia chromosome positive leukemias (CML or ALL). High or rising BCR-ABL RNA levels have been shown to increase the risk of leukemic relapse and drug-resistance mutations during TKI therapy. The failure to achieve a “major molecular response”, a 3-log drop in BCR-ABL RNA, defined as 0.1% on the BCR-ABL RNA PCR international scale (IS), is the consensus definition of a “sub-optimal” treatment that requires an alternative treatment approach. This BCR-ABL RNA PCR assay has been calibrated to the International Scale, and we are reporting the results on the IS.

Methodology:

By measuring BCR-ABL RNA levels using a sensitive real-time fluorescent PCR method, we are able to detect the presence of leukemic cells at a very low level. The sensitivity limit of the assay is approximately 1 tumor cell in 100,000 normal cells.

Turn Around :

3 Days

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