

*BloodCenter of Wisconsin
Molecular Diagnostics Laboratory offers
sensitive detection of BCR-ABL reported on the International Scale.*

BACKGROUND:

The Philadelphia chromosome, t(9;22), is found in >95% of patients with CML. It is also found in 10-20% of adults and 2-5% of children with ALL and more rarely in AML, lymphoma and myeloma. In the majority of cases the breakpoint is located in the major breakpoint cluster region resulting either the b3a2 (e14a2) or b2a2 (e13a2) variants that give rise to the p210 BCR-ABL protein. The minor breakpoint, e1a2, is more common in Ph+ ALL and gives rise to the p190 BCR-ABL protein. The BCR-ABL protein has increased tyrosine kinase activity that is implicated in the malignant transformation of hematopoietic cells. Other rare breakpoints have been reported (b3a3, b2a3, e1a3) but are not detected by this quantitative assay. These rare breakpoints can be detected with the BCR-ABL Breakpoint Analysis.

CLINICAL UTILITY

The quantitative BCR-ABL RNA assay is used to monitor minimal residual disease in Philadelphia chromosome-positive CML or ALL patients being treated with tyrosine kinase inhibitors (TKI). Levels of BCR-ABL are reported on a standardized International Scale (IS). On the IS, a major molecular response (MMR) represents a 3-log reduction in BCR-ABL and is defined as $\leq 0.1\%IS$. Achievement of MMR is associated with durable long term cytogenetic remission and a lower rate of disease progression. High or rising BCR-ABL levels may indicate the possible relapse or the presence of TKI-resistant mutations.

REASONS FOR REFERRAL:

- Quantitative minimal residual disease detection in CML.
- Monitoring tyrosine kinase inhibitor therapy.
- BCR-ABL Breakpoint Analysis (Separate order)

METHOD:

Reverse transcription of total RNA followed by real-time polymerase chain reaction to measure the b3a2, b2a2, and e1a2 BCR-ABL fusion transcripts using gene-specific hydrolysis probes. Endogenous ABL is used as a reference to report a percent relative ratio of BCR-ABL to ABL as well as to assess RNA quality. The percent BCR-ABL results are converted to the International Scale (IS) using a calibrator. Sensitivity is 0.003%IS (4.5 log reduction). Alternate breakpoints are not detected by the quantitative assay. BCR-ABL breakpoint is performed using capillary electrophoresis. Breakpoints detected are: b3a2, b2a2, e1a2, b3a3, b2a3 and e1a3.

SPECIMEN REQUIREMENTS:

10 ml of peripheral blood drawn in EDTA (lavender top) tubes. Bone marrow is also an acceptable sample, but a minimum of 3-5 ml is required. Sample should be shipped at room temperature and must be received within 48 hours of being drawn.

SHIPPING REQUIREMENTS:

Ship at room temperature. Place specimen and Molecular Diagnostics Laboratory test requisition into plastic bags and seal. Place in a Styrofoam container and seal; and then into a sturdy cardboard box and tape securely. Ship the package in compliance with your overnight carrier guidelines. Package must not arrive on weekends and holidays. Label with the following address:

Client Services/Molecular Diagnostics Laboratory
BloodCenter of Wisconsin
638 N.18th Street
Milwaukee, WI 53233-2121
800-245-3117 ext. 6250

TURNAROUND TIME: 3-6 days

BCR-ABL Quantitative Analysis:

Reference Interval: Not detected.
Positive Percent BCR-ABL: ABL ratio will be reported.
Percent International Scale (%IS) will be reported.
Log-Fold Reduction will be reported.
CPT Codes: 81206

BCR-ABL Breakpoint Analysis:

Reference Interval: Not detected.
Positive: b3a2, b2a2, e1a2 b3a3, b2a3 and e1a3 transcripts detected.
CPT Codes: 81479

REFERENCES:

- Hughes T, Hochhaus A, Branford S, et al. Long-term prognostic significance of early molecular response to imatinib in newly diagnosed chronic myeloid leukemia: an analysis from the International Randomized Study of Interferon and STI571 (IRIS). *Blood* 2010; 116:3758-3765
- Press RD, Love Z, Tronnes AA, et al. BCR-ABL mRNA levels at and after the time of a complete cytogenetic response (CCR) predict the duration of CCR in imatinib mesylate-treated patients with CML. *Blood* 2006; 107:4250-4256
- NCCN Guidelines; Chronic Myelogenous Leukemia http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf