BLOODCENTER of WISCONSIN™

BCR-ABL KINASE MUTATION ANALYSIS

BloodCenter of Wisconsin Molecular Diagnostics Laboratory offers DNA sequence analysis for the identification of BCR-ABL kinase domain mutations.

BACKGROUND:

A significant number of patients on tyrosine kinase inhibitor therapy develop resistance to the drug. Resistance can be caused by a number of mechanisms but mutations in the BCR-ABL kinase domain (KD) are frequently observed in patients with late stage disease, resistance to therapy and loss of therapeutic response. Identification of KD mutations can assist physicians with developing an appropriate therapeutic strategy for their patients by indicating whether a higher dose of imatinib, use of dasatinib or nilotinib or other therapies might be more beneficial. If KD mutations are not present, testing for other mechanisms of resistance can be considered.

REASONS FOR REFERRAL:

- Chronic phase patients with an inadequate response to tyrosine kinase inhibitors.
- Loss of response as indicated by a rise in BCR-ABL levels of at least 5-fold that has been confirmed by more than one test.
- Disease progression to accelerated or blast crisis.

BCR-ABL kinase mutation analysis can be ordered separately or in conjunction with quantitative BCR-ABL analysis.

METHOD:

RT-PCR of the major and minor BCR-ABL breakpoints followed by DNA sequence analysis of ABL kinase domain covering amino acids 236-486. This region covers all the reported kinase domain mutations.

LIMITATIONS:

Sensitivity of mutation detection is approximately 20%. The clinical significance of mutations present at <20% is not clear. Only mutations located in the analyzed exons are detected. Rare polymorphisms within primer or probe regions may interfere with detection of gene variants. Other mechanisms of drug resistance are not detected by this assay.

REFERENCE INTERVAL:

Negative, Positive

Heterozygous, Homozygous

PO Box 2178
Milwaukee, WI 53201-2178
Location/Sample Deliveries:
638 N. 18th St. Milwaukee, WI 53233-2121
p800-245-3117 | f414-937-6202 | www.bcw.edu

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

SHIPPING REQUIREMENTS:
Place the room temperature specimen and requisition in plastic bags, seal and insert in a Styrofoam container. Seal the Styrofoam container, place in 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. Address package to:

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

TURNAROUND TIME: 10-14 days

CPT CODES: 81403

REFERENCES:
Hughes, T. et al (2006) Monitoring CML patients responding to treatment with tyrosine kinase inhibitors: review and recommendations for harmonizing current methodology for detecting BCR-ABL transcripts and kinase domain mutations and for expressing results. Blood 108: 28-37.

NCCN Clinical Practice Guidelines in Oncology: Chronic Myelogenous Leukemia (2013) http://www.nccn.org/professionals/physician_gls/pdf/cml.pdf

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