



Laboratory Service Manual

Lab Dept: Anatomic Pathology

Test Name: BCR-ABL, TYROSINE KINASE INHIBITOR RESISTANCE, KINASE DOMAIN MUTATION SCREEN

General Information

Lab Order Codes: BCRM

Synonyms: BCR/ABL Mutation, ASPE; E255K; E355G; F317L; F369V; G250E; H396R; M244V; M351T; Q252H; T315I; Y253F; Y253H.

CPT Codes: 83914 x8 – Molecular diagnostics; mutation identification enzymatic ligation or primer extension, single segment, each segment.

83894 x2 – Molecular diagnostics; separation by gel electrophoresis.

83896 x8 – Molecular diagnostics; nucleic acid probe, each.

83898 x2 – Molecular diagnostics; amplification, target, each nucleic acid sequences

83909 – Molecular diagnostics; separation and identification by high-resolution technique.

83902 – Molecular diagnostics; reverse transcription

83891 – Molecular diagnostics; isolation or extraction of highly purified nucleic acid

Test Includes: Detect the presence of acquired BCR/ABL mutation associated with TKI-resistance.

Logistics



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Test Indications:

Useful for evaluating patients with chronic myeloid leukemia and Philadelphia chromosome positive B-cell acute lymphoblastic leukemia receiving tyrosine kinase inhibitor (TKI), therapy, who are apparently failing treatment.

Chronic myeloid leukemia (CML) is characterized by the presence of the t(9:22) BCR-ABL abnormality, resulting in formation of a fusion NCR-ALB mRNA and protein. The ABL component of this oncoprotein contains tyrosine kinase activity and is thought to play a central role in the proliferative phenotype of this leukemia.

Recognition of TKI resistance is important in CML, as the effect of some mutations can be overcome by increasing imatinib dosage, whereas others require switching to either a different (second generation) TKI, or alternative therapy. The common T315I KD mutation is particularly important, given that this alteration confers pan-resistance to all currently employed TKIs. Typically, TKI resistance is suspected in a CML patient who shows loss of initial therapeutic response or a significant and sustained increase in molecular BCR-ABL quantitative levels. Similar considerations are also present in patients with Philadelphia chromosome positive (Ph) B-cell acute lymphoblastic leukemia (ALL) who can also be treated using TKI therapy.

Lab Testing Sections:

Anatomic Pathology – Sendouts

Referred to:

Mayo Medical Laboratories (MML Test#: 89609)

Phone Numbers:

Minneapolis: 612-813-6280

Saint Paul: 651-220-6550

Test Availability:

Daily, 24 hours

Turnaround Time:

Results are reported in 3-5 days, testing performed Monday - Friday

Special Instructions:

Complete and submit "[MayoConnect Additional Test Information Form](#)" with the specimen. Include information: patient's name, referring (ordering) physician, specimen submitted, patient fusion type (p190 or P210), clinical morphologic suspicion & pertinent clinical history.

If BCR/ABL fusion type (p190 or p210) is not provided, BCR-ABL RNA Qualitative Mayo test #89006 will be performed.

Specimen**Specimen Type:**

Whole blood or Bone marrow

Container:

Lavender top (EDTA) tube



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Draw Volume:	3 mL blood 2 mL bone marrow
Processed Volume:	Same as Draw Volume
Collection:	Routine venipuncture; Routine bone marrow collection.
Special Processing:	Lab Staff: Do Not Centrifuge. Specimen should remain in the original collection container. Label specimen appropriately (blood or bone marrow). Store and ship at room temperature. Forward promptly. Specimen must arrive at Mayo within 72 hours of collection.
Patient Preparation:	None
Sample Rejection:	Mislabeled or unlabeled specimens; specimen other than blood or bone marrow; specimen >3 days old

Interpretive

Reference Range:	Interpretive report The presence of one or more point mutations in the translocated portion of the ABL region of the BCR-ABL fusion mRNA is considered a positive result, indicating TKI (eg, imatinib) resistance.
Critical Values:	N/A
Limitations:	This assay does not detect all possible KD mutations; thus, a negative result by this assay does not exclude the presence of a rare, less well characterized or unknown mutation that could be associated with some degree of TKI resistance. The clinical significance of such rarely occurring mutation is, however, uncertain.
Methodology:	Reverse Transcription-Polymerase Chain Reaction (RT-PCR) with Fluorescent-Bead Array Analysis Allele-Specific Primer Extension (ASPE) and Detection by Luminex Bead Array.
References:	Mayo Medical Laboratories July 2009