## 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:** 81170 – ABL1, gene analysis, variants in the kinase domain

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

### *Logistics*

**Test Indications:** Useful for evaluating patients with chronic myeloid leukemia and Philadelphia chromosome positive B-cell acute lyphoblastic 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.

See the BCR/ABL1 Ordering Guide for Blood and Bone Marrow on the Mayo Medical Laboratories website.

**Lab Testing Sections:** Anatomic Pathology – Sendouts

**Referred to:** Mayo Medical Laboratories (MML Test#: BAKDM)

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| **Phone Numbers:** | MIN Lab: 612-813-6280<br><br>STP Lab: 651-220-6550 |
| **Test Availability:** | Daily, 24 hours |
| **Turnaround Time:** | Results are reported in 5 days, testing performed Monday - Friday |
| **Special Instructions:** | Provider to complete and submit a MCL- Hematopathology Patient Information - MC1235-175 (mayocliniclabs.com) with the specimen. Include the following information: patient's name, referring (ordering) physician, specimen submitted, **patient fusion type (p190, P210, p185, p230)**, clinical morphologic suspicion & pertinent clinical history.<br><br>If BCR/ABL fusion type is not provided, BCR-ABL RNA Qualitative Mayo test BADX will be performed at an additional charge. |

## *Specimen*

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| **Specimen Type:** | Whole blood or Bone marrow |
| **Container:** | Blood: Lavender top (EDTA) tube<br><br>Bone marrow: Dry syringe immediately transferred to EDTA tube |
| **Draw Volume:** | Blood: 10 mL (Minimum: 8 mL)<br>Bone marrow: 4 mL (Minimum: 2 mL) |
| **Processed Volume:** | Same as Draw Volume |
| **Collection:** | Routine venipuncture<br><br>Routine bone marrow collection, specimen collected in dry syringe and **immediately** transferred to EDTA tube. |
| **Special Processing:** | Lab Staff: Do Not Centrifuge. Specimen should remain in the collection container. Label with specimen type (blood or bone marrow). Store and ship at refrigerated temperatures. Forward promptly**.**<br><br>Specimens are stable refrigerated (preferred) for 120 hours (5 days) from time of collection and ambient specimens must arrive within 3 days (72 hours) of collection. |
| **Patient Preparation:** | None |
| **Sample Rejection:** | Mislabeled or unlabeled specimens; specimen other than blood or bone marrow; specimens past stability timeframe; specimens in unacceptable containers/anticoagulant; gross hemolysis; moderately or severely clotted specimens. |

***Interpretive***

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| **Reference Range:** | Interpretive report<br><br>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 March 2023 |
| **Updates:** | 1/29/2013: CPT 2013 update<br>10/20/2015: Storage/shipping and change, previously ambient. Stability increase, previously 3 days.<br>1/28/2016: CPT update<br>4/27/2022: Volume update per Mayo<br>3/16/23: Added specimen stability and additional causes for rejection, updated volume requirements, fixed link to Mayo's Hematopathology request form |