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.
Lab Testing Sections:	Anatomic Pathology – Sendouts
Referred to:	Mayo Medical Laboratories (MML Test#: BAKDM)
Phone Numbers:	MIN Lab: 612-813-6280

	STP Lab: 651-220-6550
Test Availability:	Daily, 24 hours
Turnaround Time:	Results are reported in 5 days, testing performed Monday - Friday
Special Instructions:	Complete and submit a Hematopathology Patient Information Sheet, Supply T676 with the specimen. Include information: patient's name, referring (ordering) physician, specimen submitted, patient fusion type (p190, P210, p185, p230), clinical morphologic suspicion & pertinent clinical history. If BCR/ABL fusion type is not provided, BCR-ABL RNA Qualitative Mayo test BADX will be performed at an additional charge.

Specimen

Specimen Type:	Whole blood or Bone marrow
Container:	Lavender top (EDTA) tube
Draw Volume:	Blood: 3 mL (Minimum: 1 mL) Bone marrow: 2 mL (Minimum: 1 mL)
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 refrigerated temperatures. Forward promptly**.** **Specimen must arrive at Mayo within 120 hours of collection.**
Patient Preparation:	None
Sample Rejection:	Mislabeled or unlabeled specimens; specimen other than blood or bone marrow; specimen >5 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 September 2013
Updates:	1/29/2013: CPT 2013 update 10/20/2015: Storage/shipping and change, previously ambient. Stability increase, previously 3 days. 1/28/2016: CPT update