MAYO CLINIC LABORATORIES

Test Definition: BCRAB

BCR/ABL1, p210, mRNA Detection, Reverse Transcription-PCR (RT-PCR), Quantitative, Monitoring Chronic Myeloid Leukemia (CML), Varies

Overview

Useful For

Monitoring response to therapy in patients with chronic myeloid leukemia who are known to have the e13/a2 or e14/a2 *BCR/ABL1* fusion transcript forms

Testing Algorithm

For information see *BCR/ABL1* Ordering Guide for Blood and Bone Marrow.

Special Instructions

- Hematopathology Patient Information
- BCR/ABL1 Ordering Guide for Blood and Bone Marrow

Method Name

Quantitative Reverse Transcription-Polymerase Chain Reaction (RT-PCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

Specimen must arrive within 72 hours of collection. Collect and package specimen as close to shipping time as possible. Specimens greater than 3 days old at the time of receipt will be considered unacceptable.

Necessary Information

Pertinent clinical history including if the patient has a diagnosis of chronic myeloid leukemia or other BCR/ABL1-positive neoplasm information is required.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA)

Acceptable: Yellow top (ACD)
Specimen Volume: 10 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**
3. Label specimen as blood.

Specimen Type: Bone marrow
Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD)
Specimen Volume: 3 mL
Collection Instructions:
1. Invert several times to mix bone marrow.
2. Send bone marrow specimen in original tube. **Do not aliquot.**
3. Label specimen as bone marrow.

Forms

1. Hematopathology Patient Information (T676)
2. If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Specimen Minimum Volume

Blood: 4 mL
Bone marrow: 1 mL

Reject Due To

Gross hemolysis	Reject
Moderately to severely clotted	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Refrigerated (preferred)	72 hours	PURPLE OR PINK TOP/EDTA
	Ambient	72 hours	PURPLE OR PINK TOP/EDTA

Clinical & Interpretive

Clinical Information

Chronic myeloid leukemia (CML) is a hematopoietic stem cell neoplasm included in the broader diagnostic category of myeloproliferative neoplasms. CML is consistently associated with fusion of the breakpoint cluster region gene (*BCR*) at chromosome 22q11 to the Abelson gene (*ABL1*) at chromosome 9q23. This fusion is designated *BCR/ABL1* and may be seen on routine karyotype as the Philadelphia chromosome.

Although various breakpoints within the *BCR* and *ABL1* genes have been described, more than 95% of CMLs contain a consistent mRNA transcript in which either the *BCR* exon 13 (e13) or *BCR* exon 14 (e14) is fused to the *ABL1* exon 2 (a2), yielding fusion forms e13/a2 and e14/a2, respectively. The e13/a2 and e14/a2 fusion forms produce a 210-kDa protein (p210). The p210 fusion protein is an abnormal tyrosine kinase known to be critical for the clinical and pathologic features of CML, and agents that block the tyrosine kinase activity (ie, tyrosine kinase inhibitors or TKI, such as imatinib mesylate) have been used successfully for treatment. Monitoring the level of *BCR/ABL1* mRNA in CML patients during treatment is helpful for both prognosis and management of therapy.(1-3) Rising *BCR/ABL1* mRNA levels following attainment of critical therapeutic milestones (see Clinical References) can be indicative of acquired resistance mutations involving the *ABL1* portion of the *BCR/ABL1* fusion gene.

Quantitative reverse-transcription polymerase chain reaction is the most sensitive method for monitoring *BCR-ABL1* levels during treatment. This test detects the *BCR/ABL1* mRNA fusion forms found in CML (e13/a2 and e14/a2).

Reference Values

The presence or absence of *BCR/ABL1* mRNA fusion form e13/e14-a2 producing the p210 fusion protein is identified. If positive, the quantitative level is reported as the normalized ratio of *BCR/ABL1* (p210) to endogenous *ABL1* mRNA with conversion to a percentage referenced to the international scale (IS), on which 0.1% BCR/ABL1:ABL1 (also represented on a log scale as Molecular Response 3, or MR3) is designated as a major molecular response (MMR) threshold.

Interpretation

An interpretive report will be provided. When *BCR/ABL1* mRNA is present, quantitative results are reported on the international scale (IS), established from data originally reported in the IRIS (International Randomized Study of Interferon versus STI571) trial involving newly diagnosed chronic myeloid leukemia patients. Using the IS, a result of less than 0.1% *BCR/ABL1* (p210):*ABL1* is equivalent to a major molecular remission. This value is also designated on a log scale (Molecular Response, MR) as MR3. For further discussion of the international scale, see Clinical References.

Cautions

This test detects only the e13/a2 and e14/a2 fusion forms, which code for the p210 protein. Other fusion forms are not detected, including those containing the *BCR* e1 exon, which codes for the p190 protein commonly found in acute lymphoblastic leukemia (ALL). If the patient is known to carry an e1/a2 (p190) fusion form, the test BA190 / *BCR/ABL*, p190, mRNA Detection, Reverse Transcription-PCR (RT-PCR), Quantitative, Monitoring Assay, Varies should be used for monitoring.

This test should not be used to screen for *BCR/ABL1* fusions at the time of diagnosis; if a diagnostic screen for *BCR-ABL1* transcripts is desired, the test BADX / *BCR/ABL1*, Qualitative, Diagnostic Assay, Varies which is designed to detect all reported common and rare *BCR-ABL1* mRNA fusion variants, should be ordered for this purpose.

The precision of this assay at low *BCR/ABL1* levels is more variable, such that inter-run variation can be as high as + or - 0.5 log. Only level changes above 0.5 log should be considered clinically significant. For example, if a result is given as 0.1% *BCR/ABL1:ABL1,* then any result between 0.05% and 0.5% should be considered essentially equivalent. If the results are being used to make major therapeutic decisions, significant changes during monitoring should be verified with a subsequent specimen.

In general, the results of this assay cannot be directly compared with results generated from other polymerase chain reaction (PCR) assays, including identical assays performed in other laboratories. Monitoring should be performed using the same method and laboratory for each subsequent specimen.

The results of this assay cannot be directly compared with *BCR/ABL1* results obtained using FISH technology. FISH measures DNA alleles and RT-PCR-based assays measure mRNA transcripts. Because a single fusion DNA allele can produce many mRNA transcripts, the values are not directly comparable and FISH results are not applicable to the IS or to disease monitoring.

Blood is the specimen of choice for monitoring CML patients. The majority of CML patients show similar *BCR/ABL1* mRNA levels in blood and bone marrow drawn at the same time, although occasional, patients may exhibit a difference in concurrent blood and marrow levels for technical or biological reasons, requiring follow-up testing to resolve.

Clinical Reference

1. Hughes TP, Kaeda J, Branford S, et al. Frequency of major molecular responses to imatinib or interferon alfa plus cytarabine in newly diagnosed chronic myeloid leukemia. N Engl J Med. 2003;349(15):1423-1432
2. Baccarini M, Deininger MW, Rosti G, et al. European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. Blood. 2013;122(6):872-884
3. Press RD, Kamel-Reid S, Ang D. BCR-ABL1 RT-qPCR for monitoring the molecular response to tyrosine kinase inhibitors in chronic myeloid leukemia. J Mol Diagn. 2013;15(5):565-576
4. Cross NC, White HE, Muller MC, Saglio G, Hochhaus A. Standardized definitions of molecular response in chronic myeloid leukemia. Leukemia. 2012;26(10):2172-2175
5. Shah NP, Bhatia R, Altman JK, et al. Chronic Myeloid Leukemia, Version 2.2024, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2024;22(1):43-69. doi:10.6004/jnccn.2024.0007

Performance

Method Description

The assay is performed using an automated platform, GeneXpert (Cepheid). Four mL of whole blood is processed, added to an individual sample cartridge and loaded onto the GeneXpert machine. All subsequent reactions are performed within the cartridge and the results are processed and calculated by the instrument. Within the cartridge, RNA is extracted and converted to complementary DNA (cDNA).

Quantitative, reverse transcription polymerase chain reaction (PCR) is performed with a nested PCR reaction containing primers designed to amplify cDNA from the e13/a2 and e14/a2 *BCR/ABL1* fusion products. A fragment of *ABL1* cDNA is also amplified as a control for RNA degradation and for normalization of *BCR/ABL1* results. The ratio of *BCR/ABL1* (p210) to *ABL1* is calculated from the difference in the crossing thresholds of *BCR/ABL1* (p210) and *ABL1* products in relation to a lot-specific standard curve, referenced to the international scale (IS). Lot-to-lot variation in the cartridges is corrected using a calibration calculation to reference standard curve data to the IS provided by the manufacturer.(Unpublished Mayo method)

PDF Report
Supplemental

Day(s) Performed
Monday through Saturday

Report Available
3 to 6 days

Specimen Retention Time
2 weeks

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their account representative. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
81206

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
BCRAB	BCR/ABL1, p210, Quant, Monitor	55135-8

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Result ID	Test Result Name	Result LOINC® Value
MP003	Specimen Type	31208-2
19598	Final Diagnosis:	34574-4
48411	BCR/ABL1, p210 Result	55135-8