MAYO CLINIC LABORATORIES

Test Definition: P210M

BCR::ABL1, p210, mRNA Detection, Reverse Transcription-PCR (RT-PCR), Quantitative, Monitoring Chronic Myeloid Leukemia (CML), Bone Marrow

Overview

Useful For
Monitoring response to therapy in patients with chronic myeloid leukemia who are known to have the e13a2 or e14a2 *BCR::ABL1* fusion transcript forms

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

NY State Available
No

Specimen

Specimen Type
Bone Marrow

Ordering Guidance
This test detects only the e13a2 and e14a2 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 e1a2 (p190) fusion form, the test that should be used for monitoring is BA190 / *BCR*::*ABL*, p190, mRNA Detection, Reverse Transcription-PCR (RT-PCR), Quantitative, Monitoring Assay, Varies.

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, order BADX / *BCR*::*ABL1*, Qualitative, Diagnostic Assay, Varies, which is designed to detect all reported common and rare *BCR::ABL1* mRNA fusion variants.

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
The following information is required:
1. Pertinent clinical history including if the patient has a diagnosis of chronic myeloid leukemia or other *BCR*::*ABL1*-positive neoplasm
2. Date of collection

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Specimen Required

Container/Tube:

Preferred: Lavender top (EDTA)

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.

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Bone Marrow	Refrigerated (preferred)	72 hours	PURPLE TOP/EDTA
	Ambient	72 hours	PURPLE 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 CML cases contain a consistent messenger RNA (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 e13a2 and e14a2, respectively. The e13a2 and e14a2 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 [TKI], such as imatinib mesylate) have been used successfully for treatment. Monitoring the level of *BCR::ABL1* mRNA in patients with CML during their treatment is helpful for both prognosis and management of therapy.(1-3) Rising *BCR::ABL1* mRNA levels following attainment of critical therapeutic milestones can be indicative of acquired resistance variants 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 (e13a2 and e14a2).

Reference Values

An interpretive report will be provided.

Interpretation

When *BCR::ABL1* messenger RNA (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 response. This value is also designated on a log scale (molecular response [MR]) as MR3. For additional discussion of the international scale, see Clinical References.

Cautions

The precision of this assay at low *BCR::ABL1* levels is more variable, such that interassay 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 fluorescence in situ hybridization (FISH) technology. FISH measures DNA alleles and reverse transcription PCR-based assays measure messenger RNA (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 international scale or to disease monitoring.

Blood is the specimen of choice for monitoring patients with chronic myeloid leukemia (CML). The majority of patients with CML show similar *BCR::ABL1* mRNA levels in blood and bone marrow collected at the same time. Although occasionally, 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. Baccarani M, Deininger MW, Rosti G, et al. European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. Blood. 2013;122(6):872-884. doi:10.1182/blood-2013-05-501569
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. doi:10.1016/j.jmoldx.2013.04.007

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. doi:10.1038/leu.2012.104
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). Bone marrow 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 e13a2 and e14a2 *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 Friday

Report Available

1 to 8 days

Specimen Retention Time

2 weeks

Performing Laboratory Location

Mayo Clinic Jacksonville Clinical Lab

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 has been modified from the manufacturer's instructions. Its performance characteristics were determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

81206-BCR::ABL1 (t[9;22]) (eg, chronic myelogenous leukemia) translocation analysis; major breakpoint, qualitative or quantitative

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
P210M	BCR/ABL1 p210, Quant, Monitor, BM	55135-8

Result ID	Test Result Name	Result LOINC® Value
623207	Indication for Testing	42349-1
623208	Specimen	31208-2
623278	Source	31208-2
623209	Sample ID	80398-1
623210	Result	82939-0
621762	Interpretation	59465-5
623211	Method Summary	85069-3
623212	Disclaimer	62364-5
621763	Signing Pathologist	19139-5