MAYO CLINIC LABORATORIES

Test Definition: BCRFX

BCR::ABL1 Qualitative Diagnostic Assay with Reflex to BCR::ABL1 p190 Quantitative Assay or BCR::ABL1 p210 Quantitative Assay, Varies

Overview

Useful For

Initial diagnosis of *BCR::ABL1*-positive hematologic neoplasms (eg, chronic myeloid leukemia and acute lymphoblastic leukemia)

Detection and identification of *BCR::ABL1* fusion forms, including the common p210 (e13/e14a2) and p190 (e1a2) forms, as well as other rare fusion forms

Providing a baseline quantitative level of fusion forms p210 (e13/e14a2) or p190 (e1a2) when detected

This test **is not useful for** sensitive post-therapy measurable residual disease monitoring.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
B190R	BCR/ABL1, p190, Quant, Reflex	Yes, (order BA190) (Bill Only)	No
B210R	BCR/ABL1, p210, Quant, Reflex	Yes, (order BCRAB) (Bill Only)	No

Testing Algorithm

If the initial qualitative testing is negative, no additional testing will be performed.

If the initial qualitative testing is positive for the common p190 or p210 *BCR*::*ABL1* forms, reflex testing to determine the quantitative transcript level of the relevant messenger RNA will be performed at an additional charge. A normalized percentage of transcript level is provided in an integrated report. For the p210 target, the value is additionally defined using the international scale convention. These integrated results provide a baseline quantitative transcript to monitor treatment response.

If the initial qualitative testing is positive for an alternate rare form of *BCR*::*ABL1*, then BARQ / *BCR*::*ABL1* Rare Fusion Monitoring, Quantitative, Varies will be added and performed at an additional charge, with results reported separately.

For more information see:
-Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation
-Myeloproliferative Neoplasm: A Diagnostic Approach to Peripheral Blood Evaluation
-*BCR::ABL*1 Ordering Guide for Blood and Bone Marrow

Special Instructions

- Myeloproliferative Neoplasm: A Diagnostic Approach to Peripheral Blood Evaluation
- Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation

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

Highlights

Following a positive *BCR*::*ABL1* diagnostic reverse transcription polymerase chain reaction result, a reflex test will be performed to provide a quantitative measurement of *BCR*::*ABL1* messenger RNA (mRNA) transcript (either p190 or p210 types). Current National Comprehensive Cancer Network guidelines for chronic myeloid leukemia, for example, indicate that the quantitative p210 mRNA transcript level be obtained at diagnosis. The reflex test establishes the initial patient diagnostic baseline level to assess response to therapy in follow-up samples.

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test **is not indicated for** sensitive post-therapy measurable residual disease monitoring.

To monitor patients carrying *BCR::ABL1* fusion forms coding for p190 (e1a2), order BA190 / *BCR::ABL1*, p190 mRNA Detections, Reverse Transcription-PCR (RT-PCR), Quantitative, Monitoring Assay, Varies.

To monitor patients carrying *BCR::ABL1* fusion forms coding for p210 (e13/e14a2), order BCRAB / *BCR::ABL1*, p210, mRNA Detection, Reverse Transcription-PCR (RT-PCR), Quantitative, Monitoring Chronic Myeloid Leukemia (CML), Varies.

To monitor patients carrying rare *BCR::ABL1* fusion forms coding for e19a2, e13/e14a3, e1a3, e6a2, e19a3, e8a2, e12a2, e6a3, e8a3, and e12a3, order BARQ / *BCR::ABL1*, Rare Fusion Monitoring, Quantitative, Varies.

Shipping Instructions

Send specimen Monday through Friday only. Specimens must arrive within 72 hours of collection and by 10 a.m. Central time Saturday.

Specimens received after 10 a.m. Saturday or on Sunday may be canceled due to stability limitations.

Collect and package specimen as close to shipping time as possible.

Necessary Information

Pertinent clinical history including the patient diagnosis of chronic myeloid/myelogenous leukemia or other *BCR*::*ABL1* positive neoplasm **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 whole blood.

Specimen Type: Bone marrow
Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD)
Specimen Volume: 4 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

Whole blood: 8 mL; Bone marrow: 2 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

The t(9;22)/*BCR::ABL1* abnormality is associated with chronic myelogenous leukemia (CML) and "Philadelphia-positive" acute lymphoblastic leukemia of B-cell lineage (Ph+ ALL). Very rarely, this abnormality has also been identified in cases of acute myeloid leukemia and T-cell lymphoblastic leukemia/lymphoma. The fusion gene on the derivative chromosome 22q11 produces a chimeric *BCR::ABL1* messenger RNA (mRNA) transcript and corresponding translated oncoprotein. Despite substantial breakpoint heterogeneity at the DNA level, a consistent set of *BCR::ABL1* mRNA transcripts are produced that can be readily and sensitively detected by reverse transcription polymerase chain reaction (RT-PCR) technique. In CML, breakpoints in *BCR* result in either exons 13 or 14 (e13, e14) joined to exon 2 of *ABL1* (a2). The corresponding e13-a2 or e14-a2 *BCR::ABL1* mRNAs produce a 210 kDa protein (p210). Rare cases of CML are characterized by an e19-a2 type mRNA with a corresponding p230 protein. In Ph+ ALL, the majority of cases harbor an e1-a2 *BCR::ABL1* mRNA transcript, producing a p190 protein. However, chimeric mRNA type is not invariably associated with disease type, as noted by the presence of p210-positive Ph ALL and very rare cases of p190-positive CML. Therefore, positive results from a screening (diagnostic) assay for *BCR::ABL1* mRNA need to be correlated with clinical and pathologic findings.

In addition to the main transcript variants described above, rare occurrences of both CML and Ph+ ALL can have alternative break-fusion events resulting in unusual *BCR::ABL1* transcript types. Examples include e6-a2 and *BCR* exon fusions to *ABL1* exon a3 (eg, e13-a3, e14-a3, or e1-a3). In addition to detecting common *BCR::ABL1* mRNA transcripts, this assay also can identify these rarer *BCR::ABL1* transcript variants and is therefore a comprehensive screen for both usual and uncommon *BCR::ABL1* gene fusions in hematopoietic malignancies. Given the nature of genetic events in tumors however, this assay will not identify extremely rare and unexpected *BCR::ABL1* events involving other exons (eg, case report level) and is therefore not absolutely specific but is predicted to detect greater than 99.5% of *BCR::ABL1* events. Therefore, it is recommended that for diagnosis, RT-PCR plus a second method (eg, *BCR::ABL1* fluorescence in situ hybridization or cytogenetics) should be used. However, this RT-PCR assay is invaluable at diagnosis for identifying the precise *BCR::ABL1* mRNA type (eg, for future quantitative assay disease monitoring), which complementary methods cannot.

This assay is intended as a qualitative method, providing information on the presence (and specific mRNA type) or absence of the *BCR::ABL1* mRNA. Results from this test can be used to determine the correct subsequent assay for monitoring of transcript levels following therapy (eg, BCRAB / *BCR*::*ABL1*, p210, mRNA Detection, Reverse Transcription-PCR (RT-PCR), Quantitative, Monitoring Chronic Myeloid Leukemia (CML), Varies; BA190 / *BCR*::*ABL1*, p190, mRNA Detection, Reverse Transcription-PCR (RT-PCR), Quantitative, Monitoring Assay, Varies). Because the assay is analytically sensitive, it compensates for situations such as partially degraded RNA quality or low cell number, but it is not intended for quantitative or monitoring purposes.

Reference Values
An interpretive report will be provided.

Interpretation
An interpretive report will be provided.

When positive, the test identifies which specific messenger RNA fusion variant is present to guide selection of an appropriate monitoring assay. If common p210 or p190 fusion variant detected, quantitative reflex will be performed.
-Common fusion variants detected: e13-a2 or e14-a2 (p210), e1-a2 (p190), and e6-a2 (p205*)
-Rare fusion variants detected: e13-a3 (p210), e14-a3 (p210), e1-a3 (p190), e19-a2 (p230)
-Potential rare fusions detected: e12-a3, e19-a3
*This is formerly observed as the e6-a2 (p185) fusion form

Cautions
No significant cautionary statements

Clinical Reference
1. Burmeister T, Reinhardt R. A multiplex PCR for improved detection of typical and atypical BCR-ABL fusion transcripts. Leuk Res. 2008;32(4):579-585
2. Melo JV. The diversity of BCR-ABL fusion proteins and their relationship to leukemia phenotype. Blood. 1996;88(7):2375-2384
3. Melo JV. BCR-ABL gene variants. Baillieres Clin Haematol. 1997;10(2):203-222
4. 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
5. 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
6. Deininger MW, Shah NP, Altman JK, et al. Chronic Myeloid Leukemia, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2020;18(10):1385-1415. doi:10.6004/jnccn.2020.0047

Performance

Method Description
Total RNA is extracted from the patient's blood or bone marrow at the time of diagnosis and messenger RNA (mRNA) is reverse transcribed into complementary DNA (cDNA). The cDNA is then subjected to polymerase chain reaction (PCR) using 4 separate multiplex reactions. A qualitative result, which will include the relative ratio of target translocation mRNA to control *GUSB* gene mRNA, will be given by LightCycler 96 software. As this method employs a quantitative PCR platform, the results can be used to evaluate the relative expression levels of the translocation mRNA relative to control mRNA, thus providing an improved measure of RNA quality in the assay. Reporting of results will be qualitative; either *BCR::ABL1* mRNA positive/detected (with transcript type) or negative/not detected.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed
Monday through Saturday

Report Available
7 to 10 days

Specimen Retention Time
Whole blood/Bone marrow: 2 weeks; Extracted RNA: 3 months

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
81207
81208

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
BCRFX	BCR/ABL1 Reflex, Qual/Quant	In Process

Result ID	Test Result Name	Result LOINC® Value
MP039	Specimen Type	31208-2
48389	BCR/ABL1 Reflex Result	No LOINC Needed
48388	Interpretation	69047-9