

Overview

Useful For

Diagnostic workup of patients with a high probability of *BCR-ABL1*-positive hematopoietic neoplasms, predominantly chronic myeloid leukemia and acute lymphoblastic leukemia

Testing Algorithm

For more information see:

[-Myeloproliferative Neoplasm: A Diagnostic Approach to Bone Marrow Evaluation](#)

[-Myeloproliferative Neoplasm: A Diagnostic Approach to Peripheral Blood Evaluation](#)

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](#)

Method Name

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

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is only qualitative and should not be used for routine monitoring (ie, quantitative messenger RNA [mRNA] level).

Monitoring of most patients with chronic myeloid leukemia (CML) should be performed using BCRA B / *BCR/ABL*, p210, mRNA Detection, Reverse Transcription-PCR (RT-PCR), Quantitative, Monitoring Chronic Myelogenous Leukemia (CML), Varies.

Monitoring of patients known to carry a p190 fusion should be performed using BA190 / *BCR/ABL*, p190, mRNA Detection, Reverse Transcription-PCR (RT-PCR), Quantitative, Monitoring Assay, Varies.

For information on which test to order for various scenarios, see [BCR/ABL1 Ordering Guide for Blood and Bone Marrow](#)

Shipping Instructions

Refrigerate specimens must arrive within 5 days of collection, and ambient specimens must arrive with 3 days (72 hours) of collection. Collect and package specimens as close to shipping time as possible.

Necessary Information

The following information is required:

1. Pertinent clinical history including if the patient has a diagnosis of chronic myelogenous leukemia or other *BCR/ABL1*-positive neoplasm
2. Date of collection
3. Specimen source (blood or bone marrow)

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: 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.

Reject Due To

Gross hemolysis Reject
Other Moderately to severely clotted

Specimen Minimum Volume

Peripheral blood: 8 mL

Bone marrow: 2 mL

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Refrigerated (preferred)	5 days	PURPLE OR PINK TOP/EDTA
	Ambient		PURPLE OR PINK TOP/EDTA

Clinical & Interpretive

Clinical Information

The t(9;22)/*BCR-ABL1* abnormality is associated with chronic myeloid 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-lymphoblastic leukemia/lymphoma. The fusion gene on the derivative chromosome 22q11 produces a chimeric *BCR-ABL1* mRNA transcript and corresponding translated oncoprotein. Despite substantial breakpoint heterogeneity at the DNA level, a consistent set of *BCR-ABL1* messenger RNA (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 more 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 cannot be done by complementary methods.

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, BCRA190 / *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

A qualitative result is provided that indicates the presence or absence of *BCR/ABL1* messenger RNA. When positive, the fusion variant is also reported.

Interpretation

An interpretive report will be provided.

When positive, the test identifies the specific messenger RNA fusion variant present to guide selection of an appropriate monitoring assay.

Monitoring is available for common p210 or p190 fusion variant detected.

-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 Apr;32(4):579-585
2. Melo JV: The diversity of BCR-ABL fusion proteins and their relationship to leukemia phenotype. *Blood*. 1996 Oct 1;88(7):2375-2384
3. Melo JV: BCR-ABL gene variants. *Baillieres Clin Haematol*. 1997 Jun;10(2):203-222
4. [Tefferi A: The classic myeloproliferative neoplasms: Chronic myelogenous leukemia, polycythemia vera, essential thrombocythemia, and primary myelofibrosis. In: Valle DL, Antonarakis S, Ballabio A, Beaudet AL, Mitchell GA, eds. The Online Metabolic and Molecular Bases of Inherited Disease. McGraw-Hill; 2019, Accessed March 16, 2022. Available at https://ommbid.mhmedical.com/content.aspx?sectionid=225078035&bookid=2709](https://ommbid.mhmedical.com/content.aspx?sectionid=225078035&bookid=2709)

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 provided. Although 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

Specimen Retention Time

Blood/Bone marrow: 2 weeks; Extracted RNA: 3 months

Performing Laboratory Location

Rochester

Fees & Codes

Test Classification

This test was developed, and its performance characteristics 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

81207

81208

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
BADX	BCR/ABL1, RNA-Qual, Diagnostic	55135-8

Result ID	Reporting Name	LOINC®
MP001	Specimen Type	31208-2
19783	Interpretation	69047-9
39466	Diagnostic BCR/ABL1 Result	No LOINC Needed