Overview

Useful For
Diagnosis of acute promyelocytic leukemia (APL)
Detection of residual or recurrent APL
Monitoring the level of promyelocytic leukemia/retinoic acid receptor alpha (PML/RARA) in APL patients

Testing Algorithm
See Acute Promyelocytic Leukemia: Guideline to Diagnosis and Follow-up in Special Instructions.

Special Instructions
- Hematopathology Patient Information
- Acute Promyelocytic Leukemia: Guideline to Diagnosis and Follow-up

Method Name
Quantitative, Real-Time Polymerase Chain Reaction (PCR)

NY State Available
Yes

Specimen

Specimen Type
Varies

Advisory Information
This assay may not detect rare, unusual PML/RARA fusions. Therefore, if the assay is going to be used for monitoring after treatment, the test should be performed at the time of diagnosis to ensure that the test gives a positive result.

Shipping Instructions
Refrigerated specimen must arrive within 5 days (120 hours of draw), and ambient specimens must arrive within 3 days (72 hours) of draw. Draw and package specimen as close to shipping time as possible.

Necessary Information
The following information is required:

1. Pertinent clinical history
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:** EDTA (lavender top)  
**Acceptable:** ACD (yellow top)

**Specimen Volume:** 10 mL

**Collection Instructions:**

1. Invert several times to mix blood.  
2. Send specimen in original tube.  
3. Label specimen as blood.

**Specimen Type:** Bone marrow

**Container/Tube:**

**Preferred:** EDTA (lavender top)  
**Acceptable:** ACD (yellow top)

**Specimen Volume:** 4 mL

**Collection Instructions:**

1. Invert several times to mix bone marrow.  
2. Send specimen in original tube.  
3. Label specimen as bone marrow.

**Forms**

1. [Hematopathology Patient Information](#) (T676) in Special Instructions

2. If not ordering electronically, complete, print, and send a [Hematopathology/Cytogenetics Test Request](#) (T726) with the specimen.

**Specimen Minimum Volume**

Peripheral blood: 4 mL  
Bone Marrow: 2 mL

**Reject Due To**

<table>
<thead>
<tr>
<th>Gross hemolysis</th>
<th>Reject</th>
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<tbody>
<tr>
<td>Other</td>
<td>Moderately to severely clotted</td>
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Specimen Stability Information

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<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
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<tbody>
<tr>
<td>Varies</td>
<td>Refrigerated (preferred)</td>
<td>5 days</td>
<td>PURPLE OR PINK TOP/EDTA</td>
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<tr>
<td></td>
<td>Ambient</td>
<td>72 hours</td>
<td>PURPLE OR PINK TOP/EDTA</td>
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Clinical and Interpretive

Clinical Information
Acute promyelocytic leukemia (APL) accounts for 5% to 10% of acute myeloid leukemia, and generally has a good prognosis with current treatment protocols. APL cells contain a fusion gene comprised of the downstream sequences of the retinoic acid receptor alpha gene (RARA) fused to the promoter region and upstream sequences of one of several genes, the most common (>80%) being the promyelocytic leukemia gene (PML). The fusion gene is designated PML/RARA and may be seen in a karyotype as t(15;17)(q22;q12). Messenger RNA (PML/RARA) produced from the fusion gene can be detected using a PCR-based assay, and indicates the presence of neoplastic cells. The PCR-based assay has greater sensitivity than standard methods such as morphology review, karyotyping, or FISH.

Recent studies have indicated that sensitive monitoring is important because the majority of patients who remain PCR positive, or become PCR positive again following treatment, will relapse and likely benefit from early intervention for residual/recurrent disease. This quantitative assay allows PML/RARA levels to be monitored rather than simply detecting the presence or absence of disease.

Reference Values
An interpretive report will be provided.

If positive, a value representing a ratio of PML-RARA fusion transcript to the control gene ABL1 expressed as a percentage will be reported.

Interpretation
The assay is reported in the form of a normalized ratio of promyelocytic leukemia/retinoic acid receptor alpha (PML-RARA) fusion transcript to the control gene ABL1 expressed as a percentage, which is an estimate of the level of PML/RARA RNA present in the specimen, expressed in relation to the level of RNA from an internal control gene (ABL1). The normalized ratio has no units but is directly related to the level of PML/RARA detected (ie, larger numbers indicate higher levels of PML/RARA and smaller numbers indicate lower levels). A relative expression value minimizes variability in the RNA levels measured in separate specimens tested at different times. Although a quantitative PCR assay is performed, the precision of the assay is such that results must be considered semiquantitative, and it is recommended that only log changes be considered significant. Critical results, such as a change in the status of positivity, should be repeated on a separate specimen to verify the result.

Cautions
Promyelocytic leukemia/retinoic acid receptor alpha (PML/RARA) levels can only be compared reliably if tested in the same laboratory using the same procedure each time.

This assay will only detect PML/RARA RNA and will not detect RNA from the less common RARA fusion genes.
Clinical Reference


Performance

Method Description

Total RNA is extracted from blood or bone marrow and reverse transcribed to generate cDNA. Quantitative real-time PCR is performed using the LightCycler instrument platform (Roche) and the data analyzed using the dedicated software for relative quantification with calibrator normalization. Results are provided as a normalized relative value of PML-RARA/ABL1 mRNA with a reproducible analytical sensitivity of 0.003%(Unpublished Mayo method).

The normalized ratio is a relative quantification calculation as follows:

\[
\text{Normalized ratio}^* = \frac{\text{PML/RARA (sample)}}{\text{ABL1 (sample)}} \div \frac{\text{PML/RARA (calibrator)}}{\text{ABL1 (calibrator)}}
\]

*Where ABL1 mRNA is used to normalize variations in RNA quality and calibrator mRNA from a promyelocytic leukemia/retinoic acid receptor alpha (PML/RARA)-positive cell line is used to normalize variations in run conditions.

PDF Report

Supplemental

Day(s) and Time(s) Test Performed
Monday through Friday

Analytic Time
Test Definition: PMLR
PML/RARA Quantitative, PCR

4 days

Maximum Laboratory Time
8 days

Specimen Retention Time
RNA stored 3 months

Performing Laboratory Location
Rochester

Fees and 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 Regional Manager. 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. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
81315-PML/RARalpha (t(15;17)), (PML-RARA regulated adaptor molecule 1) (eg promyelocytic leukemia) translocation analysis; all breakpoints (eg, intron 3, intron 6 and variable in exon 6), qualitative or quantitative

LOINC® Information

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<th>Test Order Name</th>
<th>Order LOINC Value</th>
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<td>PML/RARA Quantitative, PCR</td>
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<table>
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