MAYO CLINIC LABORATORIES

Test Definition: PMLR

PML::RARA Quantitative, PCR, Varies

Overview

Useful For

Diagnosis of acute promyelocytic leukemia (APL)

Detection of residual or recurrent APL

Monitoring the level of *PML::RARA* (promyelocytic leukemia/retinoic acid receptor alpha) in APL patients

Testing Algorithm

For more information see Acute Promyelocytic Leukemia: Guideline to Diagnosis and Follow-up

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

Ordering Guidance

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

1. Refrigerated specimens must arrive within 5 days of collection, and ambient specimens must arrive within 3 days of collection.

2. Collect 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: 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.

Specimen Minimum Volume

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)	5 days	PURPLE OR PINK TOP/EDTA
	Ambient	72 hours	PURPLE OR PINK TOP/EDTA

Clinical & 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 produced from the fusion gene can be detected using a polymerase chain reaction (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 fluorescence in situ hybridization.

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 will 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 *PML::RARA* (promyelocytic leukemia/retinoic acid receptor alpha) 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 polymerase chain reaction 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

PML::RARA (promyelocytic leukemia/retinoic acid receptor alpha) 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

1. Grimwade D, Lo Coco F. Acute promyelocytic leukemia: a model for the role of molecular diagnosis and residual disease monitoring in directing treatment approach in acute myeloid leukemia. Leukemia. 2002;16(10):1959-1973
2. Adams J, Nassiri M. Acute promyelocytic leukemia: A review and discussion of variant translocations. Arch Pathol Lab Med. 2015;139(10):1308-1313

3. Kayser S, Schlenk RF, Platzbecker U. Management of patients with acute promyelocytic leukemia. Leukemia. 2018;32(6):1277-1294
4. Ablain J, de The H. Revisiting the differentiation paradigm in acute promyelocytic leukemia. Blood. 2011;117(22):5795-5802

Performance

Method Description

Total RNA is extracted from blood or bone marrow and reverse transcribed to generate complementary DNA. Quantitative real-time polymerase chain reaction 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 messenger RNA (mRNA) with a reproducible analytical sensitivity of 0.01%(Unpublished Mayo method).

The normalized ratio is a relative quantification calculation as follows:

$$\text{Normalized ratio}^* = \frac{\frac{\text{PML::RARA (sample)}}{\textit{ABL1}\text{ (sample)}}}{\frac{\text{PML::RARA (calibrator)}}{\textit{ABL1}\text{ (calibrator)}}}$$

*Where *ABL1* mRNA is used to normalize variations in RNA quality and calibrator mRNA from a *PML::RARA*-positive cell line is used to normalize variations in run conditions.

PDF Report

Supplemental

Day(s) Performed

Monday through Saturday

Report Available

4 to 8 days

Specimen Retention Time

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

81315-PML/RAR-alpha (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

Test ID	Test Order Name	Order LOINC® Value
PMLR	PML/RARA Quantitative, PCR	In Process

Result ID	Test Result Name	Result LOINC® Value
MP012	Specimen Type	31208-2
19449	Interpretation	69047-9
39469	PMLR Result	No LOINC Needed