Test Definition: CLLMD

Chronic Lymphocytic Leukemia (CLL) Monitoring Measurable/Minimal Residual Disease Detection, Flow Cytometry, Varies

Overview

Useful For

Confirming the presence or absence of measurable (minimal) residual disease in patients with known chronic lymphocytic leukemia who are either post-chemo/immunotherapy or post-bone marrow transplant

Method Name

Immunophenotyping

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

The preferred test for evaluating any tissue biopsy for a potential lymphoproliferative disorder is LLPT / Leukemia/Lymphoma Immunophenotyping, Flow Cytometry, Tissue.

The preferred test for a first-time evaluation of a patient with lymphocytosis is a routine flow cytometric assay; see LCMS / Leukemia/Lymphoma Immunophenotyping, Flow Cytometry, Varies.

Additional Testing Requirements

If cytogenetic tests are requested in addition to this test, an additional specimen tube should be submitted. It is important that the specimen be obtained, processed, and transported according to instructions for the other required test.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube:
Preferred: Yellow top (ACD solution A or B)
Acceptable: Lavender top (EDTA)
Specimen Volume: 6 mL
Collection Instructions:
1. Send whole blood specimen in original tube. **Do not aliquot**.

2. Label specimen as blood.

Specimen Type: Bone marrow
Container/Tube:
Preferred: Yellow top (ACD solution A or B)
Acceptable: Lavender top (EDTA)
Specimen Volume: 6 mL
Collection Instructions:
1. Submission of bilateral specimens is not required.
2. Send bone marrow specimen in original tube. **Do not aliquot**.
3. Label specimen as bone marrow.

Forms

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

Specimen Minimum Volume

1 mL

Reject Due To

Gross hemolysis	Reject
Fully clotted whole blood	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)	4 days	
	Refrigerated	4 days	

Clinical & Interpretive

Clinical Information

Chronic lymphocytic leukemia (CLL) is a low-grade, B-cell neoplasm and is the most common leukemia detected in the western world. It is primarily associated with adult patients and may present as a lymphocytosis, be detected as part of a lymphadenopathy evaluation, or be found incidentally in an otherwise asymptomatic patient. The diagnosis of CLL is based on a combination of morphologic features showing primarily small lymphoid cells with coarse chromatin and scant cytoplasm and an immunophenotype of clonal B cells with dim immunoglobulin, dim CD20, and coexpression of CD5, CD22, CD43, and CD200.

New therapeutic approaches in CLL have been increasingly successful with some patients showing no or only very little measurable (minimal) residual disease (MRD) in their peripheral blood or bone marrow specimens following a therapeutic course. Immunophenotyping studies are necessary as morphologic features are not sufficient to detect MRD. The absence of MRD is an important prognostic indicator in these patients.

Reference Values

An interpretive report will be provided.

This test will be processed as a laboratory consultation. An interpretation of the immunophenotypic findings and correlation with the morphologic features will be provided by a hematopathologist for every case.

Interpretation

An interpretive report for presence or absence of measurable (minimal) residual disease (MRD) for chronic lymphocytic leukemia (CLL) is provided.

Patients with CLL post treatment, who have detectable MRD by this assay, are considered to have residual CLL disease.

Cautions

This test is only appropriate for patients who have a previously confirmed diagnosis of chronic lymphocytic leukemia.

Supportive Data

This assay has been compared with the previously validated assay used in several clinical trials at Mayo Clinic to evaluate response to therapies in patients with chronic lymphocytic leukemia. The data showed that this assay has a better analytic sensitivity, especially for patients undergoing anti-CD19 treatment.

Clinical Reference

1. Hallek M, Cheson BD, Catovsky D, et al. Guidelines for the diagnosis and treatment of chronic lymphocytic leukemia: a report from the International Workshop on Chronic Lymphocytic Leukemia updating the National Cancer Institute-Working Group 1996 guidelines. Blood. 2008;111(12):5446-5456
2. Dimier N, Delmar P, Ward C, et al. A model for predicting effect of treatment on progression-free survival using MRD as a surrogate end point in CLL. Blood. 2018;131(9):955-962
3. Rawstron AC, Fazi C, Agathangelidis A, et al. A complementary role of multiparameter flow cytometry and high-throughput sequencing for minimal residual disease detection in chronic lymphocytic leukemia: An European Research Initiative on CLL study. Leukemia. 2016;30(4):929-936
4. Zent CS, Victoria Wang X, Ketterling RP, et al. A phase II randomized trial comparing standard and low dose rituximab combined with alemtuzumab as initial treatment of progressive chronic lymphocytic leukemia in older patients: a trial of the ECOG-ACRIN Cancer Research Group (E1908). Am J Hematol. 2016;91(3):308-312
5. Shanafelt TD, Wang XV, Kay NE, et al. Ibrutinib-Rituximab or chemoimmunotherapy for chronic lymphocytic leukemia. N Engl J Med. 2019;381(5):432-443
6. Kay NE, Strati P, LaPlant BR, et al. A randomized phase II trial comparing chemoimmunotherapy with or without bevacizumab in previously untreated patients with chronic lymphocytic leukemia. Oncotarget. 2016;7(48):78269-78280
7. Strati P, Keating MJ, O'Brien SM, et al. Eradication of bone marrow minimal residual disease may prompt early treatment discontinuation in CLL. Blood. 2014;123(24):3727-3732
8. Rawstron AC, Villamor N, Ritgen M, et al. International standardized approach for flow cytometric residual disease

monitoring in chronic lymphocytic leukaemia. Leukemia. 2007;21(5):956-964

Performance

Method Description

Flow cytometric immunophenotyping (high sensitivity) of bone marrow is performed to evaluate the presence or absence of chronic lymphocytic leukemia (CLL) measurable (minimal) residual disease (MRD) using the following antibodies: CLL, MRD Panel: CD5, CD19, CD20, CD22, CD38, CD43, CD45, CD200, and kappa and lambda immunoglobulin light chains.

The sensitivity of this assay is 0.002% (2 x 10[-5]) based on 1,000,000 total events collected and an abnormal cell immunophenotype detected in a cluster of at least 20 cells. The assay sensitivity meets or exceeds the 0.01-0.001% (10[-4]-10[-5]) level of detection by flow cytometry, as recommended by the current ERIC method and NCCN guidelines for MRD analysis in CLL.(Keren P, McCoy Jr JP, Carey J, eds. Flow Cytometry in Clinical Diagnosis. 4th ed. ASCP Press; 2007; Wierda WG, Brown J, Abramson JS, et al. NCCN Guidelines Insights: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma, Version 3.2022. J Natl Compr Canc Netw. 2022;20[6]:622-634. doi:10.6004/jnccn.2022.0031

PDF Report

No

Day(s) Performed

Preanalytical processing: Monday through Saturday
Results reported: Monday through Friday

Report Available

1 to 4 days

Specimen Retention Time

14 days

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.

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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

88184-Flow cytometry; first cell surface, cytoplasmic or nuclear marker
88185 x 9-Flow cytometry; additional cell surface, cytoplasmic or nuclear marker (each)
88188-Flow Cytometry Interpretation, 9 to 15 markers

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CLLMD	CLL Monitoring MRD Detection, V	In Process

Result ID	Test Result Name	Result LOINC® Value
608973	CLLMD Result	No LOINC Needed
608974	Final Diagnosis	22637-3
608975	Special Studies	30954-2
608976	Microscopic Description	22635-7