Test Definition: BALMF

ALL (B-cell), Specified FISH

Overview

Useful For

Detecting a neoplastic clone associated with the common chromosome abnormalities and classic rearrangements seen in patients with B-cell acute lymphoblastic leukemia/lymphoma (B-ALL/LBL) using client specified probes

An adjunct to conventional chromosome studies in patients with B-ALL/LBL

Evaluating specimens in which standard cytogenetic analysis is unsuccessful

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for 1 probe set (2 individual fluorescence in situ hybridization [FISH] probes or 3 individual FISH probes). Additional charges will be incurred for all reflex or additional probe sets performed.

If the patient is being treated for known abnormalities, indicate the abnormality and which probes should be used.

When specified, any of the following probes will be performed:

1q25 rearrangement, ABL2 break-apart

5q33 rearrangement, PDGFRB break-apart

7p-, IKZF1/CEP7

9p24.1 rearrangement, JAK2 break-apart

+9/9p-, CDKN2A/D9Z1

t(9;22) BCR/ABL1

9q34 rearrangement, ABL1 break-apart

11q23 rearrangement, MLL (KMT2A) break-apart

t(4;11)(q21;q23), AFF1/MLL

t(6;11)(q27;q23), MLLT4(AFDN)/MLL

t(9;11)(p22;q23), MLLT3/MLL

t(10;11)(p13;q23), MLLT10/MLL

t(11;19)(q23;p13.1), MLL/ELL

t(11;19)(q23;p13.3), MLL/MLLT1

-17/17p-, TP53/D17Z1

t(1;19)(q23;p13), PBX1/TCF3

Hyperdiploidy, +4,+10,+17: D4Z1/D10Z1/D17Z1

t(12;21)(p13;q22), ETV6/RUNX1 & iAMP21

12p13 rearrangement, ETV6 break-apart

14q32 rearrangement, IGH break-apart

t(Xp22.33;var) or t(Yp11.32;var), P2RY8 rearrangement

t(Xp22.33;var) or t(Yp11.32;var), CRLF2 rearrangement

t(X;14)(p22.33;q32) or t(Y;14)(p11.32;q32)), CRLF2/IGH

8q24.1 rearrangement, MYC break-apart

B-Lymphoblastic Leukemia/Lymphoma Algorithm is available in Special Instructions.

Special Instructions

- B-Lymphoblastic Leukemia/Lymphoma Algorithm

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
BALMB	Probe, Each Additional (BALMF)	No, (Bill Only)	No
BAL3B	Probe, Tri-color (BAL)	No, (Bill Only)	No

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is intended for instances when targeted B-cell acute lymphoblastic leukemia/lymphoma (B-ALL/LBL) fluorescence in situ hybridization (FISH) probes are needed based on specific abnormalities or on abnormalities identified in the diagnostic sample. The FISH probes to be analyzed must be specified on the request, otherwise test processing may be delayed in order to determine the intended analysis.

-If specific probes are not included with this test request, the test may be canceled and automatically reordered by the laboratory as BALAF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Adult, Varies or BALPF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Pediatric, Varies depending on the age of the patient.

-If this test is ordered and the laboratory is informed that the patient is on a Children's Oncology Group (COG) protocol, this test will be canceled and automatically reordered by the laboratory COGBF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Children's Oncology Group Enrollment Testing, FISH, Varies.

For an **adult** patient, if the entire B-cell ALL FISH panel is preferred, order BALAF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Adult, Varies.

For a **pediatric** patient, if the entire B-cell ALL FISH panel is preferred, order BALPF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Pediatric, Varies.

At diagnosis, both conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and either BALAF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Adult, Varies or BALPF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Pediatric, Varies should be performed.

If the patient clinically relapses, a conventional chromosome study may be useful to identify cytogenetic changes in the neoplastic clone or the possible emergence of a therapy-related myeloid clone.

For patients with B-cell lymphoma, order BLPMF / B-Cell Lymphoma, Specified FISH, Varies.

For testing paraffin-embedded tissue samples from patients with B-cell acute lymphoblastic leukemia/lymphoma, order BLBLF / B-Cell Lymphoblastic Leukemia/Lymphoma, FISH, Tissue.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. A list of probes requested for analysis is required. Probes available for this test are listed in the Testing Algorithm section.

2. A reason for testing and a flow cytometry and/or a bone marrow pathology report should be submitted with each specimen. The laboratory will not reject testing if this information is not provided, however appropriate testing and/or interpretation may be compromised or delayed in some instances. If this information is not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.

Specimen Required

Submit only 1 of the following specimens:

Preferred

Specimen Type: Bone marrow

Container/Tube:

Preferred: Yellow top (ACD)

Acceptable: Green top (heparin) or lavender top (EDTA)

Specimen Volume: 2 to 3 mL

Collection Instructions:

1. It is preferable to send the first aspirate from the bone marrow collection.

2. Invert several times to mix bone marrow.

Acceptable

Specimen Type: Blood

Container/Tube:

Preferred: Yellow top (ACD)

Acceptable: Green top (heparin) or lavender top (EDTA)

Specimen Volume: 6 mL

Collection Instructions: Invert several times to mix blood.

Forms

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

Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Minimum Volume

Blood: 2 mL

Bone Marrow: 1 mL

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

In the United States, the incidence of B-lymphoblastic leukemia/lymphoma (B-ALL/LBL) is roughly 6000 new cases per year, or approximately 1 in 50,000. B-ALL/LBL accounts for approximately 70% of all childhood leukemia cases (ages 0 to 19 years), making it the most common type of childhood cancer. It has a peak incidence at 2 to 5 years of age. This incidence decreases with age before increasing again at around 50 years of age. B-ALL/LBL is slightly more common in males than females. There is also an increased incidence of B-ALL/LBL in individuals with genetic conditions such as Down syndrome, Fanconi anemia, Bloom syndrome, ataxia telangiectasia, Li-Fraumeni syndrome, X-linked agammaglobulinemia, and severe combined immunodeficiency. The overall cure rate for B-ALL/LBL in children is approximately 90%, and about 45% to 60% of adults have long-term disease-free survival. Of note, *CRLF2/IGH* rearrangements are more commonly observed in patients with Down syndrome or of Hispanic descent.

Specific cytogenetic abnormalities are identified in the majority of cases of B-ALL/LBL, either by conventional chromosome studies or fluorescence in situ hybridization (FISH) studies. Each of the genetic subgroups are important to detect and can be critical prognostic markers. For example, a decision for early transplantation may be made if t(9;22)(q34;q11.2), *KMT2A* rearrangement, iAMP21, or a hypodiploid clone is identified. In contrast, if *ETV6/RUNX1* fusion or hyperdiploidy is identified, the patient has a more favorable prognosis and transplantation is rarely initially considered.

A newly recognized World Health Organization entity called *BCR-ABL1*-like ALL (also known as Philadelphia chromosome-like acute lymphoblastic leukemia), is increasing in importance due to the poor prognosis seen in pediatric, adolescent, and young adult ALL. Common features of this entity involve rearrangements with tyrosine kinase genes involving the following genes: *ABL2*, *PDGFRB*, *JAK2*, *ABL1*, *CRLF2*, and *P2RY8*, as well as deletions involving *IKZF1*. Patients who have failed conventional therapies have demonstrated favorable responses to targeted therapies when rearrangements involving these specific gene regions have been identified.

Evaluation of the *MYC* gene region is included in all diagnostic B-ALL panels to evaluate for Burkitt lymphoma. If a positive result is obtained, additional testing for the *BCL2* and *BCL6* gene regions may be considered.

Per National Comprehensive Cancer Network guidelines, a combination of cytogenetic and FISH testing is currently recommended in all pediatric and adult patients with B-ALL/ lymphoblastic lymphoma (LBL).

Reference Values

An interpretive report will be provided.

Interpretation

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the normal reference range for any given probe.

The absence of an abnormal clone does not rule out the presence of a neoplastic disorder.

Cautions

This test is not approved by the US Food and Drug Administration, and it is best used as an adjunct to existing clinical and pathologic information.

Bone marrow is the preferred specimen type for this fluorescence in situ hybridization test. If bone marrow is not available, a blood specimen may be used if there are malignant cells in the blood specimen (as verified by a

hematopathologist).

Supportive Data

Each probe was independently tested and verified on unstimulated peripheral blood and bone marrow specimens. Normal cutoffs were calculated based on the results of 25 normal specimens. Each probe set was evaluated to confirm the probe set detected the abnormality it was designed to detect.

Clinical Reference

1. Moorman AV, Harrison CJ, Buck GA, et al: Karyotype is an independent prognostic factor in adult acute lymphoblastic leukemia (ALL): analysis of cytogenetic data from patients treated on the Medical Research Council (MRC) UKALLXII/Eastern Cooperative Oncology Group (ECOG) 2993 trial. Blood. 2007 Apr 15;109(8):3189-3197. doi: 10.1182/blood-2006-10-051912

2. Moorman AV: The clinical relevance of chromosomal and genetic abnormalities in B-cell precursor acute lymphoblastic leukemia. Blood Rev. 2012;26:123-135. doi: 10.1016/j.blre.2012.01.001

3. Roberts KG, Li Y, Payne-Turner D, et al: Targetable kinase-activating lesions in Ph-like acute lymphoblastic leukemia. N Engl J Med. 2014 Sept;371(11):1005-1015. i: 10.1056/NEJMoa1403088

4. Mullighan CG: The genomic landscape of acute lymphoblastic leukemia in children and young adults. Hematology Am Soc Hematol Educ Program. 2014 Dec 5;2014(1):174-180. doi: 10.1182/asheducation-2014.1.174

5. Arber DA, Orazi A, Hasserjian R, et al: The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood. 2016 May 19;127(20):2391-2405. doi: 10.1182/blood-2016-03-643544

Performance

Method Description

This test is performed using commercially available and laboratory-developed probes. Deletion of the *CDKN2A* locus on chromosome 9, *TP53* on chromosome 17, deletion of *IKZF1* on chromosome 7, and gain of chromosomes 4, 10, and 17 are detected using enumeration strategy probes. Rearrangements involving *ABL2, PDGFRB, MYC,* JAK2, *ABL1, MLL, ETV6, IGH*, *MYC, CRLF2* and *P2RY8* are detected using a dual-color break-apart (BAP) strategy probe. Dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe sets are used to detect t(X/Y;14), t(9;22), t(12;21), t(1;19), and in reflex testing when rearrangements of the *MLL* gene is detected. Amplification of *RUNX1* (21q22) is detected using a D-FISH probe strategy. For enumeration and BAP strategy probe sets, 100 interphase nuclei are scored; 200 interphase nuclei are scored when D-FISH probes are used. Results are expressed as the percent abnormal nuclei.(Unpublished Mayo method)

PDF Report

No

Specimen Retention Time

4 weeks

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

88271 x2, 88275 x1, 88291 x1- FISH Probe, Analysis, Interpretation; 1 probe sets

88271 x2, 88275 x1 - FISH Probe, Analysis; each additional probe set (if appropriate)

88271 x1 –-FISH Probe; coverage for sets containing 3 probes (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
BALMF	ALL (B-cell), Specified FISH	In Process

Result ID	Reporting Name	LOINC®
614217	Result Summary	50397-9
614218	Interpretation	69965-2
614219	Result Table	93356-4
614220	Result	62356-1
GC101	Reason for Referral	42349-1
GC102	Probes Requested	78040-3
GC103	Specimen	31208-2
614221	Source	31208-2
614222	Method	85069-3
614223	Additional Information	48767-8
614224	Disclaimer	62364-5
614225	Released By	18771-6