Test Definition: BALMF

B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Specified FISH, Varies

Overview

Useful For

Detecting recurrent common chromosome abnormalities associated with B-cell acute lymphoblastic leukemia/lymphoma (B-ALL/LBL) and Philadelphia chromosome-like acute lymphoblastic leukemia (Ph-like ALL) using **client-specified** probe set(s)

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

Evaluating specimens in which chromosome studies are unsuccessful

This test **should not be used** to screen for residual B-ALL/LBL

Identifying and tracking known chromosome abnormalities in patients with B-ALL and monitoring response to therapy

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

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for one probe set (2 individual fluorescence in situ hybridization [FISH] probes). Additional charges will be incurred for all reflex or additional probe sets performed. Analysis charges will be incurred based on the number of cells analyzed per probe set. If no cells are available for analysis, no analysis charges will be incurred.

This test is performed using client-specified FISH probes and is not intended as a panel test. Specific probes must be listed in the probe request field. Reflex probes can be performed when appropriate if specified in the order request field.

When specified, any of the following probes will be performed:
t(Xp22.33;var) or t(Yp11.32;var) or *CRLF2* rearrangement, request probe CRLF2 break-apart
t(X;14)(p22.33;q32) or t(Y;14)(p11.32;q32) or *IGH::CRLF2* fusion, request probe CRLF2/IGH
t(Xp22.33;var) or t(Yp11.32;var) or *P2RY8* rearrangement, request probe P2RY8 break-apart
t(1q25;var) or *ABL2* rearrangement, request probe ABL2 break-apart
t(1;19)(q23;p13) or *TCF3::PBX1* fusion, request probe PBX1/TCF3
Hyperdiploidy or +4,+10,+17, request probe D4Z1/D10Z1/D17Z1
t(5q32;var) or *PDGFRB* rearrangement, request probe PDGFRB break-apart

7p- or *IKZF1* deletion, request probe IKZF1/CEP7
t(8;14)(q24.21;q32) or *IGH::MYC* fusion, request probe MYC/IGH
t(8q24.21;var) or *MYC* rearrangement, request probe MYC break-apart
t(3q27;var) or *BCL6* rearrangement, request probe BCL6 break-apart
t(18q21;var) or *BCL2* rearrangement, request probe BCL2 break-apart
t(14;18)(q32;q21) or *IGH::BCL2* fusion, request probe BCL2/IGH
t(9p24.1;var) or *JAK2* rearrangement, request probe JAK2 break-apart
t(9;22)(q34;q11.2) or *BCR::ABL1* fusion, request probe ABL1/BCR
t(9q34;var) or *ABL1* rearrangement, request probe ABL1 break-apart
t(11q23;var) or *KMT2A* rearrangement, request probe KMT2A break-apart
t(4;11)(q21;q23) or *KMT2A::AFF1* fusion, request probe AFF1/KMT2A
t(6;11)(q27;q23) or *KMT2A::AFDN* fusion, request probe AFDN/KMT2A
t(9;11)(p22;q23) or *KMT2A::MLLT3* fusion, request probe MLLT3/KMT2A
t(10;11)(p12;q23) or *KMT2A::MLLT10* fusion, request probe MLLT10/KMT2A
t(11;19)(q23;p13.3) or *KMT2A::MLLT1* fusion, request probe KMT2A/MLLT1
t(11;19)(q23;p13.1) or *KMT2A::ELL* fusion, request probe KMT2A/ELL
t(12;21)(p13;q22), *ETV6::RUNX1* fusion and iAMP21, request probe ETV6/RUNX1
t(12p13;var) or *ETV6* rearrangement, request probe ETV6 break-apart
t(14q32;var) or *IGH* rearrangement, request probe IGH break-apart

Appropriate ancillary probes may be performed at consultant discretion to render comprehensive assessment. Any additional probes will have the results included within the final report and will be performed at an additional charge.

For more information see:
-B-Lymphoblastic Leukemia/Lymphoma Genetic Testing Guidelines
-Acute Leukemias of Ambiguous Lineage Testing Algorithm

Special Instructions

- B-Lymphoblastic Leukemia/Lymphoma Genetic Testing Guidelines
- Acute Leukemias of Ambiguous Lineage Testing Algorithm

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is intended for instances when **limited** B-cell acute lymphoblastic leukemia (ALL) fluorescence in situ hybridization (FISH) probes are needed based on specific abnormalities or abnormalities identified in the diagnostic sample. **The FISH probes to be analyzed must be specified on the ordering request.** If targeted FISH probes are not included with this test order, test processing will be delayed and the test may be canceled and automatically reordered by the laboratory as BALAF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Adult, Varies or BALFP / Pediatric B-Lymphoblastic Leukemia/Lymphoma panel, FISH, Varies depending on the age of the patient.

At diagnosis, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and a complete B-ALL FISH panel (either BALAF or BALFP) should be performed.

If a complete B-cell ALL FISH panel is preferred for an **adult patient aged 31 years or older**, order BALAF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Adult, Varies.

If a complete B-cell ALL FISH panel is preferred for a **pediatric patient aged 30 years or younger**, order BALFP / Pediatric B-Lymphoblastic Leukemia/Lymphoma panel, FISH, Varies.

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 as COGBF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Children's Oncology Group Enrollment Testing, FISH, Varies.

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-lymphoblastic leukemia/lymphoma (B-LBL), order BLBLF / B-Cell Lymphoblastic Leukemia/Lymphoma, FISH, Tissue. If a paraffin-embedded tissue sample is submitted for this test, this test will be canceled and BLBLF will be added and performed as the appropriate test.

Additional Testing Requirements

At diagnosis, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow) and a complete BALAF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Adult, Varies or BALFP / Pediatric B-Lymphoblastic Leukemia/Lymphoma panel, FISH, Varies should be performed, depending on patient's age. If there is limited specimen available, only fluorescence in situ hybridization testing will be performed.

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 must be provided. If this information is not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.
3. 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, but appropriate testing and interpretation may be compromised or delayed.
4. If the patient has received an opposite sex bone marrow transplant, note this information on the request.
5. If the patient has Down syndrome, note this information on the request.

Specimen Required

Submit only 1 of the following specimens:

Preferred
Specimen Type: Bone marrow
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (sodium 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.
3. Send bone marrow specimen in original tube. **Do not aliquot.**

Acceptable
Specimen Type: Whole blood
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (sodium heparin) or lavender top (EDTA)
Specimen Volume: 6 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**

Forms

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

Specimen Minimum Volume

Bone marrow: 1 mL; Whole blood: 2 mL

Reject Due To

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

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 age 50. B-ALL/LBL is slightly more common in male patients than female patients. 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, *IGH::CRLF2* fusion is more commonly observed in patients with Down syndrome or of Hispanic descent.

Specific cytogenetic abnormalities are identified in most of cases of B-ALL/LBL, by conventional chromosome studies or fluorescence in situ hybridization (FISH) studies. B-ALL genetic subgroups are important to detect and can be critical prognostic markers. For example, a decision for early transplantation may be made if *BCR::ABL1* fusion, *KMT2A* rearrangement, iAMP21, or a hypodiploid clone is identified. In contrast, if the *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 pediatric 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). Additional cytogenetic techniques such as chromosomal microarray (CMAH / Chromosomal Microarray, Hematologic Disorders, Varies) may be helpful to resolve questions related to ploidy (hyperdiploid clone vs doubled hypodiploid clone) or to resolve certain clonal structural rearrangements such as the presence or absence of intra-chromosomal amplification of chromosome 21 (iAMP21). A summary of the characteristic chromosome abnormalities identified in B-ALL is listed in the following table.

Table. **Common Chromosome Abnormalities in B-cell Acute Lymphoblastic Leukemia**

Leukemia type	Cytogenetic change	Typical demographic	Risk category
B-acute lymphoblastic leukemia/lymphoma	t(12;21)(p13;q22), *ETV6::RUNX1*	Pediatric	Favorable
	Hyperdiploidy	Pediatric	Favorable
	t(1;19)(q23;p13.3), *TCF3::PBX1*	Pediatric	Intermediate to favorable
	t(9;22)(q34;q11.2), *BCR::ABL1*	All ages	Unfavorable
	iAMP21, *RUNX1*	Pediatric	Unfavorable
	t(11q23;var), *KMT2A* rearrangement	All ages	Unfavorable
	t(4;11)(q21;q23), *KMT2A::AFF1*	All ages	Unfavorable
	t(6;11)(q27;q23), *KMT2A::AFDN*	All ages	Unfavorable
	t(9;11)(p21.3;q23), *KMT2A::MLLT3*	All ages	Unfavorable
	t(10;11)(p12;q23), *KMT2A::MLLT10*	All ages	Unfavorable
	t(11;19)(q23;p13.3), *KMT2A::MLLT1*	All ages	Unfavorable
	t(11;19)(q23;p13.1), *KMT2A::ELL*	All ages	Unfavorable
	t(14q32;var), *IGH* rearrangement	All ages	Variable
	t(X;14)(p22;q32)/t(Y;14)(p11;q32), *IGH::CRLF2*	Adolescent/ young adult	Unfavorable
	t(Xp22.33;var) or t(Yp11.32;var), *CRLF2* rearrangement	All ages	Unfavorable
	t(Xp22.33;var) or t(Yp11.32;var), *P2RY8* rearrangement	All ages	Unfavorable
	t(8q24.21;var), *MYC* rearrangement *representing Burkitt or other mature B-cell lymphoma	Pediatric/ adolescent/ young adult	
	Complex karyotype (> or =4 abnormalities)	Adult	Unfavorable
	Low hypodiploidy/near-triploidy	Adult	Unfavorable
	Near-haploid/hypodiploid	All ages	Unfavorable
	del(7p) *IKZF1* deletion	All ages	Unfavorable in absence of *ERG* deletion
BCR::ABL1-like acute lymphoblastic leukemia/lymphoma	t(1q25;var), *ABL2* rearrangement	Pediatric/ adolescent/ young adult	Unfavorable
	t(5q32;var), *PDGFRB* rearrangement		
	t(9p24.1;var), *JAK2* rearrangement		
	t(9q34;var), *ABL1* rearrangement		
	t(Xp22.33;var) or t(Yp11.32;var), *CRLF2* rearrangement		
	t(Xp22.33;var) or t(Yp11.32;var), *P2RY8*		

	rearrangement		

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 set.

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 clinical and pathologic information.

Fluorescence in situ hybridization (FISH) is not a substitute for conventional chromosome studies because the latter detects chromosome abnormalities associated with other hematological disorders that would go undetected in a targeted B-cell acute lymphoblastic leukemia FISH panel test.

Bone marrow is the preferred specimen type for this FISH test. If bone marrow is not available, a blood specimen may be used if there are neoplastic cells in the blood specimen (as verified by a hematopathologist).

If no FISH signals are observed post-hybridization, the case will be released indicating a lack of FISH results.

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;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(3):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;371(11):1005-1015. doi: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;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;127(20):2391-2405. doi:10.1182/blood-2016-03-643544

Performance

Method Description

This test is performed using commercially available and laboratory-developed fluorescence in situ hybridization (FISH) probes. Deletion of *IKZF1* on chromosome 7 and gain or losses of chromosomes 4, 10, and 17 are detected using enumeration strategy probes. Rearrangements involving *CRLF2, P2RY8, ABL2, BCL3, PDGFRB, MYC, JAK2*, *ABL1, MLL, ETV6, IGH,* and *BCL2* are detected using dual-color break-apart (BAP) strategy probes. Dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe sets are used to detect t(X/Y;14), t(2;8), t(8;14), t(8;22), t(9;22), t(12;21), t(1;19), and in reflex testing when a rearrangement of the *KMT2A* gene is detected. Amplification of the *RUNX1* gene region is detected using a D-FISH probe to enumerate copies of the RUNX1 probe. 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

Day(s) Performed

Monday through Friday

Report Available

7 to 10 days

Specimen Retention Time

4 weeks

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

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)

Test Definition: BALMF

B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Specified FISH, Varies

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
BALMF	ALL (B-cell), Specified FISH	102099-9

Result ID	Test Result Name	Result LOINC® Value
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