Test Definition: PHLFD

B-Lymphoblastic Leukemia/Lymphoma with BCR::ABL1-like Features Panel, FISH, Varies

Overview

Useful For

Detecting a neoplastic clone associated with B-Lymphoblastic Leukemia/Lymphoma with BCR::ABL1-like Features particularly when a classic abnormality is not detected with the initial panel using a laboratory-designated probe set algorithm

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

Evaluating specimens in which standard cytogenetic analysis is unsuccessful

This test **should not be used** to screen for residual B-Lymphoblastic Leukemia/Lymphoma with BCR::ABL1-like Features.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
PHLBD	Probe, Each Additional (PHLFD)	No, (Bill Only)	No

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for 6 probe sets (12 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 as panel testing only using the following analysis algorithm.

The B-lymphoblastic Leukemia/Lymphoma with BCR::ABL1-like features panel includes testing for the following four kinase-activating chromosome rearrangements, as well as for *IKZF1* deletion, which often accompanies Ph-like ALL:

The **diagnostic** the B-lymphoblastic Leukemia/Lymphoma with BCR::ABL1-like features panel includes testing for the following abnormalities using the FISH probes listed:
t(1q25;var) or *ABL2* rearrangement, ABL2 break-apart probe set
t(5q32;var) or *PDGFRB* rearrangement, PDGFRB break-apart probe set
t(9p24.1;var) or *JAK2* rearrangement, JAK2 break-apart probe set
t(9q34;var) or *ABL1* rearrangement, ABL1 break-apart probe set
7p-, IKZF1/CEP7 probe set
t(Xp22.33;var) or t(Yp11.32;var) or *CRLF2* rearrangement, CRLF2 break-apart probe set

When an unbalanced CRLF2 rearrangement is identified, reflex testing will be performed using both the CRLF2/IGH fusion probe set to identify a potential t(X;14)(p22.33;q32) or t(Y;14)(p11.32;q32) cryptic translocation as well as the PRRY8 probe set to identify a potential t(Xp22.33;var) or t(Yp11.32;var), cryptic P2RY8 rearrangement

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 Algorithm.

Special Instructions

- B-Lymphoblastic Leukemia/Lymphoma Genetic Testing Guidelines

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is intended for instances when the complete B-lymphoblastic Leukemia/Lymphoma with BCR::ABL1-like features fluorescence in situ hybridization (FISH) panel is needed.

If this test is ordered concurrently with either BALAF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), FISH, Adult, Varies or BALFP / Pediatric B-Lymphoblastic Leukemia/Lymphoma Panel, FISH, Varies, this test will be canceled. The probes offered in this test are included within BALAF and BALFP, when appropriate.

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 limited B-lymphoblastic Leukemia/Lymphoma with BCR::ABL1-like features FISH probes are preferred, order BALMF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Specified FISH, Varies, and request specific probes for targeted abnormalities.

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

At follow-up, conventional cytogenetic studies (CHRBM / Chromosome Analysis, Hematologic Disorders, Bone Marrow)

and targeted B-ALL FISH probes can be evaluated based on the abnormalities identified in the diagnostic study. Order BALMF / B-Cell Acute Lymphoblastic Leukemia/Lymphoma (ALL), Specified FISH, Varies and request specific probes or abnormalities.

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

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. 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.
2. 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.

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 to3 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 an Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Specimen Minimum Volume

Bone marrow: 1 mL; Whole blood: 2 mL

Reject Due To

Fresh tissue	Reject

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

In the United States, the incidence of acute lymphoblastic leukemia (ALL) is roughly 6000 new cases per year (as of 2019). ALL accounts for approximately 70% of all childhood leukemia cases (ages 0-19 years), making it the most common type of childhood cancer. Approximately 85% of pediatric cases of ALL are of B-cell lineage (B-ALL) and 15% are of T-cell lineage (T-ALL). It has a peak incidence at age 2 to 5 years. The incidence decreases with increasing age, before increasing again at around age 50 years. ALL is slightly more common in male patients than female patients. There is an increased incidence of ALL in individuals with Down syndrome, Fanconi anemia, Bloom syndrome, ataxia telangiectasia, X-linked agammaglobulinemia, and severe combined immunodeficiency. The overall cure rate for ALL in children is about 90% and about 45% to 60% of adults have long-term disease-free survival. *CRLF2/IGH* rearrangements are more commonly observed in patients with Down syndrome or of Hispanic descent.

Specific genetic abnormalities are identified in the most of cases of B-ALL, either by conventional chromosome studies or fluorescence in situ hybridization (FISH) studies. Each of the B-ALL genetic subgroups are important to detect and can be critical prognostic markers. The decision for early transplantation may be made if *BCR::ABL1* fusion, *KMT2A* translocations, *RUNX1* duplication/amplification (iAMP21) or a hypodiploid clone is identified. In contrast, if the *ETV6::RUNX1* fusion is detected by FISH or hyperdiploidy is identified by chromosome studies, the patient has a favorable prognosis and transplantation is rarely considered.

A newly recognized World Health Organization entity *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.* Deletion of *IKZF1* often accompanies this entity. Some

patients who have failed conventional therapies have demonstrated favorable responses to targeted therapies in clinical trials when rearrangements involving these specific gene regions have been identified.

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.

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 an B-Lymphoblastic Leukemia/Lymphoma with BCR::ABL1-like Features clone or another 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 be missed by this targeted BCR::ABL1-like 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 malignant 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
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
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
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
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

Performance

Method Description

This test is performed using commercially available and laboratory-developed probes. Deletion of *IKZF1* on chromosome 7 is detected using an enumeration strategy probe set. Rearrangements involving *ABL2, PDGFRB,* JAK2, *ABL1, CRLF2,* and *P2RY8* are detected using dual-color break-apart (BAP) strategy probe sets. A dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe set is used to detect t(X/Y;14). 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

88271x12, 88275x6, 88291 x1-FISH Probe, Analysis, Interpretation; 6 probe sets
88271x2, 88275x1-FISH Probe, Analysis; each additional probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
PHLFD	BCR/ABL1-like B-ALL pnl, Diag, FISH	102100-5

Result ID	Test Result Name	Result LOINC® Value

622411	Result Summary	50397-9
622412	Interpretation	69965-2
622413	Result Table	93356-4
622414	Result	62356-1
GC156	Reason for Referral	42349-1
GC157	Specimen	31208-2
622415	Source	31208-2
622416	Method	85069-3
622417	Additional Information	48767-8
622418	Disclaimer	62364-5
622419	Released By	18771-6