MAYO CLINIC LABORATORIES

Test Definition: LCAF

Lung Cancer, ALK (2p23) Rearrangement, FISH, Tissue

Overview

Useful For

Identifying patients with non-small cell lung carcinoma who may benefit from treatment with directed tyrosine kinase inhibitors

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
_PBCT	Probe, +2	No, (Bill Only)	No
_PADD	Probe, +1	No, (Bill Only)	No
_PB02	Probe, +2	No, (Bill Only)	No
_PB03	Probe, +3	No, (Bill Only)	No
_IL25	Interphases, <25	No, (Bill Only)	No
_I099	Interphases, 25-99	No, (Bill Only)	No
_I300	Interphases, >=100	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 probes). No analysis charges will be incurred if an insufficient number of representative cells are available for analysis.

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.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Tissue

Ordering Guidance

This test does not include a pathology consultation. If a pathology consultation is requested, order PATHC / Pathology Consultation, and appropriate testing will be added at the discretion of the pathologist and performed at an additional

charge.

Multiple oncology (cancer) gene panels are also available. For more information see Hematology, Oncology, and Hereditary Test Selection Guide

Additional Testing Requirements

Confirmation testing for the presence of a possible anaplastic lymphoma kinase (ALK) fusion transcript by next generation sequencing to resolve atypical or unbalanced fluorescence in situ hybridization results is available, order MCLNR / MayoComplete Lung Rearrangements, Rapid Test, Tumor.

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

Necessary Information

1. A pathology report is required for testing to be performed. If not provided, appropriate testing and/or interpretation may be compromised or delayed. Acceptable pathology reports include working drafts, preliminary pathology, or surgical pathology reports.

2. The following information must be included in the report provided.

1. Patient name?
2. Block number - must be on all blocks, slides, and paperwork
3. Date of collection
4. Tissue Source

3. 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.

Specimen Required

Submit only 1 of the following specimens:

Preferred

Specimen Type: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tumor tissue block. Blocks prepared with alternative fixation methods will be attempted but are less favorable for successful results by FISH testing; provide fixation method used.

Additional Information:

1. Paraffin-embedded specimens can be from any anatomic location (skin, soft tissue, lymph node, etc).
2. Bone specimens that have been decalcified will be attempted for testing, but the success rate is approximately 50%.

Acceptable

Specimen Type: Tissue slides

Slides: 1 Hematoxylin and eosin stained and 4 unstained

Collection Instructions: Submit 4 consecutive unstained, positively charged, unbaked slides with 5 micron-thick sections of the tumor tissue and 1 slide stained with hematoxylin and eosin.

Forms

If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume

Slides: 1 Hematoxylin and eosin stained and 2 unstained

Reject Due To

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

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information

Rearrangements of the anaplastic lymphoma kinase (*ALK*) gene are found in approximately 3% to 5% of non-small cell lung carcinomas with the majority in adenocarcinoma and younger female patients who were light or nonsmokers. Clinical studies have shown that lung cancers harboring *ALK* rearrangements are resistant to epidermal growth factor receptor tyrosine kinase inhibitors, but may be highly sensitive to directed tyrosine kinase inhibitors.

Reference Values

An interpretative report will be provided.

Interpretation

ALK will be clinically interpreted as positive or negative.

Interpretive criteria for the anaplastic lymphoma kinase (ALK) fluorescence in situ hybridization (FISH) assays are provided by the manufacturer, Abbott Molecular.

A specimen is considered positive if greater than 50% demonstrate a signal pattern consistent with an *ALK* rearrangement and considered negative if less than 10% of cells are positive. If the results are equivocal (>10% and <50%), an additional 50 cells are scored and would be considered positive if greater than 15% of cells exhibit a signal pattern consistent with an *ALK* rearrangement and negative if less than 15% of cells exhibit an *ALK* rearrangement.

A positive result is consistent with the presence of an *ALK* rearrangement and likely reflects *ALK* fusion with a partner gene. The significance of this FISH result is dependent on additional clinical and pathologic features.

A positive result suggests that the tumor may be sensitive to directed kinase inhibitors. While results may indicate the potential response to directed tyrosine kinase inhibitors, selection of treatment remains a clinical decision.

A negative result suggests there is no rearrangement of the *ALK* gene. However, a negative result does not exclude the presence of an *ALK* fusion or exclude the possible sensitivity to targeted therapy.

Cautions

This test is intended to be used for therapeutic purposes in pulmonary carcinoma.

This fluorescence in situ hybridization (FISH) assay does not rule out other chromosome abnormalities.

While results may indicate the likely response to *ALK* inhibitor therapy, selection of treatment remains a clinical decision.

Fixatives other than formalin (eg, Prefer, Bouin's) may not be successful for FISH assays. Non-formalin fixed specimens will not be rejected.

Paraffin-embedded tissues that have been decalcified may not be successful for FISH analysis. The success rate of FISH studies on decalcified tissue is approximately 50%.

FISH studies will be attempted if sufficient tumor is present for analysis. The pathologist reviewing the hematoxylin and eosin-stained slide may find it necessary to cancel testing if insufficient tissue/tumor is available for testing.

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

Clinical Reference

1. Kwak EL, Bang YJ, Camidge DR, et al. Anaplastic lymphoma kinase inhibition in non–small-cell lung cancer. N Engl J Med, 2010;363(18):1693-1703
2. Shaw AT, Kim DW, Nakagawa K, et al. Crizotinib versus chemotherapy in advanced ALK-positive lung cancer. N Engl J Med. 2013;368(16):2385-2394
3. Peters S,Camidge DR,Shaw AT, et al. Alectinib versus crizotinib in untreated ALK-positive non-small-cell lung cancer.N Engl J Med. 2017; 377(9):829-838
4. Sholl LM, Weremowicz S, Gray SW, et al. Combined use of ALK Immunohistochemistry and FISH for optimal detection of ALK rearranged lung adenocarcinomas. J Thoraci Oncol. 2013;8(3):322–328
5. Horn L, Wang Z, Wu G, et al. Ensartinib vs crizotinib for patients with anaplastic lymphoma kinase-positive non-small cell lung cancer: A Randomized Clinical Trial. JAMA Oncol. 2021;7(11):1617-1625

Performance

Method Description

The test is performed using a US Food and Drug Administration approved anaplastic lymphoma kinase ALK (2p23) dual-color, break-apart rearrangement probe set (Abbott Molecular). Paraffin-embedded tissue samples are cut at 5 microns and mounted on positively charged glass slides. The selection of tissue and the identification of target areas on the hematoxylin and eosin (H and E)-stained slide are performed by a pathologist. Using the H and E-stained slide as a reference, target areas are etched with a diamond-tipped engraving tool on the back of the unstained slide to be assayed. The probe set is hybridized to the appropriate target areas, and 2 technologists each independently analyze 25 interphase nuclei (50 total). Results are reported based on the guidelines included with the probe kit and package insert with the results expressed as the percent of abnormal nuclei.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available
7 to 9 days

Specimen Retention Time
Slides and H&E used for analysis are retained by the laboratory in accordance with regulatory requirements. Client provided paraffin blocks and extra unstained slides (if provided) will be returned after testing is complete.

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
88271x2, 88291-DNA probe, each (first probe set), Interpretation and report
88271x2-DNA probe, each; each additional probe set (if appropriate)
88271x1-DNA probe, each; coverage for sets containing 3 probes (if appropriate)
88271x2-DNA probe, each; coverage for sets containing 4 probes (if appropriate)
88271x3-DNA probe, each; coverage for sets containing 5 probes (if appropriate)
88274 w/modifier 52-Interphase in situ hybridization, <25 cells, each probe set (if appropriate)
88274-Interphase in situ hybridization, 25 to 99 cells, each probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
LCAF	ALK (2p23), Lung Cancer, FISH, Ts	78205-2

Result ID	Test Result Name	Result LOINC® Value
52115	Result Summary	50397-9
52117	Interpretation	78210-2
54580	Result	62356-1
CG740	Reason for Referral	42349-1
52118	Specimen	31208-2

52119	Source	31208-2
52120	Tissue ID	80398-1
52121	Method	85069-3
55023	Additional Information	48767-8
52122	Released By	18771-6
53835	Disclaimer	62364-5