MAYO CLINIC LABORATORIES

Test Definition: LCAF

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

Overview

Useful For

Identifying patients with late-stage, non-small cell lung cancers who may benefit from treatment with the drug Xalkori

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 does not include a pathology consult. If a pathology consultation is requested, PATHC / Pathology Consultation should be ordered and the appropriate FISH test will be ordered and performed at an additional charge.

This test includes a charge for application of the first probe set (2 FISH probes) and professional interpretation of results.

Additional charges will be incurred for all reflex probes 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.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Tissue

Necessary Information

1. A pathology report is required in order for testing to be performed. Acceptable pathology reports include working drafts, preliminary pathology or surgical pathology reports.

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.

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Tissue
Preferred: Tissue block
Collection Instructions: Submit a formalin-fixed, paraffin-embedded (FFPE) tumor tissue block. Blocks prepared with alternative fixation methods may be acceptable; provide fixation method used.

Acceptable: Slides
Slides: Four consecutive, unstained, 5 micron-thick sections placed on positively charged slides, and 1 hematoxylin and eosin-stained slide.

Forms

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

Specimen Minimum Volume

Three consecutive, unstained, 5 micron-thick sections placed on positively charged slides and 1 hematoxylin and eosin-stained slide.

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

Lung cancer is the leading cause of cancer death in the United States. Non-small cell lung carcinoma (NSCLC) accounts for 75% to 80% of all lung cancers with an overall 5-year survival rate of 10% to 15%. Standard chemotherapy regimens have had marginal success in improving clinical outcomes. Targeted treatments may be used as novel molecular changes are identified.

Rearrangements of the anaplastic lymphoma kinase (*ALK*) locus are found in a subset of lung carcinomas and their identification may guide important therapeutic decisions for the management of these tumors. The fusion of echinoderm microtubule-associated protein-like 4 (*EML4*) gene with the *ALK* gene results from an inversion of chromosome band 2p23. The *ALK-EML4* rearrangement has been identified in 3% to 5% of NSCLC with the majority in adenocarcinoma and younger male patients who were light or nonsmokers. Lung cancers harboring *ALK* rearrangements

are resistant to epidermal growth factor receptor tyrosine kinase inhibitors, but may be highly sensitive to ALK inhibitors, like Xalkori (crizotinib).The drug Xalkori works by blocking certain kinases, including those produced by the abnormal *ALK* gene. Clinical studies have demonstrated that Xalkori treatment of patients with tumors exhibiting *ALK* rearrangements can halt tumor progression or result in tumor regression.

Reference Values

An interpretative report will be provided.

Interpretation

A positive result (*ALK* rearrangement identified) is detected when the percent of cells with an abnormality exceeds the normal cutoff for the *ALK* probe set.

A positive result suggests rearrangement of the *ALK* locus and a tumor that may be responsive to ALK inhibitor therapy.

A negative result suggests no rearrangement of the *ALK* gene region at 2p23.

A specimen is considered positive if >50% demonstrate a signal pattern consistent with an *ALK* rearrangement and considered negative if <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 >15% of cells exhibit a signal pattern consistent with an *ALK* rearrangement and negative if <15% of cells exhibit an *ALK* rearrangement.

Cautions

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

Supportive Data

Initial validation studies were performed on 40 paraffin-embedded lung tissue specimens, including 15 non-small cell lung carcinoma and 25 noncancerous lung tissue control specimens using the FDA-approved protocol. Additional verification studies were performed on 19 samples and demonstrated concordant results between the FDA method and a laboratory-developed protocol.

Clinical Reference

1. Soda M, Choi YL, Enomoto M, et al: Identification of the transforming *EML4-ALK* fusion gene in non-small-cell lung cancer. Nature 2007;448:561-566
2. Boland JM, Erdogan S, Vasmatzis G, et al: Anaplastic lymphoma kinase immunoreactivity correlates with *ALK* gene rearrangement and transcriptional up-regulation in non-small cell lung carcinomas. Hum Pathol 2009;40:1152-1158
3. Shaw AT, Yeap BY, Mino-Kenudson M, et al: Clinical features and outcome of patients with non-small-cell lung cancer who harbor *EML4-ALK*. J Clin Oncol 2009;27:4247-4253
4. Shaw AT, Yeap BY, Solomon BJ, et al: Effect of crizotinib on overall survival in patients with advanced non-small-cell lung cancer harbouring *ALK* gene rearrangement: a retrospective analysis. Lancet Oncol 2011;12:1004-1012
5. Koivunen JP, Mermel C, Zejnullahu K, et al: *EML4-ALK* fusion gene and efficacy of an ALK kinase inhibitor in lung cancer. Clin Cancer Res 2008;13:4275-4283

Performance

Method Description

The test uses an FDA-approved *ALK* (2p23) dual-color, break-apart rearrangement probe set (Abbott Molecular). Formalin-fixed, paraffin-embedded tissues are cut at 5 microns and mounted on positively charged glass slides. The selection of tissue and the target areas on the hematoxylin and eosin (H and E)-stained slide is performed by a pathologist. Using the H and E-stained slide as a reference, target areas are etched with a diamond-tipped etcher on the back of the unstained slide to be assayed. The probe set is hybridized to the appropriate target areas and 2 technologists each analyze 25 interphase nuclei (50 total). Results are reported based on the guidelines include 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 to CAP and NYS requirements. Client provided paraffin blocks and extra unstained slides (if provided) will be returned after testing is complete.

Performing Laboratory Location

Rochester

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 Regional Manager. 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. This test 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