MAYO CLINIC LABORATORIES

Test Definition: ROS1F

Lung Cancer, ROS1 (6q22) Rearrangement, FISH, Tissue

Overview

Useful For

Identifying c-ros oncogene 1 (*ROS1)* gene rearrangements in patients with late-stage, lung adenocarcinomas that are negative for epidermal growth factor receptor (*EGFR)* mutations and anaplastic lymphoma kinase (*ALK)* rearrangements

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
_I099	Interphases, 25-99	No, (Bill Only)	No
_I300	Interphases, >=100	No, (Bill Only)	No
_IL25	Interphases, <25	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
_PBCT	Probe, +2	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

Shipping Instructions

Advise Express Mail or equivalent if not on courier service.

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

Two 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 mortality in developed countries. The discovery of a variety of genetic alterations in non-small-cell lung cancer (NSCLC) has enabled the use of targeted therapy such as the anaplastic lymphoma kinase (ALK) inhibitor, crizotinib, and the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, erlotinib, for NSCLC with *ALK* rearrangements and *EGFR* mutations, respectively.

The c-ros oncogene 1 (*ROS1*), originally described in glioblastomas, has been identified as a potential relevant

therapeutic target in lung adenocarcinoma. Crizotinib has shown in vitro activity and early evidence of clinical activity in *ROS1*-rearranged tumors.

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 cutoff for the probe set.

A positive result suggests rearrangement of the *ROS1* locus and a tumor that may be responsive to ALK-inhibitor therapy.

A positive result suggests rearrangement of the c-ros oncogene 1 (*ROS1)* locus and a tumor that may be responsive to anaplastic lymphoma kinase (ALK)-inhibitor therapy

Cautions

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

Fixatives other than formalin (eg, Prefer, Bouin) may not be successful for FISH assays, however, nonformalin-fixed samples will not be rejected.

Paraffin-embedded tissues that have been decalcified are generally unsuccessful for FISH analysis. The pathologist reviewing the hematoxylin and eosin-stained slide may find it necessary to cancel testing.

Supportive Data

The probe set was independently validated in a blinded study on 20 paraffin-embedded lung adenocarcinoma tissue samples and 25 noncancerous control samples. Rearrangements of c-ros oncogene 1 (*ROS1)* were verified in samples previously identified with a *ROS1* rearrangement using reverse-transcriptase-PCR testing methods. The normal controls were used to generate a normal cutoff for this assay.

Clinical Reference

1. Suehara Y, Arcila M, Wang L, et al: Identification of *KIF5B-RET* and *GOPC-ROS1* fusions in lung adenocarcinomas through a comprehensive mRNA-based screen for tyrosine kinase fusions. Clin Cancer Res 2012;18(24):6599-6608
2. Takeuchi K, Soda M, Togashi Y, et al: *RET*, *ROS1* and *ALK* fusions in lung cancer. Nat Med 2012;18(3):378-381
3. Bergethon K, Shaw AT, Ou SH, et al: *ROS1* rearrangements define a unique molecular class of lung cancers. J Clin Oncol 2012;30(8):863-870
4. Chin LP, Soo RA, Soong R, Ou SH: Targeting *ROS1* with anaplastic lymphoma kinase inhibitors: a promising therapeutic strategy for a newly defined molecular subset of non-small-cell lung cancer. J Thorac Oncol 2012;7(11):1625-1630

Performance

Method Description

This test is performed using a laboratory developed c-ros oncogene 1 (*ROS1)* dual-color break-apart strategy probe (BAP). Paraffin-embedded tissues 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 etcher on the back of the unstained slide to be assayed. The probe is hybridized to the appropriate target areas and 2 technologists each analyze 50 interphase nuclei (100 total) with the results 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

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 account representative. For assistance, contact Customer Service.

Test Classification

This test was developed using an analyte specific reagent. Its performance characteristics were 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
ROS1F	ROS1 (6q22), FISH, Ts	81747-8

Result ID	Test Result Name	Result LOINC® Value
52235	Result Summary	50397-9
52237	Interpretation	69965-2
54595	Result	62356-1
CG755	Reason for Referral	42349-1
52238	Specimen	31208-2
52239	Source	31208-2
52240	Tissue ID	80398-1
52241	Method	85069-3
55035	Additional Information	48767-8
52242	Released By	18771-6
53821	Disclaimer	62364-5