

Overview

Useful For

Identifying non-small cell lung cancers that may benefit from treatment with epidermal growth factor receptor-tyrosine kinase or anaplastic lymphoma kinase inhibitors

Additional Tests

Test Id	Reporting Name	Available Separately	Always Performed
SLIRV	Slide Review in MG	No	Yes

Testing Algorithm

When this test is ordered, EGFR and LCAF testing will always be ordered. The *EGFR* Gene, Mutation Analysis, 29 Mutation Panel, Tumor, will always be performed. All specimens without an *EGFR* mutation will be automatically reflexed to LCAF / *ALK* (2p23), Lung Cancer, FISH Tissue. Specimens with an identified *EGFR* mutation will result in cancellation of the LCAF test.

When this test is ordered, slide review will always be performed at an additional charge.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
LCAF	ALK (2p23), Lung Cancer, FISH, Ts	Yes	No

Method Name

Polymerase Chain Reaction (PCR) and Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Pathology report **must** accompany specimen in order for testing to be performed.

Preferred:

Specimen Type: Tissue

Container/Tube: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block.

Acceptable:

Specimen Type: Tissue

Container/Tube: Slides

Specimen Volume: 12 unstained, positively charged, unbaked slides or 2 hematoxylin and eosin-stained slides (will not

be returned) and 10 unstained, positively charged, unbaked slides

Collection Instructions: Submit 12 unstained, positively charged, unbaked slides cut at 5-microns or 2 hematoxylin and eosin-stained slides and 10 unstained, positively charged, unbaked slides with 5-micron thick sections of the tumor tissue.

Forms

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

Reject Due To

Tissue Specimens that have been decalcified (all methods); specimens that have not been formalin-fixed, e paraffin-embedded

Specimen Minimum Volume

Formalin-fixed, paraffin-embedded tissue block (preferred) or 2 slides stained with hematoxylin-and-eosin and 10 unstained, positively charged, unbaked slides with 5-micron thick sections of the tumor tissue.

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Ambient (preferred)		
	Frozen		
	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. Epidermal growth factor receptor (EGFR) is activated by the binding of specific ligands, resulting in activation of the RAS/MAPK pathway. EGFR-targeted therapies (eg, gefitinib and erlotinib) have been approved by the FDA for use in treating patients with NSCLC who previously failed to respond to traditional chemotherapy. EGFR tyrosine kinase inhibitors have also been shown to increase progression-free and overall survival in patients who receive these therapies as a first-line therapy for the treatment of NSCLC. Agents such as gefitinib and erlotinib, which prevent ATP binding to EGFR kinase, do not appear to have any meaningful inhibitor activity on tumors that lack an activating *EGFR* mutation or in tumors that demonstrate the presence of drug-resistant *EGFR* mutations (eg, exon 20 insertions and T790M). Therefore, current data suggest that the efficacy of EGFR-targeted therapies in NSCLC is confined to patients with tumors demonstrating the presence of *EGFR*-activating mutations such as L858R, L861Q, G719A/S/C, S768I, or small deletions within exon 19 and the absence of drug-resistant mutations. As a result, the mutation status of *EGFR* is a critical marker for selecting patients for EGFR-targeted therapy.

Rearrangements of the anaplastic lymphoma kinase (*ALK*) locus are found in a subset of lung carcinomas (generally *EGFR* wild-type tumors) and their identification by FISH may guide important therapeutic decisions for the management of these tumors. The fusion of the *EML4* (echinoderm microtubule-associated protein-like 4) gene with the *ALK* (anaplastic large cell lymphoma kinase) 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 occurring in adenocarcinoma and younger male patients who

were light or nonsmokers. Recent studies have demonstrated that lung cancers harboring *ALK* rearrangements are resistant to epidermal growth factor receptor tyrosine kinase inhibitors, but may be highly sensitive to ALK inhibitors, like crizotinib (Xalkori). The drug crizotinib works by blocking certain kinases, including those produced by the abnormal *ALK* gene. Clinical studies have demonstrated that crizotinib treatment of patients with tumors exhibiting *ALK* rearrangements can halt tumor progression or result in tumor regression. The *ALK/EML4* FISH assay is an FDA-approved companion diagnostic test for crizotinib, which was recently approved by the FDA to treat certain patients with late-stage (locally advanced or metastatic), non-small cell lung cancers that harbor *ALK* gene rearrangements. It is useful for the identification of lung cancer patients who will benefit from crizotinib therapy.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

A negative (wild-type) *EGFR* result does not rule out the presence of a mutation that may be present, but below the limits of detection for this assay (approximately 5%).

A negative (wild-type) *EGFR* result does not rule out the presence of other activating mutations in the *EGFR* gene.

Rare polymorphisms exist that could lead to false-negative or false-positive *EGFR* results.

The *ALK* FISH test (LCAF) is intended to be used for therapeutic purposes in pulmonary carcinoma. This FISH assay does not rule out other chromosome abnormalities.

While results of these tests may indicate the likely response to epidermal growth factor receptor (EGFR)-or anaplastic lymphoma kinase (ALK)-inhibitor therapies, selection of treatment remains a clinical decision.

Clinical Reference

1. Sharma SV, Bell DW, Settleman J, Haber DA: Epidermal growth factor receptor mutations in lung cancer. *Nat Rev Cancer* 2007;7(3):169-181
2. Gao G, Ren S, Li A, et al: Epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) therapy is effective as first-line treatment of advanced non-small-cell lung cancer with mutated *EGFR*: a meta-analysis from 6 phase III randomized controlled trials. *Int J Cancer* 2012 Sep 1;131(5):E822-829
3. Mok TS: Personalized medicine in lung cancer: What we need to know. *Nat Rev Clin Oncol* 2011;8:661-668
4. Cheng L, Alexander RE, Maclennan GT, et al: Molecular pathology of lung cancer: key to personalized medicine. *Mod Path* 2012;25(3):346-369

Performance

Method Description

G719A	2239_2256del8
G719S	2239_2248TTAAGAGAAG->C
G719C	2239_2258->CA
2235_2249del15	2240_2251del12

2235_2252->AAT	2240_2257del8
2236_2253del18	2240_2254del15
2237_2251del15	2239_2251->C
2237_2254del18	2307_2308ins9
2237_2255->T	2310_2311insGGT
2236_2250del15,	2319_2320insCAC
2238_2255del18,	S768I
2238_2248->GC	T790M
2238_2252->GCA	L858R
2239_2247del9	L861Q
2239_2253del15	

PDF Report

No

Specimen Retention Time

Unused portions of blocks will be returned. Unused slides are stored indefinitely.

Performing Laboratory Location

Rochester

Fees & Codes
Test Classification

This test has been modified from the manufacturer's instructions. 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 U.S. Food and Drug Administration

CPT Code Information

EGFR Gene, Mutation Analysis, Tumor

81235-EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 deletions, L858R, T790M, G719S, L861Q)

Additional Tests:

Slide Review

88381-Microdissection, manual

Reflexed Tests (if appropriate):

Lung Cancer, ALK (2p23), FISH, Ts

88271 x 2-DNA Probe (if appropriate)

88274-Interphase in situ hybridization (if appropriate)

88291-Interpretation and report (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
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EGFR	Lung Cancer, EGFR with ALK Reflex	21665-5
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Result ID	Test Result Name	Result LOINC Value
53240	Result Summary	50397-9
53241	Result	21666-3
53242	Interpretation	69047-9
53243	Specimen	31208-2
53244	Source	31208-2
54441	Tissue ID	80398-1
53245	Released By	18771-6