Test Definition: KRASO

KRAS Mutation Analysis, Other

Overview

Useful For

Prognostic marker for cancer patients with noncolorectal tumors treated with epidermal growth factor receptor-targeted therapies

Additional Tests

Test ID	Reporting Name	Available Separately	Always Performed
SLIRV	Slide Review in MG	No, (Bill Only)	Yes

Testing Algorithm

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

Special Instructions

- Molecular Genetics: Inherited Cancer Syndromes Patient Information

Method Name

Polymerase Chain Reaction (PCR) Analysis

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: 1 stained and 5 unstained

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

Forms

1. Molecular Genetics: Inherited Cancer Syndromes Patient Information (T519) in Special Instructions.

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

Specimen Minimum Volume

Formalin-fixed, paraffin-embedded (FFPE) tissue block (preferred) or 1 slide stained with hematoxylin and eosin and 5 unstained, nonbaked slides (5-microns thick sections) of the tumor tissue.

Reject Due To

Specimens that have been decalcified (all methods) Specimens that have not been formalin-fixed, paraffin-embedded Bone marrow in EDTA	Reject

Specimen Stability Information

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

Clinical and Interpretive

Clinical Information

Lung cancer is the leading cause of cancer-related deaths in the world. Non-small cell lung cancer (NSCLC) represents 70% to 85% of all lung cancer diagnoses. Randomized trials have suggested that targeted agents alone or combined with chemotherapy may be beneficial. Because the addition of targeted therapy may lead to an increase in toxicity and cost, strategies that help to identify the individuals most likely to benefit from targeted therapies are desirable. Monoclonal antibodies against epidermal growth factor receptor (EGFR) represent a new area of targeted therapy for such patients. However, studies have shown that not all individuals with NSCLC respond to these EGFR-targeted molecules.

EGFR is a growth factor receptor that is activated by the binding of specific ligands (epiregulin and amphiregulin), resulting in activation of the RAS/MAPK pathway. Activation of this pathway induces a signaling cascade ultimately leading to cell proliferation. Dysregulation of the RAS/MAPK pathway is a key factor in tumor progression. Targeted therapies directed to EGFR, which inhibit activation of the RAS/MAPK pathway, have demonstrated some success in treating a subset of patients with NSCLC.

In NSCLC, one of the most frequently reported alterations in the EGFR-signaling pathway is the presence of a mutation in the proto-oncogene *KRAS*. *KRAS* is recruited by ligand-bound (active) EGFR to initiate the signaling cascade induced by the RAS/MAPK pathway. Because mutant *KRAS* constitutively activates the RAS/MAPK pathway downstream of EGFR, agents that prevent ligand-binding to EGFR do not appear to have any meaningful inhibitor activity on cell proliferation in the presence of mutant *KRAS*. Current data suggest that the efficacy of EGFR-targeted therapies in NSCLC is confined to patients with tumors lacking *KRAS* mutations. As a result, the mutation

status of *KRAS* can be a useful marker by which patients are selected for EGFR-targeted therapy.

At this time, this test is for unknown and/or unidentified primary tumors, primary tumors other than colorectal, and metastatic lesions from a primary other than colorectal. Please refer to KRASC / *KRAS* Mutation Analysis, 7 Mutation Panel, Colorectal for *KRAS* testing in colorectal tumors.

Reference Values

An interpretive report will be provided.

Interpretation

An interpretative report will be provided.

Cautions

Not all patients who have wild-type *KRAS* respond to epidermal growth factor receptor (EGFR)-targeted therapies.

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

Test results should be interpreted in context of clinical findings, tumor sampling, and other laboratory data. If results obtained do not match other clinical or laboratory findings, please contact the laboratory for possible interpretation. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Clinical Reference

1. Eberhard DA, Johnson BE, Amler LC, et al: Mutations in the epidermal growth factor receptor and in KRAS are predictive and prognostic indicators in patients with non-small-cell lung cancer treated with chemotherapy alone and in combination with erlotinib. J Clin Oncol 2005;23(25):5900-5909

2. Ladanyi M, Pao W: Lung adenocarcinoma: guiding EGFR-targeted therapy and beyond. Mod Pathol 2008;21 Suppl 2:S16-S22

3. Lam DC: Clinical testing for Molecular targets for personalized treatment in lung cancer. Respirology 2013 Feb;18(2):233-237 doi: 10.1111/j.1440-1843.2012.02261.x

Performance

Method Description

A PCR-based assay employing Scorpions real-time PCR and allele-specific PCR technologies is used to test for 7 mutations within codon 12 and 13 of the *KRAS* gene (G12D, G12A, G12V, G12S, G12R, G12C, and G13D). A pathology review and macrodissection to enrich for tumor cells is performed prior to DNA extraction.(Amado RG, Wolf M, Peeters M, et al: Wild-type KRAS is required for panitumumab efficacy in patients with metastatic colorectal cancer. J Clin Oncol 2008;26:1626-1634)

PDF Report

No

Day(s) and Time(s) Test Performed

Monday through Friday; Varies

Analytic Time

8 days

Maximum Laboratory Time

12 days

Specimen Retention Time

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

Performing Laboratory Location

Rochester

Fees and 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 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

81275-KRAS (v-Ki-ras2 Kirsten rat sarcoma viral oncogene) (eg, carcinoma) gene analysis, variants in codons 12 and 13

Additional Test

88381-Microdissection, manual

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
KRASO	KRAS Mutation Analysis, Other	75974-6

Result ID	Test Result Name	Result LOINC Value
53279	Result Summary	50397-9
53280	Result	82939-0
53281	Interpretation	69047-9
53282	Specimen	31208-2
53283	Source	31208-2
54446	Tissue ID	80398-1
53284	Released By	18771-6