Overview

Useful For
Identifying non-small cell lung cancers that may respond to epidermal growth factor receptor-tyrosine kinase inhibitor therapies

Additional Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLIRV</td>
<td>Slide Review in MG</td>
<td>No, (Bill Only)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

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

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, non-baked 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.

**Specimen Minimum Volume**

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

**Reject Due To**

| Specimens that have been decalcified (all methods) | Reject |
| Specimens that have not been formalin-fixed, paraffin-embedded | Reject |

**Specimen Stability Information**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varies</td>
<td>Ambient (preferred)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Refrigerated</td>
<td></td>
<td></td>
</tr>
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</table>

**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. Small molecular agents that target the tyrosine kinase domain of the epidermal growth factor receptor (EGFR) protein are approved for the treatment of locally advanced or metastatic NSCLC as a second- or third-line regimen. Subsequently, randomized trials have suggested that targeted agents alone or combined with chemotherapy may be beneficial in maintenance and first-line settings. Because the combination of targeted therapy and standard chemotherapy leads to an increase in toxicity and cost, strategies that help to identify the individuals most likely to benefit from targeted therapies are desirable.

EGFR is a growth factor receptor that is activated by the binding of specific ligands, 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 for many solid tumors. Targeted therapies directed to tumors harboring activating mutations within the *EGFR* tyrosine kinase domain (exons 18-21) have demonstrated some success in treating a subset of patients with NSCLC by preventing adenosine 5’-triphosphate (ATP)-binding at the active site. Gefitinib and erlotinib have been approved by the FDA for use in treating patients with NSCLC who previously failed to respond to the traditional platinum-based doublet chemotherapy. These 2 drugs have also recently been shown to increase progression-free and overall survival in patients who receive EGFR-tyrosine kinase inhibitor therapy 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 demonstrate the presence of the specific drug-resistant *EGFR* mutation 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 the drug-resistant mutation T790M. As a result, the
Test Definition: EGFRT
EGFR Gene, Mutation Analysis, Tumor

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

Reference Values
An interpretive report will be provided.

Interpretation
An interpretive report will be provided.

Cautions
A negative (wild type) result does not rule out the presence of a mutation that may be present but below the limits of detection for this assay (approximately 10%).

A negative (wild type) result does not rule out the presence of other activating mutations in the epidermal growth factor receptor (EGFR) gene.

The predictive value of epidermal growth factor receptor (EGFR) testing applies to EGFR--tyrosine kinase inhibitors (TKI) therapies, not to other therapeutic agents.

Not all patients that have activating EGFR mutations detected by this assay respond to EGFR-TKI therapies.

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

Clinical Reference


Performance

Method Description

A PCR-based assay employing Scorpions real-time PCR and allele-specific PCR technologies is used to test for 29 mutations within exons 18 through 21 of the EGFR gene:

<table>
<thead>
<tr>
<th>Mutation</th>
<th>Reference</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>G719A</td>
<td>2239_2256del8</td>
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<tr>
<td>G719S</td>
<td>2239_2248TTAAGAGAAG-&gt;C</td>
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<tr>
<td>G719C</td>
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<td>2307_2308ins9</td>
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</table>
A pathology review and macro dissection to enrich for tumor cells is performed prior to DNA extraction. (Package insert: EGFR RGQ PCR Kit, Qiagen, Valencia, CA, 2011)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; 10 a.m.

Analytic Time
5 days

Maximum Laboratory Time
7 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
EGFR Gene, Mutation Analysis, 29 Mutation Panel, Tumor

81235-EGFR (epidermal growth factor receptor) (eg, non-small cell lung cancer) gene analysis, common variants (eg, exon 19 LREA deletion, L858R, T790M, G719A, G719S, L861Q)
Slide Review

88381-Microdissection, manual

**LOINC® Information**

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<th>Test Order Name</th>
<th>Order LOINC Value</th>
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<td>EGFR Gene, Mutation Analysis, Tumor</td>
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<td>Result</td>
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<td>Interpretation</td>
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