Overview

Useful For
Identification of urothelial tumors that may respond to FGFR-targeted therapies

This test is **not intended for** use for hematological malignancies and **does not assess** germline alterations within the genes listed.

Genetics Test Information
This test is an FDA-approved assay for the evaluation of somatic mutations and fusions in the **FGFR3** and **FGFR2** genes to identify urothelial carcinoma patients that may be eligible for treatment with FGFR-targeted therapies such as Balversa (erdafitinib).

This test uses targeted reverse transcriptase (RT)-PCR to evaluate for somatic mutations within the **FGFR3** gene: R248C, S249C, G370C, and Y373C. RT-PCR is also used to identify certain rearrangements (fusions): **FGFR3-TACC3v3** and **FGFR3-TACC3v1**. Furthermore, this test can identify fusions: **FGFR3-BAIAP2L1**, **FGFR2-BICC1**, and **FGFR2-CASP7**, however detection of these fusions is considered off-label use of the test. For more information see Clinical Information.

Of note, this test is performed to evaluate for somatic mutations and rearrangements (fusions) within solid tumor samples. This test is not intended for use for hematological malignancies. Additionally, this test does not assess for germline alterations within the genes listed.

Additional Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
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<tbody>
<tr>
<td>SLIRV</td>
<td>Slide Review in MG</td>
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Testing Algorithm
When this test is ordered, slide review will always be performed at an additional charge.

Method Name
Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR)

NY State Available
Yes

Specimen

Specimen Type
Varies

Necessary Information
Pathology report (final or preliminary) at minimum containing the following information **must** accompany specimen in order for testing to be performed:

1. Patient name
2. Block number—must be on all blocks, slides and paperwork (can be handwritten on the paperwork)

3. Tissue collection date

4. Source of the tissue

**Specimen Required**

This assay requires at least 10% tumor nuclei.

The amount of tissue needed is dependent on a variety of preanalytical factors (e.g., cellularity, ischemic time, fixation).

The FFPE input required is equivalent to a 4â€“5 micron slide thickness with a total tumor surface area between 100 mm$^2$ and 500 mm$^2$ (inclusive). This can be created by combining material from multiple slides from one tissue block.

**Preferred:**

**Specimen Type:** Tissue block

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

**Acceptable:**

**Specimen Type:** Tissue slide

**Slides:** 1 stained and 10 unstained

**Collection Instructions:** Submit 1 slide stained with hematoxylin and eosin and 10 unstained, nonbaked slides with 5-micron thick sections of the tumor tissue.

**Specimen Minimum Volume**

See Specimen Required

**Reject Due To**

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

**Specimen Stability Information**

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<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
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Clinical and Interpretive

Clinical Information

As high as 32% of individuals with urothelial cancer have been observed to have an activating fibroblast growth factor receptor (FGFR) alteration and approximately half of those are in FGFR3. The FGFR isotypes are part of the RAS/MAPK, PI3KAKT, PLCgamma, and STAT intracellular signaling pathways involved in cell proliferation and survival. FGFR mutations, primarily those occurring in the kinase domain, result in constitutive activation and contribute to tumorigenesis. The FGFR kinase inhibitor erdafitinib (BALVERSA) is a drug therapy approved by the FDA for individuals with FGFR3 and FGFR2-mutated advanced or metastatic urothelial carcinoma after platinum-containing chemotherapy has become ineffective.

Current data suggest that the efficacy of FGFR-targeted therapy in urothelial cancer is highest in patients with tumors demonstrating the presence of the FGFR3-activating mutations R248C, S249C, G370C, Y373C, and fusions FGFR3-TACC3v3, FGFR3-TACC3v1. As a result, the mutation status of FGFR is a critical marker for selecting patients for FGFR-targeted therapy.

This FDA approved test uses RNA extracted from the tumor tissue to evaluate for the presence of mutations of R248C, S249C, G370C, and Y373C in the FGFR3 gene, as well as fusions FGFR3-TACC3v3 and FGFR3-TACC3v1. A positive result showing any of these alterations indicates the presence of an FGFR mutation and may be useful for guiding the treatment of individuals with urothelial cancer.

This test was also designed to find fusions FGFR3-BAIAP2L1, FGFR2-BICC1, and FGFR2-CASP7. However, FDA approval of this assay to detect these fusions was not gained due to lack of patient samples. Drug efficacy and safety has not been established for these fusions, which were included in clinical trials. These fusions will be reported if detected but are considered off-label use of the test.

At this time, this test is approved specifically for patients with urothelial cancer. The utilization of this test in patients with other tumor types could be considered an off-label use of this test.

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 or rearrangement (fusion) that may be present but below the limits of detection of this assay. It also does not rule out the presence of other activating mutations in the fibroblast growth factor receptor (FGFR) gene outside those that the assay was designed to detect.

The predictive value of FGFR testing applies to FGFR- kinase inhibitors therapy erdafitinib (BALSERA), not to other therapeutic agents.

Not all patients who have FGFR mutations respond to FGFR-targeted therapies.

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

Reliable results are dependent on adequate specimen collection and processing. This test has been validated on cytology slides and formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause PCR failure.
Test Definition: TFGFR
FGFR Mutation/Fusion Analysis Tumor

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


Performance

Method Description
A PCR-based assay employing real-time PCR and allele-specific PCR technologies is used to test for 4 mutations within FGFR3 (R248C, S249C, G370C and Y373C) and 2 fusions (FGFR3-TACC3v1, FGFR3-TACC3v3). Although not FDA-approved, per package insert, this test may also detect 3 additional fusions in FGFR3 and FGFR2 (FGFR3-BAIAP2L1, FGFR2-BICC1, FGFR2-CASP7,(Package insert: therascreen FGFR RGQ PCR Kit. Qiagen, 04/2019)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; Varies

Analytic Time
5 days

Maximum Laboratory Time
7 days

Specimen Retention Time
Unused portions of blocks will be returned. Unused slides: 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 cleared, approved or is exempt by the U.S. Food and Drug Administration and is used per
Test Definition: TFGFR
FGFR Mutation/Fusion Analysis Tumor

manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

CPT Code Information
0154U

Slide Review
88381

LOINC® Information

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