Test Definition: ESR1

ESR1 Mutation Analysis, Tumor

Overview

Useful For

Assisting in the clinical management of patients with metastatic breast cancer by identifying tumors with evolving resistance to endocrine therapy

Stratifying prognosis of metastatic breast cancer

This test is **not useful for** hematological malignancies.

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.

Method Name

Polymerase Chain Reaction (PCR)-Based Next-Generation Sequencing

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 20% tumor nuclei.

-Preferred amount of tumor area with sufficient percent tumor nuclei: tissue144 mm(2)

-Minimum amount of tumor area: tissue 36 mm(2).

-These amounts are cumulative over up to 10 unstained slides and must have adequate percent tumor nuclei.

-Tissue fixation: 10% neutral buffered formalin, not decalcified

-For specimen preparation guidance, see Tissue Requirement for Solid Tumor Next-Generation Sequencing in Special Instructions. In this document, the sizes are given as 4mm x 4mm x 10 slides as preferred: approximate/equivalent to 144 mm(2) and the minimum as 3mm x 1mm x 10 slides: approximate/equivalent to 36mm(2).

Preferred:

Specimen Type: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block with acceptable amount of tumor tissue.

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.

Note: The total amount of required tumor nuclei can be obtained by scraping up to 10 slides from the same block.

Specimen Type: Cytology slide (direct smears or ThinPrep)

Slides: 1 to 3 slides

Collection Instructions: Submit 1 to 3 slides stained and cover slipped with a preferred total minimum of 5000 total nucleated cells, minimum of 3000 nucleated cells.

Note: Glass coverslips are preferred; plastic coverslips are acceptable but will result in longer turnaround times.

Additional Information: Cytology slides will not be returned.

Forms

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

Specimen Minimum Volume

See Specimen Required

Reject Due To

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

Specimen Stability Information

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

Clinical and Interpretive

Clinical Information

The estrogen receptor 1 *(ESR1)* gene encodes an estrogen receptor that regulates cell growth through activation of downstream signaling pathways upon binding of estrogen. Tumors demonstrating estrogen receptor expression (ER-positive) are candidates for endocrine therapy such as selective estrogen receptor modulators (SERM) and aromatase inhibitors. *ESR1* mutations are rarely observed in primary tumors; however, mutations in the ligand-binding domain of *ESR1* have been reported at a higher frequency in ER-positive metastatic breast tumors. Preclinical data suggests that *ESR1* mutations mitigate resistance to aromatase inhibitors and decrease sensitivity to SERMs and estrogen-receptor downregulators. Studies also suggest that *ESR1* mutations are an independent indicator of poor prognosis.

This test assesses for somatic mutations in the ligand-binding domain of the *ESR1* gene associated with acquired resistance to endocrine therapy (ie, aromatase inhibitors) in patients with ER-positive metastatic breast cancer.

Reference Values

An interpretative report will be provided.

Interpretation

An interpretive report will be provided.

Cautions

This test cannot differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

DNA variants of uncertain significance may be identified.

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

Point mutations and small insertion/deletion mutations will be detected with in the *ESR1* gene only. This test does not detect large single or multiexon deletions, or duplications or genomic copy number variants.

Rare polymorphisms may be present that could lead to false-negative or false-positive results. Test results should be interpreted in the context of clinical findings, tumor sampling and other laboratory data.

If results obtained do not match other clinical or laboratory findings, contact the laboratory for updated interpretation. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

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.

Supportive Data

This next-generation sequencing assay detects somatic mutations that can be used to assist in the clinical management of metastatic breast cancer patients.

This assay has been shown to be very reproducible, having a 100% concordance for intra- and interassay reproducibility experiments. All somatic mutations that had been previously identified by various other molecular methods were detected by this assay during accuracy studies. No pathogenic variants were detected in known mutation negative samples.

Clinical Reference

1. Arenedos M, Vicier C, Loi S, et al: Precision medicine for metastatic breast cancer-limitations and solutions. Nat Rev Clin Oncol. 2015 Dec;12(12):693-704

2. Angus L, Beije N, Jager A, et al: ESR1 mutations: Moving towards guiding treatment decision-making in metastatic breast cancer patients. Cancer Treat Rev. 2017 Jan;52:33-40

3. Gradishar WJ, Anderson BO, Balassanian R, et al: NCCN Guidelines Insights: Breast Cancer, Version 1.2017. J Natl Compr Canc Netw. 2017 Apr;15(4):433-451

4. Toy W, Shen Y, Won H, et al: ESR1 ligand-binding domain mutations in hormone-resistant breast cancer. Nat Genet. 2013 Dec;45(12):1439-1445

5. Robinson DR, Wu YM, Vats P, et al: Activating ESR1 mutations in hormone-resistant metastatic breast cancer. Nat Genet. 2013 Dec;45(12):1446-1451

6. Toy W, Weir H, Razavi P, et al: Activating ESR1 Mutations Differentially Affect the Efficacy of ER Antagonists. Cancer Discov. 2017 Mar;7(3):277-287

Performance

Method Description

Next-generation sequencing is performed to test for the presence of a mutation in targeted regions of the ESR1 gene.(Unpublished Mayo method)

Gene	GenBank Accession Number	Nucleotide Start	Nucleotide End	Chromosome	Exon	Codons
ESR1	NM_000125	152415449	152415563	Chromosome 6	Exon 7	457-471
		152419879	152419997		Exon 8	522-562

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

12 to 20 days

Specimen Retention Time

Unused portions of blocks will be returned to the client. 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 was developed and its performance characteristics 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

81479

88381

LOINC® Information

Test ID	Test Order Name	Order LOINC Value
ESR1	ESR1 Mutation Analysis, Tumor	In Process

Result ID	Test Result Name	Result LOINC Value
92381	Result Summary	50397-9
92382	Result	82939-0
92383	Interpretation	69047-9
92384	Additional Information	48767-8
92385	Specimen	31208-2
92386	Source	31208-2
92387	Tissue ID	80398-1
92388	Released By	18771-6