MAYO CLINIC LABORATORIES

Test Definition: ESTUF

Endometrial Stromal Tumors (EST), 7p15 (JAZF1), 6p21.32 (PHF1), 17p13.3 (YWHAE) Rearrangement, FISH, Tissue

Overview

Useful For

Aiding in the diagnosis of endometrial stromal tumors when used in conjunction with an anatomic pathology consultation

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
_PBCT	Probe, +2	No, (Bill Only)	No
_PADD	Probe, +1	No, (Bill Only)	No
_PB02	Probe, +2	No, (Bill Only)	No
_PB03	Probe, +3	No, (Bill Only)	No
_IL25	Interphases, <25	No, (Bill Only)	No
_I099	Interphases, 25-99	No, (Bill Only)	No
_I300	Interphases, >=100	No, (Bill Only)	No

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for one probe set (2 individual fluorescence in situ hybridization [FISH] probes). Additional charges will be incurred for all reflex or additional probe sets performed. No analysis charges will be incurred if an insufficient number of representative cells are available for analysis.

Unless otherwise indicated, the JAZF1 probe set will be performed initially. In the absence of a *JAZF1* rearrangement, reflex testing using the PHF1 probe set will be performed. In the absence of a *PHF1* rearrangement, reflex testing using the YWHAE probe set will be performed.

If FISH testing for a *JAZF1* rearrangement was previously performed, reflex testing using the YWHAE and/or PHF1 probe sets may be ordered separately. A copy of the JAZF1 FISH report is required for testing to be performed. If not provided, appropriate testing and interpretation may be compromised or delayed.

Appropriate ancillary probes may be performed at consultant discretion to render comprehensive assessment. Any additional probes will have the results included within the final report and will be performed at an additional charge.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type
Tissue

Ordering Guidance
This test does not include a pathology consultation. If a pathology consultation is requested, order PATHC / Pathology Consultation, and appropriate testing will be added at the discretion of the pathologist and performed at an additional charge.

Multiple oncology (cancer) gene panels are also available. For more information see Hematology and Oncology Test Selection Guide

This test is **not intended for** male patients.

Additional Testing Requirements
Confirmation testing for the presence of a possible JAZF1, PHF1, or YWHAE fusion transcript by next-generation sequencing to resolve atypical or unbalanced fluorescence in situ hybridization results is available, order MCSRC / MayoComplete Comprehensive Sarcoma Panel, Next-Generation Sequencing, Tumor or MCRSP / MayoComplete Targeted RNA Sequencing Panel, Next-Generation Sequencing, Tumor.

Shipping Instructions
Advise Express Mail or equivalent if not on courier service.

Necessary Information
1. A pathology report is required for testing to be performed. If not provided, appropriate testing and/or interpretation may be compromised or delayed. Acceptable pathology reports include working drafts, preliminary pathology, or surgical pathology reports.
2. The following information must be included in the report provided.
-Patient name
-Block number - must be on all blocks, slides, and paperwork
-Date of collection
-Tissue source
3. A reason for testing must be provided. If this information is not provided, an appropriate indication for testing may be entered by Mayo Clinic Laboratories.

Specimen Required
Submit only 1 of the following specimens:

Preferred:
Specimen Type: Tissue block (fresh tissue is **not acceptable**)
Collection Instructions:
1. Submit a formalin-fixed, paraffin-embedded tumor tissue block.

2. Blocks prepared with alternative fixation methods (eg, Prefer, Bouin's) will be attempted but are less favorable for successful results. Provide fixation method used.

Additional Information:

1. Paraffin-embedded specimens can be from any anatomic location (skin, soft tissue, lymph node, etc).
2. Decalcified paraffin-embedded specimens will have testing attempted; however, the success rate is approximately 50%. **Testing may be canceled** if sufficient tumor tissue is not present.
3. **Submitted fresh tissue specimens will be canceled upon receipt**. If only fresh tissue is available, embed in paraffin prior to sending.

Acceptable:

Specimen Type: Tissue slides

Slides: 1 Hematoxylin and eosin-stained and 4 unstained

Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 4 consecutive unstained, positively charged, unbaked slides with 5 micron-thick sections of the tumor tissue.

Additional Information: Broken or cracked unstained slides will be rejected. Stained slides that were broken and repaired (ie, double mounted) at the client site will not be rejected, as, in most cases, they can still be reviewed under the microscope. However, due to the double mounting, digital scanning cannot be performed.

Forms

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

Specimen Minimum Volume

Slides: 1 Hematoxylin and eosin stained and 3 unstained

Reject Due To

Broken or cracked unstained slides	Reject
Broken or cracked stained slides that cannot be repaired	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Tissue	Ambient (preferred)		
	Refrigerated		

Clinical & Interpretive

Clinical Information

Endometrial stromal tumors arise from the uterus and include benign endometrial stromal nodule (ESN) and endometrial stromal sarcoma (ESS). Rearrangement of *JAZF1* occurs in approximately 70% of ESN and approximately 60% of low-grade ESS and rare high-grade ESS.

Rearrangement of *PHF1* is present in a subset of ESS and can rearrange with both known and unknown partners in addition to *JAZF1*.

YWHAE rearrangements occur in a subset of high-grade ESS.

Reference Values

An interpretive report will be provided.

Interpretation

JAZF1, YWHAE or PHF1 will be clinically interpreted as positive, negative, or equivocal.

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the respective normal cutoff for the JAZF1, YWHAE or PHF1 probe sets.

A positive result is consistent with a rearrangement of the *JAZF1, YWHAE and/or PHF1* gene regions. A positive result supports a diagnosis of an endometrial stromal tumor of various subtypes.

A negative result suggests no rearrangement of the *JAZF1, YWHAE or PHF1* gene regions are present but does not exclude the diagnosis of an endometrial stromal tumor.

A negative result suggests a *JAZF1, YWHAE or PHF1* gene rearrangement is not present.

A negative result does not exclude the presence of a neoplastic disorder.

Cautions

This test is not approved by the U.S. Food and Drug Administration, and it is best used as an adjunct to existing clinical and pathologic information.

This test is intended to be used for diagnostic purposes in endometrial stromal tumors.

This fluorescence in situ hybridization (FISH) assay does not rule out other chromosome abnormalities.

Fixatives other than formalin (eg, Prefer, Bouin's) may not be successful for FISH assays. Non-formalin fixed specimens will not be rejected.

Paraffin-embedded tissues that have been decalcified may not be successful for FISH analysis. The success rate of FISH studies on decalcified tissue is approximately 50%, but FISH will be attempted if sufficient tumor is present for analysis.

Fluorescence in situ hybridization studies will be attempted if sufficient tumor is present for analysis. The pathologist reviewing the hematoxylin and eosin-stained slide may find it necessary to cancel testing if insufficient tissue/tumor is available for testing.

If no FISH signals or a lack of sufficient tumor tissue are observed post-hybridization, the case will be released indicating a lack of FISH results.

Clinical Reference

1. WHO Classification of Tumours. Female Genital Tumours. 5th ed. IARC; 2020:286-288. WHO Classification of Tumours. Vol 4
2. Nomura Y, Tamura D, Horie M, et al. Detection of MEAF6-PHF1 translocation in an endometrial stromal nodule. Genes Chromosomes Cancer. 2020;59(12):702-708
3. Conklin CM, Longacre TA. Endometrial stromal tumors: the new WHO classification. Adv Anat Pathol. 2014;21(6):383-393
4. Antonescu CR, Kao YC, Xu B, et al. Undifferentiated round cell sarcoma with BCOR internal tandem duplications (ITD) or YWHAE fusions: a clinicopathologic and molecular study. Mod Pathol. 2020;33(9):1669-1677
5. O'Meara E, Stack D, Lee CH, et al. Characterization of the chromosomal translocation t (10; 17)(q22; p13) in clear cell sarcoma of kidney. J Pathol. 2012;227(1):72-80
6. Chiang S, Ali R, Melnyk N, et al. Frequency of known gene rearrangements in endometrial stromal tumors. Am J Surg Pathol. 2011;35(9):1364-1372
7. Lee CH, Marino-Enriquez A, Ou W, et al. The clinicopathologic features of YWHAE-FAM22 endometrial stromal sarcomas: A histologically high-grade and clinically aggressive tumor. Am J Surg Pathol. 2012;36(5):641-653
8. Panagopoulos I, Mertens F, Griffin CA, et al. An endometrial stromal sarcoma cell line with the JAZF1/PHF1 chimera. Cancer Genet Cytogenet. 2008;185(2):74-77
9. Lee CH, Ou WB, Marino-Enriquez A, et al. 14-3-3 fusion oncogenes in high-grade endometrial stromal sarcoma. Proc Natl Acad Sci U S A. 2012;109(3):929-934
10. Micci F, Panagopoulos I, Bjerkehagen B, et al. Consistent rearrangement of chromosomal band 6p21 with generation of fusion genes JAZF1/PHF1 and EPC1/PHF1 in endometrial stromal sarcoma. Cancer Res. 2006;66(1):107-112
11. Gebre-Medhin S, Nord KH, Moller E, et al. Recurrent rearrangement of the PHF1 gene in ossifying fibromyxoid tumors. Am J Pathol. 2012;181(3):1069-1077

Performance

Method Description

The test is performed using laboratory-developed JAZF1, YWHAE, PHF1 dual-color, break-apart strategy fluorescence in situ hybridization probe sets. Formalin-fixed, paraffin-embedded tissues are cut at 5 microns and mounted on positively charged glass slides. The selection of tissue and the identification of target areas on the hematoxylin and eosin (H and E)-stained slide are performed by a pathologist. Using the H and E-stained slide as a reference, target areas are etched

with a diamond-tipped engraving tool on the back of the unstained slide to be assayed. The probe set is hybridized to the appropriate target areas, and 2 technologists independently analyze 50 interphase nuclei (100 total) with the results expressed as the percent of abnormal nuclei.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
7 to 10 days

Specimen Retention Time
Slides and H and E used for analysis are retained by the laboratory in accordance with regulatory requirements. Client provided paraffin blocks and extra unstained slides will be returned after testing is complete.

Performing Laboratory Location
Mayo Clinic Laboratories - Rochester Main Campus

Fees & 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 account representative. 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. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information
88271x2
88291-DNA probe, each (first probe set), Interpretation and report
88271x2-DNA probe, each; each additional probe set (if appropriate)
88271x1-DNA probe, each; coverage for sets containing 3 probes (if appropriate)
88271x2-DNA probe, each; coverage for sets containing 4 probes (if appropriate)
88271x3-DNA probe, each; coverage for sets containing 5 probes (if appropriate)
88274 w/modifier 52-Interphase in situ hybridization, <25 cells, each probe set (if appropriate)
88274-Interphase in situ hybridization, 25 to 99 cells, each probe set (if appropriate)

LOINC® Information

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Test ID	Test Order Name	Order LOINC® Value
ESTUF	Endometrial Stromal Tumor, FISH, Ts	102086-6

Result ID	Test Result Name	Result LOINC® Value
52147	Result Summary	50397-9
52149	Interpretation	69965-2
54584	Result	62356-1
CG744	Reason for Referral	42349-1
52150	Specimen	31208-2
52151	Source	31208-2
52152	Tissue ID	80398-1
52153	Method	85069-3
55026	Additional Information	48767-8
52154	Released By	18771-6
53831	Disclaimer	62364-5