Test Definition: EOSDF

Chronic Eosinophilia, Diagnostic FISH, Varies

Overview

Useful For

Detecting a neoplastic clone associated with the common chromosome abnormalities seen in patients with myeloid/lymphoid neoplasms with eosinophilia and gene rearrangement (including PDGFRA, PDGFRB, FGFR1, JAK2, and ABL1).

Supporting the diagnosis of malignancy if a clone is present

An adjunct to conventional chromosome studies.

Reflex Tests

Test Id	Reporting Name	Available Separately	Always Performed
EOSDB	Probe, Each Additional (EOSDF)	No, (Bill Only)	No

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for 5 probe sets (11 individual fluorescence in situ hybridization [FISH] probes). Additional charges will be incurred for all reflex or additional probe sets performed.

The panel includes testing for the following kinase activating chromosome abnormalities, using the following FISH probes:
4q12 deletion or rearrangement, FIP1L1, CHIC2 ,PDGFRA
5q32 rearrangement, PDGFRB
8p11.2 rearrangement, FGFR1
9p24.1 rearrangement, JAK2
9q34 rearrangement, ABL1

In the absence of a CHIC2 deletion, if an extra or atypical CHIC2 or PDGFRA signal is identified, reflex testing will be performed using the PDGFRA break-apart probe set to evaluate for the presence or absence of a PDGFRA rearrangement.

If a PDGFRB rearrangement is identified, reflex testing using the PDGFRB/ETV6 probe set will be performed to evaluate for the presence or absence of t(5;12)(q32;p13) -PDGFRB/ETV6 fusion.

If an ABL1 rearrangement is identified, reflex testing using the ABL1/BCR probe set will be performed to evaluate for the presence or absence of t(9;22)(q34;q11.2) - ABL1/BCR fusion.

Method Name

Fluorescence In Situ Hybridization (FISH)

NY State Available

Yes

Specimen

Specimen Type

Varies

Ordering Guidance

This test is intended to be ordered when the entire chronic eosinophilia fluorescence in situ hybridization (FISH) panel is needed.

If limited chronic eosinophilia FISH probes are preferred, order EOSMF / Chronic Eosinophilia, Specified FISH, Varies.

At follow-up, targeted chronic eosinophilia probes can be evaluated based on the abnormalities identified in the diagnostic study. Order EOSMF/ Chronic Eosinophilia, Specified FISH, Varies. and request a specific probe to evaluate the known genomic abnormality.

Paraffin embedded tissue testing is not available for these probe sets.

Necessary Information

A reason for testing and a flow cytometry and/or a bone marrow pathology report should be submitted with each specimen. The laboratory will not reject testing if this information is not provided however, appropriate testing and interpretation may be compromised or delayed. If 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: Bone marrow
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (heparin) or lavender top (EDTA)
Specimen Volume: 2-3 mL
Collection Instructions:
1. It is preferable to send the first aspirate from the bone marrow collection.
2. Invert several times to mix bone marrow.
3. Send bone marrow specimen in original tube. **Do not aliquot.**

Acceptable
Specimen Type: Blood
Container/Tube:

Preferred: Yellow top (ACD)
Acceptable: Green top (heparin) or lavender top (EDTA)
Specimen Volume: 6 mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot.**

Forms
If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Specimen Minimum Volume
Blood: 2 mL
Bone Marrow: 1 mL

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

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

Clinical & Interpretive

Clinical Information
The myeloid/lymphoid neoplasms with eosinophilia and rearrangements of *PDGFRA*, *PDGFRB*, *FGFR1* and *JAK2* represent a significantly diverse group of hematologic malignancies. Despite the disparate clinical presentations, which include chronic myeloid neoplasms (chronic myelomonocytic leukemia, chronic myeloproliferative neoplasms, chronic eosinophilic leukemia) versus more acute myeloid and lymphoid neoplasms (acute myeloid leukemia, B- and T-lymphoblastic leukemia/lymphoma and mixed phenotypic acute leukemias), this diagnostic subgroup shares rearrangements involving 4 specific gene regions: *PDGFRA*, *PDGFRB*, *FGFR1*, and *JAK2*.

While conventional chromosome studies may detect many of the rearrangements associated with these gene rearrangements, several are cytogenetically "cryptic," including the most common abnormality involving *PDGFRA* activation. This one megabase submicroscopic, intrachromosomal deletion results in loss of the *CHIC2* gene region with subsequent fusion of neighboring genes *FIP1L1* and *PDGFRA*. In addition to this more common, cryptic deletion, the *PDGFRA* gene has many translocation partners described (at least 15) that similarly result in *PDGFRA* upregulation.

The *PDGFRB*, *FGFR1*, and *JAK2* gene regions similarly have numerous translocation/inversion partners described, at least 50 for *PDGFRB*, 10 for *FGFR1*, and 40 for *JAK2*. Despite the significant heterogeneity in gene partners, the identification of *PDGFRA*, *PDGFRB*, *FGFR1*, and *JAK2* rearrangements is critical for disease categorization and potential therapeutic intervention. Both *PDGFRA* and *PDGFRB* have the potential for response to targeted tyrosine kinase inhibitor therapies such as imatinib mesylate. Similarly, *JAK2* rearrangements have the potential for response to targeted inhibitor therapy.

Rearrangements of *FGFR1* are typically more aggressive and less responsive to targeted inhibitors.

While not formally included in the World Health Organization categorization of myeloid/lymphoid neoplasms with *PDGFRA*, *PDGFRB*, *FGFR1*, or *JAK2* rearrangements, rearrangements of the *ABL1* gene other than with the *BCR* locus, can result in similar clinical phenotypes. Thus, the *ABL1* gene region has been included in this fluorescence in situ hybridization panel evaluation to appropriately interrogate this gene region, particularly since these patients may not be identified by conventional karyotype analysis and may significantly benefit from targeted tyrosine kinase therapies.

Reference Values

An interpretive report will be provided.

Interpretation

A neoplastic clone is detected when the percent of cells with an abnormality exceeds the normal reference range for any given probe.

The absence of an abnormal clone does not rule out the presence of a neoplastic disorder.

Cautions

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

Fluorescence in situ hybridization (FISH) is not a substitute for conventional chromosome studies because the latter detects chromosome abnormalities associated with other hematological disorders that would be missed by this FISH panel test.

Bone marrow is the preferred sample type for this FISH test. If bone marrow is not available, a blood specimen may be used if there are neoplastic cells in the blood specimen (as verified by a hematopathologist).

Supportive Data

Each probe was independently tested and verified on unstimulated peripheral blood and bone marrow specimens. Normal cutoffs were calculated based on the results of 25 normal specimens. Each probe set was evaluated to confirm the probe set detected the abnormality it was designed to detect.

Clinical Reference

Myeloid/lymphoid neoplasms with eosinophilia and gene rearrangement. In: Swerdlow SH, Campo E, Harris NL, et al, eds. WHO Classification of Tumours. Vol 2. WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. 4th ed. IARC Press; 2017:71-80

Performance

Method Description

This test is performed using commercially available and laboratory-developed probes. Rearrangements or deletions involving *CHIC2, PDGFRA, PDGFRB, FGFR1*, *JAK2*, and *ABL1* are detected using a tri or dual-color break-apart (BAP) strategy probe. Dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe sets are used in reflex

testing when rearrangements of the *PDGFRB* and *ABL1* gene are detected. For enumeration and BAP strategy probe sets, 100 interphase nuclei are scored; 200 interphase nuclei are scored when D-FISH probes are used. All results are expressed as the percent abnormal nuclei.(Unpublished Mayo method)

PDF Report
No

Day(s) Performed
Monday through Friday

Report Available
7 to 10 days

Specimen Retention Time
4 weeks

Performing Laboratory Location
Rochester

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
88271 x11, 88275 x5, 88291 x1-FISH Probe, Analysis, Interpretation; 5 probe sets
88271 x2, 88275 x1–FISH Probe, Analysis; each additional probe set (if appropriate)

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
EOSDF	Chronic Eosinophilia, Diag FISH	In Process

Result ID	Test Result Name	Result LOINC® Value
609588	Result Summary	50397-9
609589	Interpretation	69965-2
609590	Result Table	93356-4
609591	Result	62356-1
GC080	Reason for Referral	42349-1

GC081	Specimen	31208-2
609592	Source	31208-2
609593	Method	85069-3
609594	Additional Information	48767-8
609595	Disclaimer	62364-5
609596	Released By	18771-6