Test Definition: EOSFD

Chronic Eosinophilia Panel, 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*, *ABL1* and *FLT3*) using a laboratory-designated probe set algorithm

Supporting the diagnosis of malignancy if a clone is present

Evaluating specimens in which standard cytogenetic analysis is unsuccessful

Reflex Tests

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

Testing Algorithm

This test includes a charge for the probe application, analysis, and professional interpretation of results for 6 probe sets (13 individual fluorescence in situ hybridization [FISH] probes). Additional charges will be incurred for all reflex or additional probe sets performed. Analysis charges will be incurred based on the number of cells analyzed per probe set. If no cells are available for analysis, no analysis charges will be incurred.

This test is performed as panel testing only using the following analysis algorithm.

The panel includes testing for the following kinase activating chromosome abnormalities, using the following FISH probes:
4q12 deletion or rearrangement, FIP1L1, CHIC2, PDGFRA break-apart probe set
t(5q32;var) or *PDGFRB* rearrangement, PDGFRB break-apart probe set
t(8p11.2;var) or *FGFR1* rearrangement, FGFR1 break-apart probe set
t(9p24.1;var) or *JAK2* rearrangement, JAK2 break-apart probe set
t(9q34;var) or *ABL1* rearrangement, ABL1 break-apart probe set
t(13q12.2;var) or *FLT3* rearrangement, FLT3 break-apart probe set

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 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) - *BCR::ABL1* fusion.

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
Varies

Ordering Guidance
This test is intended for instances when the complete 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, and request specific probes for targeted abnormalities.

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 specific probes for targeted abnormalities.

FISH testing using paraffin embedded tissue samples is not available for these probe sets.

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

Necessary Information
1. 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.
2. 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, but appropriate testing and interpretation may be compromised or delayed.

Specimen Required
Submit only 1 of the following specimens:

Preferred
Specimen Type: Bone marrow
Container/Tube:
Preferred: Yellow top (ACD)

Acceptable: Green top (sodium heparin) or lavender top (EDTA)
Specimen Volume: 2 to3 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: Whole Blood
Container/Tube:
Preferred: Yellow top (ACD)
Acceptable: Green top (sodium 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 an Hematopathology/Cytogenetics Test Request (T726) with the specimen.

Specimen Minimum Volume
Bone marrow: 1 mL; Whole blood: 2 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*, *JAK2,* and *FLT3* 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 5 specific gene regions: *PDGFRA*, *PDGFRB*, *FGFR1*, *JAK2* and *FLT3*.

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 set.

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

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*, *ABL1,* and *FLT3* are detected using a tri or dual-color break-apart (BAP) strategy probe set. A dual-color, dual-fusion fluorescence in situ hybridization (D-FISH) strategy probe set is used in reflex testing when rearrangements of the *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
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
88271x12, 88275x6, 88291x1-FISH Probe, Analysis, Interpretation; 6 probe sets
88271x2, 88275x1–FISH Probe, Analysis; each additional probe set (if appropriate)

LOINC® Information

Test Definition: EOSFD

Chronic Eosinophilia Panel, Diagnostic FISH, Varies

Test ID	Test Order Name	Order LOINC® Value
EOSFD	Chronic Eosinophilia pnl, Diag FISH	107544-9

Result ID	Test Result Name	Result LOINC® Value
622441	Result Summary	50397-9
622442	Interpretation	69965-2
622443	Result Table	93356-4
622444	Result	62356-1
GC165	Reason for Referral	42349-1
GC166	Specimen	31208-2
622445	Source	31208-2
622495	Method	85069-3
622496	Additional Information	48767-8
622497	Disclaimer	62364-5
622498	Released By	18771-6