MAYO CLINIC LABORATORIES

Test Definition: KITVS

KIT Asp816Val Mutation Analysis, Varies

Overview

Useful For

Diagnosing systemic mastocytosis using blood or bone marrow specimens

Testing Algorithm

For more information see:

-Mast Cell Disorder: Diagnostic Algorithm, Bone Marrow

-Eosinophilia: Bone Marrow Diagnostic Algorithm

Special Instructions

- Hematopathology Patient Information
- Mast Cell Disorder: Diagnostic Algorithm, Bone Marrow
- Eosinophilia: Bone Marrow Diagnostic Algorithm

Method Name

Allele-Specific Oligonucleotide Polymerase Chain Reaction (PCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Specimen Required

Submit only 1 of the following specimens:

Specimen Type: Whole blood
Container/Tube: Lavender top (EDTA) or yellow top (ACD)
Specimen Volume: 3 mL
Collections Instructions:
1. Invert several times to mix blood.
2. Send specimen in original tube. **Do not** aliquot.
3. Label specimen as blood.
Specimen Stability Information: Ambient (preferred) 7 days/Refrigerate 7 days

Specimen Type: Bone marrow
Container/Tube: Lavender top (EDTA) or yellow top (ACD)
Specimen Volume: 2 mL

Collections Instructions:
1. Invert several times to mix bone marrow.
2. Send specimens in original tube. **Do not** aliquot.
3. Label specimen as bone marrow.
Specimen Stability Information: Ambient (preferred) 7 days/Refrigerate 7 days

Specimen Type: Extracted DNA from blood or bone marrow
Container/Tube: 1.5- to 2-mL tube
Specimen Volume: Entire specimen
Collection Instructions:
1. Label specimen as extracted DNA from blood or bone marrow.
2. Provide indication of volume and concentration of DNA.
Specimen Stability Information: Frozen (preferred)/Refrigerated/Ambient

Forms

1. Hematopathology Patient Information (T676)
2. If not ordering electronically, complete, print, and send a Hematopathology/Cytogenetics Test Request (T726)) with the specimen.

Specimen Minimum Volume

Blood, Bone Marrow: 1 mL
Extracted DNA: 50 mcL at 20 ng/mcL concentration

Reject Due To

Gross hemolysis	Reject
Moderately to severely clotted Bone marrow biopsies Paraffin-embedded bone marrow clots Paraffin-embedded tissue Slides Paraffin shavings	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Varies		

Clinical & Interpretive

Clinical Information

Systemic mastocytosis is a hematopoietic neoplasm that can be included in the general category of chronic myeloproliferative disorders (CMPD). These neoplasms are characterized by excessive proliferation of one or more myeloid lineages, with cells filling the bone marrow and populating other hematopoietic sites. In systemic mastocytosis, mast cell proliferation is the defining feature, although other myeloid lineages and B cells are frequently part of the neoplastic clone.

Function-altering point alterations in *KIT*, a gene coding for a membrane receptor tyrosine kinase, have been found in myeloid lineage cells in the majority of systemic mastocytosis cases. The most common *KIT* alteration is an adenine to thymine base substitution (A>T) at nucleotide position 2447, which results in an aspartic acid to valine change in the protein (Asp816Val). Much less frequently, other alterations at this same location are found, and occasional cases with alterations at other locations have also been reported. Variations at codon 816 are believed to alter the protein such that it is in a constitutively activated state. The main downstream effect of *KIT* activation is cell proliferation.

Detection of a variant at codon 816 is included as one of the minor diagnostic criteria for systemic mastocytosis in the World Health Organization classification system for hematopoietic neoplasms and is also of therapeutic relevance, as it confers resistance to imatinib, a drug commonly used to treat CMPD. It is now clear that individual mast cell neoplasms are variable with respect to the number of cell lineages containing the variant; some having positivity only in mast cells and others having positivity in additional myeloid and even lymphoid lineages. The alteration has not been reported in normal tissues.

Reference Values

An interpretive report will be provided indicating the mutation status as positive or negative.

Interpretation

The test will be interpreted as positive or negative for *KIT* Asp816Val.

Cautions

Some systemic mastocytosis cases may have the variation only in mast cells. Since these cells rarely circulate in blood and are difficult to obtain in significant numbers from bone marrow aspirate specimens, false-negative results may occur if neoplastic cells are present below the sensitivity of the assay (fewer than 0.1% altered alleles).

The test is qualitative only. Reliable quantitative results cannot be issued.

Supportive Data

The analytic sensitivity of this test is 0.1% and was determined by the dilution of a cell line containing homozygous *KIT* alteration. This means that 0.1% or greater of the *KIT* alleles present in the specimen must contain the alteration to be detected by the assay. The analytic specificity was 100% in assay validation.

Clinical Reference

1. Garcia-Montero AC, Jara-Acevedo M, Teodosio C, et al. *KIT* mutation in mast cells and other bone marrow hematopoietic cell lineages in systemic mast cell disorders: a prospective study of the Spanish Network on Mastocytosis (REMA) in a series of 113 patients. Blood. 2006;108:2366-2372. doi:10.1182/blood-2006-04-015545

2. Valent P, Akin C, Sperr WR, et al. Diagnosis and treatment of systemic mastocytosis: state of the art. Br J Haematol. 2003;122:695-717. doi:10.1046/j.1365-2141.2003.04575.x
3. Jaffe ES, Harris NL, Stein H, et al. Pathology and Genetics. In: WHO Classification of Tumours of the Haematopoietic and Lymphoid Tissues. 2001:291-302. World Health Organization Classification of Tumours. Vol 2
4. Pardanani A. Systemic mastocytosis in adults: 2012 Update on diagnosis, risk stratification, and management. Am J Hematol. 2012;87:402-411. doi: 10.1002/ajh.23134.
5. Munoz-Gonzalez JI, Alvarez-Twose I, Jara-Acevedo M, et al. Frequency and prognostic impact of KIT and other genetic variants in indolent systemic mastocytosis. Blood. 2019; 134(5):456-468. doi:10.1182/blood.2018886507

Performance

Method Description

This assay detects the *KIT* alteration responsible for Asp816Val. The technique used is allele-specific oligonucleotide polymerase chain reaction (ASO-PCR) with fragment analysis on a genetic analyzer. DNA is extracted from bone marrow or blood, and PCR is used to amplify across the alteration site in 2 separate tubes; one contains a reverse primer complementary to the unaltered sequence and the other contains a reverse primer complementary to the altered sequence. Each of these is labeled with a fluorescent tag and contains an identical, non-labeled forward primer. Both primer sets amplify a 200 base pair fragment that differs only at the alteration site. The unaltered fragment should be amplified in all samples. Samples negative for *KIT* Asp816Val will not have an amplified fragment in the altered sequence reaction tube. Positive samples will have amplified fragments in both tubes. The test gives a qualitative (positive or negative) result only, as the end point PCR used is not reliable for quantification.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Friday

Report Available

4 to 7 days

Specimen Retention Time

Whole blood, bone marrow: 2 weeks; Extracted DNA: 3 Months

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

81273

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
KITVS	KIT Asp816Val Mutation Analysis, V	55201-8

Result ID	Test Result Name	Result LOINC® Value
MP055	Specimen Type	31208-2
607982	Interpretation	69047-9
607983	Signing Pathologist	19139-5