MAYO CLINIC LABORATORIES

Test Definition: IDHQ

IDH1 (R132) and IDH2 (R140 and R172) Quantitative Detection, Droplet Digital PCR, Varies

Overview

Useful For

Detecting *IDH1* R132 and *IDH2* R140 and R172 mutations in acute myeloid leukemia patients at the time of diagnosis to guide targeted therapy

Monitoring minimal residual disease during the clinical and therapeutic course

Genetics Test Information

A highly sensitive quantitative assay for the detection of 6 *IDH1* R132 mutations (R132H, R132S, R132C, R132G, R132P, and R132L) and 10 *IDH2* mutations R140 (R140Q, R140L, R140G, R140W) and R172 (R172K, R172M, R172G, R172S[G>C], R172S[G>T], R172W).

Special Instructions

- Hematopathology Patient Information

Highlights

The test can be used at the time of acute myeloid leukemia diagnosis to guide targeted therapy, as well as minimal residual disease monitoring markers during the clinical and therapeutic course of these patients.

Method Name

Droplet Digital Polymerase Chain Reaction (ddPCR)

NY State Available

Yes

Specimen

Specimen Type

Varies

Shipping Instructions

1. Refrigerated specimens **must arrive within 14 days of collection**, and ambient specimens **must arrive within 7 days of collection**.
2. Collect and package specimen as close to shipping time as possible.

Necessary Information

The following information is required:

1. Pertinent clinical history

2. Date of collection
3. Specimen source (blood or bone marrow)

Specimen Required

Submit only 1 of the following specimens

Specimen Type: Whole blood
Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD-B) or green top (heparin)
Specimen Volume: 4mL
Collection Instructions:
1. Invert several times to mix blood.
2. Send whole blood specimen in original tube. **Do not aliquot**.
3. Label specimen as blood.

Specimen Type: Bone marrow aspirate
Container/Tube:
Preferred: Lavender top (EDTA)
Acceptable: Yellow top (ACD-B) or green top (heparin)
Specimen Volume: 2mL
Collection Instructions:
1. Invert several times to mix bone marrow.
2. Send bone marrow specimen in original tube. **Do not aliquot**.
3. Label specimen as bone marrow.

Specimen Type: Extracted DNA from blood or bone marrow
Container/Tube: 1.5- to 2-mL tube with indication of volume and concentration of DNA
Specimen Volume: Entire specimen
Collection Instructions:
1. Label specimen as extracted DNA and source of specimen
2. Indicate volume and concentration of DNA on label. The required volume of DNA is at least 50 mcL at a concentration of 50 ng/mcL
Specimen Stability: Frozen (preferred)/Refrigerated

Forms

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

Specimen Minimum Volume

Whole blood: 4mL; Bone marrow: 2mL; Extracted DNA: 50 mcL at 50 ng/mcL

Reject Due To

Gross hemolysis	Reject
Moderately to severely clotted	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Varies	Refrigerated (preferred)	14 days	
	Ambient	7 days	

Clinical & Interpretive

Clinical Information

Isocitrate dehydrogenase 1 (IDH1) is a cytosolic/peroxisomal enzyme involved in citric acid cycle and other cellular metabolic processes. It catalyzes the oxidative decarboxylation of isocitrate to alpha-ketoglutarate (a-KG), generating reduced nicotinamide adenine dinucleotide phosphate (NADPH) from NADP(+). Isocitrate dehydrogenase 2 (IDH2) is a mitochondrial NADP(+)-dependent enzyme that catalyzes the oxidative decarboxylation of isocitrate to a- KG, generating NADPH from NADP(+). Mutations in codon R132 of *IDH1* or R140 or R172 in *IDH2* confer an abnormal enzyme activity that converts a-KG to D-2- hydroxyglutarate (2-HG) resulting in elevation of 2-HG and a hypermethylation state, associated in myeloid neoplasms including acute myeloid leukemia (AML). *IDH1* and *IDH2* point mutations are seen in approximately 5% to 33% *de novo* AML and 7% to 25% secondary AML.

The US Food and Drug Administration (FDA) has approved ivosidenib (AG-120) for the treatment of newly-diagnosed *IDH1*-mutated AML (patients 75 years of age and older or who have comorbidities that preclude the use of intensive induction chemotherapy) and relapsed/refractory AML in adult patients.(1) The FDA has also approved enasidenib (AG-221) for the treatment of *IDH2*-mutated relapsed/refractory AML.(2)

IDH1 and *IDH2* have also been shown to be suitable minimal residual disease markers for AML post-therapy.

Reference Values

An interpretive report will be provided.

Interpretation

The assay is reported as positive or negative. In positive cases, the mutation and its variant allele fraction (VAF) are reported.

VAF%= (mutant copy number)/(mutant copy number + wild-type number)

The precision of this quantitative assay is excellent but interassay variability may occur such that result changes should not be considered significant if 2 single measurements differ by less than 0.5 log (3.16-folds).

Cautions

Other *IDH1* or *IDH2* variants outside the 16 assay targets are not detected by this assay.

Clinical Reference

1. US Food and Drug Administration (FDA): Table of Pharmacogenomic Biomarkers in Drug Labeling. FDA; Updated September 23, 2024. January 15, 2025. Available at www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling
2. US Food and Drug Administration (FDA): FDA granted regular approval to enasidenib for the treatment of relapsed or refractory AML. FDA; August 1, 2017. Accessed January 15, 2025. Available at www.fda.gov/drugs/resources-information-approved-drugs/fda-granted-regular-approval-enasidenib-treatment-relapsed-or-refractory-aml
3. Duncavage EJ, Bagg A, Hasserjian RP, et al. Genomic profiling for clinical decision making in myeloid neoplasms and acute leukemia. Blood. 2022;140(21):2228-2247. doi:10.1182/blood.2022015853
4. Dohner H, Wei AH, Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022;140(12):1345-1377. doi:10.1182/blood.2022016867
5. Pollyea DA. New drugs for acute myeloid leukemia inspired by genomics and when to use them. Hematology Am Soc Hematol Educ Program. 2018;2018(1):45-50
6. Stein EM, DiNardo CD, Pollyea DA, Fathi AT, et al. Enasidenib in mutant IDH2 relapsed or refractory acute myeloid leukemia Blood. 2017;130(6):722-731
7. DiNardo CD, Stein EM, de Botton S, et al. Durable remissions with Ivosidenib in IDH1-mutated relapsed or refractory AML. N Engl J Med. 2018;378(25):2386-2398
8. Ok CY, Loghavi S, Sui D, et al. Persistent IDH1/2 mutations in remission can predict relapse in patients with acute myeloid leukemia. Haematologica. 2019;104(2):305-311

Performance

Method Description

This test will be performed on Bio-Rad QX200 digital polymerase chain reaction (PCR) system. Mutation-specific droplet digital PCR probes were designed using Thermo Fisher Scientific MGB (minorgroove binder) Taqman technology. The PCR reactions for each patient are placed into an 8-tube cartridge along with droplet generation oil. The cartridge is loaded onto the droplet generator instrument to partition each reaction into 20,000 nanoliter-sized droplets.

Droplets are transferred to a plate for PCR amplification. Targets are amplified by end-point PCR in each droplet. The QX200 automated droplet reader counts every acceptable droplet and measures fluorescence emissions from each droplet using two different fluorescence channels (FAM and VIC). QuantaSoft software measures the number of negative and positive droplets for each fluorophore in each sample. Poisson statistics are used to determine the concentration of mutant and wild type copies in the sample.(Unpublished Mayo method)

PDF Report

No

Day(s) Performed

Monday through Saturday

Report Available
4 to 8 days

Specimen Retention Time
Blood/bone marrow: 2 weeks; Extracted DNA: 3 months

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
81120
81121

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
IDHQ	IDH1 and IDH2, Quant, ddPCR, V	95772-0

Result ID	Test Result Name	Result LOINC® Value
MP063	Specimen Type	31208-2
618389	Interpretation	69047-9
618390	Signing Pathologist	18771-6