IDH2 Abbott RealTime PCR

Versiti offers the companion diagnostic test for *IDH2* (isocitrate dehydrogenase-2) mutations in acute myeloid leukemia (AML). The method uses the Abbott RealTime IDH2 assay[17] which is an in vitro polymerase chain reaction (PCR) assay for the qualitative detection of single nucleotide variants (SNVs) coding nine *IDH2* R140 and R172 mutations in DNA extracted from human bone marrow or blood. Versiti performs this highly sensitive test and delivers results with turnaround times which could facilitate rapid treatment decisions for patients.[16]

Indications for testing:

Abbott RealTime IDH2 is indicated as an aid in identifying acute myeloid leukemia (AML) patients with an (*IDH2*) mutation for treatment with IDHIFA® (enasidenib).

For clinical questions about laboratory tests and test utilization support, contact Versiti Client Services: 800-245-3117 x6250 (toll free).

Test method:

Abbott RealTime IDH2 detects single nucleotide variants (SNVs) coding nine *IDH2* mutations (R140Q, R140L, R140G, R140W, R172K, R172M, R172G, R172S, and R172W) by using PCR technology with homogeneous real-time fluorescent detection. The assay uses human blood or bone marrow aspirate specimens and reports a qualitative result. The table below lists the *IDH2* mutations detected by the Abbott RealTime IDH2 assay.

Mutations Detected by the Abbott RealTime IDH2

Codon	*IDH2* Mutation	SNV	Codon	*IDH2* Mutation	SNV
R140	R140Q	CAG	R172	R172K	AAG
	R140L	CTG		R172M	ATG
	R140G	GGG		R172G	GGG
	R140W	TGG		R172S	AGT and AGC
				R172W	TGG

IDH2 (isocitrate dehydrogenase-2) is a mitochondrial enzyme that helps break down nutrients and generate energy for the cell. The homodimeric enzyme catalyzes a reaction that converts isocitrate to α-ketoglutarate (α-KG) while reducing NADP to NADPH and liberating CO_2. Because of its involvement in cellular energy production, *IDH2* plays a role in the metabolism of glucose, fatty acids, and glutamine; and also contributes to the maintenance of normal cellular redox status.[1]

Mutations in the R140 and R172 codons of *IDH2* are oncogenic and can be found in several cancer types, including acute myeloid leukemia (AML) in which 8% to 19% of patients possess an *IDH2* mutation.[1,2,3,4,15] Nine *IDH2* amino acid changes have been identified in various cancer types: R140Q, R140L, R140G, R140W, R172K, R172M, R172G, R172S, and R172W.[3,5,6,7] R140 mutations account for 80% of *IDH2* mutations, with R140Q being the most prevalent, occurring in 30% to 50% of AML patients with *IDH2* mutations.[5,6,15] Mutations in R140 and R172 are associated with the ability of *IDH2* to further process α-KG to generate 2-hydroxygluturate (2-HG), an oncometabolite, which can result in concentrations that are orders of magnitude higher than normal.[8,9,10,11,12,13] Once produced, 2-HG alters the cells' genetic programming, or epigenetics, resulting in increased numbers of quickly proliferating, early hematopoietic progenitor cells, and tumorigenesis.[12,14]

Assay sensitivity and limitations:

The assay is expected to detect 99.8% or greater at mutation levels of 2% and higher for all the nine *IDH2* mutations documented with in the Abbott RealTime IDH2 product insert (R140Q, R140L, R140G, R140W, R172K, R172M, R172G, R172S, and R172W) combined or 93.5% or greater at mutation levels of 1% and higher for all the nine *IDH2* mutations documented with in the Abbott RealTime IDH2 product insert (R140Q, R140L, R140G, R140W, R172K, R172M, R172G, R172S, and R172W) combined.

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This assay detects only nine *IDH2* mutations documented with in the Abbott RealT*ime* IDH2 product insert (R140Q, R140L, R140G, R140W, R172K, R172M, R172G, R172S, and R172W).

Reporting of results:

Not detected or detected with variant notation.

Specimen requirements:

Follow the manufacturer's instructions for processing collection tubes.

Recommended Specimen Collection:

- 3-5 mL Whole blood (EDTA tube, lavender top)
- 2-5 mL Bone marrow (EDTA tube, lavender top)

Minimum Specimen Collection:

- 1mL Whole blood (EDTA tube, lavender top)
- 1mL Bone marrow (EDTA tube, lavender top)

After collection, specimen may be stored as follows:

- At 15 to 30°C for up to 48 hours
- At 2 to 8°C for up to 7 days
- At – 20°C ± 5°C for longer term

SHIP

Shipping requirements:

Ship the specimen(s) with cold packs in boxes via overnight carrier. The total time during transport should not exceed 48 hours. Place the specimen and the requisition into plastic bags and seal. Insert into a Styrofoam container, seal and place into a sturdy cardboard box, and tape securely. Ship the package in compliance with your overnight carrier guidelines. Label with the following address:

Versiti Client Services
Molecular Oncology & Genetics
638 N. 18th St.
Milwaukee, WI 53233

ORDER

Required forms:

Versiti Molecular Oncology Requisition. Clinical and laboratory history can either be recorded on the requisition form or clinical and laboratory reports can be submitted with the sample.

CPT Codes/Billing/Turnaround time:

Test Code: 7648

CPT codes: 81121

Turnaround time: 5-7 days

CPT and Order Codes are provided for reference purposes only and are subject to change. They are not intended as a guide for internal billing procedures. Institution is solely responsible for identification of correct billing codes.

For additional information related to shipping, billing or pricing, please contact, Versiti Client Services: (414) 937-6396 or 800-245-3117, Option 1, or LabInfo@versiti.org.

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17. PMA number P170005 on www.fda.gov

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