IDH1 Abbott RealTime PCR

Versiti offers the companion diagnostic test for *IDH1* (isocitrate dehydrogenase-1) mutations in acute myeloid leukemia (AML). The method uses the Abbott RealTime IDH1 assay[14] which is an in vitro polymerase chain reaction (PCR) assay for the qualitative detection of single nucleotide variants (SNVs) coding five *IDH1* R132 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.[13]

Indications for testing:

Abbott RealTime IDH1 is indicated as an aid in identifying acute myeloid leukemia (AML) patients with an isocitrate dehydrogenase-1 (*IDH1*) mutation for treatment with TIBSOVO® (ivosidenib).

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

Test method:

Abbott RealTime IDH1 detects single nucleotide variants (SNVs) coding five *IDH1* mutations (R132C, R132H, R132G, R132S, and R132L) by using PCR technology with homogeneous real-time fluorescence detection. The assay uses human blood or bone marrow aspirate specimens and reports a qualitative result. The table below lists the *IDH1* mutations detected by the Abbott RealTime IDH1 assay.

Mutations Detected by the Abbott RealTime IDH1		
Codon	*IDH1* Mutation	SNV
R132	R132C	TGT
	R132H	CAT
	R132G	GGT
	R132S	AGT
	R132L	CTT

IDH1 (isocitrate dehydrogenase-1) is a cytoplasmic enzyme involved in regulation of cellular metabolism. *IDH1* catalyzes the oxidative decarboxylation of isocitrate to produce α-ketoglutarate (α-KG). The mutated *IDH1* enzyme acquires a neomorphic activity that converts α-KG to D-2-hydroxyglutarate (2-HG) resulting in highly elevated levels of 2-HG, a rare metabolite normally present at very low levels in healthy cells.[1,2] 2-HG acts as an oncometabolite that is associated with altered gene expression, DNA and histone hypermethylation, and blocked differentiation of hematopoietic progenitor cells.[3,4,5,6,7]

Mutations in codon R132 of *IDH1* can be found in several cancer types, including acute myeloid leukemia (AML), in which 6% to 10% of patients possess an *IDH1* mutation.[6,8,9] Multiple *IDH1* amino acid changes have been identified at the arginine residue of codon R132 and include: R132H, R132C, R132L, R132G, and R132S. R132H and R132C are the most prevalent, occurring in over 50% of AML patients with *IDH1* mutations.[10,11,12]

Assay sensitivity and limitations:

The assay is expected to detect 100% at mutation levels of 2% and higher for all the five *IDH1* mutations documented within the Abbott RealTime IDH1 product insert (R132C, R132G, R132H, R132L, and R132S) combined or 98% or greater at mutation levels of 1% and higher for all the five *IDH1* mutations documented with in the Abbott RealTime IDH1 product insert (R132C, R132G, R132H, R132L, and R132S) combined.

This assay detects only five *IDH1* mutations documented within the Abbott RealTime IDH1 product insert (R132C, R132G, R132H, R132L, and R132S).

Reporting of results:

Not detected or detected with variant notation.

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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: 7647

CPT codes: 81120

Turnaround time: 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.

References:

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2. Cairns, RA and Mak, TW. Oncogenic isocitrate dehydrogenase mutations: mechanisms, models, and clinical opportunities. Cancer Discov. 2013; 3:730-741.
3. Dang, L, et al. Cancer-associated IDH1 mutations produce 2-hydroxyglutarate. Nature. 2010; 465(7300):966.
4. Clark, O et al. Molecular pathways: isocitrate dehydrogenase mutations in cancer. Clin Cancer Res. 2016; 22(8), April 15; 1837-1842.
5. Lu C. et al. IDH mutation impairs histone demethylation and results in a block to cell differentiation. Nature 2012; 483(7390):474-478.
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8. Bullinger, L et al. Genomics of Acute Myeloid Leukemia Diagnosis and Pathways. J Clin Oncol. 2017; doi: 10.1200/JCO.2016.71.2208
9. Abbas, S et al. Acquired mutations in the genes encoding IDH1 and IDH2 both are recurrent aberrations in acute myeloid leukemia: prevalence and prognostic value. Blood 2010; 116: 2122-2126.
10. Mardis, ER et al. Recurring mutations found by sequencing an acute myeloid leukemia genome. N Engl J Med. 2009; 361:1058–1066.
11. Paschka, P et al. IDH1 and IDH2 mutations are frequent genetic alterations in acute myeloid leukemia and confer adverse prognosis in cytogenetically normal acute myeloid leukemia with NPM1 mutation without FLT3internal tandem duplication. J Clin Oncol. 2010; 28;22:3636-3643.
12. Chotirat, S et al. Molecular alterations of isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2) metabolic genes and additional genetic mutations in newly diagnosed acute myeloid leukemia patients. J Hematol Oncol. 2012; 5:5.
13. Dash DP, Wise L, Harb J, et,al. A New Highly Sensitive RealTime PCR Assay with Faster Turnaround Time for Detecting IDH1 and IDH2 mutations in Acute Myeloid Leukemia (AML) Patients. Blood 2017 130:2681.
14. PMA number P170041 on www.fda.gov

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