IDH2 Abbott RealTime PCR
(FDA approved)

BloodCenter of Wisconsin offers the companion diagnostic test for IDH2 (isocitrate dehydrogenase-2) mutations in acute myeloid leukemia (AML). This is the FDA approved test to aid in identifying relapsed or refractory AML patients that may be treated with enasidenib (IDHIFA®). The method uses the Abbott RealTime IDH2 assay 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.

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 BloodCenter Client Services: (414) 937-6396.

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.

<table>
<thead>
<tr>
<th>Codon</th>
<th>IDH2 Mutation</th>
<th>SNV</th>
<th>Codon</th>
<th>IDH2 Mutation</th>
<th>SNV</th>
</tr>
</thead>
<tbody>
<tr>
<td>R140</td>
<td>R140Q</td>
<td>CAG</td>
<td>R172</td>
<td>R172K</td>
<td>AAG</td>
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<td></td>
<td>R140L</td>
<td>CTG</td>
<td></td>
<td>R172M</td>
<td>ATG</td>
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<tr>
<td></td>
<td>R140G</td>
<td>GGG</td>
<td></td>
<td>R172G</td>
<td>GGG</td>
</tr>
<tr>
<td></td>
<td>R140W</td>
<td>TGG</td>
<td></td>
<td>R172S</td>
<td>AGT and AGC</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>R172W</td>
<td>TGG</td>
</tr>
</tbody>
</table>

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 CO2. 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.

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. Nine IDH2 amino acid changes have been identified in various cancer types: R140Q, R140L, R140G, R140W, R172K, R172M, R172G, R172S, and R172W. Once produced, 2-HG alters the cell’s genetic programming, or epigenetics, resulting in increased numbers of quickly proliferating, early hematopoietic progenitor cells, and tumorigenesis.

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.

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

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:

Client Services/Molecular Oncology Laboratory
BloodCenter of Wisconsin
638 N. 18th St.
Milwaukee, WI 53233

Required forms:
Please complete all pages of the requisition form. Clinical history (including patient’s clinical diagnosis, family history and relevant laboratory findings). 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: 81403
Turnaround time: 5 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, BloodCenter Client Services: (414) 937-6396 or 800-245-3117, Option 1, or LabInfo@bcw.edu.

References: