Penn Medicine

TO: UPHS Physicians and Staff
FROM: Department of Pathology and Laboratory Medicine
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SUBJECT: Availability of targeted *IDH1* and *IDH2* variant testing

In May, targeted testing for *IDH1* and *IDH2* variants will be made available from the clinical laboratories at the Hospital of the University of Pennsylvania. These FDA-approved assays are intended for the evaluation of blood and bone marrow samples from acute myeloid leukemia (AML) patients. The identification of *IDH1* or *IDH2* variants has implications for responsiveness to certain targeted therapy in AML. These qualitative tests are designed to detect 5 variants in *IDH1* and 9 variants in *IDH2* (see below).

***IDH1* Variants**		***IDH2* Variants**		
R132C	R132G	R140Q	R140G	R172S
R132H	R132S	R140W	R172K	R172W
	R132L	R140L	R172G	R172M

Specimens with a variant in *IDH1* or *IDH2* not targeted by these assays may be reported as "Not Detected." Furthermore, if two or more variants are present in the evaluated sample, the assay cannot identify each variant separately. Instead, only the variant present at the highest allelic level will be reported. Therefore, a result of "Not Detected" does not entirely rule out the possibility of harboring an *IDH1* or *IDH2* variant, nor does the presence of an *IDH1* or *IDH2* variant rule out the possibility of having more than one variant.

Clinical Significance
IDH1 and *IDH2* variants are identified in approximately 20% of AML patients. The most common variants are R132C and R132H in *IDH1* and R140Q and R172K in *IDH2*. Patients with either *IDH1* or *IDH2* disease-associated variants may benefit from targeted therapy. While prognostic value of recurrent detection of *IDH* variants in AML remains unclear, presence of the variants suggests persistent disease. Since the absence of detectable *IDH1* or *IDH2* variants does not rule out AML, clinical correlation is required to interpret the significance of any result. These assays are not intended for use in other disease processes known to harbor *IDH1* or *IDH2* disease-associated variants.

Results and Reporting:
Results for the targeted assay will be reported as "Not Detected" or "Positive" with the relevant amino acid change. Results will be available in PennChart. The lower limit of detection is approximately 2% variant allele frequency. The reference range is "Not Detected".

Testing Information
Turnaround Time: 3-5 business days

Acceptable specimen: Peripheral blood and bone marrow collected in an EDTA (lavender) tube are the only acceptable specimen. For other specimen types, please contact the lab to discuss options.

Ordering: Patients without a known variant may be tested using PennChart order "IDH1 IDH2 Variant Analysis" (IDH12CASE). Patients with a known variant may be monitored by ordering IDH1 only "IDH1 Variant Analysis" (IDH1CASE) or IDH2 only "IDH2 Variant Analysis" (IDH2CASE).

Contact Information: Call the Molecular Pathology Laboratory (215-662-6121) weekdays during regular business hours. For information on ordering and specimen requirements, kindly consult the Lab Tests Services Guide