Penn Medicine

TO: UPHS Physicians and Staff
FROM: Department of Pathology and Laboratory Medicine
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SUBJECT: Update to targeted *IDH1* and *IDH2* variant testing to include glial tumors

In November, targeted testing for *IDH1* and *IDH2* variants will be made available for paraffin-embedded tissue samples. This targeted analysis is primarily intended for testing infiltrating gliomas in patients <55 years (see Neuro-oncology Pathway: Molecular Testing) and glial tumor samples that may not be suitable for "Solid Tumor Sequencing Panel" testing or when *IDH1* immunohistochemistry is indeterminate. These qualitative tests are designed to detect 5 *IDH1* variants and 9 *IDH2* variants (see below).

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

Assay Limitations
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
The identification of *IDH1* or *IDH2* variants has implications for diagnosis and prognosis in glial tumors. Disease associated variants in *IDH1* and *IDH2* are seen in over 80-90% of astrocytomas and oligodendrogliomas as well as approximately 10% of glioblastomas. The most prevalent variant observed in diffuse gliomas is *IDH1* R132H; however, other *IDH1* and *IDH2* variants have been observed, albeit less commonly. In addition to being an important diagnostic feature in the classification of various gliomas, the presence of an *IDH1* or *IDH2* disease-associated variant is generally associated with an improved prognosis when compared to *IDH*-wildtype tumors. Since these assays do not detect all possible *IDH1* or *IDH2* variants, a negative result does not eliminate the possibility of *IDH1* or *IDH2* associated disease. If clinically indicated, additional testing, using other methodologies, may be informative.

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. A minimum of 10% tumor is required. The reference range is "Not Detected".

Testing Information
Turnaround Time: 3-5 business days

Acceptable specimen: Formalin-fixed paraffin-embedded tissue reviewed and approved for testing by a board certified anatomic pathologist. No changes have been made to the availability of blood and bone marrow testing.

Ordering: If unfamiliar with the process for requesting testing on solid tumors, please contact the Molecular Pathology Laboratory weekdays during regular business hours (215-662-6121) for details on ordering.

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.