ARUP LABORATORIES
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Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	Unknown
Gender:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

IDH1 and IDH2 Mutation Analysis Exon 4, Formalin-Fixed, Paraffin-Embedded (FFPE) Tissue

ARUP test code 3004267

IDH1 and IDH2 Mutation Results	See Note

This result has been reviewed and approved by

BACKGROUND INFORMATION: IDH1 and IDH2 Mutation Results

CHARACTERISTICS: This test is designed to detect mutations in exon 4 of the IDH1 and IDH2 genes at "hotspots" R132 of IDH1 and R140 and R172 of IDH2 that are frequently present in gliomas and in a subset of cases of acute myeloid leukemia. IDH1/2 mutations in gliomas are generally associated with a better prognosis. In acute myeloid leukemia, the prognostic significance of IDH1 mutations is context dependent. IDH1 mutations appear to be associated with worse outcome in patients without FLT3-ITD mutations (see J Clin Oncol 2010. 28:3636 and Blood 2010. 116:2779). In acute myeloid leukemia patients with IDH2 abnormalities, IDH2 R140 mutations appear to be associated with better outcome while IDH2 R172 mutations appear associated with worse outcome (see Blood 2011. 118:409). The FDA has approved ivosidenib as a targeted therapy for acute myeloid leukemia with an IDH1 mutation, and enasidenib for AML with an IDH2 mutation. Clinical trials may be available.

METHODOLOGY: DNA is isolated from FFPE tissue, blood, or bone marrow. The DNA is amplified for IDH1 and IDH2 covering exon 4 of both genes including the important residues R132 (IDH1), R140 (IDH2) and R172 (IDH2). Sanger sequencing is then performed to detect mutations. Only mutations in R132 (IDH1), R140 and R172 (IDH2) are reported.

LIMITATIONS: Mutations in other locations within the IDH1 and IDH2 genes or in other genes will not be detected. The limit of detection for this test is 20 percent mutant allele. Results of this test must always be interpreted within the clinical context and with other relevant data, and should not be used alone for a diagnosis of malignancy. This test is not intended to detect minimal residual disease.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

IDH1-2 FFPE Source	See Note

H=High, L=Low, *=Abnormal, C=Critical

Block ID	1234567

1p19q Deletion by FISH and IDH1 R132H Point Mutation by Immunohistochemistry with Reflex to IDH1 and IDH2 Mutation Analysis, Exon 4

ARUP test code 3002135

IDH1 R132H Point Mut by IHC with Reflex	Negative IDH1 by immunohistochemistry is negative. IDH1 and IDH2 Mutation Analysis has been added and will be reported separately. INTERPRETIVE INFORMATION: IDH1 R132H Point Mut by IHC with Reflex IDH1 R132H Point Mutation by Immunohistochemistry detects the presence of mutant IDH1 R132H protein expression in diffuse gliomas and can serve as a screening tool for molecular testing. A positive result indicates a probable IDH1 R132H mutation. A negative result indicates the tumor has no R132H mutation, which will automatically reflex to IDH1 and IDH2 gene sequencing, to detect less common IDH1 or IDH2 mutations not detected by the IHC test. This test is performed on paraffin-embedded, formalin-fixed tissue. Controls were run and performed as expected. Test developed and characteristics determined by ARUP Laboratories. See Compliance Statement B: aruplab.com/CS
IDH1 Tissue Source	Tissue
IDH1 R132H Mutation Reference Number	1234567

1p/19q Deletion by FISH

ARUP test code 3001309

1p Result	Not Deleted
19q Result	Not Deleted Controls were run and performed as expected. This result has been reviewed and approved by 2000 Circle of Hope, RM 3100 Salt Lake City, UT 84112
1p/1q Ratio	0.97
1P Percent Deleted	4 %

H=High, L=Low, *=Abnormal, C=Critical

Chromosome 1 Polysomy	Not Detected
19q/19p Ratio	0.99
19Q Percent Deleted	6 %
Chromosome 19 Polysomy	Not Detected
1P Total Cell Count	50
19Q Total Cell Count	50
Scoring Method	Manual
1p19q FISH Reference Number	1234567
1p19q FISH Source	Tissue

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INTERPRETIVE INFORMATION: 1p/19q, FISH

Fluorescence in situ hybridization (FISH) analysis was performed on a section from a paraffin-embedded tissue block using differentially labeled fluorescent probes targeting 1p36/1q25 and 19p13/19q13 (Abbott Molecular). Cells were evaluated from regions of tumor identified on histopathologic review of a matching hematoxylin- and eosin-stained section. Controls performed appropriately.

This assay evaluates the average ratios of 1p to 1q and 19q to 19p, as well as the percentage of cells with a signal pattern consistent with a deletion (individual cell 1p/1q and 19q/19p ratios of 0.5 or lower). Based on the validation of this assay, 1p deletion is defined as a 1p/1q ratio below 0.80 combined with a deleted pattern in 24 percent or more of the scored cells, and 19q deletion is defined as a 19q/19p ratio below 0.80 combined with a deleted pattern in 26 percent or more of the scored cells.

Codeletion of 1p and 19q as the result of an unbalanced translocation is characteristic of oligodendrogliomas and a diagnostic feature according to the WHO Classification of Tumours of the Central Nervous System, Revised 4th Edition (2016). Codeletion is also predictive of a favorable response to combination chemotherapy. Isolated deletions of 1p or 19q are neither diagnostic nor predictive in a similar fashion. Polysomy, defined in this context as three or more signals for 1q and/or 19p in 30 percent or more of the tumor cells, suggests a less-favorable outcome in oligodendrogliomas. Based on the assay performance during test validation, the test is expected to detect 96 percent of 1p and 19q deletions in patients with oligodendrogliomas. Assay range and limit of detection were generated using normal and known positive cases respectively. Correlation with other laboratory data, especially histopathologic findings, is recommended for optimal risk stratification.

References:
1. Jenkins RB et al. A t(1;19)(q10;p10) Mediates the Combined Deletions of 1p and 19q and Predicts a Better Prognosis of Patients with Oligodendroglioma. Cancer Res 66 (20): 9852-9861, 2006.
2. Snuderl M et al. Polysomy for chromosomes 1 and 19 predicts earlier recurrence in anaplastic oligodendrogliomas with concurrent 1p/19q loss. Clin Cancer Res 15(20):6430-6437, 2009.
3. Wiens et al. Polysomy of chromosomes 1 and/or 19 is common and associated with less favorable clinical outcome in oligodendrogliomas: fluorescent in situ hybridization analysis of 84 consecutive cases. J Neuropathol Exp Neurol 71(7):618-624, 2012.
4. Clark K et al. How molecular testing can help (and hurt) in the workup of gliomas. Am J Clin Pathol 139(3):275-288, 2013.
5. Senetta R et al. A "weighted" fluorescence in situ hybridization strengthens the favorable prognostic value of 1p/19q codeletion in pure and mixed oligodendroglial tumors. J Neuropathol Exp Neurol 72(5):432-41, 2013.
6. Eckel-Passow JE et al. Glioma Groups Based on 1p/19q, IDH, and TERT Promoter Mutations in Tumors. N Engl J Med 25;372(26):2499-508, 2015.
7. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Ellison DW, Figarella-Branger D, Perry A, Reifenberger G, von Deimling A, Eds. WHO Classification of Tumours of the Central Nervous System, Revised 4th Edition. Lyon, France: International Agency for Research on Cancer, 2016.

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VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
IDH1 and IDH2 Mutation Results	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
IDH1-2 FFPE Source	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Block ID	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
IDH1 R132H Point Mut by IHC with Reflex	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
IDH1 Tissue Source	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
IDH1 R132H Mutation Reference Number	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
1p Result	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
19q Result	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
1p/1q Ratio	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
1P Percent Deleted	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Chromosome 1 Polysomy	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
19q/19p Ratio	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
19Q Percent Deleted	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Chromosome 19 Polysomy	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
1P Total Cell Count	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
19Q Total Cell Count	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Scoring Method	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
1p19q FISH Reference Number	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
1p19q FISH Source	22-213-123017	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical