G.M Malith Mahendra

AGE: 39 years | **Gender:** Male | **Coupon/UID:** NA / AOM0277

Diagnosis: Astrocytoma

MEDGENOME

MGM1341 : IDH1 and IDH2 Gene Analysis

Report Details		Specimen Information		Ordering Clinician	
Sample ID / Order ID:	9497262 / 1496708	**Specimen Site:**	Brain	**Clinician:**	Dr. Mahilal Wijekoon
Collection Date:	23rd October 2025	**Specimen Received:**	FFPE Tissue Blocks [2]	**Affiliation:**	Aegle Omics Private Limited
Date Received:	27th October 2025	**Specimen Tested:**	GJ-5572 C	**Serviced By:**	18718
Report Date & Time:	5th Nov 2025 14:26 PM	**Tumor Content (%):**	70	**Report Status:**	Final

Clinical Summary: Cerebellar lesion biopsy - Diffuse astrocytoma, WHO grade 3

TEST RESULT SUMMARY

Next Generation Sequencing (NGS) Test Result

Result - POSITIVE

CLINICALLY RELEVANT VARIANT/S DETECTED

AMP Classification ^	CDS variant details	Interpretation	Treatment Recommendations	$Treatment Response
***IDH2* p.Arg172Gly (MISSENSE)** Variant Allele Frequency - 40.93%				
Tier I	c.514A>G (ENST00000330062.3)	Oncogenic	NA	Prognostic

^Refer to Glossary section for the classification criteria details.

$Drug Approvals are based on US-FDA Guidelines. Kindly refer to local guidelines if required.

ADDITIONAL BIOMARKERS DETECTED

This section provides information about variants that do not have any therapeutic value. However, these variants may or may not have a likely oncogenic effect.

No other biomarkers that warrants to be reported was detected

ACTIONABLE BIOMARKER DETAILS

IDH2 (p.Arg172Gly) - MISSENSE

Gene: *IDH2*	**Exon:** 4	**Variant Allele Frequency:** 40.93%
Nucleotide change: chr15:g.90631839T>C	**Protein change:** p.Arg172Gly	**Population MAF:** 0 (1000G);0(gnomAD);
cDNA change: c.514A>G	**Variant Type:** MISSENSE	**In-silico Predictions:** D_lc(SIFT); D(LRT); PrD(Polyphen2)
Transcript ID: ENST00000330062.3	**Variant Allele Depth/Total depth:** 61305/149789x	**Gene Function:** Oncogene

Gene Summary: Isocitrate dehydrogenases catalyze the oxidative decarboxylation of isocitrate to 2-oxoglutarate. These enzymes belong to two distinct subclasses, one of which utilizes NAD(+) as the electron acceptor and the other NADP(+). Five isocitrate dehydrogenases have been reported: three NAD(+)-dependent isocitrate dehydrogenases, which localize to the mitochondrial matrix, and two NADP(+)-dependent isocitrate dehydrogenases, one of which is mitochondrial and the other predominantly cytosolic. Each NADP(+)-dependent isozyme is a homodimer. The protein encoded by *IDH2* is the NADP(+)-dependent isocitrate dehydrogenase found in the mitochondria. It plays a role in intermediary metabolism and energy production. This protein may tightly associate or interact with the pyruvate dehydrogenase complex. Alternative splicing results in multiple transcript variants.

Clinical and Therapeutic Relevance: In a study with 811 glioma samples, *IDH2* mutations were identified in 18 samples (2.2%). *IDH2* mutations were found in 0.5 % of primary glioblastoma (1/215), 3.4 % of secondary glioblastoma (1/29) and 2.8 % (16/577) of low-grade gliomas [PMID: 27245697]. The presence of *IDH1/2* mutation has become one of the most critical biomarkers for molecular classification and prognostication in adult diffuse gliomas. From 2016 WHO classification of tumors of the Central Nervous System, the adult diffuse gliomas are grouped as diffuse astrocytic tumors or oligodendroglial tumors based on the presence of IDH mutations (typically *IDH1*-Arg132 and *IDH2*-Arg172) and 1p/19q codeletion [PMID: 28899049]. Patients harboring *IDH1* mutation showed longer PFS (Progression Free Survival) as compared to wild-type *IDH1* [PMID: 22034964, 22291938]. IDH-inhibitors like IDH305 are under preclinical studies which have showed potential for therapy in glioma and have moved into clinical studies [PMID: 31165048]. **In patients with grade 2 IDH-mutant glioma, vorasidenib significantly improved progression-free survival and delayed the time to the next intervention** [PMID: 37272516, https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-vorasidenib-grade-2-astrocytoma-or-oligodendroglioma-susceptible-idh1-or-idh2-mutation].
Ivosidenib can extend progression-free survival and reduce tumor growth in predominantly non-enhancing *IDH1*-mutated gliomas [PMID: 32530764]. As per NCCN guidelines, in patients with predominantly non-enhancing *IDH1*-mutant gliomas, rather than enhancing disease, ivosidenib can be considered in appropriate cases [www.nccn.org].

PubMed References: 27245697, 28899049, 22034964, 22291938, 31165048, 37272516, 32530764

AMP-ASCO-CAP CLASSIFICATION CRITERIA

Genetic test results are reported based on the somatic variant classification recommendations of College of American Pathologists (CAP) /American society for Clinical Oncology (ASCO)/Association of Molecular Pathologists (AMP) [PMID: 27993330] as described in the table below:

Tier	Criteria
Tier I	Variants of strong clinical significance.
Tier II	Variants of potential clinical significance.
Tier III	Variants of unknown clinical significance
Tier IV	Benign or likely benign variants

DISCLAIMER

- **Decisions regarding treatment action plans should not be solely based on these test results. These findings are highly recommended to be correlated with the patient's clinical, pathological, radiological and family history for decisions on diagnosis, prognosis, or therapeutics.**
- The therapy information provided in this report is based on FDA approved drugs data, NCCN guidelines, peer reviewed published literature, standard clinical databases, and strength of biomarker results till date. These therapies may or may not be suitable/beneficial to a particular patient. This clinical report summarises potentially effective medications, potentially ineffective medications, and medications that may pose a higher risk of adverse reactions by mapping the patient's genetic alterations to the biomedical reference information. The report may also provide prognostic and diagnostic biomarkers detected or shown for the given disease context.The treatment recommendations for the variants classified in Tier II are not provided.
- The clinical trials information provided in this report is compiled from www.clinicaltrials.gov as per currently available data, however completeness of information provided herein cannot be guaranteed. This information should only be used as a guide and specific eligibility criteria should be reviewed thoroughly for the concerned patient. MedGenome Labs does not guarantee or promise an enrolment in any clinical trials.
- The identification of a genomic biomarker does not necessarily imply pharmacological effectiveness or ineffectiveness. The medications identified by the treating physician may or may not be suitable for use on a particular patient. Thus, the clinical report does not guarantee that any particular agent will be effective in the treatment of any particular condition. Also, the absence of a treatment option does not determine the effectiveness or predict an ineffective or safety-relevant effect of a medication selected by the treating physician.
- The classification and clinically relevant information for the reported variants is based on peer-reviewed publications, public clinical databases, medical guidelines (NCCN, ASCO, AMP) or other publicly available information and it has been ensured that the information provided is up to date at the time of report generated, however continuous updates may happen in public domains. Also, the classification of variants can change based on the updated literature evidence. Re-analysis of the results can be requested at additional cost.
- **This test is performed on the patient's tumor sample without a paired blood sample; therefore, it may include variations which may be of germline origin. However, this test is designed and validated for the detection and reporting of somatic genomic variants only and does not discriminate between germline and somatic variants. If clinically warranted, appropriate germline testing and genetic counselling for the patient should be considered for further evaluation.**
- Due to poor quality of FFPE tissue blocks, the QC parameters for extracted DNA may not pass to proceed further with the testing, therefore there is a possibility of assay failure at various steps (DNA QC, Library QC, Bioinformatics QC) or compromised results that include low gene coverage and low variant depth. However, sample status in such scenarios shall be sent through mail to the ordering clinician.
- This test has been validated at MedGenome Labs and the limit of detection (LOD) of allele fraction for SNVs and InDels is ≥5%. However, the report may include, at the discretion of laboratory director, the variants with lower allele burden (3-5%) having strong or potential clinical significance or those have been reported earlier in the patient. Variants with <1% allele fraction and variants of uncertain

significance with <5% allele fraction are not routinely reported. However, possibility of false negative or false positive below the limit of detection of this assay cannot be ruled out.

- Large deletions and deep intronic variations are not detected in this assay.
- **Additional case specific disclaimer : None**

TEST DESCRIPTION

IDH1 and IDH2 gene mutation analysis by NGS is a high throughput next-generation sequencing assay that covers clinically significant hotspot mutations associated with tumorigenesis, prognostication and predictive therapeutics in different tumor types.

TEST METHODOLOGY

Sample type: FFPE Specimen; A histopathologic review is performed to determine the tumor content in the FFPE block/curls.

Extraction and Library Preparation: Tumor DNA is extracted from FFPE (Formalin fixed) tissue block and used to perform targeted gene capture and sequencing.

Sequencing: The QC passed libraries are sequenced to a minimum depth of 250X on validated Illumina sequencing platform.

Data Analysis: The sequences are processed using a customized and validated analysis pipeline designed to accurately detect all classes of genomic alterations (SNVs and InDels).

Variant Annotation and Reporting:: The variants are annotated using our in-house annotation pipeline. Reportable genomic alterations are prioritized, classified, and reported based on AMP-ASCO-CAP guidelines [PMID: 27993330] and NCCN guidelines.

Limit of Detection (LOD): The LOD for SNVs and InDels is 5% Variant allele Frequency (VAF).

The transcript used for clinical reporting generally represents the canonical transcript (according to Ensembl release 99 human gene model), which is usually the longest coding transcript with strong/multiple supporting evidence. However, clinically relevant variants annotated in alternate complete coding transcripts could also be reported. Variants annotated on incomplete, and nonsense mediated decay transcripts are not reported.

§This test is developed, and its performance characteristics is determined by MedGenome Labs Ltd.

GENES ANALYSED

SNVs/InDels	
IDH1	*IDH2*

CLINICAL TRIALS

The following trials are potentially best suited for your patient's indication, considering all reported treatment recommendations. See https://clinicaltrials.gov (clinical trials from NCT) or https://trialsearch.who.int (clinical trials from other registries) for more information.

Clinical trials in total : 0 **Trial countries :** IN-India, US-United States

S.No	Title	Phase and ID	Intervention	Disease	Age & Sex
No Clinical Trials.					

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END OF REPORT