Patient ID	Patient Name		Birth Date	Sex	Age
SA00174977	TESTINGRNV, ABNORMAL		1984-01-11	F	41
Order Number	Client Order Number	Ordering Physician	Report Notes		
SA00174977	SA00174977	CLIENT,CLIENT			
Account Information		Collected			
C7028846 DLMP Rochester		28 Mar 2025 00:00			

IDH1/IDH2 Mutations Analysis, Tumor

Result

MCR

Provided diagnosis: oligodendroglioma, WHO grade II

The following CLINICALLY RELEVANT VARIANT was detected:
Gene: IDH2
DNA Change: c.515G>T (Exon 4)
Amino Acid Change: p.R172M (Arg172Met)
Variant Allele Frequency: 39%

No other reportable sequence variants were detected within the analyzed regions of the tested gene(s) listed in the method description.

Interpretation

MCR

IDH2 c.515G>T (p.R172M) (Exon 4)

IDH2 encodes a mitochondrial dehydrogenase enzyme that participates in cellular metabolism and oxidative damage control. IDH2 mutations involving codons 140 and 172 result in reduction of the IDH2 enzyme physiological activity and gain of a neomorphic ability to generate oncometabolite R(-)-2-hydroxyglutarate [PMID:20171147, PMID:22343901]. This oncometabolite is thought to mediate gliomagenesis by inducing genome-wide epigenetic changes that characterize the glioma CpG island methylator phenotype (G-CIMP)[PMID:22343889, PMID:22899282]. G-CIMP is associated with suppression of cell differentiation and disruption of chromosomal topology leading to altered regulatory interactions and oncogene activation [PMID:22343901, PMID:26700815].

IDH mutations result in reduction of the enzyme physiological activity and gain of a neomorphic ability to generate oncometabolite R(-)-2-hydroxyglutarate [PMID: 2017114, PMID: 21598255, PMID: 22343901]. This oncometabolite is thought to mediate gliomagenesis by inducing genome-wide epigenetic changes that characterize the glioma CpG island methylator phenotype (G-CIMP)[PMID: 22343889, PMID: 22899282]. G-CIMP is associated with suppression of cell differentiation and disruption of chromosomal topology leading to altered regulatory interactions and oncogene activation [PMID: 22343901, PMID: 26700815].

IDH mutations are a diagnostic molecular biomarker for astrocytoma, IDH-mutant and for oligodendroglioma, IDH-mutant and 1p/19q-codeleted [WHO Classification of Tumours Editorial Board. Central nervous system tumours. Lyon (France): International Agency for Research on Cancer, 5th ed., vol. 6, 2021]. For astrocytoma, IDH-mutant, the IDH1 R132C mutation is enriched in Li-Fraumeni patients [PMID:19340432], IDH1 non-R132H mutations are associated with longer survival than IDH1 R132H-mutant tumors [PMID:33740099], and IDH1-mutant tumors in children and young adults are enriched for germline mutations in mismatch repair genes [PMID:32895736]. IDH mutations have also been recurrently reported in medulloblastoma and meningioma [PMID:23894344, PMID:28726821, PMID:32179909]. In other central nervous system and in peripheral nervous system tumors, IDH2 mutations are rare or have not been reported [COSMIC, cBioPortal for Cancer Genomics].

The PRESENCE of a mutation in IDH2 supports the diagnosis of any of these tumor types and should be interpreted in correlation with histopathological and clinico-radiological findings and other genetic test results.

Clinically approved targeted therapy is available for patients with grade 2 astrocytoma or oligodendroglioma and acute myeloid leukemia whose tumors harbor an IDH2 mutation [fda.gov/drugs].

Additional studies are needed to assess the efficacy of approved targeted therapy and the therapeutic significance of IDH2 mutations in other tumor types.

Performing Site Legend

Code	Laboratory	Address	Lab Director	CLIA Certificate
MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	Nikola Baumann Ph.D.	24D0404292

MAYO CLINIC LABORATORIES

Patient ID	Patient Name		Birth Date	Sex	Age
SA00174977	TESTINGRNV, ABNORMAL		1984-01-11	F	41
Order Number	Client Order Number	Ordering Physician	Report Notes		
SA00174977	SA00174977	CLIENT,CLIENT			
Account Information		Collected			
C7028846 DLMP Rochester		28 Mar 2025 00:00			

Additional Information

MCR

CLINICAL TRIALS

Possible clinical trials of benefit for this patient can be found at the following sites:
1) ClinicalTrials.gov:
www.clinicaltrials.gov/ct2/search/advanced
2) Mayo Clinic: www.mayo.edu/research/clinical-trials/ 3) National Cancer Institute: www.cancer.gov/clinicaltrials/search

REFERENCE TRANSCRIPT

Sequence variant nomenclature is based on the following RefSeq accession number (build GRCh37 (hg19)): IDH2 NM_002168.

Specimen

MCR

Tissue, Tumor

Tissue ID

MCR

12345

Method

MCR

Microscopic examination is performed by a pathologist to identify areas of tumor for enrichment by macrodissection. DNA is extracted from FFPE or cytology slides, and next generation sequencing is performed to evaluate the presence of a mutation in all coding regions and exon/intron boundaries of the IDH1 and IDH2 genes.

Variant nomenclature is based on build GRCh37 (hg19). For details about gene transcripts (RefSeq accession numbers), specific targeted regions of each gene, and additional information on this test, see www.mayocliniclabs.com (Test ID IDHT).

Disclaimer

1 MCR

This test cannot differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

DNA variants of uncertain significance may be identified.

A negative result does not rule out the presence of a variant that may be present but below the limits of detection of this assay. The analytical sensitivity of this assay for sequence reportable alterations is 5% mutant allele frequency with a minimum coverage of 500X in a sample with at least 20% tumor content.

Point mutations and small insertion/deletion mutations will be detected in the IDH1 and IDH2 genes only. This test may detect single exon deletions but does not detect multi-exon deletions, duplications, larger-scale genomic copy number variants, copy neutral loss of heterozygosity (LOH), or epigenetic modifications such as promoter methylation. DELINS of 1,000 bp or less are detectable with at least 50 or more supporting reads.

Variant allele frequency (VAF) is the percentage of sequencing reads supporting a specific variant divided by the total sequencing reads at that position. In somatic testing, VAF should be interpreted in the context of several factors including, but not limited to: tumor purity/heterogeneity/copy number status (ploidy, gains/losses, loss of heterozygosity) and sequencing artifact/misalignment [PMID: 27144058, PMID: 29769535].

Rare polymorphisms may be present that could lead to false-negative or false-positive results.

The presence or absence of a variant may not be predictive of response to therapy in all patients.

Test results should be interpreted in the context of clinical, tumor sampling, histopathological, and other laboratory data. If results obtained do not match other clinical or laboratory findings, contact the laboratory for discussion. Misinterpretation of results may occur if the information provided is inaccurate and/or incomplete.

Reliable results are dependent on adequate specimen collection and processing. This test has been validated on cytology slides and formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause PCR failure.

Performing Site Legend

Code	Laboratory	Address	Lab Director	CLIA Certificate
MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	Nikola Baumann Ph.D.	24D0404292

MAYO CLINIC LABORATORIES

Patient ID	Patient Name		Birth Date	Sex	Age
SA00174977	TESTINGRNV, ABNORMAL		1984-01-11	F	41
Order Number	**Client Order Number**	**Ordering Physician**	**Report Notes**		
SA00174977	SA00174977	CLIENT,CLIENT			
Account Information		**Collected**			
C7028846 DLMP Rochester		28 Mar 2025 00:00			

Released By MCR

Katherine B. Geiersbach, M.D.

Received: 29 Mar 2025 10:57 **Reported:** 08 Apr 2025 15:21

Laboratory Notes

1 This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

Performing Site Legend

Code	Laboratory	Address	Lab Director	CLIA Certificate
MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	Nikola Baumann Ph.D.	24D0404292