Taipei Veterans General Hospital

Department of Pathology and Laboratory Medicine
No.201, Sec. 2, Shipai Rd., Beitou District, Taipei City, Taiwan
11217, R.O.C.
Tel: 02-2875-7449

Sample Information

Patient Name: 蘇玉秀
Gender: Female
ID No.: R202531390
History No.: 24974274
Age: 72

Ordering Doctor: DOC3109L 邱昭華
Ordering REQ.: C21JEME
Signing in Date: 2020/09/16

Path No.: S109-89602
MP No.: F20073
Assay: Oncomine Focus Assay
Sample Type: FFPE
Block No.: S109-20426A
Percentage of tumor cells: 70%
Note:

Sample Cancer Type: Liver Cancer

Report Highlights

1 Relevant Biomarkers
0 Therapies Available
3 Clinical Trials

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*IDH1 p.(R132C) c.394C>T* isocitrate dehydrogenase (NADP(+)) 1, cytosolic Allele Frequency: 13.51%	None	None	3

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], ESMO
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
IDH1	p.(R132C)	c.394C>T	COSM28747	chr2:209113113	13.51%	NM_005896.3	missense	1999
JAK1	p.(=)	c.2199A>G	.	chr1:65310489	49.25%	NM_002227.3	synonymous	1994
JAK1	p.(=)	c.2097C>G	.	chr1:65311214	45.05%	NM_002227.3	synonymous	2000

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
ALK	p.(D1529E)	c.4587C>G	.	chr2:29416366	99.95%	NM_004304.4	missense	1998
ALK	p.(I1461V)	c.4381A>G	.	chr2:29416572	100.00%	NM_004304.4	missense	2000
ALK	p.(=)	c.3375C>A	.	chr2:29445458	100.00%	NM_004304.4	synonymous	1995
FGFR3	p.(=)	c.1953G>A	.	chr4:1807894	99.75%	NM_000142.4	synonymous	1992
PDGFRA	p.(=)	c.1701A>G	.	chr4:55141055	99.80%	NM_006206.5	synonymous	1999
FGFR4	p.(P136L)	c.407C>T	.	chr5:176517797	99.65%	NM_213647.2	missense	2000
FGFR4	p.(=)	c.483A>G	.	chr5:176517985	14.36%	NM_213647.2	synonymous	1998
RET	p.(=)	c.2307G>T	.	chr10:43613843	48.77%	NM_020975.4	synonymous	1997
MAP2K2	p.(=)	c.192C>T	.	chr19:4117528	54.38%	NM_030662.3	synonymous	1999

Gene Fusions (RNA)

Genes	Variant ID	Locus
BAG4-FGFR1	BAG4-FGFR1.B1F2.Non-Targeted	chr8:38034657 - chr8:38315052

Biomarker Descriptions

IDH1 (isocitrate dehydrogenase (NADP(+)) 1, cytosolic)

Background: The IDH1 and IDH2 genes encode homologous isocitrate dehydrogenase enzymes that catalyze the conversion of isocitrate to α-ketoglutarate (α-KG)[1]. The IDH1 gene encodes the NADP+ dependent cytoplasmic isocitrate dehydrogenase enzyme; IDH2 encodes the mitochondrial isoform.

Alterations and prevalence: Recurrent somatic mutations in IDH1 and IDH2 are mutually exclusive and observed in several malignancies including glioma, chondrosarcoma, intrahepatic cholangiocarcinoma, acute myeloid leukemia (AML), and myelodysplastic syndrome (MDS)[2]. Recurrent IDH1 variants include predominately R132H/C plus other substitutions at lower frequencies. These gain of function variants confer neomorphic enzyme activity[3]. Although wild-type enzymatic activity is ablated, recurrent IDH1 variants catalyze the conversion of α-KG to D-2-hydroxyglutarate, an oncometabolite with diverse effects on cellular metabolism, epigenetic regulation, redox states, and DNA repair[1,4]. Recurrent IDH1 mutations are present in 5-10% of patients with AML and 5% of patients with MDS[5,6,7]. Recurrent IDH1 mutations are present in nearly 80% of lower grade diffuse gliomas[8,9].

Potential relevance: Ivosidenib[10] is FDA approved (2018) for the treatment of AML patients with IDH1 R132C/G/H/L/S variants[11]. IDH1 mutations are associated with inferior leukemia-free survival in primary myelofibrosis (PMF) and inferior overall survival in polycythemia vera (PV) but have been shown to confer improved prognosis in lower grade gliomas[12,13,14].

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ⊘ Contraindicated ⚠ Both for use and contraindicated ✖ No evidence

IDH1 p.(R132C) c.394C>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
niraparib	✖	✖	✖	✖	● (II)
olaparib	✖	✖	✖	✖	● (II)
olaparib, ceralasertib	✖	✖	✖	✖	● (II)

* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.

Signatures

Testing Personnel:

2020.09.21
17:21:46 +08'00'

Laboratory Supervisor:

2020.09.21
17:21:57 +08'00'

Pathologist:

2020.09.21
17:22:11 +08'00'

References

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6. Chou et al. The prognostic impact and stability of Isocitrate dehydrogenase 2 mutation in adult patients with acute myeloid leukemia. Leukemia. 2011 Feb;25(2):246-53. PMID: 21079611
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