Taipei Veterans General Hospital

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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

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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: FDA1, 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.

Variants (Exclude variant in Taiwan BioBank with >1% allele frequency)

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

Variants (Exclude variant in Taiwan BioBank with >1% allele frequency) (continued)

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

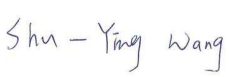
IDH1 p.(R132C) c.394C>T

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:



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Laboratory Supervisor:

2020.09.21
17:23:50 +08'00'

Pathologist:

2020.09.21
17:24:04 +08'00'

References

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