Taipei Veterans General Hospital

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Sample Information

Patient Name: 徐士文
Gender: Male
ID No.: G121749965
History No.: 49213458
Age: 33

Ordering Doctor: DOC6258D 林益庭
Ordering REQ.: 0CERHJR
Signing in Date: 2023/01/12

Path No.: M112-00004
MP No.: MY23002
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2023/01/06

Reporting Doctor: DOC5466K 葉奕成 (Phone: 8#5466)

Note:

Sample Cancer Type: Acute Myeloid Leukemia

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Relevant Acute Myeloid Leukemia Variants

Gene	Finding	Gene	Finding
ABL1	None detected	MECOM	None detected
ASXL1	None detected	MLLT3	None detected
CEBPA	None detected	MYH11	None detected
CREBBP	None detected	NPM1	None detected
FLT3	None detected	NUP214	None detected
IDH1	None detected	RARA	None detected
IDH2	None detected	RUNX1	None detected
KMT2A	None detected	TP53	None detected

Relevant Biomarkers

No clinically significant biomarkers found in this sample.

Prevalent cancer biomarkers without relevant evidence based on included data sources
PTPN11 p.(D61N) c.181G>A, NRAS p.(A59T) c.175G>A

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
NRAS	p.(A59T)	c.175G>A	COSM578	chr1:115256536	3.60%	NM_002524.5	missense	1999
PTPN11	p.(D61N)	c.181G>A	COSM13012	chr12:112888165	42.30%	NM_002834.5	missense	2000

Biomarker Descriptions

NRAS (NRAS proto-oncogene, GTPase)

Background: The NRAS proto-oncogene encodes a GTPase that functions in signal transduction and is a member of the RAS superfamily which also includes KRAS and HRAS. RAS proteins mediate the transmission of growth signals from the cell surface to the nucleus via the PI3K/AKT/MTOR and RAS/RAF/MEK/ERK pathways, which regulate cell division, differentiation, and survival[1,2,3].

Alterations and prevalence: Recurrent mutations in RAS oncogenes cause constitutive activation and are found in 20-30% of cancers. NRAS mutations are particularly common in melanomas (up to 25%) and are observed at frequencies of 5-10% in acute myeloid leukemia, colorectal, and thyroid cancers[4,5]. The majority of NRAS mutations consist of point mutations at G12, G13, and Q61[4,6]. Mutations at A59, K117, and A146 have also been observed but are less frequent[7,8].

Potential relevance: Currently, no therapies are approved for NRAS aberrations. The EGFR antagonists, cetuximab[9] and panitumumab[10], are contraindicated for treatment of colorectal cancer patients with NRAS mutations in exon 2 (codons 12 and 13), exon 3 (codons 59 and 61), and exon 4 (codons 117 and 146)[8]. The FDA has granted fast track designation to the pan-RAF inhibitor, KIN-2787[11], for the treatment of NRAS mutation positive metastatic or unresectable melanoma. NRAS mutations are associated with poor prognosis in patients with low-risk myelodysplastic syndrome[12] as well as melanoma[13]. In a phase III clinical trial in patients with advanced NRAS-mutant melanoma, binimetinib improved progression free survival (PFS) relative to dacarbazine with median PFS of 2.8 and 1.5 months, respectively[14].

PTPN11 (protein tyrosine phosphatase non-receptor type 11)

Background: The PTPN11 gene encodes a tyrosine phosphatase non-receptor type 11 protein, and is also known as Src homology region 2 domain-containing phosphatase-2 (SHP-2)[15]. PTPN11 is a member of the protein tyrosine phosphatase (PTP) family that is ubiquitously expressed and regulates cellular growth, differentiation, mitotic cycle, and oncogenic transformation. PTPN11 contains two tandem N-terminal Src homology-2 domains (N-SH2 and C-SH2), a PTP catalytic domain, and uncharacterized C-terminal domain[16]. PTPN11 regulates various signaling processes including the RAS/RAF/MEK/ERK, PI3K/AKT/MTOR, and JAK/STAT pathways[17,18]. Germline mutations in PTPN11 are associated with LEOPARD syndrome and Noonan syndrome with a predisposition to juvenile myelomonocytic leukemia (JMML) or myeloproliferative neoplasms (MPN)[12,19]. Somatic mutations in PTPN11 are associated with JMML[20,21] and solid tumors such as lung, colon, and thyroid[16,22]

Alterations and prevalence: Somatic alterations in PTPN11 include mutations and amplification[19,23]. PTPN11 mutations occur in 6% of uterine carcinoma and 5% of acute myeloid leukemia (AML) cases[7]. Mutations including E76K and D61Y result in PTPN11 activation and are associated with 30% of JMML[18].

Potential relevance: Currently, no therapies are approved for PTPN11 aberrations. Somatic mutations in PTPN11 confer drug resistance to venetoclax and azacitidine in AML[24,25].

Signatures

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Laboratory Supervisor: 2023.01.19 11:59:00 +08'00'

Pathologist: Yi-Chu Yeh 2023.01.19 11:59:10 +08'00'

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