Taipei Veterans General Hospital

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Sample Information

Patient Name: 魏慧珍
Gender: Female
ID No.: J221117841
History No.: 18365441
Age: 53

Ordering Doctor: DOC1697J 蔡淳光
Ordering REQ.: H44EEBK
Signing in Date: 2022/10/06

Path No.: S111-97920
MP No.: MY22029
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2022/09/26

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

Note:

Sample Cancer Type: Myelodysplastic Syndrome

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Relevant Myelodysplastic Syndrome Variants

Gene	Finding	Gene	Finding
ASXL1	None detected	NPM1	None detected
BCOR	None detected	NRAS	None detected
CBL	None detected	NUP214	None detected
CREBBP	None detected	RUNX1	None detected
ETV6	None detected	SF3B1	***SF3B1 p.(K700E) c.2098A>G***
EZH2	None detected	SRSF2	None detected
FLT3	None detected	STAG2	None detected
GATA2	None detected	TP53	None detected
IDH2	None detected	U2AF1	None detected
KIT	None detected	WT1	None detected
KMT2A	None detected	ZRSR2	None detected
MECOM	None detected		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*SF3B1 p.(K700E) c.2098A>G* splicing factor 3b subunit 1 Allele Frequency: 34.67% **Prognostic significance:** NCCN: Favorable	luspatercept	None	0

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], ESMO
Public data sources included in prognostic and diagnostic significance: NCCN, ESMO

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
SF3B1	p.(K700E)	c.2098A>G	COSM84677	chr2:198266834	34.67%	NM_012433.4	missense	1647
TET2	p.(L1210P)	c.3629T>C	.	chr4:106164761	41.89%	NM_001127208.2	missense	1998

Biomarker Descriptions

SF3B1 (splicing factor 3b subunit 1)

Background: The SF3B1 gene encodes the splicing factor 3b subunit 1 protein, a core component of the U2 small nuclear ribonucleoprotein (snRNP) complex of the spliceosome responsible for RNA splicing. SF3B1 is involved in recognition of the branch point sequence during selection of the 3' splice site. Recurrent somatic mutations in SF3B1 and other components of the splicing machinery including SRSF2, U2AF1, and ZRSR2, are common in myelodysplasia. These components experience mutations in a mutually exclusive manner suggesting a common impact on RNA splicing and the pathogenesis of myelodysplasia[1]. SF3B1 mutations are believed to contribute to aberrant post-translational inactivation of the regulatory complex PPP2R5A of protein phosphatase 2A (PP2A), leading to the activation and stabilization of MYC activation and impairing apoptosis[2].

Alterations and prevalence: SF3B1 mutations occur in the majority (70-80%) of myelodysplastic syndromes (MDS) with ring sideroblasts (RS) and at lower frequency in other myeloid neoplasms including MDS without RS (7%), chronic myelomonocytic leukemia (5-6%), therapy-related acute myeloid leukemia (AML) or AML with MDS features (5%), and de novo AML (3%)[1,3,4]. Recurrent somatic SF3B1 mutations are also common in certain solid cancers including uveal melanoma (20-30%) and breast cancer (2%) and at lower frequencies in diverse cancer types[5,6,7,8,9,10,11,12]. Cancer-associated recurrent missense mutations in SF3B1 occur within the HEAT repeat domains 5-9 at codon positions R625, K666, K700, G742, and D781[13]. The functional significance of recurrent SF3B1 mutations is to alter branch point selection thus inducing cryptic 3' splice site selection[13,14,15]

Potential relevance: Currently, no therapies are approved for SF3B1 aberrations. SF3B1 mutations are associated with aggressive disease and shorter survival in patients diagnosed with chronic lymphocytic leukemia (CLL)[16]. Investigational inhibitors of the spliceosome are in early clinical development[17,18].

Relevant Therapy Summary

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types ✖ No evidence

SF3B1 p.(K700E) c.2098A>G

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
luspatercept	✖	✖	✖	●	✖

Relevant Therapy Details

Current ESMO Information

● In this cancer type ○ In other cancer type ◑ In this cancer type and other cancer types

ESMO information is current as of 2022-08-01. For the most up-to-date information, search www.esmo.org.

SF3B1 p.(K700E) c.2098A>G

● **luspatercept**

Cancer type: Myelodysplastic Syndrome **Variant class:** SF3B1 mutation

ESMO Level of Evidence/Grade of Recommendation: I / A

Population segment (Line of therapy):
- Refractory (Second-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Myelodysplastic Syndromes [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.11.002]

Prognostic Details

Current NCCN Information

NCCN information is current as of 2022-08-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

SF3B1 p.(K700E) c.2098A>G

Prognostic significance: NCCN: Favorable

Cancer type: Myelodysplastic Syndrome **Variant class:** SF3B1 K700E mutation

NCCN Recommendation category: 2A

Summary:
- NCCN Guidelines® independently associate the biomarker with favorable prognosis

Reference: NCCN Guidelines® - NCCN-Myelodysplastic Syndromes [Version 3.2022]

Signatures

Testing Personnel: Yuk_Shing Lam 2022.10.07 13:05:38 +08'00'

Laboratory Supervisor: 2022.10.07 13:06:29 +08'00'

Pathologist: 2022.10.07 13:07:10 +08'00'

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