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Sample Information

Patient Name: 陳詮鈞
Gender: Male
ID No.: F121825665
History No.: 43467909
Age: 50

Ordering Doctor: DOC1751J 蕭樑材
Ordering REQ.: 0CQBFUM
Signing in Date: 2023/08/24

Path No.: M112-00230
MP No.: MY23062
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2023/08/22

Reporting Doctor: DOC5444B 楊靜芬 (Phone: 8#5444)

Note:

Sample Cancer Type: Acute Myeloid Leukemia

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Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*ASXL1 p.(A640Gfs*13)* *c.1919_1932delCCATCGGAGGGGGG* ASXL transcriptional regulator 1 Allele Frequency: 51.54%	allogeneic stem cells azacitidine cytarabine cytarabine + daunorubicin cytarabine + daunorubicin + etoposide cytarabine + etoposide + idarubicin cytarabine + fludarabine + idarubicin + filgrastim cytarabine + idarubicin cytarabine + mitoxantrone decitabine liposomal cytarabine-daunorubicin CPX-351 venetoclax + chemotherapy	None	0

Public data sources included in relevant therapies: FDA[1], NCCN, **EMA**[2], 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
ASXL1	p.(A640Gfs*13)	c.1919_1932delCCATCGGAGGGGGG	.	chr20:31022433	51.54%	NM_015338.6	frameshift Deletion	1327
CEBPA	p.(H195_P196dup)	c.589_590insACCCGC	.	chr19:33792731	39.01%	NM_004364.4	nonframeshift Insertion	423

Biomarker Descriptions

ASXL1 (ASXL transcriptional regulator 1)

Background: The ASXL1 gene encodes the ASXL transcriptional regulator 1 protein, a ligand-dependent co-activator and epigenetic scaffolding protein involved in transcriptional regulation[1,2]. ASXL1 belongs to the ASXL gene family, which also includes ASXL2 and ASXL3[2]. ASXL proteins contain a conserved c-terminal plant homeodomain (PHD) which facilitates interaction with DNA and histones[2,3]. ASXL1 influences chromatin remodeling and transcription through interaction with BAP1 and polycomb repressive complex (PRC) proteins, as well as other transcriptional activators and repressors[2,4]. In cancer, ASXL1 is the target of somatic mutations which often result in a truncated ASXL1 protein and loss of its PHD[5,6,7]. Such mutations can lead to impaired protein function and consequent upregulation of HOXA gene expression, supporting a tumor suppressor role for ASXL1[8].

Alterations and prevalence: Missense, nonsense, and frameshift mutations in ASXL1 are reported in 3-6% of de novo acute myeloid leukemia (AML), up to 36% of secondary AML, approximately 15% of myelodysplastic syndromes (MDS), up to 23% of myeloproliferative neoplasms (MPN), up to 30% of systemic mastocytosis (SM), and approximately 45% of chronic myelomonocytic leukemia (CMML)[4,9,10,11,12,13,14,15,16]. The ASXL1 G646Wfs*12 mutation accounts for over 50% of ASXL1 mutated cases in myeloid malignancies[6,11,17]. This mutation results from a single nucleotide expansion that occurs within an eight base pair guanine repeat that extends from c.1927 to c.1934. It is proposed that the high prevalence of the G646Wfs*12 variant is due to replication slippage which can occur in areas of repetitive sequence[18]. As a consequence, detection of G646Wfs*12 may result as an artifact of PCR and/or sequencing[19]. However, multiple studies observe an increase in the frequency of G646Wfs*12 in myeloid cancer relative to normal suggesting that G646Wfs*12 is a bona fide somatic mutation[9,18,20].

Potential relevance: The majority of frameshift and nonsense mutations in ASXL1 that result in protein truncation and removal of the PHD domain are considered pathogenic[21]. Mutations in ASXL1 confer poor/adverse risk in AML[16,22]. Additionally, ASXL1 nonsense or frameshift mutations are independently associated with poor prognosis in MDS and CMML[23]. Moreover, ASXL1 mutations are independently associated with inferior overall survival (OS) in patients with MPN or SM[24,25].

Relevant Therapy Summary

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

ASXL1 p.(A640Gfs*13) c.1919_1932delCCATCGGAGGGGGG

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
Allogeneic hematopoietic stem cell transplantation	✖	●	✖	✖	✖
azacitidine	✖	●	✖	✖	✖
cytarabine	✖	●	✖	✖	✖
cytarabine + daunorubicin	✖	●	✖	✖	✖
cytarabine + daunorubicin + etoposide	✖	●	✖	✖	✖

Relevant Therapy Summary (continued)

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

ASXL1 p.(A640Gfs*13) c.1919_1932delCCATCGGAGGGGGG (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
cytarabine + etoposide + idarubicin	✖	●	✖	✖	✖
cytarabine + fludarabine + idarubicin + filgrastim	✖	●	✖	✖	✖
cytarabine + idarubicin	✖	●	✖	✖	✖
cytarabine + mitoxantrone	✖	●	✖	✖	✖
decitabine	✖	●	✖	✖	✖
liposomal cytarabine-daunorubicin CPX-351	✖	●	✖	✖	✖
venetoclax + azacitidine	✖	●	✖	✖	✖
venetoclax + cytarabine	✖	●	✖	✖	✖
venetoclax + cytarabine + fludarabine + idarubicin + filgrastim	✖	●	✖	✖	✖
venetoclax + decitabine	✖	●	✖	✖	✖

Relevant Therapy Details

Current NCCN Information

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

NCCN information is current as of 2023-06-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/what-we-do/international-adaptations.

Some variant specific evidence in this report may be associated with a broader set of alterations from the NCCN Guidelines. Specific variants listed in this report were sourced from approved therapies or scientific literature. These therapeutic options are appropriate for certain population segments with cancer. Refer to the NCCN Guidelines® for full recommendation.

ASXL1 p.(A640Gfs*13) c.1919_1932delCCATCGGAGGGGGG

● **azacitidine**

Cancer type: Acute Myeloid Leukemia

Variant class: ASXL1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

ASXL1 p.(A640Gfs*13) c.1919_1932delCCATCGGAGGGGGG (continued)

cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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cytarabine + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

Allogeneic hematopoietic stem cell transplantation

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Consolidation therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

ASXL1 p.(A640Gfs*13) c.1919_1932delCCATCGGAGGGGGG (continued)

azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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cytarabine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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cytarabine + mitoxantrone

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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liposomal cytarabine-daunorubicin CPX-351

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

ASXL1 p.(A640Gfs*13) c.1919_1932delCCATCGGAGGGGGG (continued)

venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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venetoclax + cytarabine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Consolidation therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

ASXL1 p.(A640Gfs*13) c.1919_1932delCCATCGGAGGGGGG (continued)

azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Maintenance therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

ASXL1 p.(A640Gfs*13) c.1919_1932delCCATCGGAGGGGGG (continued)

venetoclax + cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 3

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** ASXL1 mutation

NCCN Recommendation category: 3

Population segment (Line of therapy):
- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]

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