



Sample Information

Patient Name: 徐律哲  
Gender: Male  
ID No.: F122002166  
History No.: 16917218  
Age: 60  
  
Ordering Doctor: DOC1697J 蔡淳光  
Ordering REQ.: H47F21P  
Signing in Date: 2023/08/17

Path No.: M112-00216  
MP No.: MY23057  
Assay: Oncomine Myeloid Assay  
Sample Type: Bone Marrow  
Bone Marrow Aspirating Date: 2023/08/15

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

Note:

Sample Cancer Type: Myelodysplastic Syndrome

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Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	ASXL1 p.(S852*) c.2555C>A ASXL transcriptional regulator 1 Allele Frequency: 15.75%	None	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	0

Public data sources included in relevant therapies: FDA1, NCCN, EMA2, ESMO

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.07(006). The content of this report has not been evaluated or approved by FDA, EMA or other regulatory agencies.

## Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	<b><i>U2AF1 p.(Q157P) c.470A&gt;C</i></b> U2 small nuclear RNA auxiliary factor 1 Allele Frequency: 39.75%	None	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	0

Public data sources included in relevant therapies: FDA1, NCCN, EMA2, 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.(S852*)	c.2555C>A	.	chr20:31023070	15.75%	NM_015338.6	nonsense	2000
U2AF1	p.(Q157P)	c.470A>C	COSM211534	chr21:44514777	39.75%	NM_006758.2	missense	2000
CEBPA	p.(H195_P196dup)	c.589_590insACCCG C	.	chr19:33792731	12.45%	NM_004364.4	nonframeshift Insertion	
U2AF1L5	p.(Q84P)	c.251A>C	COSM211534	chr21:44514777	39.75%	NM_001320651.1	missense	2000

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

**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)<sup>4,9,10,11,12,13,14,15,16</sup>. The ASXL1 G646Wfs\*12 mutation accounts for over 50% of ASXL1 mutated cases in myeloid malignancies<sup>6,11,17</sup>. 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<sup>18</sup>. As a consequence, detection of G646Wfs\*12 may result as an artifact of PCR and/or sequencing<sup>19</sup>. 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<sup>9,18,20</sup>.

**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<sup>21</sup>. Mutations in ASXL1 confer poor/adverse risk in AML<sup>16,22</sup>. Additionally, ASXL1 nonsense

## Biomarker Descriptions (continued)

or frameshift mutations are independently associated with poor prognosis in MDS and CMML<sup>23</sup>. Moreover, ASXL1 mutations are independently associated with inferior overall survival (OS) in patients with MPN or SM<sup>24,25</sup>.

### U2AF1 (U2 small nuclear RNA auxiliary factor 1)

**Background:** The U2AF1 gene encodes the U2 small nuclear RNA auxiliary factor 1 protein that belongs to the splicing factor SR family of genes involved in RNA splicing<sup>1,26</sup>. U2AF1, also known as U2AF35, mediates the recruitment of the U2AF complex to the 3' end of that pre-mRNA that is being spliced<sup>27</sup>. U2AF1 is the smaller subunit of the U2 auxiliary factor and along with the larger subunit, U2AF65 regulates the removal of introns from pre-mRNAs to produce mature mRNAs for translation during protein synthesis<sup>28</sup>. Mutations in U2AF1 alter the differential splicing of genes that are involved in various biological pathways, including DNMT3B in DNA methylation, ATR along with FANCA in DNA damage response, and H2AFY in X-chromosome inactivation<sup>29</sup>. Spliceosomal genes such as U2AF1 are common targets of somatic mutations in myelodysplastic syndrome (MDS) and are associated with the progression of MDS to acute myeloid leukemia (AML)<sup>29,30,31</sup>.

**Alterations and prevalence:** Recurrent mutations in U2AF1 occur at S34 and Q157 and are observed in 8-12% of MDS<sup>23</sup>. Somatic mutations in U2AF1 are also observed in 10% of uterine carcinoma, 4% of AML, as well as 2% of lung adenocarcinoma and stomach adenocarcinoma<sup>32</sup>.

**Potential relevance:** U2AF1 mutations including S34 and Q157 are associated with poor prognosis in MDS<sup>23</sup>. U2AF1 mutations are associated with inferior overall survival and adverse risk in primary myelofibrosis (PMF) and AML<sup>16,22,24</sup>. Specifically, the Q157 mutation is associated with a significantly shorter overall survival than U2AF1 S34 mutated and U2AF1 unmutated myeloproliferative neoplasms (MPN)<sup>24</sup>.

## Relevant Therapy Summary

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ No evidence

### ASXL1 p.(S852\*) c.2555C>A

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
Allogeneic hematopoietic stem cell transplantation	×	○	×	×	×
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 + azacitidine	×	○	×	×	×
venetoclax + cytarabine	×	○	×	×	×
venetoclax + cytarabine + fludarabine + idarubicin + filgrastim	×	○	×	×	×

## Relevant Therapy Summary (continued)

☒ In this cancer type    
 ☐ In other cancer type    
 ☒ In this cancer type and other cancer types    
 ✕ No evidence

### ASXL1 p.(S852\*) c.2555C>A (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
venetoclax + decitabine	✕	<input type="radio"/>	✕	✕	✕

### U2AF1 p.(Q157P) c.470A>C

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
Allogeneic hematopoietic stem cell transplantation	✕	<input type="radio"/>	✕	✕	✕
azacitidine	✕	<input type="radio"/>	✕	✕	✕
cytarabine	✕	<input type="radio"/>	✕	✕	✕
cytarabine + daunorubicin	✕	<input type="radio"/>	✕	✕	✕
cytarabine + daunorubicin + etoposide	✕	<input type="radio"/>	✕	✕	✕
cytarabine + etoposide + idarubicin	✕	<input type="radio"/>	✕	✕	✕
cytarabine + fludarabine + idarubicin + filgrastim	✕	<input type="radio"/>	✕	✕	✕
cytarabine + idarubicin	✕	<input type="radio"/>	✕	✕	✕
cytarabine + mitoxantrone	✕	<input type="radio"/>	✕	✕	✕
decitabine	✕	<input type="radio"/>	✕	✕	✕
liposomal cytarabine-daunorubicin CPX-351	✕	<input type="radio"/>	✕	✕	✕
venetoclax + azacitidine	✕	<input type="radio"/>	✕	✕	✕
venetoclax + cytarabine	✕	<input type="radio"/>	✕	✕	✕
venetoclax + cytarabine + fludarabine + idarubicin + filgrastim	✕	<input type="radio"/>	✕	✕	✕
venetoclax + decitabine	✕	<input type="radio"/>	✕	✕	✕

## 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](http://www.nccn.org). For NCCN International Adaptations & Translations, search [www.nccn.org/global/what-we-do/international-adaptations](http://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.(S852\*) c.2555C>A

##### ☐ 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]

##### ☐ 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]

##### ☐ 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]

##### ☐ 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]

**ASXL1 p.(S852\*) c.2555C>A (continued)****○ 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]

**○ 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]

**○ 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]

**○ 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]

**ASXL1 p.(S852\*) c.2555C>A (continued)****○ 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]

**○ 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]

**○ 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]

**○ 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]

**○ 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]

**ASXL1 p.(S852\*) c.2555C>A (continued)****○ 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]

**○ 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]

**○ 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]

**○ 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]

**○ 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]



**ASXL1 p.(S852\*) c.2555C>A (continued)****○ 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]

**○ 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]

**○ 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]

**○ 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]

## U2AF1 p.(Q157P) c.470A>C

### ☐ azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Maintenance therapy)

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

### ☐ cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Induction therapy)

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

### ☐ cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Induction therapy)

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

### ☐ cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Induction therapy)

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

### ☐ cytarabine + idarubicin

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):

- (Induction therapy)

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

## U2AF1 p.(Q157P) c.470A>C (continued)

### ○ Allogeneic hematopoietic stem cell transplantation

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Consolidation therapy); Preferred intervention

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

### ○ azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Maintenance therapy)

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

### ○ cytarabine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Consolidation therapy)

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

### ○ cytarabine + mitoxantrone

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

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

### ○ decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

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

## U2AF1 p.(Q157P) c.470A>C (continued)

### ☐ liposomal cytarabine-daunorubicin CPX-351

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Consolidation therapy)

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

### ☐ venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Consolidation therapy)

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

### ☐ venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

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

### ☐ venetoclax + cytarabine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

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

### ☐ venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Consolidation therapy)

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

## U2AF1 p.(Q157P) c.470A>C (continued)

### ☐ venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

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

### ☐ azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Induction therapy)

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

### ☐ cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Induction therapy)

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

### ☐ cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Induction therapy)

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

### ☐ cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Induction therapy)

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

## U2AF1 p.(Q157P) c.470A>C (continued)

### ☐ decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Maintenance therapy)

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

### ☐ venetoclax + cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 3

Population segment (Line of therapy):

- (Induction therapy)

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

### ☐ venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: U2AF1 mutation

NCCN Recommendation category: 3

Population segment (Line of therapy):

- (Induction therapy)

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

## References

1. O'Leary et al. Reference sequence (RefSeq) database at NCBI: current status, taxonomic expansion, and functional annotation. *Nucleic Acids Res.* 2016 Jan 4;44(D1):D733-45. PMID: 26553804
2. Katoh. Functional and cancer genomics of ASXL family members. *Br. J. Cancer.* 2013 Jul 23;109(2):299-306. PMID: 23736028
3. Gelsi-Boyer et al. Mutations of polycomb-associated gene ASXL1 in myelodysplastic syndromes and chronic myelomonocytic leukaemia. *Br. J. Haematol.* 2009 Jun;145(6):788-800. PMID: 19388938
4. Gelsi-Boyer et al. Mutations in ASXL1 are associated with poor prognosis across the spectrum of malignant myeloid diseases. *J Hematol Oncol.* 2012 Mar 21;5:12. doi: 10.1186/1756-8722-5-12. PMID: 22436456
5. Larsson et al. The changing mutational landscape of acute myeloid leukemia and myelodysplastic syndrome. *Mol. Cancer Res.* 2013 Aug;11(8):815-27. PMID: 23645565
6. Alvarez et al. ASXL1 mutations in myeloid neoplasms: pathogenetic considerations, impact on clinical outcomes and survival. *Curr Med Res Opin.* 2018 May;34(5):757-763. PMID: 28027687
7. Yang et al. Gain of function of ASXL1 truncating protein in the pathogenesis of myeloid malignancies. *Blood.* 2018 Jan 18;131(3):328-341. PMID: 29113963
8. Abdel-Wahab et al. ASXL1 mutations promote myeloid transformation through loss of PRC2-mediated gene repression. *Cancer Cell.* 2012 Aug 14;22(2):180-93. PMID: 22897849
9. Alberti et al. Discriminating a common somatic ASXL1 mutation (c.1934dup; p.G646Wfs\*12) from artifact in myeloid malignancies using NGS. *Leukemia.* 2018 Aug;32(8):1874-1878. PMID: 29959414
10. Kakosaiou et al. ASXL1 mutations in AML are associated with specific clinical and cytogenetic characteristics. *Leuk. Lymphoma.* 2018 Oct;59(10):2439-2446. PMID: 29411666
11. Paschka et al. ASXL1 mutations in younger adult patients with acute myeloid leukemia: a study by the German-Austrian Acute Myeloid Leukemia Study Group. *Haematologica.* 2015 Mar;100(3):324-30. PMID: 25596267
12. Weinstein et al. The Cancer Genome Atlas Pan-Cancer analysis project. *Nat. Genet.* 2013 Oct;45(10):1113-20. PMID: 24071849
13. Jawhar et al. The clinical and molecular diversity of mast cell leukemia with or without associated hematologic neoplasm. *Haematologica.* 2017 Jun;102(6):1035-1043. PMID: 28255023
14. Jawhar et al. KIT D816 mutated/CBF-negative acute myeloid leukemia: a poor-risk subtype associated with systemic mastocytosis. *Leukemia.* 2019 May;33(5):1124-1134. PMID: 30635631
15. Damaj et al. ASXL1 but not TET2 mutations adversely impact overall survival of patients suffering systemic mastocytosis with associated clonal hematologic non-mast-cell diseases. *PLoS ONE.* 2014;9(1):e85362. PMID: 24465546
16. NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 3.2023]
17. Boulton et al. Frequent mutation of the polycomb-associated gene ASXL1 in the myelodysplastic syndromes and in acute myeloid leukemia. *Leukemia.* 2010 May;24(5):1062-5. doi: 10.1038/leu.2010.20. Epub 2010 Feb 25. PMID: 20182461
18. Yannakou et al. ASXL1 c.1934dup;p.Gly646Trpfs\*12-a true somatic alteration requiring a new approach. *Blood Cancer J.* 2017 Dec 15;7(12):656. doi: 10.1038/s41408-017-0025-8. PMID: 29242575
19. Abdel-Wahab et al. The most commonly reported variant in ASXL1 (c.1934dupG;p.Gly646TrpfsX12) is not a somatic alteration. *Leukemia.* 2010 Sep;24(9):1656-7. doi: 10.1038/leu.2010.144. Epub 2010 Jul 1. PMID: 20596031
20. Montes-Moreno et al. Clinical molecular testing for ASXL1 c.1934dupG p.Gly646fs mutation in hematologic neoplasms in the NGS era. *PLoS ONE.* 2018;13(9):e0204218. PMID: 30222780
21. Landrum et al. ClinVar: improving access to variant interpretations and supporting evidence. *Nucleic Acids Res.* 2018 Jan 4;46(D1):D1062-D1067. PMID: 29165669
22. Döhner et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. *Blood.* 2022 Sep 22;140(12):1345-1377. PMID: 35797463
23. NCCN Guidelines® - NCCN-Myelodysplastic Syndromes [Version 1.2023]
24. NCCN Guidelines® - NCCN-Myeloproliferative Neoplasms [Version 1.2023]
25. NCCN Guidelines® - NCCN-Systemic Mastocytosis [Version 1.2020]
26. Long et al. The SR protein family of splicing factors: master regulators of gene expression. *Biochem. J.* 2009 Jan 1;417(1):15-27. PMID: 19061484
27. Zuo et al. The splicing factor U2AF35 mediates critical protein-protein interactions in constitutive and enhancer-dependent splicing. *Genes Dev.* 1996 Jun 1;10(11):1356-68. PMID: 8647433
28. Ruskin et al. A factor, U2AF, is required for U2 snRNP binding and splicing complex assembly. *Cell.* 1988 Jan 29;52(2):207-19. PMID: 2963698

## References (continued)

29. Ilagan et al. U2AF1 mutations alter splice site recognition in hematological malignancies. *Genome Res.* 2015 Jan;25(1):14-26. PMID: 25267526
30. Graubert et al. Recurrent mutations in the U2AF1 splicing factor in myelodysplastic syndromes. *Nat. Genet.* 2011 Dec 11;44(1):53-7. PMID: 22158538
31. Papaemmanuil et al. Clinical and biological implications of driver mutations in myelodysplastic syndromes. *Blood.* 2013 Nov 21;122(22):3616-27; quiz 3699. PMID: 24030381
32. Cerami et al. The cBio cancer genomics portal: an open platform for exploring multidimensional cancer genomics data. *Cancer Discov.* 2012 May;2(5):401-4. PMID: 22588877