Taipei Veterans General Hospital

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Sample Information

Patient Name: 石添明
Gender: Male
ID No.: G101813124
History No.: 45648600
Age: 69

Ordering Doctor: DOC6266E 徐千富
Ordering REQ.: 0CPLGYS
Signing in Date: 2023/08/09

Path No.: M112-00210
MP No.: MY23053
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2023/08/07

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	*RUNX1 p.(G170Rfs*10)* *c.507_508insCGTCCCGTCGG* RUNX family transcription factor 1 Allele Frequency: 40.34%	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: FDA[1], NCCN, **EMA**[2], ESMO

Relevant Biomarkers (continued)

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*SRSF2 p.(P95L) c.284C>T* serine and arginine rich splicing factor 2 Allele Frequency: 26.54%	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
IIC	*STAG2 p.(M904Efs*2) c.2709_2710delAA* STAG2 cohesin complex component Allele Frequency: 81.76%	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: FDA[1], NCCN, **EMA**[2], ESMO

Prevalent cancer biomarkers without relevant evidence based on included data sources

*TET2 p.(Q1034Rfs*3) c.3100_3101insGCATCTGAAGC*

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
TET2	p.(Q1034Rfs*3)	c.3100_3101insGCATCTGAAGC	.	chr4:106158188	40.62%	NM_001127208.2	frameshift Insertion	1989
SRSF2	p.(P95L)	c.284C>T	COSM146288	chr17:74732959	26.54%	NM_003016.4	missense	1929
RUNX1	p.(G170Rfs*10)	c.507_508insCGTCCCGTCGG	.	chr21:36252854	40.34%	NM_001754.4	frameshift Insertion	1983
STAG2	p.(M904Efs*2)	c.2709_2710delAA	.	chrX:123211841	81.76%	NM_001042749.2	frameshift Deletion	1546
KIT	p.(?)	c.-21G>T	.	chr4:55524161	46.05%	NM_000222.3	unknown	2000
TET2	p.(C1289Y)	c.3866G>A	.	chr4:106180838	41.74%	NM_001127208.2	missense	1998
EZH2	p.(R25*)	c.73C>T	.	chr7:148544318	10.26%	NM_004456.5	nonsense	1999

Biomarker Descriptions

RUNX1 (RUNX family transcription factor 1)

Background: The RUNX1 gene encodes the runt-related transcription factor (RUNX) 1, part of the RUNX family of transcription factors which also includes RUNX2 and RUNX3[1]. All RUNX proteins share several conserved regions with similar functionality including a highly conserved N-terminal 'runt' domain responsible for binding DNA, a C-terminal region composed of an activation domain, inhibitory domain, protein interacting motifs, and a nuclear matrix targeting signal[2]. Each of these proteins are capable of interacting with core binding factor beta (CBFβ) to form the core binding factor (CFB) complex. Consequently, RUNX1, RUNX2, and RUNX3 are collectively known as core binding factor alpha (CBFα) since they can each function as the alpha subunit of CBF. Specifically, CBFβ binds to the 'runt' domain of RUNX1 leading to RUNX1 stabilization and increased affinity of the CFB complex for promoters involved in hematopoietic differentiation and cell cycle regulation[3,4]. RUNX1 is frequently mutated in various hematological malignancies[4]. Germline mutations in RUNX1 result in a rare autosomal dominant condition known as familial platelet disorder, with predisposition to acute myeloid leukemia (FPD/AML)[5,6]. Somatic mutations and chromosomal translocations in RUNX1 are often observed in myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), and chronic myelomonocytic leukemia (CMML)[4].

Alterations and prevalence: RUNX1 is frequently rearranged in hematological malignancies with over 50 different observed translocations[7]. The most recurrent translocation, t(12;21)(q34;q11), results in ETV6-RUNX1 fusion and is observed in 20-25% of childhood ALL[8,9,10]. This translocation is also observed in adult ALL at a lower frequency (2%)[9,10]. Another recurrent translocation, t(8;21)(q22;q22), results in RUNX1-RUNX1T1 fusion and is observed in 5-10% of AML[11]. The RUNX1-RUNX1T1 fusion, consists of the RHD domain of RUNX1 and the majority of RUNX1T1, which promotes oncogenesis by altering transcriptional regulation of RUNX1 target genes[4,11]. Somatic mutations in RUNX1 include missense, nonsense, and frameshift mutations resulting in loss of function or dominant negative effects[4]. RUNX1 mutations are reported in approximately 10% of de novo AML as well as 10-15% of MDS[4,12,13,14].

Potential relevance: AML with RUNX1-RUNX1T1 fusions is considered a distinct molecular subtype by the World Health Organization (WHO)[12,15]. Translocations involving RUNX1, specifically t(8;21)(q22;q22)/RUNX1-RUNX1T1 in AML and t(12;21)(q34;q11)/ETV6-RUNX1 in ALL, are associated with favorable risk[12,16,17]. On the other hand, mutations in RUNX1 confer poor prognosis in AML, MDS, and systemic mastocytosis (SM)[12,13,18]

SRSF2 (serine and arginine rich splicing factor 2)

Background: The SRFS2 gene encodes the serine/arginine (SR)-rich splicing factor 2, a member of the SR-rich family of pre-mRNA splicing factors which make up part of the spliceosome. SRFS2 contains an RNA recognition motif (RRM) that recognizes and binds exonic splicing enhancers (ESE) in a sequence-specific manner[19]. SR proteins are essential regulators of alternative RNA splicing due to their ability to bind RNA and interact with other splicing factors. These proteins can influence the exclusion of cassette exons, a form of alternative splicing also known as exon skipping, which allows for the production of different protein isoforms[19,20]. SRSF2 is the target of somatic missense mutations and in-frame deletions in hematological malignancies, particularly myelodysplastic syndromes (MDS), chronic myelomonocytic leukemia (CMML), and myeloproliferative neoplasms (MPN)[21,22,23]. Such mutations in SRSF2 result in a differential gain of function which influences cassette exon exclusion, thereby supporting an oncogenic role in cancer[24].

Alterations and prevalence: Mutations in SRSF2 are observed in approximately 10% of MDS cases and 30-40% of CMML[22,25,26]. Missense mutations at P95 are most recurrent, which leads to an amino acid change from proline to histidine (H), leucine (L), or arginine (R)[26]. Specifically, the P95H substitution alters SRSF2 affinity for ESEs and drives preferential recognition of cassette exons containing C- versus G-rich ESEs[23,24]. Although less prevalent, recurrent in-frame deletions (P95H_R102del) are observed in primary myelofibrosis (PMF)[27]. This mutation results in the deletion of 8 amino acids which has been shown to exhibit greater variation of splicing events relative to the P95 missense mutation alone[28].

Potential relevance: Mutation of SRSF2 considered is one of the molecular abnormalities that defines acute myeloid leukemia, myelodysplasia related (AML-MR) according to the World Health Organization (WHO)[15]. SRSF2 mutations confer poor prognosis and risk in MDS, systemic mastocytosis (SM), and acute myeloid leukemia (AML) and are associated with decreased overall survival (OS)[12,13,17,18,29]. In MPN, SRSF2 mutations are considered high-risk mutations and are independently associated with inferior OS as well as leukemia-free survival[30,31]. Additionally, SRSF2 mutations are predictive of leukemic transformation in patients with PMF[30].

STAG2 (STAG2 cohesin complex component)

Background: The STAG2 gene encodes the stromal antigen 2 protein, one of the core proteins in the cohesin complex, which regulates the separation of sister chromatids during cell division[32,33]. Components of the cohesion complex include SMC1A, SMC3, and RAD21, which bind to STAG1/STAG2 paralogs[34,35]. Inactivating mutations in STAG2 contribute to X-linked neurodevelopmental disorders, aneuploidy, and chromosomal instability in cancer[34,36].

Alterations and prevalence: Somatic mutations in STAG2 include nonsense, frameshift, splice site variants[13]. Somatic mutations in STAG2 are observed in various solid tumors including 14% of bladder cancer, 10% of uterine cancer, 3% of stomach cancer, and 4%

Biomarker Descriptions (continued)

of lung adenocarcinoma[37]. In addition, mutations in STAG2 are observed in 5-10% of myelodysplastic syndrome(MDS), 3% of acute myeloid leukemia, and 2% of diffuse large B-cell lymphoma[13,37].

Potential relevance: Mutations in STAG2 are associated with poor prognosis and adverse risk in MDS and Acute Myeloid Leukemia[12,13,17]. Truncating mutations in STAG2 lead to a loss of function in bladder cancer and are often identified as an early event associated with low grade and stage tumors[38].

TET2 (tet methylcytosine dioxygenase 2)

Background: TET2 encodes the tet methylcytosine dioxygenase 2 protein and belongs to a family of ten-eleven translocation (TET) proteins that also includes TET1 and TET3[39]. TET2 is involved in DNA methylation, specifically in the conversion of 5-methylcytosine to 5-hydroxymethylcytosine[40,41]. The TET proteins contain a C-terminal core catalytic domain that contains a cysteine-rich domain and a double stranded ß-helix domain (DSBH)[42]. TET2 is a tumor suppressor gene. Loss of function mutations in TET2 are associated with loss of catalytic activity and transformation to hematological malignancies[39,40,41]

Alterations and prevalence: Somatic TET2 mutations, including nonsense, frameshift, splice site, and missense, are observed in 20-25% of myelodysplastic syndrome (MDS) associated diseases, including 40%-60% chronic myelomonocytic leukemia (CMML)[13]. TET2 mutations at H1881 and R1896 are frequently observed in myeloid malignancies[40,43]. TET2 mutations are also observed in 9% of uterine, 8% of melanoma and acute myeloid leukemia (AML), as well as 6% of diffuse large B-cell lymphoma (DLBCL).

Potential relevance: The presence of TET2 mutations may be used as one of the major diagnostic criteria in pre-primary myelofibrosis (pre-PMF) and overt PMF in the absence of JAK2/CALR/MPL mutations[30]. TET2 mutations are associated with poor prognosis in PMF and increased rate of transformation to leukemia[30,44]

Relevant Therapy Summary

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

RUNX1 p.(G170Rfs*10) c.507_508insCGTCCCGTCGG

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

RUNX1 p.(G170Rfs*10) c.507_508insCGTCCCGTCGG (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
venetoclax + decitabine	✖	○	✖	✖	✖

SRSF2 p.(P95L) c.284C>T

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	✖	○	✖	✖	✖
venetoclax + decitabine	✖	○	✖	✖	✖

STAG2 p.(M904Efs*2) c.2709_2710delAA

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	✖	○	✖	✖	✖

Relevant Therapy Summary (continued)

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

STAG2 p.(M904Efs*2) c.2709_2710delAA (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
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.

RUNX1 p.(G170Rfs*10) c.507_508insCGTCCCGTCGG

○ azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: RUNX1 mutation

NCCN Recommendation category: 1

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

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

RUNX1 p.(G170Rfs*10) c.507_508insCGTCCCGTCGG (continued)

cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** RUNX1 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:** RUNX1 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:** RUNX1 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:** RUNX1 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:** RUNX1 mutation

NCCN Recommendation category: 2A

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

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

RUNX1 p.(G170Rfs*10) c.507_508insCGTCCCGTCGG (continued)

azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** RUNX1 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:** RUNX1 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:** RUNX1 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:** RUNX1 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:** RUNX1 mutation

NCCN Recommendation category: 2A

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

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

RUNX1 p.(G170Rfs*10) c.507_508insCGTCCCGTCGG (continued)

venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** RUNX1 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:** RUNX1 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:** RUNX1 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:** RUNX1 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:** RUNX1 mutation

NCCN Recommendation category: 2A

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

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

RUNX1 p.(G170Rfs*10) c.507_508insCGTCCCGTCGG (continued)

azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** RUNX1 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:** RUNX1 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:** RUNX1 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:** RUNX1 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:** RUNX1 mutation

NCCN Recommendation category: 2B

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

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

RUNX1 p.(G170Rfs*10) c.507_508insCGTCCCGTCGG (continued)

venetoclax + cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia **Variant class:** RUNX1 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:** RUNX1 mutation

NCCN Recommendation category: 3

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

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

SRSF2 p.(P95L) c.284C>T

azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** SRSF2 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:** SRSF2 mutation

NCCN Recommendation category: 1

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

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

SRSF2 p.(P95L) c.284C>T (continued)

cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia **Variant class:** SRSF2 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:** SRSF2 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:** SRSF2 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:** SRSF2 mutation

NCCN Recommendation category: 2A

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

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

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azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** SRSF2 mutation

NCCN Recommendation category: 2A

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

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

SRSF2 p.(P95L) c.284C>T (continued)

cytarabine

Cancer type: Acute Myeloid Leukemia **Variant class:** SRSF2 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:** SRSF2 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:** SRSF2 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:** SRSF2 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:** SRSF2 mutation

NCCN Recommendation category: 2A

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

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

SRSF2 p.(P95L) c.284C>T (continued)

venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** SRSF2 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:** SRSF2 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:** SRSF2 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:** SRSF2 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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azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** SRSF2 mutation

NCCN Recommendation category: 2B

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

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

SRSF2 p.(P95L) c.284C>T (continued)

cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia **Variant class:** SRSF2 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:** SRSF2 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:** SRSF2 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:** SRSF2 mutation

NCCN Recommendation category: 2B

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

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

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venetoclax + cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia **Variant class:** SRSF2 mutation

NCCN Recommendation category: 3

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

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

SRSF2 p.(P95L) c.284C>T (continued)

venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** SRSF2 mutation

NCCN Recommendation category: 3

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

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

STAG2 p.(M904Efs*2) c.2709_2710delAA

azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** STAG2 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:** STAG2 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:** STAG2 mutation

NCCN Recommendation category: 1

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

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

STAG2 p.(M904Efs*2) c.2709_2710delAA (continued)

cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** STAG2 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:** STAG2 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:** STAG2 mutation

NCCN Recommendation category: 2A

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

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

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azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** STAG2 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:** STAG2 mutation

NCCN Recommendation category: 2A

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

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

STAG2 p.(M904Efs*2) c.2709_2710delAA (continued)

cytarabine + mitoxantrone

Cancer type: Acute Myeloid Leukemia **Variant class:** STAG2 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:** STAG2 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:** STAG2 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:** STAG2 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:** STAG2 mutation

NCCN Recommendation category: 2A

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

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

STAG2 p.(M904Efs*2) c.2709_2710delAA (continued)

venetoclax + cytarabine

Cancer type: Acute Myeloid Leukemia **Variant class:** STAG2 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:** STAG2 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:** STAG2 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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azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** STAG2 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:** STAG2 mutation

NCCN Recommendation category: 2B

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

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

STAG2 p.(M904Efs*2) c.2709_2710delAA (continued)

○ cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** STAG2 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:** STAG2 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:** STAG2 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:** STAG2 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:** STAG2 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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