Taipei Veterans General Hospital

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Sample Information

Patient Name: 留麗絹
Gender: Female
ID No.: P220769096
History No.: 18478267
Age: 61

Ordering Doctor: DOC6372L 張彥安
Ordering REQ.: 0CHBPDY
Signing in Date: 2023/03/16

Path No.: M112-00041
MP No.: MY23013
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2023/03/08

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

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	***NPM1 p.(W288Cfs*12) c.863_864insTCTG***
FLT3	***FLT3 ITD mutation***	NUP214	None detected
IDH1	None detected	RARA	None detected
IDH2	None detected	RUNX1	None detected
KMT2A	None detected	TP53	None detected

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.02(005).The content of this report has not been evaluated or approved by FDA, EMA or other regulatory agencies.

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*FLT3 ITD mutation* fms related receptor tyrosine kinase 3 Allele Frequency: 8.60%, 22.30% (2 variants)	**gilteritinib** [1, 2] **midostaurin + chemotherapy** [1, 2] cytarabine + daunorubicin cytarabine + daunorubicin + etoposide cytarabine + etoposide + idarubicin cytarabine + fludarabine + idarubicin + filgrastim cytarabine + idarubicin cytarabine + mitoxantrone gemtuzumab ozogamicin + chemotherapy sorafenib sorafenib + chemotherapy venetoclax + chemotherapy	None	0
	Prognostic significance: ELN 2017: Favorable to Intermediate			
IA	*NPM1 p.(W288Cfs*12) c.863_864insTCTG* nucleophosmin 1 Allele Frequency: 44.61%	cytarabine + daunorubicin cytarabine + daunorubicin + etoposide cytarabine + etoposide + idarubicin cytarabine + fludarabine + idarubicin + filgrastim cytarabine + idarubicin cytarabine + mitoxantrone gemtuzumab ozogamicin + chemotherapy midostaurin + chemotherapy	None	0
	Prognostic significance: ELN 2017: Favorable to Intermediate **Diagnostic significance:** Acute Myeloid Leukemia			

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

Prevalent cancer biomarkers without relevant evidence based on included data sources

*TET2 p.(I1873N) c.5618T>A, TET2 p.(L1111Ffs*19) c.3332_3333insT*

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.(L1111Ffs*19)	c.3332_3333insT	.	chr4:106158429	50.25%	NM_001127208.2	frameshift Insertion	1986
TET2	p.(I1873N)	c.5618T>A	.	chr4:106197285	5.80%	NM_001127208.2	missense	2000
NPM1	p.(W288Cfs*12)	c.863_864insTCTG	COSM17559	chr5:170837547	44.61%	NM_002520.6	frameshift Insertion	408
FLT3	p.(E598_F612dup)	c.-1_0insAATATGATCTCAAATGGGAGTTTCCAAGAGAAAATTTAGAGTTTG	.	chr13:28608218	8.60%	NM_004119.3	nonframeshift Insertion	1965

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Variants (Exclude variant in Taiwan BioBank with >1% allele frequency) (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
FLT3	p.(Y597_L610dup)	c.1787_1787delAinsA ATATGAATATGATC TCAAATGGGAGTTT CCAAGAGAAAATTT	.	chr13:28608269	22.30%	NM_004119.3	nonframeshift Block Substitution	
ASXL1	p.(N986S)	c.2957A>G	.	chr20:31023472	50.10%	NM_015338.6	missense	2000

Biomarker Descriptions

FLT3 (fms related receptor tyrosine kinase 3)

Background: The FLT3 gene encodes the fms related tyrosine kinase 3, a tyrosine kinase receptor that is a member of the class III receptor tyrosine kinase family that also includes PDGFR, FMS, and KIT[1]. FLT3 is highly expressed in hematopoietic progenitor cells[2]. Genomic alterations in FLT3 activate downstream oncogenic pathways including PI3K/AKT/mTOR and RAS/RAF/MEK/ERK pathways which promote cellular proliferation, survival, and inhibition of differentiation[1].

Alterations and prevalence: Somatic mutations occur in approximately 30% of acute myeloid leukemia (AML), 7-10% of melanoma, and up to 8% of uterine cancer[3,4,5,6]. The most common activating FLT3 mutations are internal tandem duplications (ITD) that range from 3 to 400 base pairs in length within exons 14 and 15 in the juxtamembrane (JM) domain[7]. The second most frequent mutations are point mutations in exon 20 within the tyrosine kinase domain (TKD)[8]. FLT3 is amplified in up to 8% of colorectal cancer, 3% of stomach cancer, and is commonly overexpressed in AML[5,6,9].

Potential relevance: The presence of FLT3-ITD confers poor prognosis in myelodysplastic syndrome (MDS) and AML[10,11]. Similarly, the FLT3 TKD mutation D835 confers poor prognosis in MDS[10]. Midostaurin[12] (2017) and gilteritinib[13] (2018) are kinase inhibitors approved for AML patients with FLT3-ITD and TKD mutations including D835 and I836 mutations. The FDA granted fast track designations in 2017 to crenolanib[14] and in 2022 to tuspetinib (HM43239)[15] for FLT3 mutation-positive relapsed or refractory AML. In 2018 the FDA granted breakthrough therapy designation to quizartinib[16] for AML with FLT3-ITD. A phase II trial testing crenolanib in 34 patients with FLT3-ITD and TKD mutated relapsed/refractory AML, reported that FLT3 inhibitor naïve patients demonstrated a longer overall survival (OS) and event free survival (EFS) in comparison to previously treated patients (median OS: 55 weeks vs 13 weeks; median EFS: 13 weeks vs 7 weeks)[17]. Another phase II trial of crenolanib with chemotherapy in newly diagnosed FLT3 mutated AML reported complete remission in 24/29 (83%) patients[18]. Several multi-targeted tyrosine kinase inhibitors such as sorafenib (2005), sunitinib (2006), cabozantinib (2012), and ponatinib (2012) are FDA approved and include FLT3 as a target. Sorafenib is recommended in combination with chemotherapy in FLT3-ITD mutated AML[11].

NPM1 (nucleophosmin 1)

Background: The NPM1 gene encodes the nucleophosmin protein, a histone chaperone of the nucleophosmin/nucleoplasmin family, which also includes NPM2 and NPM3[19]. NPM1 functions as an oncogene and tumor suppressor, and is important in maintaining genomic stability, DNA repair, and apoptosis[19,20]. NPM1 has a highly conserved N-terminal region which constitutes the core domain responsible for oligomerization, an acidic domain, a nuclear localization signal, and a disorganized C-terminal region which is required for nucleolar localization[19]. Oligomerization of NPM1 localizes the protein in the nucleus of proliferating cells where it binds to Akt in response to growth factor stimulation and escapes proteolytic degradation by caspase activity, thereby promoting cell survival[19,20]. NPM1 is one of the most frequently altered genes in hematological cancers[21]. Most NPM1 mutations occur in the C-terminus, impacting protein folding or the nucleolar localization signal, and result in the localization of NPM1 to the cytoplasm (NPMc) instead of to the nucleus[19].

Alterations and prevalence: NPM1 mutations are observed in 45-60% of AML with a normal karyotype (NK-AML), 28-35% of de novo acute myeloid leukemia (AML) and are frequently co-mutated with DNMT3A and/or FLT3-ITD[11,22,23]. NPM1 fusions are associated with distinct partner genes in acute promyelocytic leukemia (APL), anaplastic large-cell lymphoma (ALCL), AML, and myelodysplasia[21]. Specifically, NPM1-ALK fusion is found in 30% of all ALCL and this specific fusion is observed in 85% of ALK-positive ALCL[19]. The t(5;17)(q35;q21) translocation that results in NPM1-RARA fusion is observed in APL[24].

Potential relevance: NPM1 mutated AML is recognized as a distinct diagnostic disease entity by the World Health Organization (WHO)[25]. NPM1 mutations are associated with better outcomes, increased complete remission, and improved overall survival in AML[11,23]. NPM1 without FLT3-ITD mutations or with <0.5 allelic ratio FLT3-ITD mutations are associated with favorable risk in AML[11]. Concurrent NPM1 and with >0.5 allelic ratio FLT3-ITD mutations confer intermediate risk in AML, whereas wild-type NPM1 confers

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Biomarker Descriptions (continued)

poor/adverse risk[11]. The NPM1 frameshift mutation W288fs*12 is associated with poor prognosis in myelodysplastic syndrome (MDS)[10]. The ALK-NPM1 fusion, and translocation t(2;5)(p23;q35) which leads to an ALK-NPM1 fusion, is diagnostic of ALK-positive anaplastic large cell lymphoma[26,27].

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[28]. TET2 is involved in DNA methylation, specifically in the conversion of 5-methylcytosine to 5-hydroxymethylcytosine[29,30]. The TET proteins contain a C-terminal core catalytic domain that contains a cysteine-rich domain and a double stranded ß-helix domain (DSBH)[31]. TET2 is a tumor suppressor gene. Loss of function mutations in TET2 are associated with loss of catalytic activity and transformation to hematological malignancies[28,29,30]

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)[10]. TET2 mutations at H1881 and R1896 are frequently observed in myeloid malignancies[29,32]. 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[25,33]. TET2 mutations are associated with poor prognosis in PMF and increased rate of transformation to leukemia[33,34]

Relevant Therapy Summary

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

FLT3 ITD mutation

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
gilteritinib	●	●	●	●	✖
midostaurin + cytarabine + daunorubicin	●	●	●	●	✖
cytarabine + daunorubicin	✖	●	✖	✖	✖
cytarabine + daunorubicin + etoposide	✖	●	✖	✖	✖
cytarabine + etoposide + idarubicin	✖	●	✖	✖	✖
cytarabine + fludarabine + idarubicin + filgrastim	✖	●	✖	✖	✖
cytarabine + idarubicin	✖	●	✖	✖	✖
cytarabine + mitoxantrone	✖	●	✖	✖	✖
gemtuzumab ozogamicin + cytarabine + daunorubicin	✖	●	✖	✖	✖
midostaurin + cytarabine	✖	●	✖	✖	✖
sorafenib	✖	●	✖	✖	✖
sorafenib + azacitidine	✖	●	✖	✖	✖
sorafenib + decitabine	✖	●	✖	✖	✖
venetoclax + azacitidine	✖	●	✖	✖	✖
venetoclax + cytarabine	✖	●	✖	✖	✖

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Relevant Therapy Summary (continued)

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

FLT3 ITD mutation (continued)

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

NPM1 p.(W288Cfs*12) c.863_864insTCTG

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
cytarabine + daunorubicin	✖	●	✖	✖	✖
cytarabine + daunorubicin + etoposide	✖	●	✖	✖	✖
cytarabine + etoposide + idarubicin	✖	●	✖	✖	✖
cytarabine + fludarabine + idarubicin + filgrastim	✖	●	✖	✖	✖
cytarabine + idarubicin	✖	●	✖	✖	✖
cytarabine + mitoxantrone	✖	●	✖	✖	✖
gemtuzumab ozogamicin + cytarabine + daunorubicin	✖	●	✖	✖	✖
midostaurin + cytarabine + daunorubicin	✖	●	✖	✖	✖

Relevant Therapy Details

Current FDA Information

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

FDA information is current as of 2023-01-18. For the most up-to-date information, search www.fda.gov.

FLT3 ITD mutation

● **gilteritinib**

Cancer type: Acute Myeloid Leukemia **Label as of:** 2022-01-12 **Variant class:** FLT3 ITD mutation

Indications and usage:
XOSPATA® is a kinase inhibitor indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with a FLT3 mutation as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/211349s003lbl.pdf

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FLT3 ITD mutation (continued)

midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Label as of:** 2021-11-15 **Variant class:** FLT3 ITD mutation

Indications and usage:

RYDAPT® is a kinase inhibitor indicated for the treatment of adult patients with:

- Newly diagnosed acute myeloid leukemia (AML) that is FLT3 mutation-positive as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation.

  Limitations of Use: RYDAPT® is not indicated as a single-agent induction therapy for the treatment of patients with AML.
- Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL).

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/207997s008lbledt.pdf

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.02(005).

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 2023-01-03. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

FLT3 ITD mutation + NPM1 p.(W288Cfs*12) c.863_864insTCTG

● cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- (Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

● cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- (Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

● cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- (Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

● cytarabine + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- (Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.02(005).

FLT3 ITD mutation + NPM1 p.(W288Cfs*12) c.863_864insTCTG (continued)

cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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cytarabine + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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cytarabine + mitoxantrone

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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gemtuzumab ozogamicin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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FLT3 ITD mutation + NPM1 p.(W288Cfs*12) c.863_864insTCTG (continued)

cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

cytarabine + fludarabine + idarubicin + filgrastim

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

FLT3 ITD mutation

gilteritinib

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- Relapsed, Refractory (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.02(005).

FLT3 ITD mutation (continued)

midostaurin + cytarabine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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sorafenib

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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sorafenib + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Induction therapy); Other recommended intervention
- Relapsed, Refractory (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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FLT3 ITD mutation (continued)

sorafenib + decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Induction therapy); Other recommended intervention
- Relapsed, Refractory (Line of therapy not specified)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 mutation

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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venetoclax + cytarabine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):
- (Induction therapy); Other recommended intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

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venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.02(005).

Current EMA Information

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

EMA information is current as of 2023-01-18. For the most up-to-date information, search www.ema.europa.eu/ema.

FLT3 ITD mutation

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Label as of:** 2021-09-08 **Variant class:** FLT3 ITD mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/xospata-epar-product-information_en.pdf

● midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Label as of:** 2022-09-23 **Variant class:** FLT3 ITD mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/rydapt-epar-product-information_en.pdf

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.02(005).

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 2023-01-03. For the most up-to-date information, search www.esmo.org.

FLT3 ITD mutation

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

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

Population segment (Line of therapy):
- Relapsed, Refractory (Line of therapy not specified)

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

● midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 ITD mutation

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

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

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.02(005).

Prognostic Details

Current NCCN Information

NCCN information is current as of 2023-01-03. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

FLT3 ITD mutation + NPM1 p.(W288Cfs*12) c.863_864insTCTG

Prognostic significance: ELN 2017: Intermediate

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

NCCN Recommendation category: 2A

Summary:
- FLT3-ITD^{high}; High defined as allelic ratio (≥0.5).

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 2.2022]

Current ESMO Information

ESMO information is current as of 2023-01-03. For the most up-to-date information, search www.esmo.org.

FLT3 ITD mutation + NPM1 p.(W288Cfs*12) c.863_864insTCTG

Prognostic significance: ELN 2017: Intermediate

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

Summary:
- FLT3-ITD^{High}; High defined as allelic ratio (≥0.5)

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

Prognostic significance: ELN 2017: Favorable

Cancer type: Acute Myeloid Leukemia **Variant classes:** FLT3 ITD mutation & NPM1 mutation

Summary:
- FLT3-ITD^{Low}; Low defined as allelic ratio (<0.5)

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

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Diagnostic Details

Current ESMO Information

ESMO information is current as of 2023-01-03. For the most up-to-date information, search www.esmo.org.

NPM1 p.(W288Cfs*12) c.863_864insTCTG

Diagnostic significance: Acute Myeloid Leukemia

Variant class: NPM1 mutation

Diagnostic notes:
- AML with recurrent genetic abnormalities; WHO classification of AML

Reference: ESMO Clinical Practice Guidelines - ESMO-Acute Myeloblastic Leukaemia in Adult Patients [Ann Oncol (2020); 31(6): 697-712.]

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2023-01-18. For the most up-to-date information, search www.fda.gov.

FLT3 ITD mutation

crenolanib

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 mutation

Supporting Statement:

The FDA has granted Fast Track Designation to the benzimidazole type I kinase inhibitor, crenolanib, for:
- FLT3 mutation-positive relapsed or refractory acute myeloid leukemia (AML)
- PDGFRA D842V mutated unresectable or metastatic gastrointestinal stromal tumors (GIST)

Reference:

https://www.globenewswire.com/news-release/2017/12/01/1216122/0/en/Arog-Pharmaceuticals-Receives-FDA-Fast-Track-Designation-for-Crenolanib-in-Relapsed-or-Refractory-FLT3-Positive-AML.html

tuspetinib

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 mutation

Supporting Statement:
The FDA has granted Fast Track Designation to tuspetinib (HM43239), a myeloid kinome inhibitor, for relapsed or refractory (R/R) acute myeloid leukemia (AML) with FLT3 mutation.

Reference:

https://www.aptose.com/news-media/press-releases/detail/230/aptose-receives-fast-track-designation-for-hm43239-in

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Signatures

Testing Personnel: Shu-Ying Wang 2023.03.21 11:05:14 +08'00'

Laboratory Supervisor: 2023.03.21 11:05:27 +08'00'

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