Taipei Veterans General Hospital

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Sample Information

Patient Name: 郭照娟
Gender: Female
ID No.: P220945649
History No.: 48430871
Age: 49

Ordering Doctor: DOC1751J 蕭樑材
Ordering REQ.: 0CXPJGL
Signing in Date: 2024/02/23

Path No.: M113-00053
MP No.: MY24006
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2024/02/22

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

Note:

Sample Cancer Type: Acute Myeloid Leukemia

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Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*FLT3 p.(D835Y) c.2503G>T* FLT3 TKD mutation fms related receptor tyrosine kinase 3 Allele Frequency: 25.69%	**gilteritinib** [1, 2] **midostaurin + chemotherapy** [1, 2] allogeneic stem cells azacitidine decitabine gilteritinib + chemotherapy midostaurin sorafenib sorafenib + chemotherapy venetoclax + chemotherapy	None	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
IA	*FLT3 ITD mutation* fms related receptor tyrosine kinase 3 Allele Frequency: 10.50%	**gilteritinib** [1, 2] **midostaurin + chemotherapy** [1, 2] **quizartinib** [1, 2] **quizartinib + chemotherapy** [1, 2] allogeneic stem cells azacitidine decitabine gilteritinib + chemotherapy midostaurin sorafenib sorafenib + chemotherapy venetoclax + chemotherapy	None	0
IA	*STAG2 c.2096+1G>A* STAG2 cohesin complex component Allele Frequency: 37.22%	allogeneic stem cells azacitidine cytarabine cytarabine + daunorubicin cytarabine + daunorubicin + etoposide cytarabine + etoposide + idarubicin cytarabine + fludarabine + idarubicin + filgrastim cytarabine + idarubicin cytarabine + mitoxantrone decitabine liposomal cytarabine-daunorubicin CPX-351 venetoclax + chemotherapy	None	0

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

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

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
FLT3	p.(D835Y)	c.2503G>T	COSM783	chr13:28592642	25.69%	NM_004119.3	missense	1985
FLT3	p.(R595_E596insFPADFR)	c.1775_1776insTGATTTCAGATTCCCCGC	.	chr13:28608280	10.50%	NM_004119.3	nonframeshift Insertion	1991
STAG2	p.(?)	c.2096+1G>A	.	chrX:123199797	37.22%	NM_001042749.2	unknown	1975
JAK2	p.(W659R)	c.1975T>C	.	chr9:5077563	41.90%	NM_004972.4	missense	2000

Biomarker Descriptions

STAG2 c.2096+1G>A

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[1,2]. Components of the cohesion complex include SMC1A, SMC3, and RAD21, which bind to STAG1/STAG2 paralogs[3,4]. Inactivating mutations in STAG2 contribute to X-linked neurodevelopmental disorders, aneuploidy, and chromosomal instability in cancer[3,5].

Biomarker Descriptions (continued)

Alterations and prevalence: Somatic mutations in STAG2 include nonsense, frameshift, splice site variants[6]. 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% of lung adenocarcinoma[7]. 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[6,7].

Potential relevance: Mutations in STAG2 are associated with poor prognosis and adverse risk in MDS and Acute Myeloid Leukemia[6,8,9]. 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[10].

FLT3 p.(D835Y) c.2503G>T (FLT3 TKD mutation), FLT3 ITD mutation

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[11]. FLT3 is highly expressed in hematopoietic progenitor cells[12]. 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[11].

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[7,13,14,15]. 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[16]. The second most frequent mutations are point mutations in exon 20 within the tyrosine kinase domain (TKD)[17]. FLT3 is amplified in up to 8% of colorectal cancer, 3% of stomach cancer, and is commonly overexpressed in AML[7,15,18].

Potential relevance: FLT3 rearrangements are recognized by the World Health Organization (WHO) as one of the possible molecular abnormality requirements that define myeloid/lymphoid neoplasms with eosinophilia and tyrosine kinase gene fusions[19].The presence of FLT3-ITD confers poor prognosis in myelodysplastic syndrome (MDS)[6]. Concurrent expression of FLT-ITD with mutant or wild-type NPM1 (when lacking adverse risk genetic lesions) confers intermediate risk in AML[8,9]. FLT3 TKD mutation at D835 confers poor prognosis in MDS[6]. Midostaurin[20] (2017) and gilteritinib[21] (2018) are kinase inhibitors approved for AML patients with FLT3-ITD and TKD mutations including D835 and I836 mutations. Quizartinib dihydrochloride[22] (2023) is also a kinase inhibitor approved for AML patients with FLT3-ITD mutations. The FDA granted fast track designations in 2017 to crenolanib[23] and in 2022 to tuspetinib (HM43239)[24] for FLT3 mutation-positive relapsed or refractory AML. 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)[25]. Another phase II trial of crenolanib with chemotherapy in newly diagnosed FLT3 mutated AML reported complete remission in 24/29 (83%) patients[26]. 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[8].

Relevant Therapy Summary

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

FLT3 p.(D835Y) c.2503G>T

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

Relevant Therapy Summary (continued)

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

FLT3 p.(D835Y) c.2503G>T (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
midostaurin	✖	●	✖	✖	✖
midostaurin + cytarabine	✖	●	✖	✖	✖
midostaurin + cytarabine + idarubicin	✖	●	✖	✖	✖
sorafenib	✖	●	✖	✖	✖
sorafenib + azacitidine	✖	●	✖	✖	✖
sorafenib + decitabine	✖	●	✖	✖	✖
venetoclax + azacitidine	✖	●	✖	✖	✖
venetoclax + cytarabine	✖	●	✖	✖	✖
venetoclax + decitabine	✖	●	✖	✖	✖

FLT3 ITD mutation

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
gilteritinib	●	●	●	●	✖
midostaurin + cytarabine + daunorubicin	●	●	●	●	✖
quizartinib	●	●	●	✖	✖
quizartinib + cytarabine	●	●	●	✖	✖
quizartinib + anthracycline + cytarabine	●	✖	●	✖	✖
Allogeneic hematopoietic stem cell transplantation	✖	●	✖	✖	✖
azacitidine	✖	●	✖	✖	✖
decitabine	✖	●	✖	✖	✖
gilteritinib + azacitidine	✖	●	✖	✖	✖
midostaurin	✖	●	✖	✖	✖
midostaurin + cytarabine	✖	●	✖	✖	✖
midostaurin + cytarabine + idarubicin	✖	●	✖	✖	✖
quizartinib + cytarabine + daunorubicin	✖	●	✖	✖	✖
quizartinib + cytarabine + idarubicin	✖	●	✖	✖	✖
sorafenib	✖	●	✖	✖	✖
sorafenib + azacitidine	✖	●	✖	✖	✖
sorafenib + decitabine	✖	●	✖	✖	✖
venetoclax + azacitidine	✖	●	✖	✖	✖

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 + cytarabine	✖	●	✖	✖	✖
venetoclax + decitabine	✖	●	✖	✖	✖

STAG2 c.2096+1G>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	✖	●	✖	✖	✖
venetoclax + decitabine	✖	●	✖	✖	✖

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 2024-01-17. For the most up-to-date information, search www.fda.gov.

FLT3 p.(D835Y) c.2503G>T

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Label as of:** 2022-01-12 **Variant class:** FLT3 D835 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

● midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Label as of:** 2023-05-22 **Variant class:** FLT3 D835 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/2023/207997s010lbl.pdf

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

FLT3 ITD mutation (continued)

midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Label as of:** 2023-05-22 **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/2023/207997s010lbl.pdf

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quizartinib, quizartinib + cytarabine, quizartinib + anthracycline + cytarabine

Cancer type: Acute Myeloid Leukemia **Label as of:** 2023-07-20 **Variant class:** FLT3 ITD mutation

Indications and usage:
VANFLYTA® is a kinase inhibitor indicated in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive as detected by an FDA-approved test.

Reference:

https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216993s000lbl.pdf

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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 2024-01-02. To view the most recent and complete version of the guideline, go online to 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.

FLT3 p.(D835Y) c.2503G>T

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 D835 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 6.2023]

● midostaurin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 D835 mutation

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

● midostaurin + cytarabine + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 D835 mutation

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

FLT3 p.(D835Y) c.2503G>T (continued)

venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 D835 mutation

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 D835 mutation

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

Allogeneic hematopoietic stem cell transplantation

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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azacitidine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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decitabine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

FLT3 p.(D835Y) c.2503G>T (continued)

midostaurin + cytarabine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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midostaurin + cytarabine + daunorubicin

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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midostaurin + cytarabine + idarubicin

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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sorafenib

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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sorafenib + azacitidine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

FLT3 p.(D835Y) c.2503G>T (continued)

sorafenib + decitabine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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venetoclax + cytarabine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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gilteritinib

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

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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gilteritinib + azacitidine

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Induction therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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midostaurin

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

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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 6.2023]

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midostaurin + cytarabine + daunorubicin

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

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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midostaurin + cytarabine + daunorubicin

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

Other criteria: NPM1 wild type

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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midostaurin + cytarabine + idarubicin

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

Other criteria: NPM1 wild type

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

FLT3 ITD mutation (continued)

midostaurin + cytarabine + idarubicin

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

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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quizartinib + cytarabine + daunorubicin

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

Other criteria: NPM1 wild type

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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quizartinib + cytarabine + daunorubicin

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

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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quizartinib + cytarabine + idarubicin

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

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

FLT3 ITD mutation (continued)

quizartinib + cytarabine + idarubicin

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

Other criteria: NPM1 wild type

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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venetoclax + azacitidine

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

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

Allogeneic hematopoietic stem cell transplantation

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 6.2023]

Allogeneic hematopoietic stem cell transplantation

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

Other criteria: NPM1 wild type

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

FLT3 ITD mutation (continued)

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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midostaurin + cytarabine

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

Other criteria: NPM1 wild type

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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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 6.2023]

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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):
- Residual (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

FLT3 ITD mutation (continued)

midostaurin + cytarabine + idarubicin

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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quizartinib

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 6.2023]

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quizartinib + 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 6.2023]

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quizartinib + cytarabine

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

Other criteria: NPM1 wild type

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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quizartinib + cytarabine + daunorubicin

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

FLT3 ITD mutation (continued)

quizartinib + cytarabine + idarubicin

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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sorafenib

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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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 6.2023]

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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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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sorafenib + decitabine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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venetoclax + cytarabine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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venetoclax + decitabine

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

NCCN Recommendation category: 2A

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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gilteritinib

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

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

FLT3 ITD mutation (continued)

gilteritinib + azacitidine

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

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Induction therapy); Useful in certain circumstances

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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midostaurin

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

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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quizartinib

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

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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quizartinib

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

NCCN Recommendation category: 2B

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

STAG2 c.2096+1G>A

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 6.2023]

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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 6.2023]

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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 6.2023]

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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 6.2023]

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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 6.2023]

STAG2 c.2096+1G>A (continued)

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)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 6.2023]

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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 6.2023]

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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 6.2023]

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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 6.2023]

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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 6.2023]

STAG2 c.2096+1G>A (continued)

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 6.2023]

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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 6.2023]

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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 6.2023]

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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 6.2023]

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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 6.2023]

STAG2 c.2096+1G>A (continued)

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 6.2023]

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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 6.2023]

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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 6.2023]

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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 6.2023]

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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 6.2023]

STAG2 c.2096+1G>A (continued)

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 6.2023]

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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 6.2023]

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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 6.2023]

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 2024-01-17. For the most up-to-date information, search www.ema.europa.eu/ema.

FLT3 p.(D835Y) c.2503G>T

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Label as of:** 2023-11-07 **Variant class:** FLT3 D835 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:** 2023-07-26 **Variant class:** FLT3 D835 mutation

Reference:

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

FLT3 ITD mutation

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Label as of:** 2023-11-07 **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:** 2023-07-26 **Variant class:** FLT3 ITD mutation

Reference:

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

● quizartinib, quizartinib + cytarabine, quizartinib + anthracycline + cytarabine

Cancer type: Acute Myeloid Leukemia **Label as of:** 2023-11-21 **Variant class:** FLT3 ITD mutation

Reference:

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

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 2024-01-02. For the most up-to-date information, search www.esmo.org.

FLT3 p.(D835Y) c.2503G>T

● gilteritinib

Cancer type: Acute Myeloid Leukemia **Variant class:** FLT3 D835 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 D835 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.]

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.]

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2024-01-17. For the most up-to-date information, search www.fda.gov.

FLT3 p.(D835Y) c.2503G>T

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

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

FLT3 ITD mutation (continued)

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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