Taipei Veterans General Hospital

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Sample Information

Patient Name: 呂朝輝
Gender: Male
ID No.: F122419554
History No.: 46079043
Age: 61

Ordering Doctor: DOC4205A 柯博伸
Ordering REQ.: H4768E2
Signing in Date: 2023/07/14

Path No.: M112-00181
MP No.: MY23041
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2023/07/06

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

Note:

Sample Cancer Type: Myelodysplastic Syndrome

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Report Highlights

2 Relevant Biomarkers
18 Therapies Available
0 Clinical Trials

Relevant Myelodysplastic Syndrome Variants

Gene	Finding	Gene	Finding
ASXL1	None detected	NPM1	None detected
BCOR	None detected	NRAS	None detected
CBL	None detected	NUP214	None detected
CREBBP	None detected	RUNX1	None detected
ETV6	None detected	SF3B1	None detected
EZH2	None detected	SRSF2	None detected
FLT3	None detected	STAG2	None detected
GATA2	None detected	TP53	***TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T***
IDH2	None detected	U2AF1	None detected
KIT	None detected	WT1	None detected
KMT2A	None detected	ZRSR2	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 2023.06(005). The content of this report has not been evaluated or approved by FDA, EMA or other regulatory agencies.

Relevant Myelodysplastic Syndrome Variants (continued)

Gene	Finding	Gene	Finding
MECOM	None detected		

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T* tumor protein p53 Allele Frequency: 22.30%, 20.96% (2 variants)	None	**idelalisib + rituximab** [2] acalabrutinib allogeneic stem cells azacitidine cytarabine cytarabine + daunorubicin + etoposide cytarabine + etoposide + idarubicin cytarabine + fludarabine + idarubicin + filgrastim daunorubicin decitabine ibrutinib idarubicin liposomal cytarabine-daunorubicin CPX-351 mitoxantrone obinutuzumab + venetoclax rituximab + venetoclax venetoclax venetoclax + chemotherapy	0

Diagnostic significance: Myelodysplastic Syndrome

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

Alerts informed by public data sources: ⊘ Contraindicated, Resistance

TP53 c.920-2A>G, TP53 p.(R342) c.1024C>T*	lenalidomide

Public data sources included in alerts: 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
TP53	p.(R342*)	c.1024C>T	COSM11073	chr17:7574003	20.96%	NM_000546.5	nonsense	1999
TP53	p.(?)	c.920-2A>G	.	chr17:7576928	22.30%	NM_000546.5	unknown	2000
PRPF8	p.(N1023=)	c.3069C>T	.	chr17:1577966	47.47%	NM_006445.4	synonymous	1997
CALR	p.(P243L)	c.728C>T	.	chr19:13051380	50.90%	NM_004343.4	missense	2000
CEBPA	p.(H195_P196dup)	c.589_590insACCCGC	.	chr19:33792731	40.19%	NM_004364.4	nonframeshift Insertion	1463

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Biomarker Descriptions

TP53 (tumor protein p53)

Background: The TP53 gene encodes the p53 tumor suppressor protein that binds to DNA and activates transcription in response to diverse cellular stresses to induce cell cycle arrest, apoptosis, or DNA repair. In unstressed cells, TP53 is kept inactive by targeted degradation via MDM2, a substrate recognition factor for ubiquitin-dependent proteolysis. Alterations in TP53 is required for oncogenesis as they result in loss of protein function and gain of transforming potential[1]. Germline mutations in TP53 are the underlying cause of Li-Fraumeni syndrome, a complex hereditary cancer predisposition disorder associated with early-onset cancers[2,3].

Alterations and prevalence: TP53 is the most frequently mutated gene in the cancer genome with approximately half of all cancers experiencing TP53 mutations. Ovarian, head and neck, esophageal, and lung squamous cancers have particularly high TP53 mutation rates (60-90%)[4,5,6,7,8,9]. Approximately two-thirds of TP53 mutations are missense mutations and several recurrent missense mutations are common including substitutions at codons R158, R175, Y220, R248, R273, and R282[4,5]. Invariably, recurrent missense mutations in TP53 inactivate its ability to bind DNA and activate transcription of target genes[10,11,12,13].

Potential relevance: The small molecule p53 reactivator, PC14586, received a fast track designation (2020) by the FDA for advanced tumors harboring a TP53 Y220C mutation[14]. The FDA has granted fast track designation (2019) to the p53 reactivator, eprenetapopt,[15] and breakthrough designation[16] (2020) in combination with azacitidine or azacitidine and venetoclax for acute myeloid leukemia patients (AML) and myelodysplastic syndrome (MDS) harboring a TP53 mutation, respectively. In addition to investigational therapies aimed at restoring wild-type TP53 activity, compounds that induce synthetic lethality are also under clinical evaluation[17,18]. TP53 mutations confer poor prognosis in multiple blood cancers including AML, MDS, myeloproliferative neoplasms (MPN), and chronic lymphocytic leukemia (CLL)[19,20,21,22,23]. In mantle cell lymphoma, TP53 mutations are associated with poor prognosis when treated with conventional therapy including hematopoietic cell transplant[24]. Mono- and bi-allelic mutations in TP53 confer unique characteristics in MDS, with multi-hit patients also experiencing associations with complex karyotype, few co-occuring mutations, and high-risk disease presentation as well as predicted death and leukemic transformation independent of the IPSS-R staging system[25].

Relevant Therapy Summary

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

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
Allogeneic hematopoietic stem cell transplantation	✖	○	✖	✖	✖
azacitidine	✖	○	✖	✖	✖
cytarabine	✖	○	✖	✖	✖
cytarabine + daunorubicin + etoposide	✖	○	✖	✖	✖
cytarabine + etoposide + idarubicin	✖	○	✖	✖	✖
cytarabine + fludarabine + idarubicin + filgrastim	✖	○	✖	✖	✖
daunorubicin	✖	○	✖	✖	✖
decitabine	✖	○	✖	✖	✖
idarubicin	✖	○	✖	✖	✖
liposomal cytarabine-daunorubicin CPX-351	✖	○	✖	✖	✖
mitoxantrone	✖	○	✖	✖	✖
venetoclax + azacitidine	✖	○	✖	✖	✖
venetoclax + cytarabine	✖	○	✖	✖	✖

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.06(005).

Relevant Therapy Summary (continued)

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

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T (continued)

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
venetoclax + cytarabine + fludarabine + idarubicin + filgrastim	✖	○	✖	✖	✖
venetoclax + decitabine	✖	○	✖	✖	✖
idelalisib + rituximab	✖	✖	○	○	✖
acalabrutinib	✖	✖	✖	○	✖
ibrutinib	✖	✖	✖	○	✖
obinutuzumab + venetoclax	✖	✖	✖	○	✖
rituximab + venetoclax	✖	✖	✖	○	✖
venetoclax	✖	✖	✖	○	✖

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 2023-05-01. 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.

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T

○ azacitidine

Cancer type: Acute Myeloid Leukemia

Variant class: TP53 mutation

NCCN Recommendation category: 1

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

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

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.06(005).

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T (continued)

cytarabine + daunorubicin + etoposide

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 1

Population segment (Line of therapy):
- (Maintenance therapy); Preferred intervention
- (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:** TP53 mutation

NCCN Recommendation category: 1

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

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

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daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 1

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

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

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idarubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 1

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

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

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.06(005).

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T (continued)

Allogeneic hematopoietic stem cell transplantation

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 2A

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

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

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azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 2A

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

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

---

cytarabine

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 2A

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

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

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decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 2A

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

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

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.06(005).

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T (continued)

liposomal cytarabine-daunorubicin CPX-351

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 2A

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

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

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mitoxantrone

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 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 + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 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 + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 2A

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

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

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venetoclax + cytarabine

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 2A

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

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

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.06(005).

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T (continued)

venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 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:** TP53 mutation

NCCN Recommendation category: 2A

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

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

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azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Maintenance 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:** TP53 mutation

NCCN Recommendation category: 2B

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

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

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TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T (continued)

cytarabine + etoposide + idarubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Maintenance 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:** TP53 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Maintenance 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:** TP53 mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):
- (Maintenance therapy)
- (Induction 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:** TP53 mutation

NCCN Recommendation category: 3

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

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

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.06(005).

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T (continued)

venetoclax + decitabine

Cancer type: Acute Myeloid Leukemia

Variant class: TP53 mutation

NCCN Recommendation category: 3

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

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

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.06(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 2023-05-17. For the most up-to-date information, search www.ema.europa.eu/ema.

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T

○ idelalisib + rituximab

Cancer type: Chronic Lymphocytic Leukemia **Label as of:** 2021-10-06 **Variant class:** TP53 mutation

Reference:

https://www.ema.europa.eu/en/documents/product-information/zydelig-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 2023.06(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 2023-05-01. For the most up-to-date information, search www.esmo.org.

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T

○ acalabrutinib

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

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

Population segment (Line of therapy):
- Symptomatic, Relapsed (Subsequent therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Lymphocytic Leukaemia [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.09.019.(published)]

○ ibrutinib

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

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

Population segment (Line of therapy):
- Symptomatic, Relapsed (Subsequent therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Lymphocytic Leukaemia [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.09.019.(published)]

○ rituximab + venetoclax

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

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

Population segment (Line of therapy):
- Symptomatic, Relapsed (Subsequent therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Lymphocytic Leukaemia [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.09.019.(published)]

○ idelalisib + rituximab

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

ESMO Level of Evidence/Grade of Recommendation: II / B

Population segment (Line of therapy):
- Symptomatic, Relapsed (Subsequent therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Lymphocytic Leukaemia [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.09.019.(published)]

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TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T (continued)

acalabrutinib

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

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

Population segment (Line of therapy):
- Early-stage; Symptomatic (First-line therapy)
- Advanced-stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Lymphocytic Leukaemia [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.09.019.(published)]

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ibrutinib

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

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

Population segment (Line of therapy):
- Early-stage; Symptomatic (First-line therapy)
- Advanced-stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Lymphocytic Leukaemia [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.09.019.(published)]

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idelalisib + rituximab

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

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

Population segment (Line of therapy):
- Early-stage; Symptomatic (First-line therapy)
- Advanced-stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Lymphocytic Leukaemia [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.09.019.(published)]

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obinutuzumab + venetoclax

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

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

Population segment (Line of therapy):
- Early-stage; Symptomatic (First-line therapy)
- Advanced-stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Lymphocytic Leukaemia [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.09.019.(published)]

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TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T (continued)

venetoclax

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

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

Population segment (Line of therapy):
- Early-stage; Symptomatic (First-line therapy)
- Advanced-stage (First-line therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Lymphocytic Leukaemia [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.09.019.(published)]

venetoclax

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

ESMO Level of Evidence/Grade of Recommendation: III / B

Population segment (Line of therapy):
- Symptomatic, Relapsed (Subsequent therapy)

Reference: ESMO Clinical Practice Guidelines - ESMO-Chronic Lymphocytic Leukaemia [Annals of Oncology (2020), https://doi.org/10.1016/j.annonc.2020.09.019.(published)]

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.06(005).

Diagnostic Details

Current NCCN Information

NCCN information is current as of 2023-05-01. 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.

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T

Diagnostic significance: Myelodysplastic Syndrome

Variant class: TP53 mutation

NCCN Recommendation category: 2A

Diagnostic notes:
- 2022 WHO Classification of Myelodysplastic Neoplasms (MDS); MDS-Biallelic (or multi-hit) TP53 mutation: ≥2 TP53 mutations or 1 mutation with TP53 copy number loss or cnLOH at the 17p TP53 locus, usually with complex karyotype, or a VAF >23%.

Reference: NCCN Guidelines® - NCCN-Myelodysplastic Syndromes [Version 1.2023]

Alerts Informed By Public Data Sources

Current FDA Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

FDA information is current as of 2023-05-17. For the most up-to-date information, search www.fda.gov.

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T

eprenetapopt + azacitidine, eprenetapopt + venetoclax + azacitidine

Cancer type: Myelodysplastic Syndrome **Variant class:** TP53 mutation

Supporting Statement:

The FDA has granted Breakthrough Designation to the small molecule inhibitor, eprenetapopt, in combination with azacitidine or azacitidine and venetoclax for TP53 mutant myelodysplastic syndrome (MDS).

Reference:

http://vp280.alertir.com/en/pressreleases/karolinska-development%27s-portfolio-company-aprea-therapeutics-receives-fda-breakthrough-therapy-designation-1769167

eprenetapopt + azacitidine, eprenetapopt + venetoclax + azacitidine

Cancer type: Acute Myeloid Leukemia **Variant class:** TP53 mutation

Supporting Statement:

The FDA has granted Fast Track Designation to the small molecule inhibitor, eprenetapopt, in combination with azacitidine or azacitidine and venetoclax for TP53 mutant acute myeloid leukemia (AML).

Reference:

https://ir.aprea.com//news-releases/news-release-details/aprea-therapeutics-receives-fda-fast-track-designation

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.06(005).

Current NCCN Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

NCCN information is current as of 2023-05-01. 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.

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T

chemoimmunotherapy

Cancer type: Chronic Lymphocytic Leukemia, Small Lymphocytic Lymphoma **Variant class:** TP53 mutation

Summary:
NCCN Guidelines® include the following supporting statement(s):
- "Chemoimmunotherapy is not recommended since del(17p)/TP53 mutation is associated with low response rates."

Reference: NCCN Guidelines® - NCCN-Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma [Version 2.2023]

Current ESMO Information

Contraindicated Not recommended Resistance Breakthrough Fast Track

ESMO information is current as of 2023-05-01. For the most up-to-date information, search www.esmo.org.

TP53 c.920-2A>G, TP53 p.(R342*) c.1024C>T

lenalidomide

Cancer type: Myelodysplastic Syndrome **Variant class:** TP53 mutation

Summary:
ESMO Clinical Practice Guidelines include the following supporting statement:
- "TP53 gene mutations, found in ~20% of lower-risk MDS with del(5q), confer resistance to LEN and a higher risk of AML progression."

Reference: ESMO Clinical Practice Guidelines - ESMO-Myelodysplastic Syndromes [Ann of Oncol (2020), https://doi.org/10.1016/j.annonc.2020.11.002]

Disclaimer: The data presented here is from a curated knowledgebase of publicly available information, but may not be exhaustive. The data version is 2023.06(005).

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