



Sample Information

Patient Name: 李阮鴻
Gender: Male
ID No.: A129004289
History No.: 45478715
Age: 35

Ordering Doctor: DOC1697J 蔡淳光
Ordering REQ.: H443BNF
Signing in Date: 2022/08/18

Path No.: S111-97852
MP No.: MY22023
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2022/08/08

Reporting Doctor: DOC5466K 葉奕成 (Phone: 8#5466)

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	CEBPA p.(Q312dup) c.936_937insCAG	MYH11	None detected
CREBBP	None detected	NPM1	None detected
FLT3	None detected	NUP214	None detected
IDH1	None detected	RARA	None detected
IDH2	None detected	RUNX1	None detected
KMT2A	None detected	TP53	None detected

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	CEBPA p.(Q312dup) c.936_937insCAG CCAAT enhancer binding protein alpha Allele Frequency: 56.70% Prognostic significance: ELN 2017: Favorable Diagnostic significance: Acute Myeloid Leukemia	cytarabine + daunorubicin cytarabine + idarubicin cytarabine + mitoxantrone gemtuzumab ozogamicin + chemotherapy	None	0

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

Public data sources included in prognostic and diagnostic significance: NCCN, ESMO

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
CEBPA	p.(Q312dup)	c.936_937insCAG	COSM18466	chr19:33792384	56.70%	NM_004364.4	nonframeshift Insertion	1455
IDH1	p.(G105=)	c.315C>T	.	chr2:209113192	36.59%	NM_005896.3	synonymous	1875

Biomarker Descriptions

CEBPA (CCAAT enhancer binding protein alpha)

Background: The CEBPA gene encodes the enhancer binding protein alpha, a member of the basic region leucine zipper family of transcription factors that recognizes the CCAAT promoter¹. CEBPA gives rise to two protein isoforms— p42 and p30, where p30 is the shorter isoform lacking the N-terminal 117 amino acids that is present in p42. Both isoforms contain the basic leucine zipper (bZip) domain involved in hetero/homo-dimerization with other CEBP family members and are required for DNA binding¹. CEBPA is a tumor suppressor gene that plays a critical role in the development of granulocytes¹. Specifically, CEBPA can influence the expression of granulocyte colony-stimulating factor (G-CSF) and interleukin 6 (IL-6), which are required for neutrophil maturation^{2,3}. CEBPA also directly interacts and inhibits cell cycle kinases, including CDK2 and CDK4, thereby hindering cell proliferation⁴. CEBPA is the target of monoallelic or biallelic mutations leading to a loss of function, which can promote the development of cancers such as acute myeloid leukemia (AML)⁵. Germline mutations in CEBPA are also frequent among AML patients and are associated with predisposition to the disease^{6,7}.

Alterations and prevalence: Mutations in CEBPA are reported in 6-18% of all AML cases^{8,9,10,11}. In AML, CEBPA mutations are observed to occur as either monoallelic (single mutant) or bi-allelic (double mutant)^{11,12,13}. Biallelic CEBPA mutations are heterozygous and occur as a specific combination of an N-terminal frameshift on one allele and a C-terminal in frame mutation on the other, referred to as an N/C mutant^{13,14}. Frameshift mutations result in the N-terminal truncation of approximately 120 amino acids while preserving the remaining 300 amino acids that are initiated further downstream¹⁴. C-terminal in-frame mutations disrupt the bZip domain which interferes with DNA binding and hetero/homo-dimerization with other CEBP family members. Specifically, N/C mutants possess one N-terminal truncated allele coding for the p30 isoform while the other allele codes for either p30 or p42 isoforms harboring C-terminal mutations¹³.

Potential relevance: Biallelic CEBPA mutations are recognized as a diagnostic entity for AML by the World Health Organization (WHO)¹⁵. Biallelic CEBPA mutations are associated with favorable risk and improved prognosis in AML^{11,15,16,17,18}.

Relevant Therapy Summary

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

CEBPA p.(Q312dup) c.936_937insCAG

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

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 2022-06-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

CEBPA p.(Q312dup) c.936_937insCAG

● cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia

Variant class: CEBPA mutation

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2022]

● cytarabine + idarubicin

Cancer type: Acute Myeloid Leukemia

Variant class: CEBPA mutation

NCCN Recommendation category: 1

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

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2022]

CEBPA p.(Q312dup) c.936_937insCAG (continued)**● cytarabine + daunorubicin**

Cancer type: Acute Myeloid Leukemia

Variant class: CEBPA mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2022]

● cytarabine + idarubicin

Cancer type: Acute Myeloid Leukemia

Variant class: CEBPA mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2022]

● cytarabine + mitoxantrone

Cancer type: Acute Myeloid Leukemia

Variant class: CEBPA mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2022]

● gemtuzumab ozogamicin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia

Variant class: CEBPA mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy); Preferred intervention

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2022]

● gemtuzumab ozogamicin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia

Variant class: CEBPA mutation

NCCN Recommendation category: 2A

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2022]

CEBPA p.(Q312dup) c.936_937insCAG (continued)**● gemtuzumab ozogamicin + cytarabine + fludarabine + idarubicin + filgrastim**

Cancer type: Acute Myeloid Leukemia

Variant class: CEBPA mutation

NCCN Recommendation category: 2B

Population segment (Line of therapy):

- (Induction therapy)

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2022]

Prognostic Details

Current NCCN Information

NCCN information is current as of 2022-06-01. For the most up-to-date information, search www.nccn.org.
For NCCN International Adaptations & Translations, search www.nccn.org/global/international_adaptations.aspx.

CEBPA p.(Q312dup) c.936_937insCAG

Prognostic significance: ELN 2017: Favorable

Cancer type: Acute Myeloid Leukemia

Variant class: CEBPA mutation

NCCN Recommendation category: 2A

Summary:

- Genetic Abnormality: Biallelic mutated CEBPA.

Reference: NCCN Guidelines® - NCCN-Acute Myeloid Leukemia [Version 1.2022]

Current ESMO Information

ESMO information is current as of 2022-06-01. For the most up-to-date information, search www.esmo.org.

CEBPA p.(Q312dup) c.936_937insCAG

Prognostic significance: ELN 2017: Favorable

Cancer type: Acute Myeloid Leukemia

Variant class: CEBPA mutation

Summary:

- Double-mutant CEBPA

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

Diagnostic Details

Current ESMO Information

ESMO information is current as of 2022-06-01. For the most up-to-date information, search www.esmo.org.

CEBPA p.(Q312dup) c.936_937insCAG

Diagnostic significance: Acute Myeloid Leukemia

Variant class: CEBPA mutation

Diagnostic notes:

- CEBPA biallelic mutations; 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.]

Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:

References

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