Taipei Veterans General Hospital

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## Sample Information

**Patient Name:** 李瀛春
**Gender:** Male
**ID No.:** O100157464
**History No.:** 32050401
**Age:** 65

**Ordering Doctor:** DOC6266E 徐千富
**Ordering REQ.:** 0BXSWTC
**Signing in Date:** 2022/07/28

**Path No.:** S111-97805
**MP No.:** MY22020
**Assay:** Oncomine Myeloid Assay
**Sample Type:** Bone Marrow
**Bone Marrow Aspirating Date:** 2022/07/18

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

**Note:**

## Sample Cancer Type: Acute Myeloid Leukemia

### Table of Contents



### Report Highlights

1 Relevant Biomarkers
4 Therapies Available
0 Clinical Trials

## Relevant Acute Myeloid Leukemia Variants

| Gene | Finding | Gene | Finding |
|---|---|---|---|
| ABL1 | None detected | MECOM | None detected |
| ASXL1 | None detected | MLLT3 | None detected |
| CEBPA | ***CEBPA p.(D107*) c.318_319insT*** | 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.(D107*) c.318_319insT*<br>CCAAT enhancer binding protein alpha<br>Allele Frequency: 75.90%<br><br>**Prognostic significance:** ELN 2017: Favorable<br>**Diagnostic significance:** Acute Myeloid Leukemia | cytarabine + daunorubicin<br>cytarabine + idarubicin<br>cytarabine + mitoxantrone<br>gemtuzumab ozogamicin + chemotherapy | None | 0 |

**Public data sources included in relevant therapies: FDA**[1], NCCN, **EMA**[2], ESMO
**Public data sources included in prognostic and diagnostic significance:** NCCN, 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 |
|---|---|---|---|---|---|---|---|---|
| CEBPA | p.(D107*) | c.318_319insT | . | chr19:33793002 | 75.90% | NM_004364.4 | nonsense | 809 |
| PRPF8 | p.(F2267=) | c.6801C>T | . | chr17:1554454 | 48.40% | NM_006445.4 | synonymous | 2000 |
| CEBPA | p.(H195_P196dup) | c.589_590insACCCGC | . | chr19:33792731 | 11.14% | NM_004364.4 | nonframeshift Insertion | |
| RUNX1 | p.(V452G) | c.1355T>G | . | chr21:36164520 | 49.67% | NM_001754.4 | missense | 1999 |

## 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 promoter[1]. 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 binding[1]. CEBPA is a tumor suppressor gene that plays a critical role in the development of granulocytes[1]. 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 proliferation[4]. 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 downstream[14]. 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 mutations[13].

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.(D107*) c.318_319insT

| 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.(D107*) c.318_319insT

#### ● 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.(D107*) c.318_319insT (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]

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### 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]

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### 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]

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### 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]

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### 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]

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## CEBPA p.(D107*) c.318_319insT (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.(D107*) c.318_319insT

### 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.(D107*) c.318_319insT

### 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.(D107*) c.318_319insT

### Diagnostic significance: Acute Myeloid Leukemia

**Variant class:** CEBPA mutation

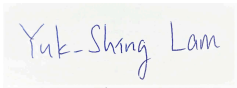
**Diagnostic notes:**

- 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:**



2022.07.29
10:56:16 +08'00'

**Laboratory Supervisor:**

2022.07.29
10:56:28 +08'00'

**Pathologist:**

2022.07.29
10:56:40 +08'00'

## References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