Taipei Veterans General Hospital

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Sample Information

Patient Name: 許丕煌
Gender: Male
ID No.: W100071546
History No.: 42673063
Age: 57

Ordering Doctor: DOC1697J 蔡淳光
Ordering REQ.: 0CPWDUH
Signing in Date: 2023/08/21

Path No.: M112-00228
MP No.: MY23060
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2023/08/17

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

Note:

Sample Cancer Type: Acute Myeloid Leukemia

Report Highlights

1 Relevant Biomarkers
1 Therapies Available
0 Clinical Trials

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IA	*CBFB::MYH11 fusion* core-binding factor subunit beta - myosin heavy chain 11 **Diagnostic significance:** Acute Myeloid Leukemia	gemtuzumab ozogamicin + chemotherapy	None	0

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

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

Gene Fusions (RNA)

Genes	Variant ID	Locus	Read Count
CBFB-MYH11	CBFB-MYH11.C5M33	chr16:67116211 - chr16:15814908	720

Biomarker Descriptions

CBFB (core-binding factor subunit beta)

Background: The CBFB gene encodes the core-binding factor subunit beta, a member of the PEBP2/CBF transcription factor family[1]. CBFB is capable of heterodimerization with the RUNX protein family (RUNX1, RUNX2, and RUNX3) which results in the formation of the core binding factor (CFB) complex, a transcription factor complex responsible for the regulation of many critical functions in hematopoiesis and osteogenesis[2,3,4]. Although possessing no DNA-binding activity, CBFB has been observed to enhance stability and transcriptional activity of RUNX proteins, thereby exhibiting a critical role in RUNX mediated transcriptional regulation[3,4]. In cancer, mutations in CBFB have been implicated in decreased protein stability and loss of function, supporting a tumor suppressor role for CBFB[4]

Alterations and prevalence: Somatic mutations in CBFB are observed in 2% of diffuse large B-cell lymphoma, breast invasive carcinoma, and uterine corpus endometrial carcinoma[5]. Biallelic deletions in CBFB are found in 2% of ovarian serous cystadenocarcinoma, prostate adenocarcinoma, and breast invasive carcinoma[5]. Translocations including inv(16) and t(16;16) have been observed to be recurrent in de novo AML, occurring in 7-10% of patients, and have been associated with the AML M4 with bone barrow eosinophilia (M4Eo) subtype[6]. Translocations often result in CBFB-MYH11 fusion, which can exist as one of multiple transcripts, depending on the exons fused[6].

Potential relevance: Currently, no therapies are approved for CBFB aberrations. In AML, CBFB translocations, including inv(16) and t(16;16) which result in CBFB-MYH11 fusion, are associated with favorable prognosis and define a distinct molecular subtype of AML according to the World Health Organization (WHO)[7,8,9].

MYH11 (myosin heavy chain 11)

Background: MYH11 encodes myosin heavy-chain 11 which is a key contractile protein involved in smooth muscle movement, protein transport, and cell-cell interaction[10]. MYH11 belongs to the myosin family of motor proteins that function to convert chemical energy into mechanical energy through ATP hydrolysis[11,12]. MYH11 consists of two pairs of light chains and two heavy chains produced from the MYH11 gene[1]. MYH11 is frequently translocated in acute myeloid leukemia (AML) where the C-terminal of MYH11 protein that contains a coiled-coil smooth muscle myosin heavy chain (SMMHC) is fused with the core binding factor ß (CBFß) gene[13,14]. The CBFB-MYH11 fusion dimerizes with RUNX1, a key transcription factor in myelodysplastic malignancies, and inhibits RUNX1's function in hematopoiesis[15].

Alterations and prevalence: Somatic missense, nonsense, and splice-site mutations of MYH11 are observed in 13% of melanoma, 10% of uterine, 6% of stomach as well as bladder cancers, and 2% of AML cases[16]. The inv(16)(p13.1;q22) or t(16;16)(p13.1;q22) translocation results in the CBFB-MYH11 fusion and is observed in over 5% of AML cases[14].

Potential relevance: The inv(16)(p13.1;q22)/t(16;16)(p13.1;q22) that results in CBFB-MYH11 fusion is recognized by the World Health Organization (WHO) as one of the possible molecular abnormality requirements for the diagnosis of myelodysplasia-related AML (AML-MR)[7,9]. The CBFB-MYH11 fusion is also associated with favorable risk stratification in AML[7,8].

Relevant Therapy Summary

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

CBFB::MYH11 fusion

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
gemtuzumab ozogamicin + cytarabine + daunorubicin	✖	✖	✖	●	✖

Relevant Therapy Details

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 2023-06-01. For the most up-to-date information, search www.esmo.org.

CBFB::MYH11 fusion

● gemtuzumab ozogamicin + cytarabine + daunorubicin

Cancer type: Acute Myeloid Leukemia **Variant class:** MYH11-CBFB fusion [t(16;16)(p13;q22)]

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

Population segment (Line of therapy):
- Core Bindig Factor (Induction therapy)

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

Diagnostic Details

Current NCCN Information

NCCN information is current as of 2023-06-01. 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.

CBFB::MYH11 fusion

Diagnostic significance: Acute Myeloid Leukemia

Variant class: inv(16)

NCCN Recommendation category: 2A

Diagnostic notes:
- Karyotypes t(8;21), inv16, and t(15;17) are considered to be Acute Myeloid Leukemia even if the marrow blast count is less than 20%

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

Current ESMO Information

ESMO information is current as of 2023-06-01. For the most up-to-date information, search www.esmo.org.

CBFB::MYH11 fusion

Diagnostic significance: Acute Myeloid Leukemia

Variant class: MYH11-CBFB fusion [t(16;16)(p13;q22)]

Diagnostic notes:
- Core Binding Factor-Acute Myeloid Leukemia; 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.]

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