



## Sample Information

**Patient Name:** 張如平**Gender:** Female**ID No.:** A228771961**History No.:** 22456695**Age:** 77**Ordering Doctor:** DOC8537C 鄭菀韻**Ordering REQ.:** 0AVNUQQ**Signing in Date:** 2020/08/31**Path No.:** S109-99930**MP No.:** MY20001**Assay:** Oncomine Myeloid Assay**Sample Type:** Bone Marrow**Bone Marrow Aspirating Date:** 2020/08/26**Note:**

## Sample Cancer Type: Myelodysplastic Syndrome

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### Report Highlights

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## Relevant Myelodysplastic Syndrome Findings

Gene	Finding	Gene	Finding
ASXL1	Not detected	NPM1	Not detected
BCOR	Not detected	NRAS	Not detected
CBL	Not detected	NUP214	Not detected
CREBBP	Not detected	RUNX1	Not detected
ETV6	Not detected	SF3B1	Not detected
EZH2	Not detected	SRSF2	Not detected
FLT3	Not detected	STAG2	Not detected
GATA2	Not detected	TP53	Not detected
IDH2	Not detected	U2AF1	Not detected
KIT	Not detected	WT1	Not detected
KMT2A	Not detected	ZRSR2	Not detected
MECOM	Not detected		



## Relevant Biomarkers

Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
<b>TET2 p.(F868L) c.2604T&gt;G</b> tet methylcytosine dioxygenase 2 Allele Frequency: 50.85% <b>Prognostic significance:</b> None <b>Diagnostic significance:</b> None	None	None	1

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
TET2	p.(F868L)	c.2604T>G	COSM87107	chr4:106157703	50.85%	NM_001127208.2	missense	1996
SF3B1	p.(=)	c.2631T>C	.	chr2:198265526	49.37%	NM_012433.3	synonymous	1999
TET2	p.(P29R)	c.86C>G	.	chr4:106155185	49.25%	NM_001127208.2	missense	2000
TET2	p.(I1762V)	c.5284A>G	.	chr4:106196951	48.47%	NM_001127208.2	missense	1999
IKZF1	p.(=)	c.1176C>T	.	chr7:50467941	49.65%	NM_006060.5	synonymous	2000
WT1	p.(=)	c.1107A>G	.	chr11:32417945	99.90%	NM_024426.4	synonymous	2000
ETV6	p.(=)	c.258G>A	.	chr12:11992168	88.25%	NM_001987.4	synonymous	2000
KRAS	p.(=)	c.483G>A	.	chr12:25368462	99.25%	NM_033360.3	synonymous	1997
SH2B3	p.(W262R)	c.784T>C	.	chr12:111884608	99.65%	NM_005475.2	missense	1993
TP53	p.(P72R)	c.215C>G	.	chr17:7579472	47.17%	NM_000546.5	missense	1999
NF1	p.(=)	c.702G>A	.	chr17:29508775	48.19%	NM_001042492.2	synonymous	1880
NF1	p.(=)	c.2034G>A	.	chr17:29553485	47.75%	NM_001042492.2	synonymous	1998
SRSF2	p.(=)	c.144C>T	.	chr17:74733099	99.75%	NM_003016.4	synonymous	2000
CALR	p.(?)	c.-4C>T	.	chr19:13049490	50.00%	NM_004343.3	unknown	2000
CEBPA	p.(H195_P196dup)	c.589_590insACCCG C	.	chr19:33792731	57.17%	NM_004364.4	nonframeshift Insertion	1039
CEBPA	p.(P189H)	c.566C>A	.	chr19:33792755	27.33%	NM_004364.4	missense	1050
ASXL1	p.(L815P)	c.2444T>C	.	chr20:31022959	100.00%	NM_015338.5	missense	1995
ASXL1	p.(=)	c.3759T>C	.	chr20:31024274	99.95%	NM_015338.5	synonymous	2000
ZRSR2	p.(=)	c.864C>T	.	chrX:15838366	46.42%	NM_005089.3	synonymous	1997
BCOR	p.(S897L)	c.2690C>T	.	chrX:39931909	48.00%	NM_001123385.1	missense	2000
BCOR	p.(S637C)	c.1910C>G	.	chrX:39932689	49.75%	NM_001123385.1	missense	2000



## Variant Details (continued)

### DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect	Coverage
BCOR	p.(=)	c.1692A>G	.	chrX:39932907	100.00%	NM_001123385.1	synonymous	1920
BCOR	p.(=)	c.1260T>C	.	chrX:39933339	100.00%	NM_001123385.1	synonymous	1997

## Biomarker Descriptions

### TET2 (tet methylcytosine dioxygenase 2)

**Background:** TET2 encodes the tet methylcytosine dioxygenase 2 protein and belongs to a family of ten-eleven translocation (TET) proteins that also includes TET1 and TET3<sup>1</sup>. TET2 is involved in DNA methylation, specifically in the conversion of 5-methylcytosine to 5-hydroxymethylcytosine<sup>2,3</sup>. The TET proteins contain a C-terminal core catalytic domain that contains a cysteine-rich domain and a double stranded  $\beta$ -helix domain (DSBH)<sup>4</sup>. TET2 is a tumor suppressor gene. Loss of function mutations in TET2 are associated with loss of catalytic activity and transformation to hematological malignancies<sup>1,2,3</sup>.

**Alterations and prevalence:** Somatic TET2 mutations, including nonsense, frameshift, splice site, and missense, are observed in 20-25% of myelodysplastic syndrome (MDS) associated diseases, including 40%-60% chronic myelomonocytic leukemia (CMML)<sup>5</sup>. TET2 mutations at H1881 and R1896 are frequently observed in myeloid malignancies<sup>2,6</sup>. TET2 mutations are also observed in 9% of uterine, 8% of melanoma and acute myeloid leukemia (AML), as well as 6% of diffuse large B-cell lymphoma (DLBCL).

**Potential relevance:** The presence of TET2 mutations may be used as one of the major diagnostic criteria in pre-primary myelofibrosis (pre-PMF) and overt PMF in the absence of JAK2/CALR/MPL mutations<sup>7,8</sup>. TET2 mutations are associated with poor prognosis in PMF and increased rate of transformation to leukemia<sup>8,9</sup>.

## Relevant Therapy Summary

☒ In this cancer type
 ☐ In other cancer type
 ☒ In this cancer type and other cancer types
 ☒ Contraindicated
 ☒ Both for use and contraindicated
 ☒ No evidence

### TET2 p.(F868L) c.2604T>G

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
supplement, chemotherapy	✗	✗	✗	✗	● (II)

\* Most advanced phase (IV, III, II/III, II, I/II, I) is shown and multiple clinical trials may be available.



## Signatures

Testing Personnel:

Laboratory Supervisor:

Pathologist:



## References

1. Pan et al. The TET2 interactors and their links to hematological malignancies. *IUBMB Life*. 2015 Jun;67(6):438-45. PMID: 26099018
2. Ko et al. Impaired hydroxylation of 5-methylcytosine in myeloid cancers with mutant TET2. *Nature*. 2010 Dec 9;468(7325):839-43. PMID: 21057493
3. Solary et al. The Ten-Eleven Translocation-2 (TET2) gene in hematopoiesis and hematopoietic diseases. *Leukemia*. 2014 Mar;28(3):485-96. PMID: 24220273
4. An et al. TET family dioxygenases and DNA demethylation in stem cells and cancers. *Exp. Mol. Med*. 2017 Apr 28;49(4):e323. PMID: 28450733
5. NCCN Guidelines® - NCCN-Myelodysplastic Syndromes [Version 2.2020]
6. Kosmider et al. TET2 mutation is an independent favorable prognostic factor in myelodysplastic syndromes (MDSs). *Blood*. 2009 Oct 8;114(15):3285-91. PMID: 19666869
7. Arber et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. 2016 May 19;127(20):2391-405. PMID: 27069254
8. NCCN Guidelines® - NCCN-Myeloproliferative Neoplasms [Version 1.2020]
9. Lundberg et al. Clonal evolution and clinical correlates of somatic mutations in myeloproliferative neoplasms. *Blood*. 2014 Apr 3;123(14):2220-8. PMID: 24478400