Taipei Veterans General Hospital

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Sample Information

Patient Name: 林徐秀英
Gender: Female
ID No.: G200335525
History No.: 6547213
Age: 71

Ordering Doctor: DOC4205A 柯博伸
Ordering REQ.: H45N3FC
Signing in Date: 2023/02/21

Path No.: M112-00032
MP No.: MY23009
Assay: Oncomine Myeloid Assay
Sample Type: Bone Marrow
Bone Marrow Aspirating Date: 2023/02/16

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

Note:

Sample Cancer Type: Chronic Myelomonocytic Leukemia

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Relevant Chronic Myelomonocytic Leukemia Variants

Gene	Finding
ASXL1	None detected

Relevant Biomarkers

No clinically significant biomarkers found in this sample.

Prevalent cancer biomarkers without relevant evidence based on included data sources
CSF3R p.(T618I) c.1853C>T

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
CSF3R	p.(T618I)	c.1853C>T	COSM1737962	chr1:36933434	41.55%	NM_156039.3	missense	2000
CSF3R	p.([L827=;V828I])	c.2481_2482delGGinsAA	.	chr1:36932068	38.10%	NM_156039.3	synonymous, missense	1995
CSF3R	p.(G825=)	c.2475G>A	.	chr1:36932075	38.59%	NM_156039.3	synonymous	1998
CSF3R	p.(W818*)	c.2453G>A	.	chr1:36932097	39.45%	NM_156039.3	nonsense	2000

Biomarker Descriptions

CSF3R (colony stimulating factor 3 receptor)

Background: The CSF3R gene encodes the colony stimulating factor 3 trans-membrane receptor for the granulocyte colony-stimulating factor (G-CSF) ligand. CSF3R is a class I membrane-bound cytokine receptor, which lacks intrinsic kinase activity and therefore must interact with downstream proteins for activation[1]. Upon ligand activation, CSF3R activates downstream oncogenic pathways by interacting with intracellular signaling proteins through its cytoplasmic tyrosine residues, including proteins from the JAK/STAT, MAPK/ERK, and PI3K/AKT pathways[1,2]. Nonsense and frameshift mutations in CSF3R target and truncate its cytoplasmic tail, subsequently impairing the internalization signal of the receptor and leading to an overexpression CSF3R on the cell surface[3,4,5]. Missense mutations in the proximal membrane lead to increased dimerization of the receptor, independent of G-CSF binding[3,4,5]. These mutations promote constitutive oncogenic JAK-STAT signaling, and increase granulocyte proliferation and survival signaling of hematopoietic progenitor cells[1,6].

Alterations and prevalence: CSF3R activating mutations are observed in up to 80% of patients with chronic neutrophilic leukemia (CNL), and in up to 59% of patients with atypical chronic myelogenous leukemia (aCML)[3,7]. CSF3R mutations occur in 0.5-1% of adult acute myeloid leukemia (AML) and in 2.4% of pediatric AML[7]. In solid malignancies, CSF3R mutations are observed in up to 5% of uterine carcinosarcoma and skin cutaneous melanoma[8,9]. Somatic mutations identified in CNL and AML include T615A, T618I, and T640N missense mutations, as well as truncating mutations at Q749, Q754, Y767, S783, Y787, and P820[7]. T618I mutation is the most frequent variant observed in CNL[10].

Potential relevance: CSF3R activating mutations including T618I are a diagnostic criteria for CNL as defined by the World Health Organization (WHO)[11]. Mutations in CSF3R are observed in patients with severe congenital neutropenia, which can progress to AML. CSF3R mutations frequently co-occur with CEBPA, and these co-mutations are associated with unfavorable prognosis in AML[7,12,13]. In independent reports, a CNL patient and an aCML patient with the proximal membrane T618I mutation demonstrated sensitivity to JAK1/2 inhibitor, ruxolitinib[3,14].

Signatures

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Laboratory Supervisor: 2023.03.02 14:54:51 +08'00'

Pathologist: Yi-Chu Yeh 2023.03.02 14:55:04 +08'00'

References

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