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Patient Name: 조희만
Gender: Male
Sample ID: N25-21

Primary Tumor Site: lymph node
Collection Date: 2025.05.13

Sample Cancer Type: Peripheral T-Cell Lymphoma

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Relevant Biomarkers

No biomarkers associated with relevant evidence found in this sample

Prevalent cancer biomarkers without relevant evidence based on included data sources
ARID1A p.(Q1334del) c.3999_4001delGCA, KMT2D p.(Q4557) c.13669C>T, STAT3 p.(D661Y) c.1981G>T*

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
ARID1A	p.(Q1334del)	c.3999_4001delGCA	COSM298325	chr1:27100181	5.77%	NM_006015.6	nonframeshift Deletion
KMT2D	p.(Q4557*)	c.13669C>T	.	chr12:49424678	41.45%	NM_003482.4	nonsense
STAT3	p.(D661Y)	c.1981G>T	.	chr17:40474420	63.37%	NM_139276.3	missense
ID3	p.(T105A)	c.313A>G	.	chr1:23885498	99.85%	NM_002167.5	missense
ARID1A	p.(G864C)	c.2590G>T	.	chr1:27089634	6.91%	NM_006015.6	missense
TENT5C	p.(H67Q)	c.201C>G	.	chr1:118165691	51.88%	NM_017709.4	missense
CCND3	p.(S259A)	c.775T>G	.	chr6:41903782	99.95%	NM_001760.5	missense
KLLN	p.(?)	c.-1616AG>G	.	chr10:89623860	100.00%	NM_001126049.2	unknown
PTEN	p.(?)	c.-367CT>C	.	chr10:89623860	100.00%	NM_000314.8	unknown
ATM	p.(N1983S)	c.5948A>G	.	chr11:108183167	99.60%	NM_000051.4	missense
KMT2D	p.(R5224H)	c.15671G>A	.	chr12:49420078	49.15%	NM_003482.4	missense
KMT2D	p.(A476T)	c.1426G>A	.	chr12:49446040	4.45%	NM_003482.4	missense
FOXO1	p.(D82N)	c.244G>A	.	chr13:41240106	48.40%	NM_002015.4	missense
DIS3	p.(T899R)	c.2696C>G	.	chr13:73334764	50.53%	NM_014953.5	missense
DIS3	p.(N269S)	c.806A>G	.	chr13:73350079	99.35%	NM_014953.5	missense

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
TP53	p.(P72R)	c.215C>G	.	chr17:7579472	83.24%	NM_000546.6	missense
SMARCA4	p.(F1234L)	c.3702C>A	.	chr19:11144121	14.86%	NM_001128849.3	missense
MEF2B	p.(G328Afs*75)	c.981_984delCGGG	.	chr19:19256728	10.12%	NM_001145785.2	frameshift Deletion
MEF2B	p.(R307S)	c.919C>A	.	chr19:19256794	58.64%	NM_001145785.2	missense
EP300	p.(M2010V)	c.6028A>G	.	chr22:41573743	3.30%	NM_001429.4	missense

Biomarker Descriptions

STAT3 p.(D661Y) c.1981G>T

signal transducer and activator of transcription 3

Background: The STAT3 gene encodes the signal transducer and activator of transcription 3 (STAT3)[1]. STAT3, a transcription factor, is a member of a highly conserved signal transducer and activator of transcription (STAT) family which also includes STAT1-4, STAT5A, STAT5B, and STAT6[2]. Inactive STAT transcription factors in the cytoplasm are activated by tyrosine phosphorylation, resulting in STAT dimerization and nuclear translocation[2]. Following translocation to the nucleus, STAT dimers interact with specific enhancers and promote transcriptional initiation of target genes[2]. Activation of STAT3 is catalyzed by phosphorylation from upstream receptor tyrosine kinases including epidermal growth factor receptor (EGFR), vascular endothelial growth factor receptor (VEGFR), platelet derived growth factor receptor (PDGFR), and non-receptor tyrosine kinases including Src and abl, as well as serine kinases of the MAPK family[1,2]. Specifically, STAT3 is involved in the regulation of proliferation, differentiation, apoptosis, angiogenesis, and immune response[1]. Constitutive STAT3 activation is detected in the majority of cancer cell lines and tumor tissues, suggesting an oncogenic role for STAT3[2].

Alterations and prevalence: Somatic mutations in STAT3 are observed in 14% of diffuse large B-cell lymphoma, 6% of uterine carcinosarcoma, and 4% of melanoma[3,4]. In a study of enteropathy-associated T-cell lymphoma, STAT3 activating mutations, generally occurring in the SH2 domain, were observed in 16% of tumors[5]. Somatic mutations including Y640F, N647I, E638Q, I659L, and K657R have also been observed in large granular lymphocyte leukemia (LGLL) and natural killer cell (NK) leukemias[6]. Amplifications are observed in 2% of esophageal cancer and diffuse large B-cell lymphoma (DLBCL)[3,4]. Phosphorylated STAT3 (pSTAT3), indicative of STAT3 activation, has been observed in 38% of peripheral T-cell lymphoma (PTCL) and 43% of adult T-cell lymphoma/leukemia (ATLL), with 27%-93% of specific lymphoma subtypes expressing pSTAT3[5,7].

Potential relevance: Currently, no therapies are approved for STAT3 aberrations. Much research has focused on targeting STAT3 directly or indirectly. Mechanisms to disrupt STAT3 signaling focus on inhibiting the DNA binding domain and preventing binding with upstream regulatory inhibitors such as Src and JAKs[1]. Identification of STAT3 mutation status in hepatosplenic T-cell lymphoma and T-cell large granular lymphocyte leukemia is useful in certain circumstances for diagnosis due to the prevalence of STAT3 mutations in these cancer types[6]. pSTAT3 is associated with better overall survival and progression free survival in select lymphoma subtypes including PTCL and ATLL[5,7].

ARID1A p.(Q1334del) c.3999_4001delGCA

AT-rich interaction domain 1A

Background: The ARID1A gene encodes the AT-rich interaction domain 1A tumor suppressor protein[8]. ARID1A, also known as BAF250A, belongs to the ARID1 subfamily that also includes AR1D1B[8,9]. ARID1A and ARID1B are mutually exclusive subunits of the BAF variant of the SWI/SNF chromatin-remodeling complex[9,10]. The BAF complex is a multisubunit protein that consists of SMARCB1/IN1, SMARCC1/BAF155, SMARCC2/BAF170, SMARCA4/BRG1 or SMARCA2/BRM, and ARID1A or ARID1B[10]. The BAF complex remodels chromatin at promoter and enhancer elements to alter and regulate gene expression[10,11]. ARID1A binds to transcription factors and coactivator/corepressor complexes to alter transcription[9]. Recurrent inactivating mutations in BAF complex subunits, including ARID1A, lead to transcriptional dysfunction thereby, altering its tumor suppressor function[9].

Alterations and prevalence: Mutations in SWI/SNF complex subunits are the most commonly mutated chromatin modulators in cancer and have been observed in 20% of all tumors[11]. The majority of ARID1A inactivating mutations are nonsense or frameshift mutations[9].

Biomarker Descriptions (continued)

Somatic mutations in ARID1A have been identified in 50% of ovarian clear cell carcinoma, 30% of endometrioid carcinoma, and 24-43% of uterine corpus endometrial carcinoma, bladder urothelial carcinoma, and stomach adenocarcinoma[3,4,10]. In microsatellite stable (MSS) colorectal cancer, mutations in ARID1A have been observed to correlate with increased tumor mutational burden (TMB) and expression of genes involved in the immune response[12].

Potential relevance: Currently, no therapies are approved for ARID1A aberrations. However, the FDA has granted fast track designation (2022) to HSF1 pathway inhibitor, NXP-800[13], for the treatment of platinum resistant ARID1A-mutated ovarian carcinoma. Tulmimetostat[14], dual inhibitor of EZH2 and EZH1, was also granted a fast track designation (2023) for the treatment of patients with advanced, recurrent or metastatic endometrial cancer harboring ARID1A mutations and who have progressed on at least one prior line of treatment.

KMT2D p.(Q4557*) c.13669C>T

lysine methyltransferase 2D

Background: The KMT2D gene encodes the lysine methyltransferase 2D protein, a transcriptional coactivator and histone H3 lysine 4 (H3K4) methyltransferase[8]. KMT2D belongs to the SET domain protein methyltransferase superfamily[15]. KMT2D is known to be involved in the regulation of cell differentiation, metabolism, and tumor suppression due to its methyltransferase activity[15]. Mutations or deletions in the enzymatic SET domain of KMT2D are believed to result in loss of function and may contribute to defective enhancer regulation and altered gene expression[15].

Alterations and prevalence: Somatic mutations in KMT2D are predominantly missense or truncating and are observed in 29% of diffuse large B-cell lymphoma (DLBCL), 28% of bladder urothelial carcinoma, 27% of uterine corpus endometrial carcinoma, 22% of lung squamous cell carcinoma, 21% of skin cutaneous melanoma, 17% of stomach adenocarcinoma, 15% of head and neck squamous cell carcinoma, and 14% of cervical squamous cell carcinoma[3,4].

Potential relevance: Currently, no therapies are approved for KMT2D aberrations.

Genes Assayed

ARID1A, ATM, B2M, BCL2, BCL6, BIRC3, BRAF, BTK, CARD11, CCND1, CCND3, CD79B, CDKN2A, CREBBP, CXCR4, DIS3, DNMT3A, EP300, ETV6, EZH2, TENT5C, FAS, FBXW7, FOXO1, GNA13, HRAS, ID3, IDH2, IRF4, KMT2D, KRAS, MAP2K1, MEF2B, MYC, MYD88, NFKBIE, NOTCH1, NOTCH2, NRAS, PAX5, PIM1, PLCG2, POT1, PRDM1, PTEN, RHOA, RPS15, SAMHD1, SF3B1, SGK1, SMARCA4, SOCS1, STAT3, STAT5B, STAT6, TET2, TNFAIP3, TNFRSF14, TP53, XPO1

Thermo Fisher Scientific's Ion Torrent Oncomine Reporter software was used in generation of this report. Software was developed and designed internally by Thermo Fisher Scientific. The analysis was based on Oncomine Reporter (6.0.2 data version 2025.04(004)). The data presented here are from a curated knowledge base of publicly available information, but may not be exhaustive. FDA information was sourced from www.fda.gov and is current as of 2025-03-19. NCCN information was sourced from www.nccn.org and is current as of 2025-03-03. EMA information was sourced from www.ema.europa.eu and is current as of 2025-03-19. ESMO information was sourced from www.esmo.org and is current as of 2025-03-03. Clinical Trials information is current as of 2025-03-03. For the most up-to-date information regarding a particular trial, search www.clinicaltrials.gov by NCT ID or search local clinical trials authority website by local identifier listed in 'Other identifiers.' Variants are reported according to HGVS nomenclature and classified following AMP/ASCO/CAP guidelines (Li et al. 2017). Based on the data sources selected, variants, therapies, and trials listed in this report are listed in order of potential clinical significance but not for predicted efficacy of the therapies.

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