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Patient Name: 조병옥
Gender: F
Sample ID: N25-40

Primary Tumor Site: lymph node
Collection Date: 2025.5.23

Sample Cancer Type: Diffuse Large B-Cell Lymphoma

Report Highlights
2 Relevant Biomarkers
0 Therapies Available
1 Clinical Trials

Relevant Biomarkers

Tier	Genomic Alteration	Relevant Therapies (In this cancer type)	Relevant Therapies (In other cancer type)	Clinical Trials
IIC	*CD79B p.(Y197D) c.589T>G* CD79b molecule Allele Frequency: 49.82% Locus: chr17:62006799 Transcript: NM_001039933.3 **Diagnostic significance:** Diffuse Large B-Cell Lymphoma	None*	None*	1
IIC	*MYD88 p.(L252P) c.755T>C* myeloid differentiation primary response 88 Allele Frequency: 51.40% Locus: chr3:38182641 Transcript: NM_002468.5 **Diagnostic significance:** Diffuse Large B-Cell Lymphoma	None*	None*	1

*** Public data sources included in relevant therapies: FDA**[1], NCCN, **EMA**[2], ESMO
*** Public data sources included in prognostic and diagnostic significance:** NCCN, ESMO
Line of therapy: I: First-line therapy, II+: Other line of therapy
Tier Reference: Li et al. *Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists.* J Mol Diagn. 2017 Jan;19(1):4-23.

Prevalent cancer biomarkers without relevant evidence based on included data sources
*TET2 p.(Y1724Lfs*5) c.5170_5171insT*

Variant Details

DNA Sequence Variants

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
MYD88	p.(L252P)	c.755T>C	COSM85940	chr3:38182641	51.40%	NM_002468.5	missense
TET2	p.(Y1724Lfs*5)	c.5170_5171insT	.	chr4:106196835	60.69%	NM_001127208.3	frameshift Insertion
CD79B	p.(Y197D)	c.589T>G	COSM1737939	chr17:62006799	49.82%	NM_001039933.3	missense
TNFRSF14	p.(K17R)	c.50A>G	.	chr1:2488153	49.60%	NM_003820.3	missense

Variant Details (continued)

DNA Sequence Variants (continued)

Gene	Amino Acid Change	Coding	Variant ID	Locus	Allele Frequency	Transcript	Variant Effect
ID3	p.(T105A)	c.313A>G	.	chr1:23885498	99.85%	NM_002167.5	missense
ARID1A	p.(G864C)	c.2590G>T	.	chr1:27089634	4.81%	NM_006015.6	missense
IRF4	p.(G22V)	c.65G>T	.	chr6:393217	20.86%	NM_002460.4	missense
CCND3	p.(S259A)	c.775T>G	.	chr6:41903782	7.99%	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	99.95%	NM_000051.4	missense
ATM	p.(M3011I)	c.9033G>C	.	chr11:108236097	20.55%	NM_000051.4	missense
ETV6	p.(?)	c.-54G>A	.	chr12:11803008	19.62%	NM_001987.5	unknown
ETV6	p.(?)	c.26_33+7delGCATTAA GGTAAAAA	.	chr12:11803086	27.31%	NM_001987.5	unknown
KMT2D	p.(Q3471H)	c.10413G>C	.	chr12:49428392	36.35%	NM_003482.4	missense
KMT2D	p.(T2952A)	c.8854A>G	.	chr12:49432285	40.25%	NM_003482.4	missense
KMT2D	p.(A476T)	c.1426G>A	.	chr12:49446040	3.35%	NM_003482.4	missense
DIS3	p.(N269S)	c.806A>G	.	chr13:73350079	99.90%	NM_014953.5	missense
CREBBP	p.(Q1491K)	c.4471C>A	.	chr16:3786740	62.85%	NM_004380.3	missense
TP53	p.(P72R)	c.215C>G	.	chr17:7579472	80.47%	NM_000546.6	missense
GNA13	p.(?)	c.-3GGCA>A	.	chr17:63052714	65.76%	NM_006572.6	unknown
BCL2	p.(P40Rfs*112)	c.119_120delCG	.	chr18:60985779	99.72%	NM_000633.3	frameshift Deletion
EP300	p.(S507G)	c.1519A>G	.	chr22:41527628	28.81%	NM_001429.4	missense

Biomarker Descriptions

MYD88 p.(L252P) c.755T>C

myeloid differentiation primary response 88

Background: The MYD88 gene encodes the myeloid differentiation factor 88, a general adaptor protein involved in signaling by the toll-like receptor (TLR) and interleukin-1 (IL-1) receptor[1,2]. The MYD88 protein includes an N-terminal death domain, an intermediate linker domain, and a C-terminal toll-interleukin-1 receptor (TIR) domain[2]. Upon TLR activation, MYD88 is recruited as an intermediate signaling protein between the TLR and IRAK4 through its intermediate domain[3]. IRAK4 then recruits and phosphorylates IRAK1 and IRAK2 to form the 'Myddosome' complex, which promotes cell survival through activation of the NFkB and MAPK pathways[4]. Inappropriate activation of TLRs due to somatic gain-of-function mutations are implicated in hematological cancers and are suggested to be a potent driver of constitutively active NFkB signaling in tumors[5].

Alterations and prevalence: MYD88 L252P mutation (NM_002468.5) is also referred to as L260P (NM_001172567.2), L265P (NM_002468.4), or L273P (NM_001172567.1). The recurrent MYD88 L252P mutation is a gain-of-function driver mutation that triggers IRAK-mediated NF-kB signaling[6]. MYD88 L252P mutation is observed in 87-91% of Waldenstrom macroglobulinemia (WM), 74% of testicular diffuse large B-cell lymphoma (DLBCL), 75% of central nervous system DLBCL, 54% of leg type DLBCL, 54% of immunoglobulin M (IgM) monoclonal gammopathy of undetermined significance (MGUS), and 29% of activated B-cell-like (ABC)

Biomarker Descriptions (continued)

DLBCL[4,5,7]. MYD88 L252P mutation is also observed in less than 10% of B-cell disorders with overlapping clinical features to WM, such as chronic lymphocytic leukemia (CLL), multiple myeloma, splenic marginal zone lymphoma, and immunoglobulin G (IgG) MGUS[8].

Potential relevance: Due to its prevalence, the MYD88 L252P (also referred to as L260P/L265P/L273P) mutation is considered diagnostic of WM and is also believed to be a direct oncogenic driver of the disease[4,9,10].

TET2 p.(Y1724Lfs*5) c.5170_5171insT

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[11]. TET2 is involved in DNA methylation, specifically in the conversion of 5-methylcytosine to 5-hydroxymethylcytosine[12,13]. The TET proteins contain a C-terminal core catalytic domain that contains a cysteine-rich domain and a double stranded ß-helix domain (DSBH)[14]. TET2 is a tumor suppressor gene. Loss of function mutations in TET2 are associated with loss of catalytic activity and transformation to hematological malignancies[11,12,13]

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)[15]. TET2 mutations at H1881 and R1896 are frequently observed in myeloid malignancies[12,16]. 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[17]. TET2 mutations are associated with poor prognosis in PMF and increased rate of transformation to leukemia[17,18]

CD79B p.(Y197D) c.589T>G

CD79b molecule

Background: The CD79B gene encodes the cluster of differentiation 79b molecule, also known as B29[19]. CD79B, along with CD79A, are two distinct proteins that heterodimerize to form the CD79 transmembrane protein complex[20]. CD79 is a member of the immunoglobulin superfamily of cell surface and soluble proteins, and is physically linked to membrane immunoglobulin to form the B-cell antigen receptor complex present on the surface of B-cells[19]. Specifically, CD79B is essential for B-cell development and acts as a signal transducer after antigen recognition by surface immunoglobulin[21]. Due to its exclusivity to B-cells, CD79 is considered a useful marker for the detection of various B-cell neoplasms[19]. Mutations in CD79B or CD79A lead to chronic activation of B-cell receptor (BCR) signaling, supporting an oncogenic role for CD79B[19].

Alterations and prevalence: Somatic mutations in CD79B are observed in 12% of diffuse large B-cell lymphoma (DLBCL)[22,23]. Oncogenic missense mutations at Y196 located in the ITAM domain is shown to result in constitutive BCR signaling[24]. Amplifications in CD79B are observed in 6% of breast invasive carcinoma, 5% of mesothelioma, 3% of liver cancer, and 2% of bladder cancer[22,23]. CD79B is expressed in 80-90% of mature B-cell neoplasms, and is also observed in 96% of mantle cell lymphoma, 83% of follicular lymphoma, and 80% of DLBCL[19].

Potential relevance: Currently, no therapies are approved for CD79B aberrations. Polatuzumab vedotin is a CD79B targeting antibody-drug conjugate with a payload of microtubule inhibitor monomethyl auristatin E (MMAE) approved by the FDA in 2019 for the treatment of releapsed/refractory DLBCL in combination with bendamustine and rituximab[25].

Genes Assayed

Genes Assayed for the Detection of DNA Sequence Variants

BRAF, BTK, CARD11, GNA13, HIST1H1E, MTOR, SF3B1, XPO1

Genes Assayed for the Detection of Copy Number Variations

BRAF, CARD11, GNA13, HIST1H1E, MTOR, SF3B1, XPO1

Genes Assayed (continued)

Genes Assayed with Full Exon Coverage

ARID1A, ATM, B2M, BCL2, BCL6, CD79B, CDKN2A, CREBBP, EZH2, KMT2D, MYC, MYD88, PIM1, SOCS1, TNFAIP3, TNFRSF14, TP53

Relevant Therapy Summary

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

CD79B p.(Y197D) c.589T>G

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
zanubrutinib, chemotherapy	✖	✖	✖	✖	● (IV)

MYD88 p.(L252P) c.755T>C

Relevant Therapy	FDA	NCCN	EMA	ESMO	Clinical Trials*
zanubrutinib, chemotherapy	✖	✖	✖	✖	● (IV)

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

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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