

Summit™ Report

Patient Information	Provisional Diagnosis	Specimen	Physician Information
Name: John Smith DOB: 01/01/2000 Sex Assigned at Birth: Female MRN: 11xx22xx33	Diagnosis: Diffuse Large B-Cell Lymphoma ICD10: C85.99	Type: CSF Collected: 7/2/2025 Received: 7/3/2025 Specimen ID: CASE 3 Lymphoma	Institution: Belay Diagnostics Referring Physician: Provider Test

RESULT SUMMARY

POSITIVE

Clinically Significant Alterations Detected	MYD88 L265P (Tier 1A)	Actionability Summary	0 therapeutic responses 0 trials
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Comments
The previously reported MYD88 L265P variant was identified in the submitted CSF specimen.

ALTERATION DETAILS

Clinically Significant Genomic Variants				
Alteration	VAF	Type of Alteration	Classification	Clinical Implications
MYD88 p.L265P c.794T>C	0.7%	Substitution - Missense	Tier 1A	Prognostic Implications; Diagnostic Implications

Aneuploidy Variants (Chromosome Arm Level Loss or Gain): None
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Clinical Implications: Associated with drug response = related to drug sensitivity or resistance as described in Drug Response section of this report; Potentially relevant clinical trials = gene is related to a trial in the Clinical Trials section of this report; Prognostic Implications = related to prognosis as described in Prognostic Implications section of this report; Diagnostic Implications = related to diagnosis as described in Diagnostic Implications section of this report
VAF: Variant Allelic Frequency

Variants of Unknown Significance (Tier 3): None
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ACTIONABILITY SUMMARY

FDA / NCCN Therapies for the Patient's Tumor Type (Tier 1A): None
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FDA / NCCN Therapies with Resistance / Decreased Response (Tier 1A): None
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Prognostic Implications per NCCN			
Biomarker	Prognostic Association	Diseases	Note
MYD88 L265P	Unfavorable	Primary Cutaneous Diffuse Large B-Cell Lymphoma, Leg Type	In PCDLBCL, leg type, MYD88 L265P is associated with inferior prognosis.

Diagnostic Implications per WHO		
Biomarker	Diseases	Note

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MYD88 L265P	Lymphocytic Neoplasm	MYD88 mutations have been identified in many lymphocytic neoplasms: lymphoplasmacytic lymphoma (LPL)/Waldenstrom macroglobulinemia (WM), marginal zone lymphoma (MZL), and many other B-cell neoplasms. MYD88 mutations are detectable in up to 80% of IgM Monoclonal gammopathy of undetermined significance (MGUS). IgM MGUS patients with mutated MYD88 are at higher risk of progression to WM. The demonstration of MYD88 p.L265P mutation favors a LPL diagnosis. The presence of EBV has been reported to be mutually exclusive with either MYD88 and/or CD79A mutations. Detection of MYD88 hotspot mutations can aid in diagnosis of primary central nervous system diffuse large B-cell lymphoma (PCNS-DLBCL), primary vitreoretinal lymphoma-large B-cell lymphoma (PVRL-LBCL), and primary testicular lymphoma-large B-cell lymphoma (PTL-LBCL). The absence of MYD88 mutation helps to exclude other B-cell lymphomas (splenic MZL, follicular lymphoma, extranodal MZL, and mantle cell lymphoma), and can help support a diagnosis of nodal MZL.
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CLINICAL TRIALS / INVESTIGATIONAL THERAPIES

None

TIER 1A THERAPY DETAILS

None

TEST DETAILS

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SNVs and Indels (32 genes, 112 amplicons)			
AKT1 NM_001014432.1	ERBB2 NM_004448.2	GNAS NM_000516.4	NRAS NM_002524.4
APC NM_000038.5	ERBB3 NM_001982.3	H3-3A NM_002107.4	PIK3CA NM_006218.2
BRAF NM_004333.4	ERCC2 NM_000400.3	HRAS NM_005343.2	PTEN NM_000314.4
CD79B NM_000626.2	FBXW7 NM_033632.3	IDH1 NM_005896.2	RAF1 NM_002880.3
CDH1 NM_004360.3	FGFR2 NM_000141.4	IDH2 NM_002168.2	SMAD4 NM_005359.5
CDKN2A NM_000077.4	FGFR3 NM_000142.4	KRAS NM_004985.3	TERT NM_198253.2
CTNNB1 NM_001904.3	FUS NM_004960.3	MYD88 NM_002468.4	TP53 NM_000546.5
EGFR NM_005228.3	GATA3 NM_001002295.1	NFE2L2 NM_006164.4	VHL NM_000551.3

Aneuploidy (chromosome arm level loss and gain)									
chr1p	chr3p	chr5p	chr7p	chr9p	chr11p	chr13q	chr16q	chr18q	chr20q
chr1q	chr3q	chr5q	chr7q	chr9q	chr11q	chr14q	chr17p	chr19p	chr21q
chr2p	chr4p	chr6p	chr8p	chr10p	chr12p	chr15q	chr17q	chr19q	chr22q
chr2q	chr4q	chr6q	chr8q	chr10q	chr12q	chr16p	chr18p	chr20p	

Methods and Limitations

The Summit™ next-generation sequencing (NGS) test investigates tumor DNA (tDNA) extracted from cerebrospinal fluid (CSF) for clinically relevant single/multi nucleotide variants (SNVs, MNVs, indels) and aneuploidy events associated with primary and metastatic central nervous system (CNS) cancers. Methodology involves targeted duplex sequencing of 32 key genes (SNVs, MNVs and indels) and low pass whole genome sequencing (>0.1x) for the detection of chromosomal arm level loss or gain, aneuploidy (PMID: 37014860). Post target enrichment libraries, generated from 20-40ng of tDNA, are sequenced on the Illumina NovaSeq XPlus, generating 100 bp paired-end sequence reads. The LOD (limit of detection) for SNVs, MNVs and Indels was determined as 0.3% variant allelic fraction (VAF). Variants (mutations and aneuploidy) are called against the human genome build reference hg19 using the Summit™ Genome Analytics (SGA) pipeline (SNVs, MNVs, and Indels - version 1.0.0 and aneuploidy - version 0.6.0), developed at Belay Diagnostics.

Tertiary analysis is performed using the precision oncology workbench (GenomOncology) based on the joint AMP/ASCO/CAP consensus guidelines for interpretation of sequence variants in cancer (PMID: 27993330). Please reach out to contact@belaydiagnostics.com for additional information or queries.

Disclaimers

This test was developed, and its performance characteristics determined by Belay Diagnostics Laboratory (CLIA# 14D2302605), which is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity testing. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). This test may be used for clinical purposes. However, the results of this test do not establish a diagnosis and should not be used alone for diagnosis or patient care decisions or otherwise replace the judgment of a treating physician and must always be interpreted in the context of all relevant clinical and pathological data.

This test is performed only to evaluate for somatic (i.e., tumor-specific) variants within the genes listed and cannot distinguish between germline and somatic alterations with absolute certainty. This test therefore does not report on incidental findings as defined by the American College for Medical Genetics and Genomics (ACMG) (PMID: 37347242). If a germline variant is suspected, follow-up germline testing using non-neoplastic (normal) tissue

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should be performed by a laboratory permitted to perform germline genetic testing along with genetic counseling. It is possible for a genomic variant to be present yet go undetected by our assay either due to the heterogeneous nature of the specimen or the limits of detection of our assay. Therefore, to the extent a particular genomic variant is not reported, Belay Diagnostics LLC does not guarantee that the variant does not exist in the specimen provided. Likely benign, and benign variants are not reported. For any reported variant of uncertain significance (VUS), if the classification changes, there is no obligation to send out a new report updating this information.

The information presented in the clinical trials and therapeutic sections of this report is compiled from public sources which are continuously updated. While we strive to ensure this information is accurate and complete, we cannot guarantee the accuracy or completeness of this information. This public sourced information is not ranked in order of potential or predicted efficacy and may not be complete. Specific eligibility criteria should be reviewed as applicable. This information may include associations between a genomic variant (or lack of a variant) and one or more therapeutic agents with potential clinical benefit (or lack of clinical benefit), including agents that are being studied in clinical research. The finding of a genomic variant does not necessarily indicate or demonstrate pharmacologic effectiveness (or lack thereof) of any agent or treatment regimen found in public source information. Similarly, the finding of "no clinically significant variant" does not necessarily indicate or demonstrate lack of pharmacologic effectiveness (or lack of effectiveness) of any agent or treatment regimen found in public source information. Belay Diagnostics expressly disclaims, and makes no representation of or warranty of, the accuracy or completeness with respect to the publicly available information included herein or reviewed or collected during creation of this report.

ACTIONABILITY REFERENCES

FDA: U.S. Food & Drug Administration ([fda.gov](https://www.fda.gov))

NCCN: National Comprehensive Cancer Network® (NCCN®). Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. The NCCN Guidelines® and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN. To view the most recent and complete version of the guideline, go online to [NCCN.org](https://www.nccn.org). NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

WHO: World Health Organization Classification of Tumours online (tumourclassification.iarc.who.int)

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