

Patient ID SA00105299	Patient Name TESTINGRNV, LPLFXMOLHEME	Birth Date 1984-09-11	Gender M	Age 33
Order Number SA00105299	Client Order Number SA00105299	Ordering Physician CLIENT, CLIENT	Report Notes	
Account Information C7028846 DLMP Rochester		Collected 15 Mar 2018 14:59		

Reflex Testing of MYD88 and CXCR4

Specimen Type

Peripheral blood

MCR

LPLFX Reflex Result

see interpretation

MCR

Final Diagnosis

1 MCR

Peripheral blood, MYD88 L265P Mutation Analysis, Allele-specific PCR : Positive for MYD88 L265P alteration.

Comment: The MYD88 L265P abnormality is highly associated (>90%) with the pathologic diagnosis of lymphoplasmacytic lymphoma and the clinical syndrome of Waldenstrom macroglobulinemia (LPL/WM), particularly in the setting of an elevated IgM serum monoclonal paraprotein. A positive molecular result therefore supports the possibility of LPL/WM; however, this mutation has also been reported in other B-cell neoplasms, including IgM monoclonal gammopathy of uncertain significance, a small subset of marginal zone lymphomas (approximately 10%). The MYD88 L265P mutation is also identified in some diffuse large B-cell lymphomas (DLBCL), with a higher prevalence observed in "immune privileged" sites (e.g. central nervous system, testis, breast, skin). Clinical, laboratory and pathologic correlation is required for final diagnosis and interpretation of these results. The analytical sensitivity of this assay is approximately 1% mutation detection in a wild type background.

Method Comment: DNA was extracted from the specimen and subjected to allele-specific polymerase chain reaction (PCR) using an allele specific forward primer that distinguishes the presence of the MYD88 L265P mutation. The reaction also contains a wild-type forward 5' of the mutation site and a single reverse primer. Expected fragment lengths of PCR products are interpreted using capillary electrophoresis.

Peripheral blood, CXCR4 Mutation Analysis : Positive. The following pathogenic nonsense mutation was

detected in CXCR4: g.136872485G>C, c.1013C>G

This translates into the following predicted protein change: p.Ser338*

In lymphoplasmacytic lymphoma/Waldenstrom's macroglobulinemia (LPL/WM), WHIM-like somatic mutations (C-terminus nonsense/frameshift mutations) of CXCR4 have been reported in approximately 30% of cases, commonly coexisting with a MYD88 L265P mutation. A MYD88-L265P/CXCR4-WHIM molecular signature is associated with similar overall survival, lower response to ibrutinib in previously treated patients, similar or higher bone marrow disease burden and serum IgM levels, and less adenopathy in comparison to those with a MYD88-L265P/CXCR4-WT (wild type) molecular signature. CXCR4 WHIM-like somatic mutations have also been described in approximately 6–20% IgM-MGUS and a small percentage of splenic marginal zone lymphoma, nodal marginal zone lymphoma and rarely, diffuse large B-cell lymphoma (Treon et al., 2014, 24553177; 2015, 25853747; Poulain et al., 2016, 26490317; Roccaro et al., 2014, 24711662; Cao et al., 2017, 28280994). Interpretation of the result in context of all available clinical, laboratory, and morphologic information is recommended.

Method Summary - The C-terminus end of CXCR4 (NM_003467.2, c.898–1059) is amplified from extracted genomic DNA by polymerase chain reaction (PCR), followed by Sanger sequencing and capillary electrophoresis analysis. Review of the sequence data is performed using a combination of automated calls and manual inspection (Unpublished Mayo method). The hotspot mutation c.1013 C>A/G (p.S338X) is examined using bridge nucleic acids (BNA) clamping-enhanced Sanger sequencing with an analytic sensitivity of 1%. All other genetic variants in the test region are examined by regular Sanger sequencing with the analytic sensitivity of 15–20%.

Signing Pathologist: BENJAMIN BAILEY

Received: 16 Mar 2018 15:04

Reported: 16 Mar 2018 16:11

Performing Site Legend

Code	Laboratory	Address	Lab Director	CLIA Certificate
MCR	Mayo Clinic Laboratories - Rochester Main Campus	200 First Street SW, Rochester, MN 55905	William G. Morice M.D. Ph.D	24D0404292



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Test
Environment
LTCSEQ Template

Laboratory Notes

- 1 This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

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