Does MYD88 status impact disease presentation and outcome?

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By specific PCR (sensitivity ~10^{-3}), we evaluated the MYD88 L265P mutation in 487 patients with Waldenström's Macroglobulinemia (WM) or B-cell Lymphoproliferative Disorders. The mutation was seen in 182/221 (82%) WM patients, 37/53 (70%) IgM monoclonal gammopathies of uncertain significance (MGUS), 11/358 (3%) chronic lymphocytic B-cell leukemias and high-risk B-cell lymphocytosis (restricted to mutated cases, 4,6%), 3/36 (8%) splenic marginal zone lymphomas, and 10/77(13%) diffuse large B-cell lymphoma, mostly non-germinal center. The mutation was absent in 53 hairy cell leukemias, 72 non-IgM MGUS, 67 multiple myelomas, 9 amyloidosis, 11 lymphoplasmacytic lymphomas, and 1 IgM-related neuropathy. CXCR4 mutations were present in 32% of WM patients, and it was restricted to $MYD88^{L265P}$ cases.

Among WM and IgM-MGUS, MYD88 L265P mutation was associated with some differences in clinical & biological characteristics at presentation, but usually minor; wild-type MYD88 cases had a higher frequency of female gender (43% vs. 24%, p=0.001),a trend to a smaller M-component (2.05 vs. 2.62 g/dL, *P* = 0.12), more cases with lymphocytosis (24% vs. 5%, *P*=0.006) but less bone marrow infiltration (23% vs. 33%, P=0.005), higher LDH level (371 vs. 265 UI/L,*P* = 0.002) atypical immunophenotype (CD23-CD27++FMC7++), less IGVH somatic hypermutation (69% vs. 96%, P = 0.02) and less VH3-23 gene selection (8% vs. 24%, *P* = 0.05). This diversity did not lead to relevant differences in time to first therapy, response to treatment, or progression-free or overall survival.However, theevent free survival was longer for $MYD88^{L265P}$ respect to $MYD88^{WT}$ patients (94 vs. 45 months, p=0.02).However, mortality related to WM and probability to develop a DLBCL development was slightly higher for $MYD88^{L265P}$ cases (again with no statistically significant differences), which was responsible for a similar OS for MYD88 mutated and wild type cases.