4. SPECIAL CONDITIONS

TP53 MUTATION AND MSS-WM IDENTIFY HIGH RISK WALDENSTROM MACROGLOBULINEMIA IN A REAL WORLD COHORT

U. Calis[1], S. Yuksel[2], M. Kurt Yuksel[1], P. Topcuoglu[1], I. Kuzu[2], O. Arslan[1], M. Ozcan[1], T. Demirer[1], S. Kocak Toprak[1], M. Beksac[3], G. Cengiz Seval[1]

[1]Department of Hematology, Ankara University Faculty of Medicine, Turkey; [2]Department of Pathology, Ankara University Faculty of Medicine, Turkey; [3]Department of Hematology Istinye University, Ankara Liv Hospital, Turkey

https://doi.org/10.3324/haematol.2026.s2.14096

Background. Waldenstrom macroglobulinemia (WM) is a rare lymphoplasmacytic lymphoma with heterogeneous clinical behavior. Real world data integrating clinical staging systems with molecular risk factors remain limited, particularly regarding the prognostic value of TP53 mutation and the recently proposed Modified Staging System for WM (MSS-WM).

Methods. We performed a retrospective single center study including patients diagnosed with WM and followed at Ankara University between January 2005 and July 2025. Clinical and laboratory parameters at diagnosis were recorded. MYD88, CXCR4, TP53 and additional mutations were assessed using targeted next generation sequencing panels. Risk stratification was performed using IPSS-WM and MSS-WM. Overall survival (OS) and progression free survival (PFS) were analyzed by Kaplan-Meier method and Cox regression.

Results. Forty patients were included; median age was 70 years and 77.5 percent were male. MYD88 mutation was detected in 87.5 percent, CXCR4 in 20 percent and TP53 in 15.8 percent of patients. First line therapy was initiated in 90 percent of patients, most commonly with bortezomib based regimens or DRC. Overall response rate to first line therapy was 60 percent. Plasma exchange was required in 45 percent of patients due to IgM related complications. TP53 mutation was associated with significantly inferior OS (hazard ratio 3.75, p=0.036) and PFS (hazard ratio 3.26, p=0.030). MYD88 and CXCR4 mutation status were not associated with survival outcomes. Among patients receiving ibrutinib, disease progression was observed only in CXCR4 mutated cases, although this did not reach statistical significance. IPSS-WM risk categories did not show significant discrimination for OS. In contrast, high risk MSS-WM was associated with significantly increased mortality compared with low risk group (hazard ratio 9.21, p=0.039). Achievement of objective response was associated with significantly prolonged OS and PFS compared with non responding patients.

Conclusions. In this real world cohort with long term follow up, TP53 mutation identifies a high risk subgroup of WM patients with significantly inferior survival. MSS-WM provided superior prognostic discrimination compared with IPSS-WM, supporting its clinical utility across heterogeneous patient populations. Integration of molecular and simplified clinical risk stratification may improve identification of high risk WM patients and should be validated in larger prospective multicenter cohorts.