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POSTER ABSTRACTS

623.MANTLE CELL, FOLLICULAR, AND OTHER INDOLENT B CELL LYMPHOMAS: CLINICAL AND EPIDEMIOLOGICAL

Modified Staging System for Waldenström Macroglobulinemia (MSS-WM): A Multi-Institutional Externally Validated Prognostic Model for Active/Symptomatic Waldenström Macroglobulinemia

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Background: Waldenström Macroglobulinemia (WM) is an indolent lymphoma with heterogeneous outcomes. The recently developed, Revised International Prognostic Scoring System for WM (rIPSS-WM) did not examine the prognostic impact of *MYD88* ^{L265P}, a somatic alteration present in most patients with WM. Moreover, rIPSS-WM could only be partially validated in an external cohort. Here, we report the performance of rIPSS-WM and propose a refined prognostic model with external validation.

Methods: We reviewed medical records of treatment-naïve patients with active WM consecutively seen at Mayo Clinic, Rochester (MCR) between 01/01/1996 and 12/31/2017. We applied the rIPSS-WM model in patients with data available for all required parameters, including age, serum beta-2 microglobulin (β2M), serum lactate dehydrogenase (LDH) and serum albumin at diagnosis to assess the prognostic utility of this model. We then identified the dichotomized clinical and laboratory parameters prognostic for overall survival (OS) by univariate analyses (UVA) in our cohort. The significant parameters were analyzed to independently predict OS in a multivariable analysis (MVA) and to create a prognostic model, which was subsequently validated in an independent multi-institutional cohort.

Results: We identified 889 patients with active WM at MCR, with a median follow-up of 8.2 [95% confidence interval (CI): 7.5-9] years. The estimated median OS for this cohort was 10.6 (95%CI: 9.7-11.4) years. Patients with available data in this cohort for the validation of rIPSS-WM (n=241) were risk stratified into very low (n=46), low (n=64), intermediate (n=58), high (n=46) and very-high risk groups (n=27) per rIPSS-WM, with the respective 5-year OS rates of 96%, 76%, 72%, 77% and 32%, demonstrating overlapping survival curves for the low, intermediate and the high-risk groups. Because rIPSS-WM could not

be validated, we used the data from the MCR cohort and identified age at diagnosis of active WM, LDH >upper limit of normal (ULN), β2M >3μg/mL and albumin <3.5g/dL as statistically significant prognostic markers for OS on UVA. Notably, the presence of *MYD88* ^{L265P} did not impact OS [median 11.4 years (95%CI: 10.1-not reached (NR) for *MYD88* ^{L265P} genotype (n=231) *versus* 10 years (95% CI: 8.1-NR) for *MYD88* ^{WT} genotype (n=65); p=0.33]. On MVA, LDH >ULN (HR 2.34), serum albumin <3.5 g/dL (HR 1.5) and age groups 65-75 years (HR 1.4) and >75 years (HR 2.6) were independently prognostic. Based on comparable HRs, we assigned a score of 1 point each to serum albumin <3.5 g/dL and age group 66-75 years and similarly, 2 points each for age >75 years and serum LDH >ULN per their impact on OS. Patients with the composite scores of 0, 1 and 2 were categorized as low risk, low- intermediate risk and intermediate risk, respectively. Due to similar OS for the scores of 3 to 5, these were combined to form the high-risk group of our proposed model: Modified Staging System for WM (MSS-WM). The median OS was 14.6 years [95%CI: 9.1 years-NR] for low-risk (score 0, n=71, 21%), 11.2 years (95% CI: 9.1-15.2 years) for low-intermediate risk (score 1, n=110, 32%), 8.1 years (95% CI: 6.4-12.2) for intermediate risk (score 2, n=81, 24%) and 5.5 years (95 % CI: 3.9-11 years) for the high-risk group (score ≥3, n=79, 23%); p<0.0001. In this derivation cohort, the 5-year OS rate was 93%, 82%, 69% and 55% and 10-year OS rate was 60%, 53%, 45% and 30% for the low, low-intermediate, intermediate, and high-risk cohort, respectively (**Figure 1A**). We also validated MSS-WM using competing risk analysis (p=0.001) and in the cohort of rituximab treated patients (p<0.0001). We then used data from an independent series of 335 treatment-naïve symptomatic patients from academic institutions (n=5) across the US and Europe for external validation of the MSS-WM model. The median follow-up for the validation cohort was 6.3 years (95% CI: 5.5-7.2 years). The 5-year OS was 93%, 90%, 75% and 57% and the estimated 10-year OS was 91%, 80%, 64% and 35% for the low risk (n= 86, 26%), low-intermediate (n=107, 32%), intermediate (n=86, 26%) and high-risk (n=59, 18%) cohorts, respectively (p<0.0001, **Figure 1B**).

Conclusions: Our proposed model, MSS-WM, is a simple, clinically useful, externally validated model that reliably risk stratifies previously untreated patients with active WM into four groups that have distinct outcomes based on the composite scores derived from the patients' age, serum albumin and serum LDH at diagnosis.

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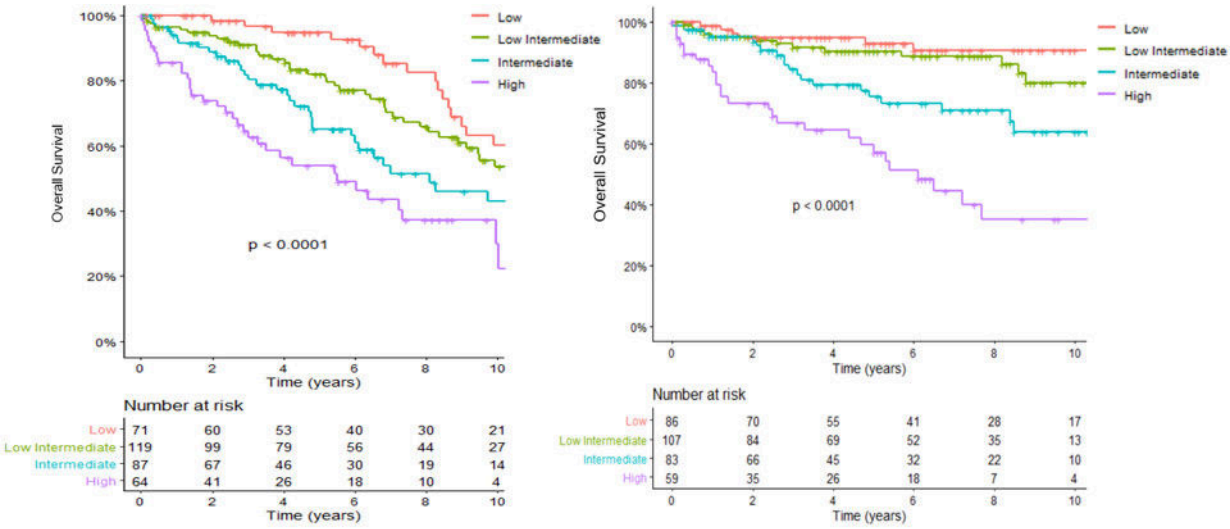

Figure 1A. Derivation Cohort

Figure 1B. Validation Cohort

Figure 1

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