



## BEYOND THE DIPSS: THE ROLE OF INFLAMMATION IN MYELOFIBROSIS

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**Introduction:** Chronic inflammation plays a pivotal role in the pathogenesis and prognosis of myelofibrosis (MF), contributing to fibrosis, immune dysregulation, and cardiovascular comorbidities. Traditional prognostic tools, such as the Dynamic International Prognostic Scoring System (DIPSS), do not consider inflammatory status, despite evidence significance of linking of inflammatory indices—including neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and systemic inflammation response index (SIRI) - with disease progression and survival. This study aimed to assess the prognostic relevance of these indices in MF patients treated with ruxolitinib and to develop a new inflammation-integrated prognostic model.

**Methods:** We retrospectively analyzed 166 MF patients (98 PMF and 68 SMF) followed at the Hematology Units of Pisa and Catania (Italy) between 2013 and 2023. All patients received ruxolitinib and met WHO 2008/2016 diagnostic criteria. Inflammatory parameters (NLR, MLR, PLR, WLR, SII, SIRI) were calculated at diagnosis. Survival analyses were performed using Kaplan-Meier curves and Cox regression models. Variables significant in univariate analysis were included in multivariate models. Based on these results, a new prognostic score (DiMoL) combining DIPSS and MLR was proposed.

**Results:** Median patient age was 68 years; (M:F=1,2). JAK2V617F mutation was detected in 76%, CALR in 16%,

and MPL in 1%. According to DIPSS, 11% were low-risk, 36% intermediate-1, 40% intermediate-2, and 13% high-risk. Median overall survival (OS) was 84 months, with a 6-year OS of 54%. In univariate analysis, OS was significantly affected by DIPSS category, age >65 years, and symptom burden, but not by gender, splenomegaly, or driver mutation. Among inflammatory indices, elevated MLR ( $p < 0.01$ ) and high SIRI ( $p < 0.008$ ) were associated with poorer OS, although only MLR maintained significance in multivariate analysis (HR 1.80,  $p = 0.03$ ). The DiMoL score, integrating DIPSS and MLR, identified three risk categories with distinct survival outcomes: 6-year OS of 90% (low), 52% (intermediate), and 22% (high), offering improved stratification compared with DIPSS alone by reallocating part of the intermediate-risk group.

**Conclusions:** Inflammation, as reflected by MLR, is an independent prognostic factor in MF patients treated with ruxolitinib. The novel DiMoL score effectively refines risk stratification, identifying more homogeneous subgroups than DIPSS and highlighting the clinical value of easily measurable inflammatory parameters. Incorporating inflammation into prognostic models may improve individualized management, support early therapeutic intervention in high-risk patients, and encourage the evaluation of anti-inflammatory strategies—such as statins or interferon—in future prospective studies.