Optimizing Treatment Strategies in Higher MF and Beyond

Sung-Eun Lee
Department of Hematology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea

Myelofibrosis (MF), encompassing primary MF (PMF), post–essential thrombocythemia MF (post-ET/MF), and post–polycythemia vera MF (post-PV/MF), is a complex myeloid neoplasm characterized by clonal ineffective hematopoiesis, extramedullary hematopoiesis, progressive bone marrow fibrosis, and an inherent risk of leukemic transformation. The identification of recurrent driver mutations involving *JAK2*, *CALR*, and *MPL* has significantly advanced our understanding of MF pathogenesis and enabled the development of targeted therapies, particularly Janus kinase (JAK) inhibitors. These therapeutic advances have resulted in meaningful improvements in splenomegaly, symptom burden, quality of life, and potentially overall survival. However, despite the development of medical therapies and the refinement of prognostic models reflecting evolving risk profiles, substantial limitations remain in the management of patients with higher-risk MF, particularly with respect to therapeutic strategies aimed at modifying disease biology. In addition, although allogeneic hematopoietic stem cell transplantation remains the only potentially curative option, its clinical application is complicated by challenges in optimal candidate selection, timing of transplantation, and the integration of pre- and post-transplant JAK inhibitor therapy. Finally, the management of advanced MF, including accelerated-phase disease and leukemic transformation, represents a major unmet clinical need. Outcomes in this setting remain poor, and evidence-based treatment strategies are limited. This presentation will review current evidence and unmet clinical needs in higher-risk and advanced MF, and discuss future directions for optimizing treatment strategies beyond conventional approaches.