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REVIEW

Highlights from MPN Asia 2025: Advances in Molecular Pathogenesis and Therapeutic Strategies in Myeloproliferative Neoplasms

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Abstract

Purpose of Review This report summarizes key insights from the 8th Annual International Symposium on Myeloproliferative Neoplasms (MPN Asia 2025). The symposium brought together global experts to discuss advancements in MPN biology, diagnostics, and therapeutics, with a focus on emerging molecular understanding, novel treatment strategies and real-world data.

Recent Findings Molecular profiling has become essential in MPN risk stratification and therapeutic decision-making. High-risk mutations (e.g., ASXL1, TP53) and inflammatory pathways (e.g., IL-17, NF-κB) were shown to correlate with disease progression and transformation. Interferon-based therapy is increasingly used in younger, low-risk, or treatment-naïve patients, and is also being investigated in myelofibrosis and essential thrombocythemia. Ropeginterferon alfa-2b, a novel interferon-based therapy, demonstrated durable clinical efficacy in polycythemia vera. Its high initial-dose and accelerated titration (HIDAT) regimen led to fast achievement of complete hematologic response, rapid reductions in *JAK2*V617F allele burden, and high complete molecular response rate. Combination regimens involving ruxolitinib and agents such as pelabresib, selinexor, and interferon showed potential for enhanced efficacy. Population-based studies from Asia contributed regional epidemiological and treatment data, reinforcing the role of real-world evidence. Modern prognostic models such as MIPSS70+ v2.0 and GIPSS were discussed for more precise risk prediction. Preliminary findings also suggest ropeginterferon alfa-2b may be a safe option during pregnancy.

Summary MPN Asia 2025 highlighted the growing role of molecular diagnostics and targeted therapeutics in the management of MPNs. Ropeginterferon alfa-2b has emerged as a therapeutic potential across the MPN spectrum. Its early use and personalized strategies are increasingly recognized. Real-world data and regional insights are shaping a more nuanced, globally informed approach to MPN care.

The 8th Annual International Symposium on Myeloproliferative Neoplasms (MPN Asia 2025), held in Beijing, brought together leading hematologists and researchers from across Asia, Europe, and North America to share novel insights into the evolving landscape of Myeloproliferative Neoplasm (MPN) biology and therapeutics. The conference featured data from clinical trials, real-world evidence, and translational research, highlighting an emerging consensus on personalized, molecularly informed treatment strategies.

Expanding the Molecular Understanding of Myeloproliferative Neoplasms

New molecular insights continue to refine the classification and management of MPNs. Presentations at MPN Asia 2025 underscored the critical role of driver mutations such as *JAK2*V617F, *CALR*, and *MPL*, alongside the growing importance of high-risk co-occurring mutations in genes such as *TET2*, *DNMT3A*, *IDH1/2*, *ASXL1*, *EZH2*, *SRSF2*, *U2AF1* and *TP53*. These co-occurring mutations, detectable

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via next-generation sequencing (NGS), are now widely used in prognostication and therapeutic decisions in MPN [1–7].

Specific high-risk mutations, particularly when accompanied by elevated *JAK2*V617F allele burden in polycythemia vera (PV) [8], can predict transformation to post-PV myelofibrosis (MF) or acute myeloid leukemia (AML). Such molecular characteristics are increasingly being integrated into treatment decisions, including the selection of therapies following *JAK* inhibitor failure.

At the conference, the pro-inflammatory nature of MPN was highlighted and discussed. Transcriptomic, proteomic, and cytokine profiling studies have shown that inflammatory pathways, including IL-17 signaling, NF-κB activation, and chemokine cascades, are upregulated in MPNs and are particularly associated with disease progression and thrombotic risk [9–13].

MPNs are still largely unrecognized and underdiagnosed chronic blood cancers which may lead to delayed or missed opportunities for treatment [14]. Early detection and diagnosis may be achieved by screening patients with a "high-risk MPN profile". For example, patients who had an ischemic stroke were 2.4 times more likely to carry the JAK2V617F mutation than matched individuals without history of ischemic stroke [15].

Ropeginterferon Alfa-2b: Establishing a New Therapeutic Backbone

A central theme of the conference was the transformative potential of ropeginterferon alfa-2b, a long-acting, monopegylated interferon, across the MPN spectrum. Multiple presentations, spanning clinical trials in Europe [16–21], China [22–24], Korea [25, 26], Japan [27, 28], and real-world data from the United States [29], and Taiwan [30], demonstrated its robust and durable efficacy in PV. Notably, the **h**igh **i**nitial-**d**ose and **a**ccelerated dose-titration **t**reatment (HIDAT), 250–350–500 µg every two weeks, was associated with faster achievement of complete hematologic response, more rapid reductions in *JAK2*V617F allele burden and higher complete molecular remission rate compared with the conventional dose-titration regimen [23, 31–33].

Interferon therapy is being increasingly investigated as front line treatment option in younger patients with MPN [34, 35], as well as in those who are treatment-naïve [36] or classified as low-risk [20, 21], and also in individuals who are intolerant or resistant to hydroxyurea and/or anagrelide [30, 37, 38]. The use of interferon alfa is also being assessed in patients with early stage MPN, where early intervention may offer the potential to achieve molecular remission and delay disease progression [8, 18, 39–42].

Early and Targeted Therapy in Myelofibrosis: A Shifting Paradigm

Early intervention and prompt treatment of patients with MF can lead to better outcomes, reducing symptom burden and improving survival [43, 44]. Evidence from the primary analysis of JUMP study and post-hoc analyses of the COMFORT trials, as well as data from national registries, suggest that initiating ruxolitinib earlier in the disease course may improve overall response rates and outcomes [45, 46].

The development of combination regimens, such as ruxolitinib with pelabresib (a BET inhibitor) [47], bomedemstat (LSD1 inhibitor) [48], selinexor (XPO1 inhibitor) [49, 50] or with interferon [51], are being evaluated for their potential to increase response in first-line therapy of patients with MF and potentially improve disease modification and molecular responses.

Intervention with pegylated interferon in pre-fibrotic MF, or in primary MF and essential thrombocythemia (ET), aims at reducing progression to fibrotic phase MF and other adverse outcomes. Emerging evidence suggests that ropeginterferon alfa-2b may also be effective in treating patients with MF as a monotherapy, especially in early and low-risk MF [43, 44].

Asian Real-World and Population-Based Evidence

Large-scale real-world data analysis can help understand the disease better and design personalized treatment strategies. A real-world study of 338 patients with MF in China has confirmed the differences in clinical characteristics, cytogenetics, molecular biology, and prognosis among overt PMF, post-ET MF and post-PV MF [52]. Epidemiologic data on MPN in Asia remains limited, however, a multicenter cohort study from Zhejiang Province, in China, encompassing over 3,000 patients across 58 hospitals was discussed at the conference. The results provide valuable clinical and molecular insights into PV, ET, and MF in China. This dataset highlights regional mutation patterns and supports expanded molecular diagnostics.

Two nationwide population-based studies from South Korea have been published. Lim et al. analyzed the incidence, prevalence and survival trends in MPNs using National Health Insurance data [53], while Byun et al. provided further characterization of clinical features and treatment patterns in patients with PV, ET, and MF [54]. In Taiwan, a recent population-based cross-sectional study reported treatment patterns and clinical outcomes on 2,647 patients with PV using the National Health Insurance Research Database [55].

Toward Personalized Risk Stratification and Therapy in MF

Emerging evidence continues to support the integration of molecular data into clinical risk models of MF. Prognostic scoring systems such as the updated MIPSS70+v2.0 [56], MYSEC-PM [57], and GIPSS [56] that integrate clinical, cytogenetic and genetic data more accurately identify patients at risk of MF disease progression or leukemic transformation than conventional prognostic methods.

Special Considerations: Ropeginterferon alfa-2b in Pregnancy

In limited real-world cases, ropeginterferon alfa-2b was reported to be safe in pregnancy [58, 59], similarly to pegylated interferon alfa-2a. Pharmacokinetics data showed minimal placental transfer and virtually undetectable levels in breastmilk, supporting cautious use in women of reproductive age when alternative cytoreductive therapies are contraindicated [Tashi et al., manuscript in preparation].

Conclusion and Future Outlook

MPN Asia 2025 highlighted a field in rapid evolution, fueled by advances in molecular diagnostics, targeted therapeutics and potential personalized medicine approaches based on molecular profiles, as well as a need for global collaboration. There is growing international alignment on the early use of interferon-based therapies, especially ropeginterferon alfa-2b, across the MPN disease spectrum and the use of combination regimens to achieve disease modification and better outcomes. Increasingly, treatment strategies are shifting from symptom control and thrombosis reduction toward long-term disease remission and even treatment-free remission. As molecular monitoring becomes more routine and genomic classifiers are increasingly integrated into clinical practice, personalized care for patients with PV, ET, and MF will become more precise and more effective.

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Declarations

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