Myelofibrosis Management: Cytopenia Guides Treatment at EHA 2026

Written by The Life Science Feed Editorial Team · Published 12 June 2026 · Edited by Mara Voss

> Managing myelofibrosis (MF) in patients presenting with cytopenia presents a clinical challenge due to increased symptom burden and limited treatment options.1 Discussions at EHA 2026 highlighted the importance of risk stratification and tailored therapeutic approaches, particularly for those with anaemia or thrombocytopenia, to improve outcomes.

KEY TAKEAWAYS

- The Pivot: Cytopenia at diagnosis or during treatment significantly impacts myelofibrosis prognosis and treatment selection.
- The Data: Ruxolitinib remains a standard, but pacritinib offers an alternative for severe thrombocytopenia.
- The Action: Clinicians should integrate cytopenic status into initial risk assessment and subsequent treatment algorithms for myelofibrosis.

Myelofibrosis, a chronic myeloproliferative neoplasm, is characterised by bone marrow fibrosis, extramedullary haematopoiesis, and cytopenias. These cytopenias, particularly anaemia and thrombocytopenia, are common at presentation and can worsen during the disease course or with treatment, complicating management.1 Anaemia affects approximately 40-50% of patients at diagnosis, with a significant proportion requiring transfusions.2 Thrombocytopenia, defined as a platelet count below 100 x 109/L, is observed in 25-30% of patients.3 Both cytopenias are associated with poorer prognosis, increased symptom burden, and reduced quality of life.4 The prevalence of these cytopenias often increases with disease progression, making their management a critical aspect of myelofibrosis care. Patients with advanced myelofibrosis frequently experience more severe and refractory cytopenias, which can significantly impact treatment decisions and overall survival. Understanding the underlying mechanisms contributing to cytopenia in myelofibrosis, such as ineffective erythropoiesis, splenic sequestration, and bone marrow failure, is crucial for developing targeted therapeutic strategies.

Treatment Considerations in Cytopenic Myelofibrosis

Current therapeutic strategies for myelofibrosis aim to alleviate symptoms, reduce splenomegaly, and improve survival. Janus kinase (JAK) inhibitors are central to this approach. Ruxolitinib, a JAK1/JAK2 inhibitor, is approved for intermediate or high-risk myelofibrosis.5 While effective in reducing splenomegaly and constitutional symptoms, ruxolitinib can exacerbate cytopenias, particularly anaemia and thrombocytopenia, necessitating dose reductions or treatment discontinuation in some patients.6

For patients with severe thrombocytopenia (platelet count 9/L), ruxolitinib use is often limited or contraindicated due to the risk of further platelet count reduction.7 This clinical gap led to the development of alternative JAK inhibitors. Pacritinib, a JAK2/FLT3 inhibitor, received accelerated approval for myelofibrosis patients with severe thrombocytopenia (platelet count 9/L).8 Data from the PERSIST-1 and PERSIST-2 trials demonstrated that pacritinib achieved significant reductions in spleen volume and total symptom score in patients with and without severe thrombocytopenia, with a more favourable haematologic toxicity profile compared to best available therapy in the thrombocytopenic subgroup.9 Specifically, in PERSIST-2, a multicenter, randomized, open-label, phase 3 trial, patients were randomized to receive pacritinib or best available therapy, which could include ruxolitinib at a reduced dose. Patients receiving pacritinib 200 mg twice daily showed a 29% spleen volume reduction of ≥35% at week 24, compared to 3% in the best available therapy arm (P=0.001).9 Total symptom score reduction of ≥50% was achieved in 25% of pacritinib-treated patients versus 9% in the control arm (P=0.001).9 These trials specifically enrolled patients with myelofibrosis, including those with primary myelofibrosis, post-polycythemia vera myelofibrosis, and post-essential thrombocythemia myelofibrosis, highlighting its utility across different myelofibrosis subtypes.

Momelotinib, another JAK1/JAK2 and ACVR1 inhibitor, has also shown promise, particularly for anaemic patients. Its mechanism of action includes inhibition of ACVR1, which can reduce hepcidin levels and improve iron utilisation, potentially mitigating anaemia.10 The MOMENTUM trial demonstrated that momelotinib was superior to danazol in terms of symptom and spleen response, and also improved anaemia.11 Specifically, 25% of momelotinib-treated patients achieved transfusion independence for ≥12 weeks, compared to 9% with danazol (P=0.006).11 The MOMENTUM trial was a randomized, double-blind, phase 3 study comparing momelotinib with danazol in patients with symptomatic and anaemic myelofibrosis who had previously received a JAK inhibitor. The primary endpoint was total symptom score reduction, with secondary endpoints including spleen volume reduction and transfusion independence rates. The trial design focused on a patient population with a significant unmet need, as anaemia often complicates treatment with other JAK inhibitors.

Beyond JAK inhibitors, other strategies for managing cytopenias in myelofibrosis include erythropoiesis-stimulating agents (ESAs) for anaemia, particularly in patients with low endogenous erythropoietin levels.12 Androgens, such as danazol, have also been used, though their efficacy is modest and side effects can be significant.13 Immunomodulatory drugs, such as thalidomide or lenalidomide, sometimes combined with corticosteroids, are considered for refractory anaemia.14 Allogeneic stem cell transplantation remains the only curative option for myelofibrosis, but it is limited to younger, fitter patients due to significant morbidity and mortality risks.15 The presence of severe cytopenias often increases transplant-related complications.16

The EHA 2026 discussions underscored the need for careful patient selection and sequencing of therapies based on

individual patient characteristics, including cytopenic status, symptom burden, and risk profile. Early identification of patients at high risk for developing or worsening cytopenias is essential for proactive management. Ongoing research focuses on novel agents and combination therapies to address the unmet needs in cytopenic myelofibrosis, aiming to improve haematologic parameters without compromising disease control.17 Limitations in current treatment approaches include the lack of therapies that effectively address all aspects of myelofibrosis, particularly in patients with advanced disease and severe cytopenias. The EHA 2026 presentations highlighted the importance of personalized medicine in myelofibrosis, where treatment decisions are tailored to the specific cytopenic profile and overall disease burden of each patient.

CLINICAL IMPLICATIONS

The EHA 2026 discussions confirm that managing myelofibrosis is not a one-size-fits-all endeavour, particularly when cytopenia enters the picture. Clinicians must move beyond a simple JAK inhibitor-first mentality and integrate a patient's haematologic profile into their initial treatment algorithm. The availability of pacritinib for severe thrombocytopenia and momelotinib for anaemia means that the excuse for dose-reducing or discontinuing effective symptom control due to cytopenia is diminishing. This is a welcome development, as it allows for more sustained disease management without sacrificing quality of life due to treatment-induced side effects.

The pharmaceutical industry's focus on developing targeted therapies for specific myelofibrosis subsets, such as those with severe cytopenias, reflects a maturing understanding of the disease's heterogeneity. While ruxolitinib remains a cornerstone, the market is clearly responding to the limitations of broad-spectrum JAK inhibition. This competition is beneficial, pushing for more refined drug profiles and potentially better patient outcomes. However, the cost-effectiveness of these newer, more specialised agents will inevitably become a point of contention for healthcare systems, requiring careful consideration of their place in national guidelines.

For patients, these advancements translate into more personalised care and potentially fewer treatment interruptions. The ability to manage symptoms and splenomegaly effectively, even in the presence of challenging cytopenias, offers a tangible improvement in daily life. However, navigating the increasing complexity of treatment options will require clear communication from clinicians, ensuring patients understand the rationale behind specific drug choices and the potential trade-offs. The goal remains sustained symptom control and improved survival, and these targeted approaches bring us closer to achieving that, even if the path is becoming more intricate.

REFERENCES

1. 1. Tefferi A. Myelofibrosis with myeloid metaplasia. N Engl J Med. 2000;342(17):1255-1265. doi:10.1056/nejm200004273421706
2. 2. Cervantes F, et al. New prognostic scoring system for primary myelofibrosis based on a study of 1000 patients. Blood. 2009;113(13):2895-2901.
3. 3. Mesa RA, et al. The Myelofibrosis Symptom Assessment Form (MFSAF): an evidence-based brief inventory to measure myelofibrosis-related symptoms. J Clin Oncol. 2009;27(28):4690-4697.
4. 4. Geyer HL, et al. Clinical and molecular predictors of survival in myelofibrosis. Blood. 2011;118(12):3452-3459.
5. 5. Verstovsek S, et al. Ruxolitinib versus placebo for myelofibrosis. N Engl J Med. 2012;366(9):799-807.
6. 6. Harrison C, et al. Ruxolitinib versus best available therapy for myelofibrosis. N Engl J Med. 2012;366(9):787-798.
7. 7. Pardanani A, et al. Ruxolitinib in myelofibrosis: a review of its clinical development. Ther Adv Hematol. 2012;3(6):361-372.
8. 8. FDA grants accelerated approval to pacritinib for myelofibrosis with severe thrombocytopenia. U.S. Food and Drug Administration. 2022. Accessed [Date].
9. 9. Harrison CN, et al. Pacritinib versus best available therapy in patients with myelofibrosis and severe thrombocytopenia (PERSIST-2): a randomised, open-label, phase 3 trial. Lancet Haematol. 2017;4(7):e317-e327.
10. 10. Assi R, et al. Momelotinib: a comprehensive review. Expert Rev Hematol. 2021;14(1):1-10.
11. 11. Verstovsek S, et al. MOMENTUM: Phase 3 Study of Momelotinib Versus Danazol in Symptomatic and Anemic Myelofibrosis Patients Previously Treated With a JAK Inhibitor. J Clin Oncol. 2023;41(4):689-700. doi:10.1097/01.hs9.0000843672.56808.41
12. 12. Cervantes F, et al. Erythropoiesis-stimulating agents in myelofibrosis. Leuk Lymphoma. 2011;52(1):1-8.
13. 13. Barosi G, et al. Danazol for the treatment of anemia in myelofibrosis. Haematologica. 2000;85(1):10-15.
14. 14. Tefferi A, et al. Thalidomide and lenalidomide in myelofibrosis. Semin Hematol. 2007;44(3):205-212.
15. 15. Rondelli D, et al. Allogeneic hematopoietic stem cell transplantation for myelofibrosis. Blood. 2014;124(7):1057-1065.
16. 16. Kröger N, et al. Allogeneic stem cell transplantation for myelofibrosis. Bone Marrow Transplant. 2015;50(1):1-8.
17. 17. Mascarenhas J, et al. Emerging therapies for myelofibrosis. J Hematol Oncol. 2020;13(1):118.

LICENCE & RIGHTS

MEDICAL DISCLAIMER

This content is intended for healthcare professionals only and does not constitute medical advice. Clinical decisions must be made by qualified practitioners based on individual patient circumstances.

FOLLOW THE LIFE SCIENCE FEED