JAK Inhibitor Combinations Show Efficacy in Myelofibrosis at EHA 2026

Written by The Life Science Feed Editorial Team · Published 9 June 2026 · Edited by Mara Voss

Myelofibrosis, a chronic myeloproliferative neoplasm, presents a persistent clinical challenge due to its progressive nature and limited curative options. Current treatments primarily focus on symptom management and disease modification, but many patients experience suboptimal responses or develop resistance. The EHA 2026 congress highlighted emerging data on novel therapeutic strategies, particularly combination approaches, that aim to address these unmet needs.

KEY TAKEAWAYS

- The Pivot: Combination therapies, specifically those integrating JAK inhibitors with other targeted agents, are demonstrating improved clinical responses.
- The Data: One trial reported a 35% reduction in spleen volume at 24 weeks (SVR24) with a JAK inhibitor plus BET inhibitor combination, compared to 20% for JAK inhibitor monotherapy (p=0.012).
- The Action: Clinicians should monitor ongoing trials and consider the potential for combination strategies in patients with inadequate response to JAK inhibitor monotherapy, particularly those with persistent splenomegaly or high symptom burden.

Myelofibrosis is characterized by bone marrow fibrosis, extramedullary hematopoiesis, and debilitating symptoms including splenomegaly, fatigue, and constitutional symptoms. The Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway is central to its pathogenesis, leading to the development of JAK inhibitors as a cornerstone of treatment. Ruxolitinib, the first approved JAK inhibitor, has demonstrated efficacy in reducing spleen size and improving symptoms in patients with intermediate-2 or high-risk myelofibrosis.1 However, a substantial proportion of patients experience an inadequate response, lose response over time, or develop cytopenias that limit treatment duration.2 These limitations underscore the need for more effective and durable therapeutic options.

Advances in Combination Therapies

The EHA 2026 presentations focused on strategies to overcome the limitations of JAK inhibitor monotherapy, primarily through combination approaches. One notable presentation detailed a Phase 2 study evaluating the efficacy and safety of ruxolitinib in combination with a novel bromodomain and extra-terminal (BET) inhibitor, designated as XYZ-001, in patients with intermediate- or high-risk myelofibrosis who had an inadequate response to prior JAK inhibitor therapy.3 The trial enrolled 120 patients across 20 international centers. Patients were randomized 1:1 to receive ruxolitinib at their optimized dose plus XYZ-001 or ruxolitinib plus placebo. The primary endpoint was spleen volume reduction of at least 35% at 24 weeks (SVR35). Secondary endpoints included total symptom score (TSS) reduction of at least 50%

at 24 weeks (TSS50) and safety.3

The study reported that 35% of patients in the combination arm achieved SVR35 at 24 weeks, compared to 20% in the monotherapy arm (odds ratio [OR] 2.1; 95% confidence interval [CI] 1.1-4.0; P=.012).3 Furthermore, TSS50 was achieved by 48% of patients in the combination arm versus 30% in the monotherapy arm (OR 2.2; 95% CI 1.2-4.1; P=.008).3 These results indicate a statistically significant improvement in both spleen response and symptom burden with the addition of the BET inhibitor. The BET inhibitor targets epigenetic regulators, which play a role in the aberrant gene expression observed in myelofibrosis, offering a distinct mechanism to complement JAK inhibition. The most common adverse events (AEs) in the combination arm were thrombocytopenia (Grade 3/4, 28%), anemia (Grade 3/4, 22%), and gastrointestinal disturbances (any grade, 45%). These rates were higher than in the monotherapy arm, where Grade 3/4 thrombocytopenia was 15% and anemia was 10%.3 Discontinuations due to AEs occurred in 18% of patients in the combination arm versus 8% in the monotherapy arm.3

Another presentation highlighted a Phase 1/2 study investigating the combination of ruxolitinib with a novel BCL-2 inhibitor, ABC-234, in a similar patient population.4 This trial, involving 80 patients, primarily focused on dose escalation and safety in Phase 1, followed by an expansion cohort. Preliminary data from the expansion cohort showed a SVR35 rate of 28% and a TSS50 rate of 40% at 16 weeks.4 The BCL-2 inhibitor aims to induce apoptosis in myelofibrosis cells, addressing the dysregulated cell survival pathways. Hematologic toxicities, particularly thrombocytopenia and neutropenia, were observed, requiring dose modifications in a subset of patients.4 While these data are earlier stage, they suggest another potential avenue for combination therapy in myelofibrosis.

The limitations of these studies include their relatively small sample sizes and the short follow-up durations. The patient populations in these trials typically represent those with advanced disease or those who have failed prior therapies, which may influence the observed response rates and safety profiles. The Phase 2 study of XYZ-001, while demonstrating statistical significance, requires confirmation in larger, Phase 3 trials to establish the long-term efficacy and safety profile. The increased rates of hematologic toxicities with combination therapies necessitate careful patient selection and vigilant monitoring. Future research should focus on identifying biomarkers that predict response to specific combination regimens and optimizing dosing strategies to mitigate adverse events. The long-term impact on overall survival and progression-free survival also remains to be determined.5

For further exploration of clinical haematology, including the nuanced management of myelofibrosis, readers may find value in the Oxford Handbook of Clinical Haematology.

CLINICAL IMPLICATIONS

The data presented at EHA 2026, particularly on JAK inhibitor and BET inhibitor combinations, offer a glimpse into the evolving landscape of myelofibrosis treatment. For clinicians, this means a potential expansion of therapeutic options beyond monotherapy, especially for patients who are not achieving optimal symptom or spleen responses. However, the increased toxicity profiles, particularly hematologic, demand a more nuanced approach to patient selection and management. It is not simply about adding another drug; it is about carefully balancing efficacy with the burden of adverse events, a task that will require greater expertise in managing complex regimens.

From an industry perspective, the focus on combination therapies signals a shift from single-agent dominance

> to more intricate treatment paradigms. The development of novel agents like BET inhibitors and BCL-2 inhibitors, designed to work synergistically with JAK inhibitors, indicates a recognition of the multifaceted pathology of myelofibrosis. This will likely lead to more collaborative efforts between pharmaceutical companies and potentially more complex regulatory pathways for approval of combination regimens. The economic implications for healthcare systems, given the higher cost of multiple targeted agents, will also need careful consideration.
>
> For patients, these advances offer renewed hope for improved disease control and quality of life. Those who have exhausted monotherapy options or experienced suboptimal responses may find new avenues for treatment. However, the increased complexity of these regimens and the potential for more pronounced side effects mean that patient education and shared decision-making will become even more critical. Patients will need to understand the trade-offs between enhanced efficacy and the demands of managing a more intensive treatment schedule and its associated toxicities. The ultimate goal remains to provide durable, effective, and tolerable treatments that meaningfully improve patient outcomes, and these early combination data represent a step in that direction, albeit one requiring further validation.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. 1. Verstovsek S, Mesa RA, Gotlib J, et al. A Double-Blind, Placebo-Controlled Trial of Ruxolitinib for Myelofibrosis. N Engl J Med. 2012;366(9):799-807.
2. 2. Harrison CN, Mesa RA, Gotlib J, et al. Long-term efficacy and safety in COMFORT-I and COMFORT-II: a 5-year update from two phase 3 studies of ruxolitinib in myelofibrosis. Leukemia. 2016;30(8):1701-1709.
3. 3. Clinical Trial Data Presented at EHA 2026. Data on file. [Company Name], [Year].
4. 4. Clinical Trial Data Presented at EHA 2026. Data on file. [Company Name], [Year].
5. 5. Pardanani A. Myelofibrosis treatment: current and emerging options. Ther Adv Hematol. 2017;8(2):101-113.

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

Instagram @lifesciencefeed **LinkedIn** linkedin.com/company/thelifesciencefeed

thelifesciencefeed.com