Cancer Therapy & Oncology
International Journal
ISSN: 2473-554X

Juniper Publishers
key to the Researchers

Editorial
Volume 30 Issue 4 - December 2025
DOI: 10.19080/CTOIJ.2025.30.556297

Cancer Ther Oncol Int J

Treatment Options for Myelofibrosis Related Anemia

Nahla A. M. Hamed*

Professor of Hematology, Faculty of Medicine, Alexandria University, Egypt

Submission: November 16, 2025; **Published**: December 03, 2025

Corresponding author: Nahla A. M. Hamed, Professor of Hematology, Faculty of Medicine, Alexandria University, Egypt

Abstract

Anemia is a frequent and clinically significant complication of myelofibrosis (MF). It contributes to poor prognosis, reduced quality of life, and therapeutic challenges. Its pathogenesis is multifactorial. It results from progressive bone marrow fibrosis, ineffective erythropoiesis, iron sequestration driven by elevated hepcidin, hypersplenism, and treatment-related myelosuppression. Current management strategies include transfusion support, erythropoiesis-stimulating agents, androgens and immunomodulatory drugs, but their efficacy and responses are often limited. Future therapies—such as novel JAK inhibitors, hepcidin antagonists, activin receptor ligand traps, and telomerase inhibitors—may offer promise in alleviating anemia and addressing the biology of the disease. However, ongoing research into mechanisms and targeted interventions are still needed.

Keywords: Anemia; Myelofibrosis; JAK inhibitors; Activin; Erythropoietin

Abbreviations: MF: myelofibrosis; JAK-STAT: Janus kinase–signal transducer and activator of transcription; MPN: myeloproliferative neoplasm; ESAs: erythropoiesis-stimulating agents; RR6 model: Response to Ruxolitinib After 6 Months

Introduction

Anemia defined as a hemoglobin level less than 10g/dL is present in 30% to 40% of patients with myelofibrosis (MF) at the time of initial diagnosis. Anemia rates increased from 38% at the time of diagnosis to 58% after 1 year following diagnosis according to one study. Another study found that 47% of non-anemic patients at diagnosis developed anemia after a median of 3.3 years and nearly all patients eventually become anemic over time. Furthermore, the proportion of patients requiring red blood cell (RBC) (transfusions dependent) doubled (rising from 24% to 46%) from diagnosis to 1 year later highlighting the progressive worsening of anemia over time as the disease progresses [1].

Pathogenesis of Anemia

The pathogenesis of anemia in MF is multifactorial. Contributions of several disease-related mechanisms to anemia pathogenesis suggest that anemia is an intrinsic feature of MF. Key mechanisms include pro-inflammatory cytokine signaling due to aberrant Janus kinase–signal transducer and activator of transcription (JAK-STAT) pathway signaling, leading to bone marrow fibrosis and ineffective extramedullary hematopoiesis [2]. Dysfunctional erythropoiesis may result also from non–JAK-STAT molecular pathway signaling alterations [1]. Additional contributing factors include RBC sequestration associated with splenomegaly, dilutional effects from associated increase in plasma volume, RBCs loss through bleeding or intravascular destruction [1], decreased erythropoiesis due to high hepcidin levels leading to iron sequestration in the reticuloendothelial system and hypersplenism [2]. The myelosuppressive JAK inhibitors (ruxolitinib and fedratinib), used in the treatment of MF can provide spleen and symptom relief in many patients but can induce or worsen anemia [1]. MF-related anemia is linked to a negative impact on survival [3].

Treatment of MF-Related Anemia

Treatment of anemia associated with MF is challenging and mortality due to MF-related complications is high [2]. Selecting the appropriate therapeutic agent requires consideration of multiple factors, including whether the patient is present with isolated anemia or if they have a constellation of MF-related symptoms, such as fever, weight loss or abdominal discomfort. Symptoms

can be assessed using the Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF). Understanding whether anemia arises from the underlying disease or a consequence of therapy can also guide treatment decisions [4]. The guidelines revealed a lack of unified standards of care for the management of MF-related anemia, and a lack of standardized direction for starting anemia treatment and transfusion requirements [3].

Treatment Options for MF-Related Anemia

Currently, the only curative therapy is allogenic stem cell transplantation, but this is an option only for younger and fit patients and is associated with high risk of treatment-related death and morbidity [2]. Current treatments options for MF-related anemia include red blood cell (RBC) transfusions, erythropoiesis-stimulating agents (ESAs), androgens, steroids, splenectomy, and immunomodulatory drugs (IMiD® agents), all of which have limited efficacy and durability of response and are associated with multiple side effects [2].

JAK Inhibitors

- **Ruxolitinib**

The JAK inhibitors are disease-modifying therapy. Ruxolitinib is the cornerstone of treatment though it is not suitable in all situations. It has been shown to confer an overall survival benefit. Multiple studies reported improved outcome and a decrease in the spleen volume among patients who received a dose of 20 mg for at least six months. It may be administered in combination with other treatments. Anemia is a common adverse effect in patients taking ruxolitinib for MF. Dose reduction is often considered in such cases, but patients may tolerate a certain amount of anemia in some cases to achieve a spleen volume reduction or MPN symptom control. The RR6 model provides a useful tool to predict survival in MF based on a clinical response to ruxolitinib [4].

- **Pracritinib and Momelotinib**

Novel JAK and ACVR1/ALK2 inhibitors (pracritinib and momelotinib) have demonstrated an ability to improve anemia-related outcomes in the PERSIST-2 and MOMENTUM studies, respectively [5]. Momelotinib (ACVR1/JAK1/2 inhibitor) and pacritinib (ACVR1/JAK2 inhibitor) are the preferred JAK inhibitors for MF patients with cytopenias (anemia, thrombocytopenia) [6]. Real-life treatment with Momelotinib demonstrates its significant effect in improving anemia among MF patients, with high rates of patients achieving transfusion independence (TI) regardless of prior iJAK exposure. Moreover, Momelotinib has shown to be effective in alleviating symptoms and managing splenomegaly in patients previously treated with ruxolitinib, with an acceptable toxicity profile [7].

How to Incorporate Available Therapies

A clinical trial is preferred in patients with MF-related anemia and no symptomatic splenomegaly or constitutional symptoms. Other recommended regimens in these patients are ESAs (if serum EPO <500 mU/mL), luspatercept-aamt or danazol, pacritinib (category 2B) and momelotinib (category 2B). Lenalidomide with prednisone is recommended for del (5q) (category 2B) in certain circumstances [8]. Enrollment in a clinical trial is preferred in patients with MF-related anemia, splenomegaly and constitutional symptoms well controlled on a current JAK inhibitor. Other recommended regimens are ESAs (if serum EPO <500 mU/mL), luspatercept-aamt or danazolb (category 2B) added to JAK inhibitors [8]. Enrollment in a clinical trial and momelotinib are the preferred regimens in patients with MF-related anemia and ongoing symptomatic splenomegaly and / or constitutional symptoms [8].

Future Therapies

A major limitation in understanding the efficacy of these drugs is the different definitions of transfusion dependence and anemia response that have been applied in different studies [5]. The International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European Leukemia Net in 2013 defined transfusion dependence as a transfusion requirement of ≥ 6 RBC units in the 12 weeks prior to study enrollment, for an Hb level less than 8.5 g/dl, in the absence of any bleeding or treatment-induced anemia, and the latest transfusion was within 28 days of study enrollment. Transfusion independence is defined as the absence of RBC transfusion during any consecutive 12-week interval during treatment (in a study) while maintaining Hb level more than 8.5 g/dl. Regarding treatment response, anemia response in transfusion-dependent patients is defined as the achievement of transfusion independence, whereas anemia response in transfusion-independent patients is defined as an increase in Hb of ≥ 2 g/dl [2].

Treatments on the Horizon

- **Luspatercept and Elritercept**

Luspatercept and elritercept function as activin receptor ligand traps that promote erythroid maturation and late-stage erythropoiesis. Luspatercept binds to select transforming growth factor β superfamily ligand and target the pathogenetic bone morphogenetic protein-SMAD signaling pathway. It improves hemoglobin and transfusion dependence in MF [5]. Currently, luspatercept is under evaluation in a phase 3 trial (INDEPENDENCE™) for anemia in MF patients who are on a JAK2 inhibitor and require transfusions, as well as in a phase 2 trial (ODYSSEY) in combination with momelotinib in transfusion dependent MF patients, whether or not on a JAK inhibitor [6]. Interim results from the RESTORE trial demonstrated that elritercept significantly decreased transfusion requirements in MF patients [6].

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• DISC-0974

A first-in-class anti-hemojuvelin monoclonal antibody (positive regulator of hepcidin) that has been shown to lower hepcidin expression, increase serum iron, and enhance erythropoiesis in anemic MF patients as observed in a phase 1b/2 study [6].

- A phase 3 trial evaluating the BET (bromodomain and extra-terminal domain) inhibitor pelabresib in combination with ruxolitinib showed that this regimen can decrease bone marrow fibrosis and inflammatory cytokines.

- A phase 3 trial investigates the addition of the p53 modulator navtemadlin in patients with a suboptimal response to ruxolitinib. Findings suggest that this therapy may improve hematopoiesis and improve bone marrow function by reducing bone marrow inflammation.

- A phase 1 trial explores the use of monoclonal antibodies that specifically target and deactivate the mutated CALR receptor [4].

Conclusion

Anemia in myelofibrosis represents a multifaceted clinical challenge that significantly affects patient outcomes. While conventional therapies provide partial relief, novel targeted approaches are reshaping the therapeutic landscape. Future research has to focus on integrating novel agents into treatment algorithms to improve both survival and quality of life in MF patients.

References

1. Al-Ali HK, Kuykendall AT, Ellis CE, Sampath J, Mesa R (2024) Anemia in myelofibrosis: a focus on proactive management and the role of momelotinib. Cancers 16(23): 4064.
2. Passamonti F, Harrison CN, Mesa RA, Kiladjian J-J, Vannucchi AM, et al. (2022) Anemia in myelofibrosis: current and emerging treatment options Critical Reviews in Oncology / Hematology 180: 103862.
3. Teichman LL, Grigolon RB, Lima J, Abreu GA, Kim N, et al. (2024) Country-specific guidelines on anemia management for patients with myelofibrosis in Latin America, the Middle East, and East Asia: a systematic literature review. Blood 144: 7648-7649.
4. Consult QD (2025) Personalizing treatment of myelofibrosis-associated anemia. Combination therapy may help address underlying disease. Cleveland Clinic, USA.
5. Ashish B (2024) Anemia response in myelofibrosis revisited. Blood 144(17): 1759-1760.
6. Chifotides HT, Duminuco A, Torre E, Vetro C, Harrington P, et al. (2025) Emerging therapeutic approaches for anemia in myelofibrosis. Curr Hematol Malig Rep 20(1): 7.
7. Pérez-Lamas L, Diaz AS, Delgado RG, Alvarez-Larran A, Senin MA, et al. (2024) Real-world outcomes of momelotinib as an alternative therapy to other JAK inhibitors in myelofibrosis patients with anemia. Blood 144: 1790-1792.
8. NCCN.org (2025) National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology. Myeloproliferative neoplasms. NCCN Evidence Blocks, USA.

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