Managing Myelofibrosis-Associated Anemia

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Current Guideline Updates for MF-Associated Anemia[1]

Presence of symptomatic splenomegaly and/or constitutional symptoms

Controlled on a JAKi

Preferred	Other Recommended Regimens	Useful in Certain Circumstances
• Clinical Trial	• Ruxolitinib combination ➢ Add luspatercept ➢ Add ESA (if serum EPO <500 mU/mL) ➢ Danazol (Category 2B)	• Change to momelotinib • Change to pacritinib

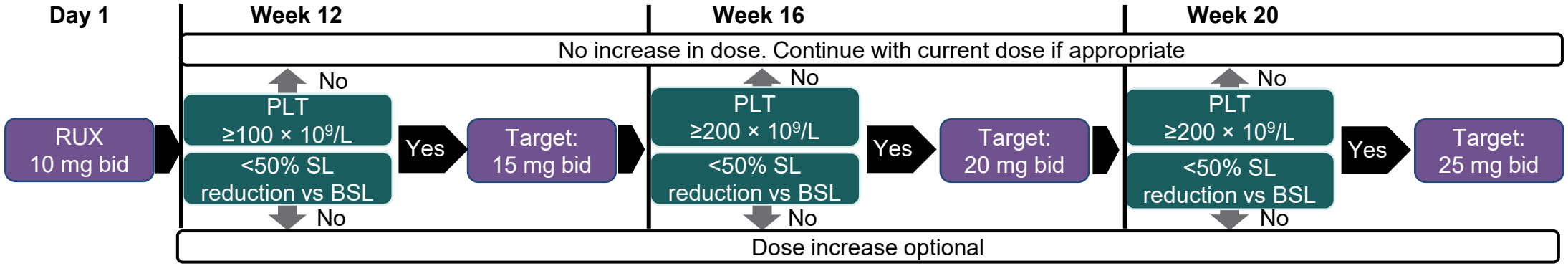
Not Controlled

Preferred	Other Recommended Regimens
• Clinical Trial • Momelotinib	• Pacritinib • Ruxolitinib combination ➢ Luspatercept ➢ ESAs (if serum EPO <500 mU/mL) ➢ Danazol (category 2B)

EPO, erythropoietin; ESA, erythropoiesis-stimulating agent; JAKi, Janus-associated kinase inhibitor.

1. Gerds AT, et al. NCCN Guidelines. Myeloproliferative Neoplasms (Version 1.2024). NCCN.org.

Ruxolitinb[a] Dosing Strategy Based on Spleen Length Reduction, PLT Counts, and Efficacy



Parameters

- Patients with ANC >0.5 × 10^9/L and Hb ≥6.5 g/dL were eligible for dose increases
- Dose increases were optional for those patients who achieved ≥50% reduction in SL from BL
- Patients received study treatment for as long as it was beneficial, up to 48 weeks after the last patient's first treatment

56% (28/50) of patients met the primary endpoint of a ≥50% reduction in SL by week 24

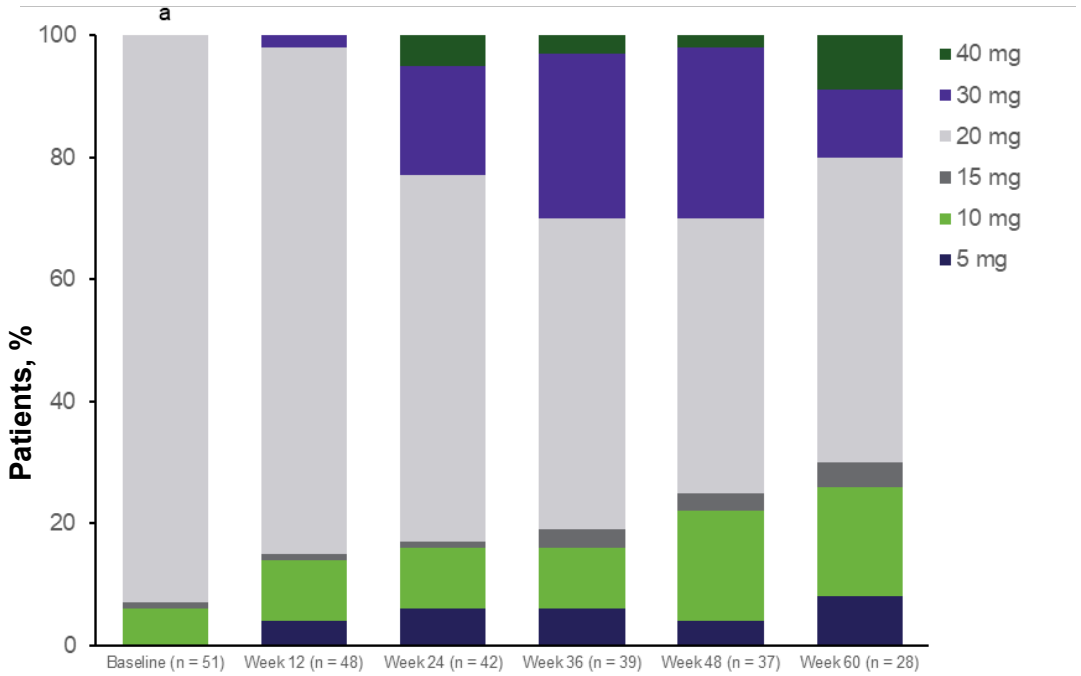
- Of the patients who were TD at baseline, 67% (6/9) had a ≥50% reduction in SL by week 24

ANC, absolute neutrophil count; bid, twice daily; BL, baseline; BSL, baseline spleen length; Hb, hemoglobin; JAK, Janus-associated kinase; LCM, left costal margin; MF, myelofibrosis; PLT, platelet; RUX, ruxolitinib; SL, spleen length; TD, transfusion dependent. [a] REALISE was an open-label, single-arm, phase 2 study to evaluate the efficacy and safety of a novel dosing strategy of ruxolitinib in adult patients with MF and anemia. Patients were required to have a palpable spleen (≥5 cm below LCM), peripheral blood blast <10%, and a Hb level <10 g/dL. Exclusion criteria included prior treatment with any JAK1 or JAK2 inhibitor, Inadequate bone marrow reserve at BL visit,[b] and a history of malignancy in the past 3 years, except for treated early-stage squamous or basal cell carcinoma. The primary endpoint was ≥50% reduction in SL at week 24.
[b] As demonstrated by at least one of the following: ANC ≤1 × 10^9/L, platelet count <50 × 10^9/L, and Hb ≤6.5 g/dL despite transfusions.

Cervantes F, et al. *Leukemia*. 2021;35(12):3455-3465.

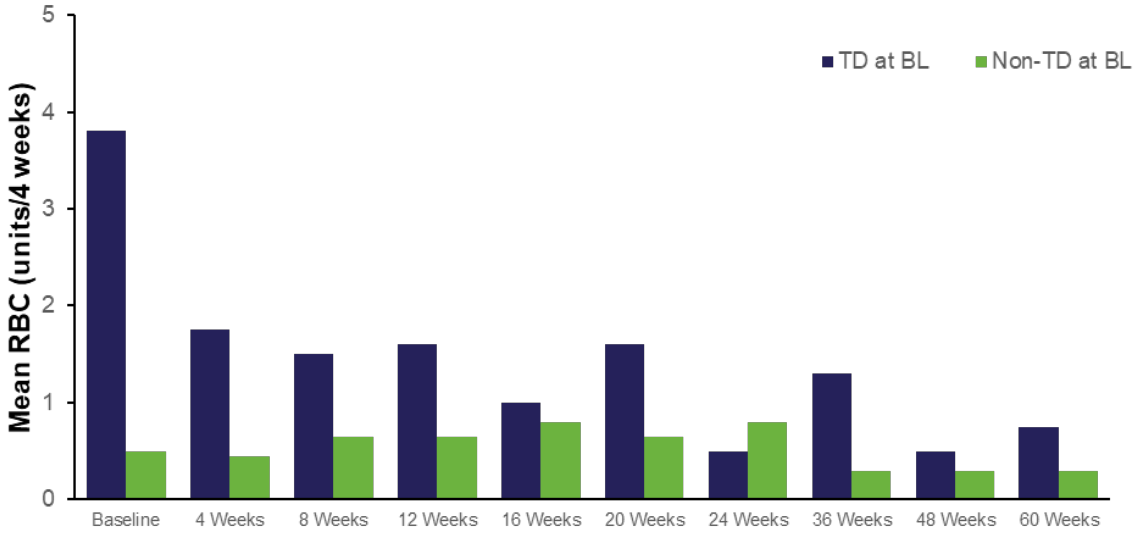
Changes in Ruxolitinib Dosing and Transfusion Requirements

Total Daily Dose of RUX Over Time



- By week 24, 26.2% (11/42 patients) received a total daily dose of ≥30 mg, and by week 48, 32.4% (12/37) patients with dose data received daily doses ≥30 mg

Transfusion Requirement Over Time



The requirements for RBC transfusions (units/4 weeks):

- Decreased for TD patients
- Remained at similar levels for non-TD patients

BL, baseline; RBC, red blood cell; RUX, ruxolitinib; TD, transfusion dependent.

[a] Three patients started the study at 10 mg. Two of these were dosing errors that were corrected within 5 and 6 days. The third was a physician decision for a patient who did not continue with the next phase of the study.

Cervantes F et al. *Leukemia*. 2021;35(12):3455-3465.

Adverse Events With a Reduced Starting Dose With Delayed Up-Titration With Ruxolitinib in Anemic Patients With MF

Adverse Events Occurring in ≥5% of Patients by MedDRA Preferred Term

MedDRA Preferred Term	All Grades, n (%)	Grade ≥3, n (%)
Anemia	18 (35.3)	16 (31.4)
Thrombocytopenia	15 (29.4)	10 (19.6)
γ-glutamyltransferase increase	6 (11.8)	2 (3.9)
Asthenia	6 (11.8)	1 (2.0)
Diarrhea	6 (11.8)	0 (0.0)
ALT/AST increase	5 (9.8)	0 (0.0)
Fatigue	5 (9.8)	0 (0.0)
Urinary tract infection	5 (9.8)	0 (0.0)

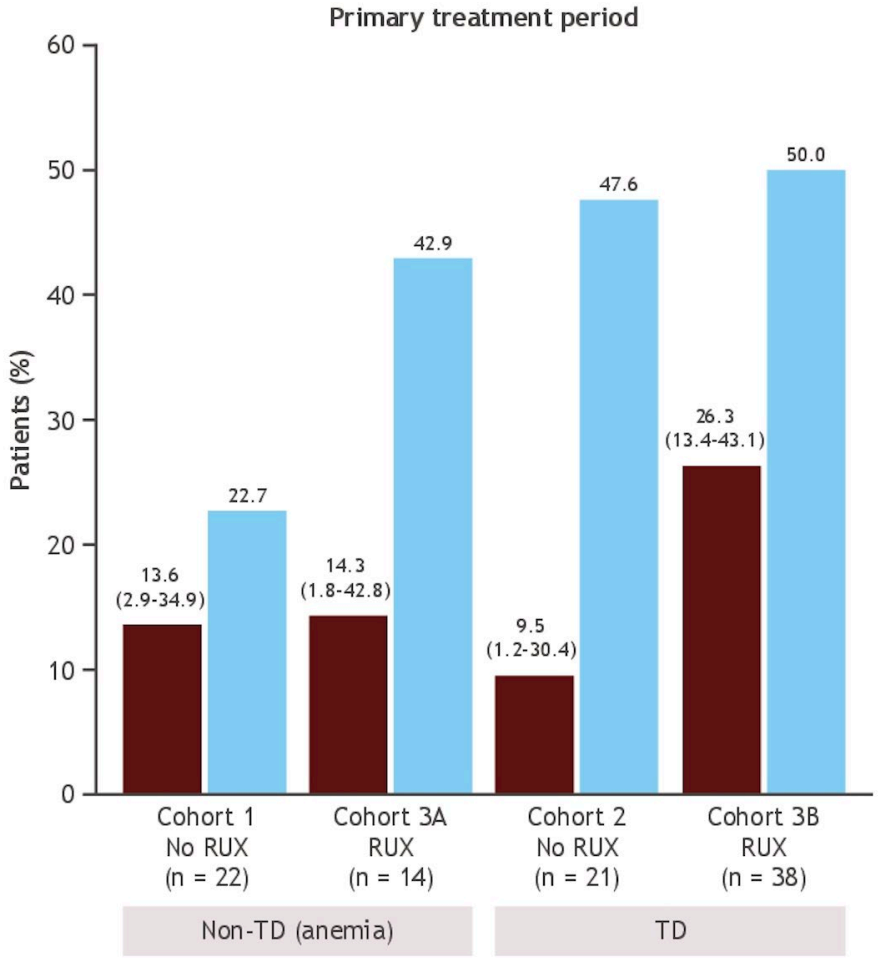
ALT, alanine transaminase; AST, aspartate transaminase; MedDRA, Medical Dictionary for Regulatory Activities.

Cervantes F et al. *Leukemia.* 2021;25(12):3455-3465.

Luspatercept Shows Efficacy in the Setting of MF-Induced Anemia

- Phase 2 trial assessing erythroid maturation agent luspatercept in patients with MF-associated anemia ± transfusion dependence[1]
- Safety profile of luspatercept consistent with previous studies
- Treatment with luspatercept induced improvements in anemia and transfusion burden in all cohorts

Use of luspatercept for MF-induced anemia in patients with transfusion dependence on JAK2i therapy is being assessed in the phase 3 INDEPENDENCE study[2]



1. Gerds AT, et al. ASCO 2023. Abstract 7016. 2. ClinicalTrials.gov identifier: NCT04717414.

Summary

- Pacritinib and momelotinib can improve hemoglobin in patients with myelofibrosis
- To mitigate anemia with ruxolitinib:
  - Start with a low dose and escalate to the maximal tolerated dose, or
  - Add additional anemia-specific agents
    - ESA
    - Luspatercept
    - Danazol