

How and When to Manage Ruxolitinib Failure

John Mascarenhas, MD

Professor of Medicine

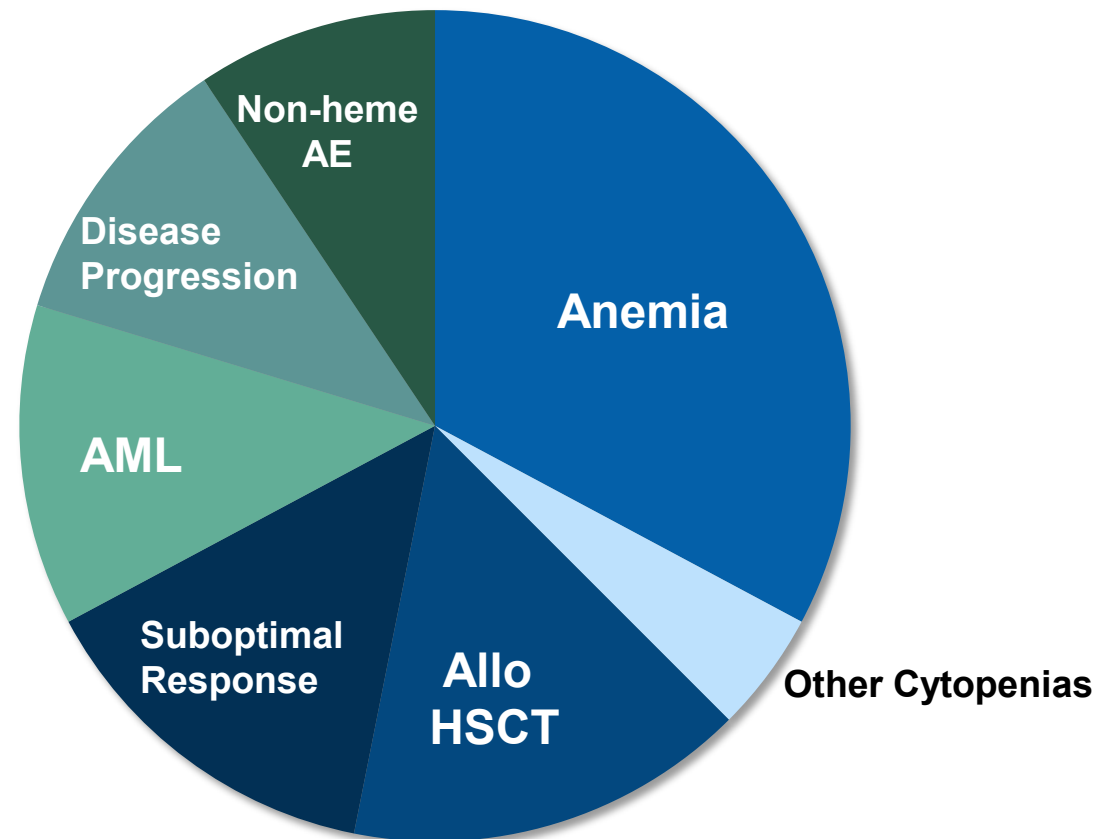
Icahn School of Medicine at Mount Sinai

New York, NY



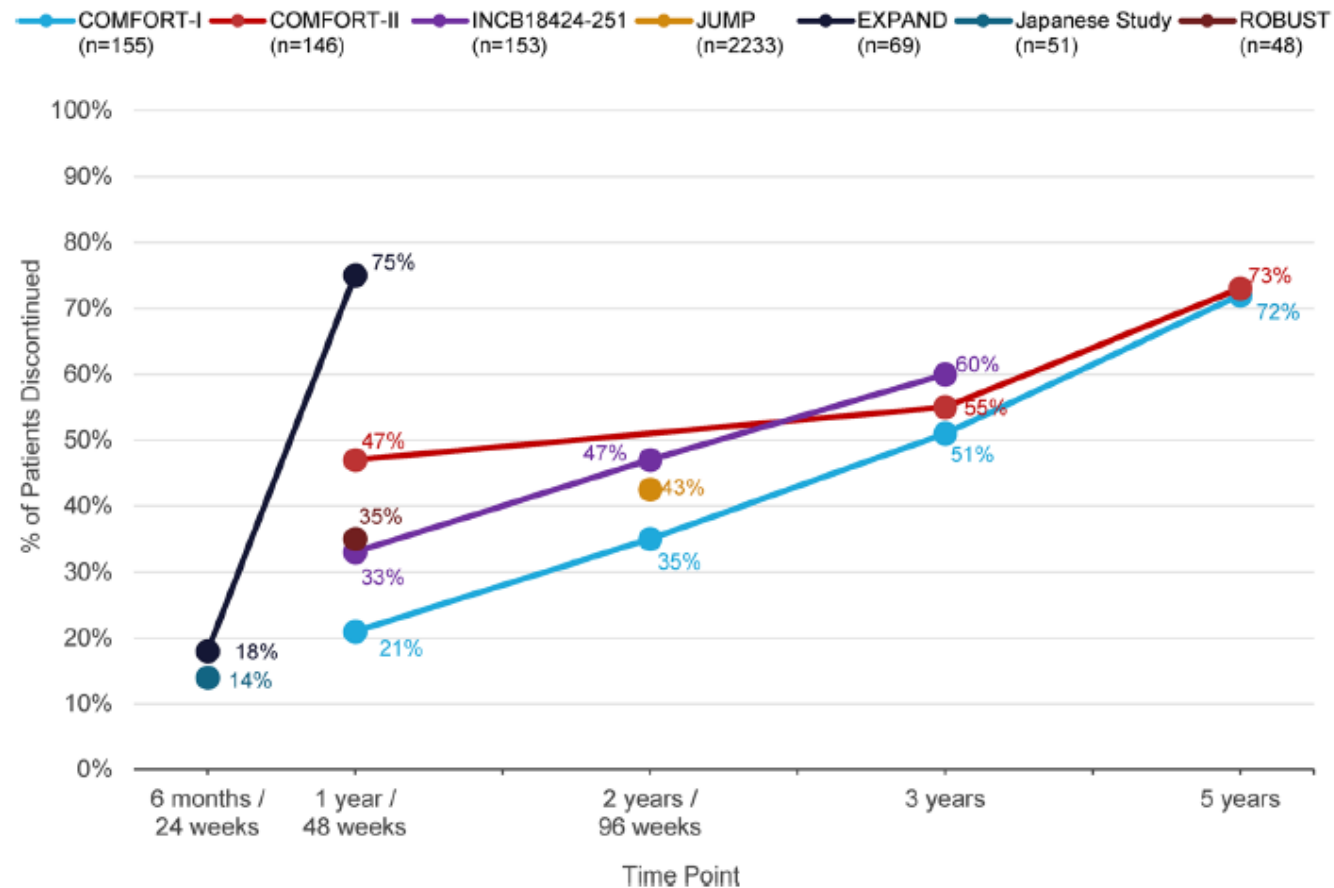
Reasons for Stopping Ruxolitinib

Anemia appears to be the leading cause of ruxolitinib discontinuations



AE, adverse event; Allo HSCT, allogeneic hematopoietic stem-cell transplant; AML, acute myeloid leukemia.
Kuykendall AT, et al. *Ann Hematol.* 2018;97(3):435-441.

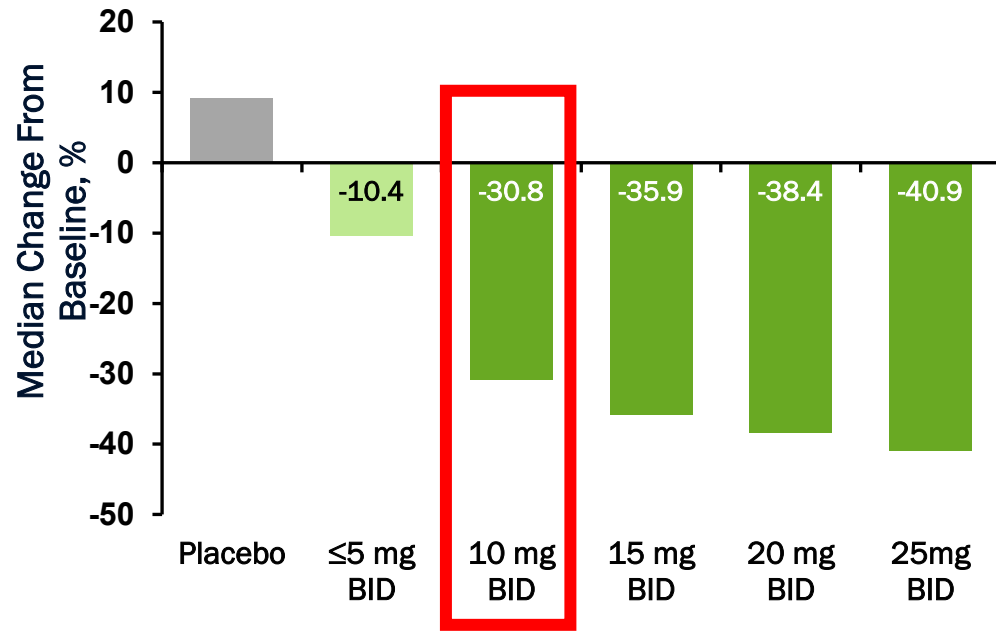
Rates of Ruxolitinib Treatment Discontinuation at Various Time Points in Large Clinical Trials



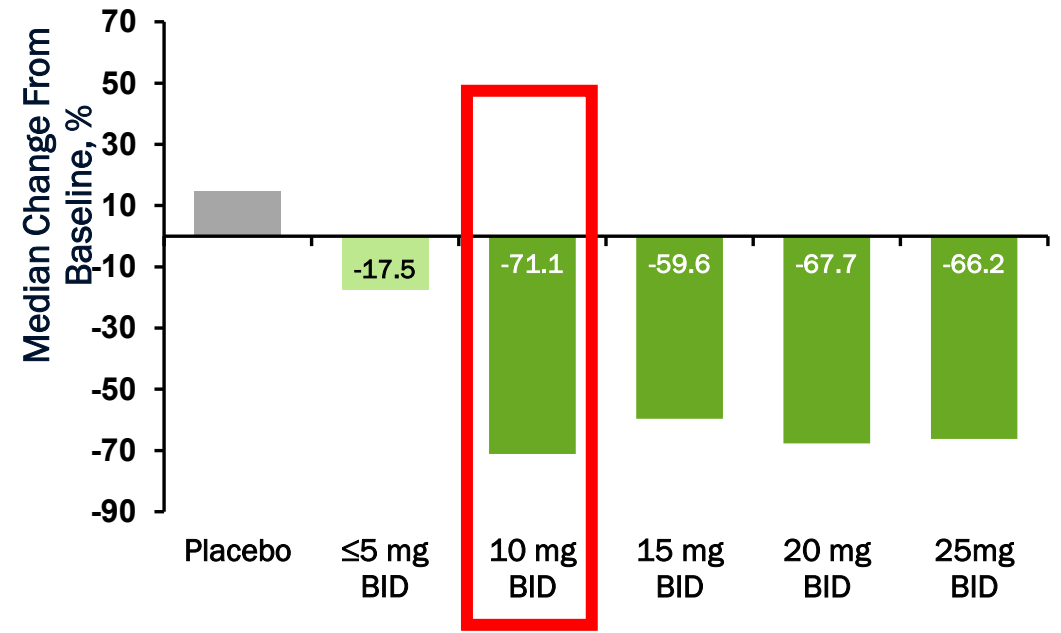
COMFORT-I: Spleen Volume and Symptom Scores

- Limited change from baseline in spleen volume and TSS with low-dose ruxolitinib^{1*}
- Long-term maintenance with low-dose ruxolitinib has not shown responses in patients with myelofibrosis²

Spleen Volume at Week 24 by Ruxolitinib Dose¹



TSS at Week 24 by Ruxolitinib Dose²



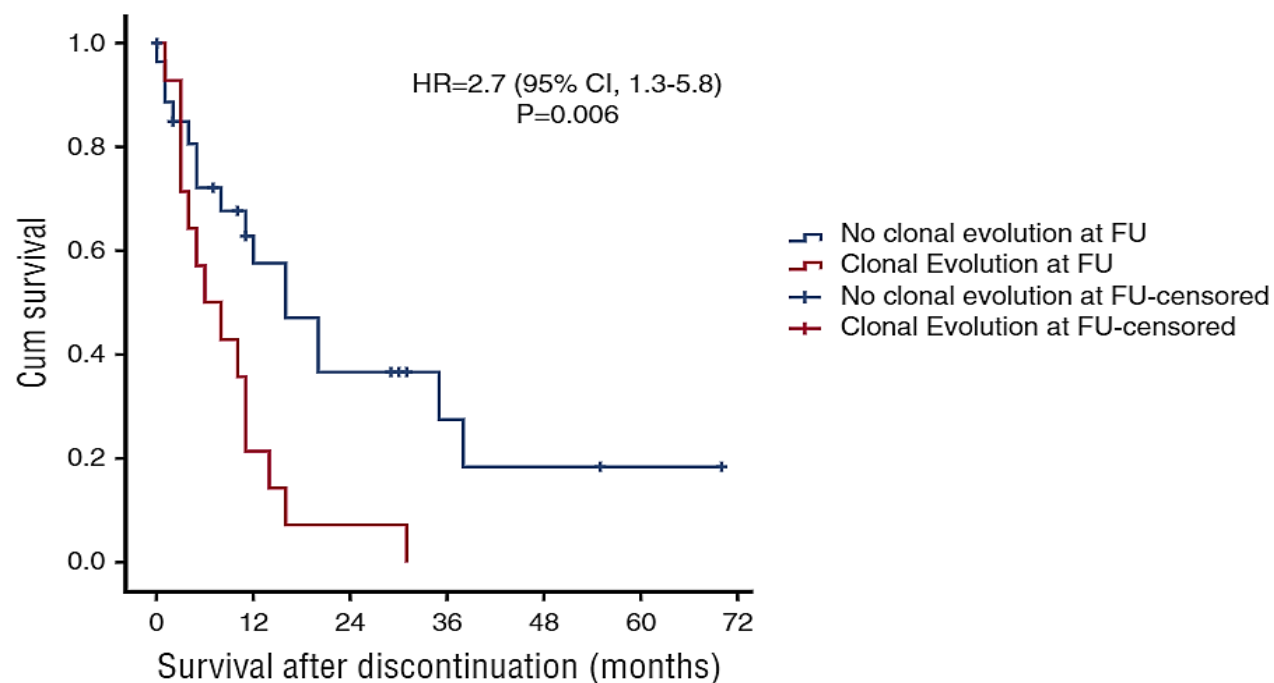
* ≤ 5 mg twice daily.

BID, twice daily; TSS, total symptom score.

1. Verstovsek S, et al. *Onco Targets Ther.* 2013;7:13-21. 2. Ruxolitinib. Prescribing information; 2021.

Outcomes After Ruxolitinib Discontinuation

- Retrospective analysis of clonal evolution and outcomes after ruxolitinib discontinuation in an open-label phase 1/2 study (N = 56)

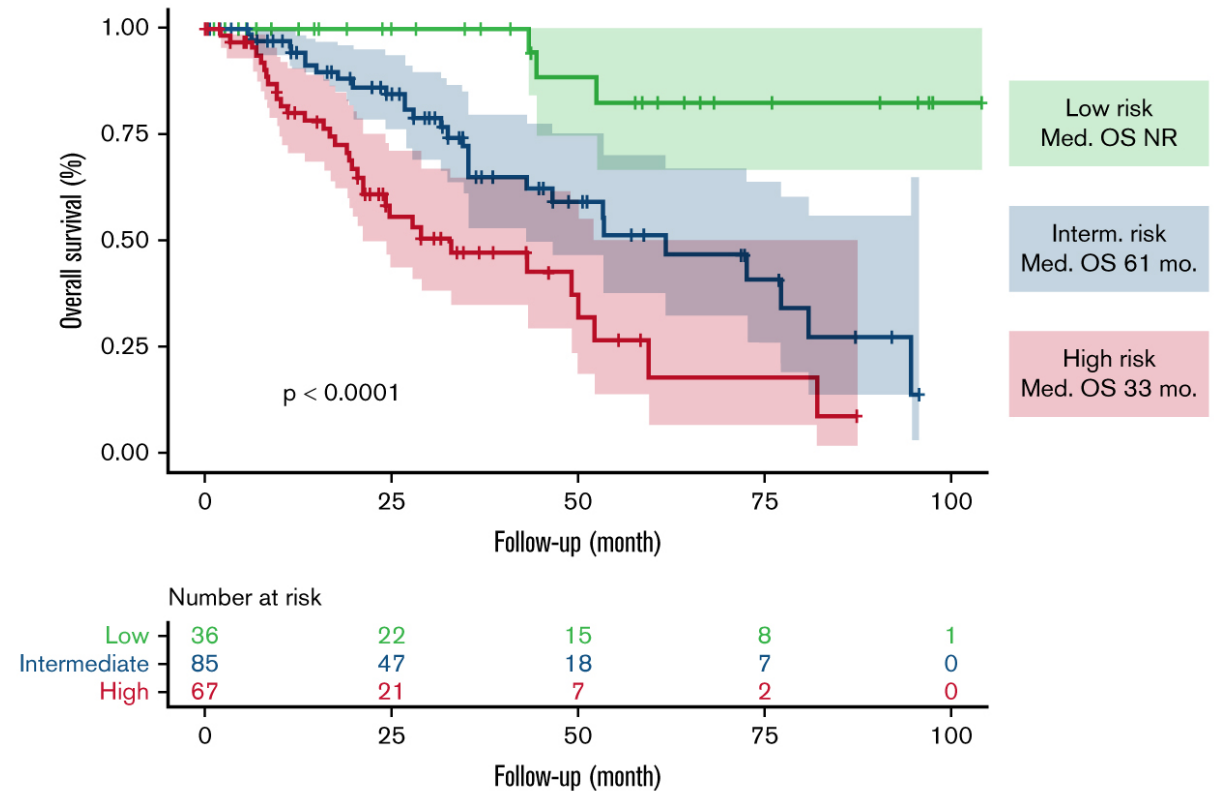
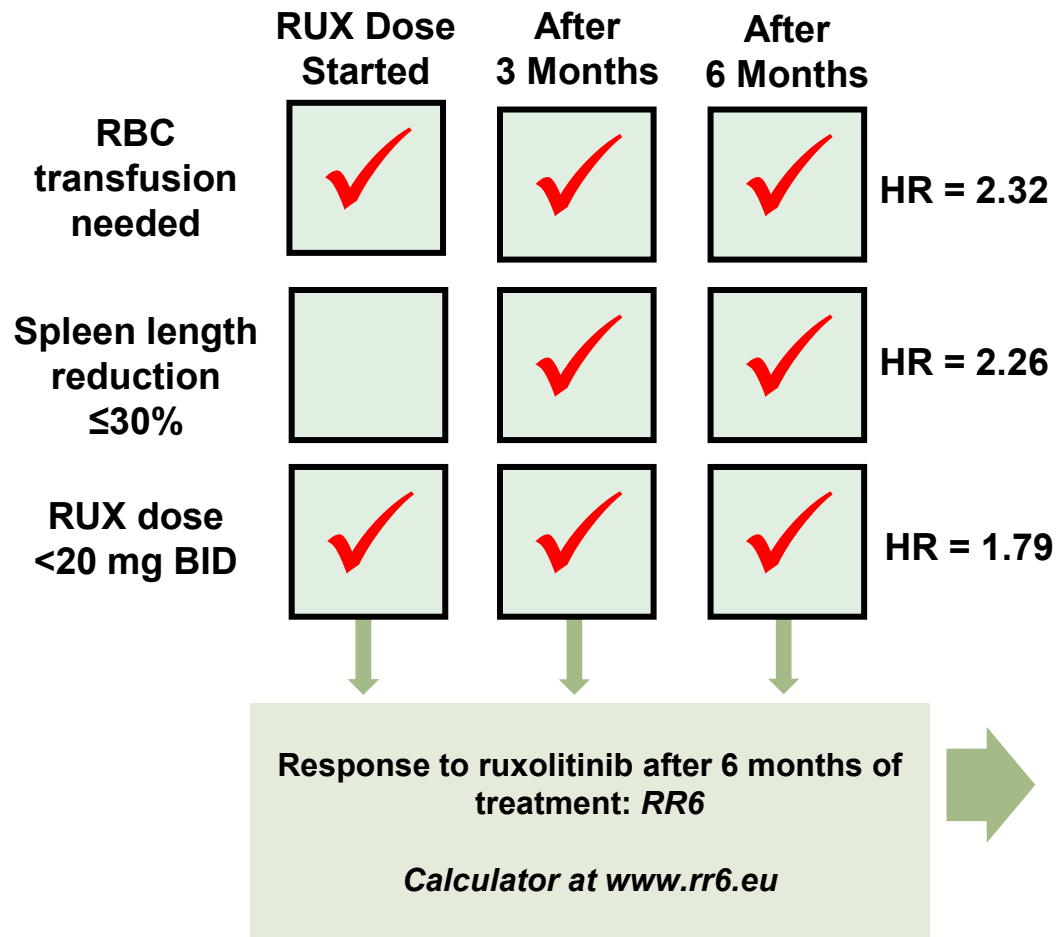


- Median OS = 14 mo
- Survival improved if baseline platelets ≥ 260 vs $< 260 \times 10^9/L$ (HR = 2.7; P = 0.006)
- Survival improved if follow-up platelets ≥ 100 vs $< 100 \times 10^9/L$ (HR = 4.1; P = 0.001)
- 35% of patients acquired a new mutation while on ruxolitinib, most commonly *ASXL1*

Hashed lines = censored.

Newberry KJ, et al. *Blood*. 2017;130(9):1125-1131.

RR6 Model: 3 Factors Predict Survival Benefit



The RR6 model was validated in another cohort of patients ($n = 40$; $P = 0.0276$) treated with ruxolitinib at Moffitt Cancer Center.

Summary

- Anemia is one of the leading causes for discontinuing ruxolitinib
- Dose of ruxolitinib matters
 - Higher doses lead to better spleen reduction and better outcomes
- Patient outcomes are generally poor when ruxolitinib is discontinued
- RR6 model can be used to predict survival when used within the first 6 months of ruxolitinib treatment