

Comparative Efficacy, Hematologic Safety, and Treatment Persistence of FDA-Approved Janus Kinase Inhibitors in Myelofibrosis: Integrating the 2026 Approval of Once-Daily Ruxolitinib XR – A Systematic Review and Bayesian Network Meta-Analysis

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INTRODUCTION

The therapeutic landscape of myelofibrosis (MF) has evolved rapidly following approvals of multiple Janus kinase inhibitors (JAKi), including once-daily ruxolitinib extended-release (XR) in 2026. However, direct comparative trials among approved JAKi remain limited, complicating evidence-based treatment selection across distinct clinical phenotypes including anemia and thrombocytopenia.

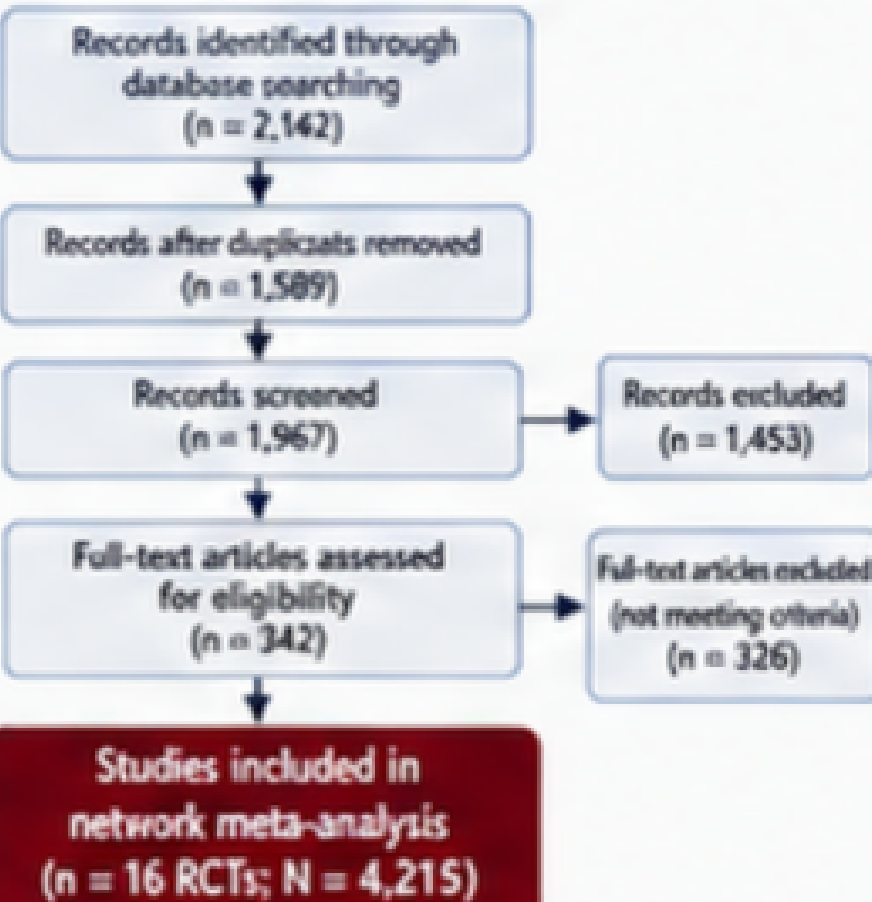
OBJECTIVE

To compare the efficacy, hematologic safety, and treatment persistence of FDA-approved JAK inhibitors in myelofibrosis using a Bayesian network meta-analysis, incorporating once-daily ruxolitinib XR approved in 2026.

METHODS

- Databases:** PubMed, Embase, Cochrane CENTRAL, ClinicalTrials.gov
- Study design:** Systematic review and Bayesian network meta-analysis of Phase II/III RCTs
- Population:** Adults with primary or secondary myelofibrosis
- Interventions:** FDA-approved JAK inhibitors (ruxolitinib IR/XR, fedratinib, momelotinib, pacritinib)
- Outcomes:** SVR35 at Week 24, TSS50, Grade ≥ 3 anemia, thrombocytopenia, treatment persistence
- Follow-up:** 24–72 weeks
- Statistical analysis:** Bayesian NMA using netmeta package in R
- Risk of bias:** RoB 2.0 tool across included studies

STUDY FLOW DIAGRAM



STUDY & PATIENT CHARACTERISTICS

Baseline Characteristics (N = 4,215)

Median age, years (range)	67 (35–86)
Male, n (%)	2,443 (58%)
PMF / Post-PV / Post-ET, n (%)	2,676 (63%) / 987 (23%) / 556 (13%)
DIPSS risk: Intermediate-2 / High, n (%)	2,995 (71%)
Median follow-up, weeks (range)	48 (24–72)
Median spleen volume, mL (range)	1,650 (900–3,800)

Included Randomized Controlled Trials (n = 16)

JAK Inhibitor	No. of RCTs	Patients (n)
Ruxolitinib IR/XR	6	1,826
Fedratinib	4	1,042
Momelotinib	4	896
Pacritinib	2	451
Total	16	4,215

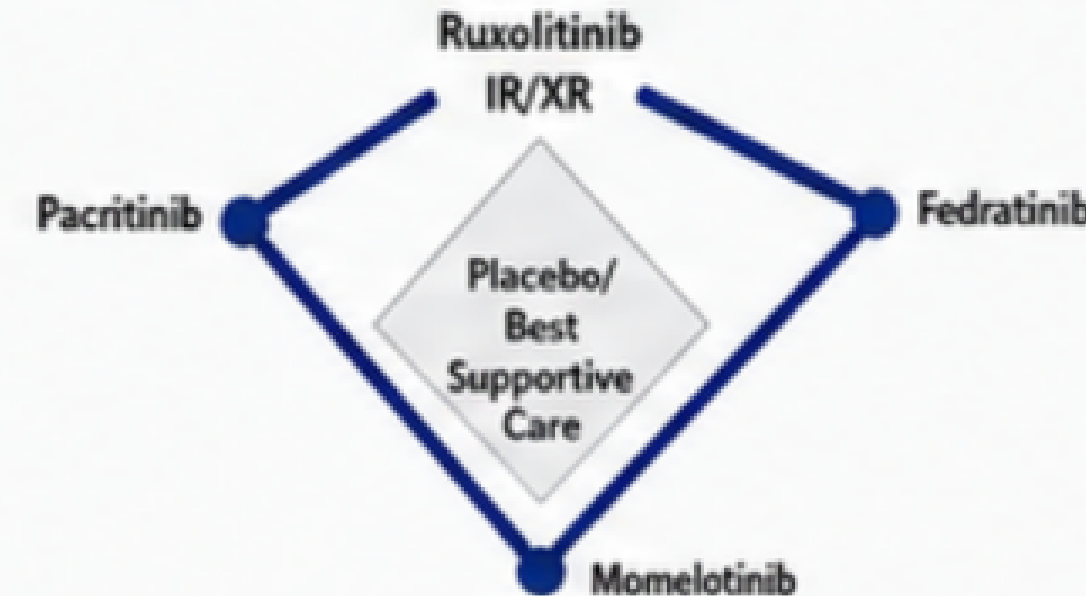
RISK OF BIAS (RoB 2.0)

Summary of Risk of Bias Across 16 RCTs

D1 Randomization Process	D2 Deviations from Intended Interventions	D3 Missing Outcome Data	D4 Measurement of the Outcome	D5 Selection of Reported Result	Overall Risk of Bias
Low risk	Low risk	Some concerns	Low risk	Low risk	Low risk

NETWORK GEOMETRY

Evidence Network for Efficacy Outcomes

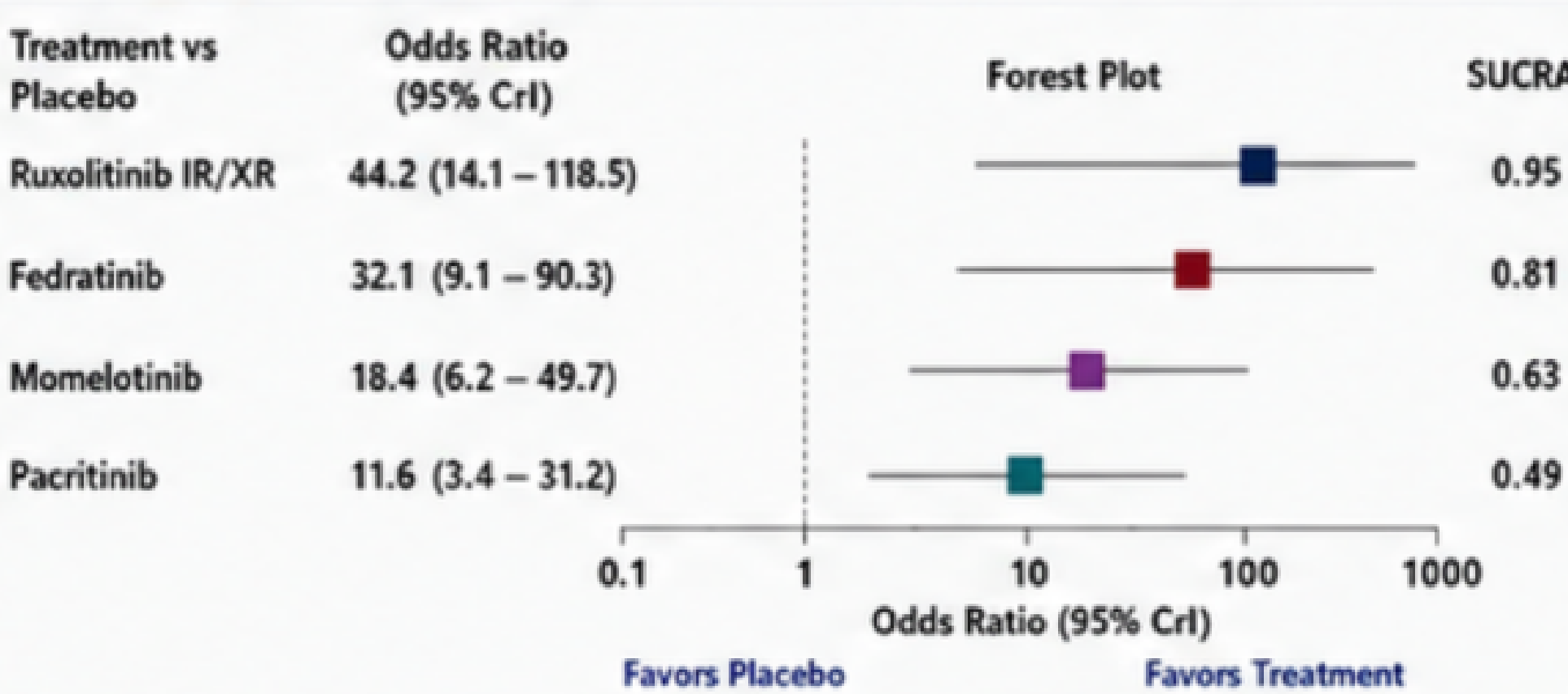


SUCRA RANKINGS (Higher is better)

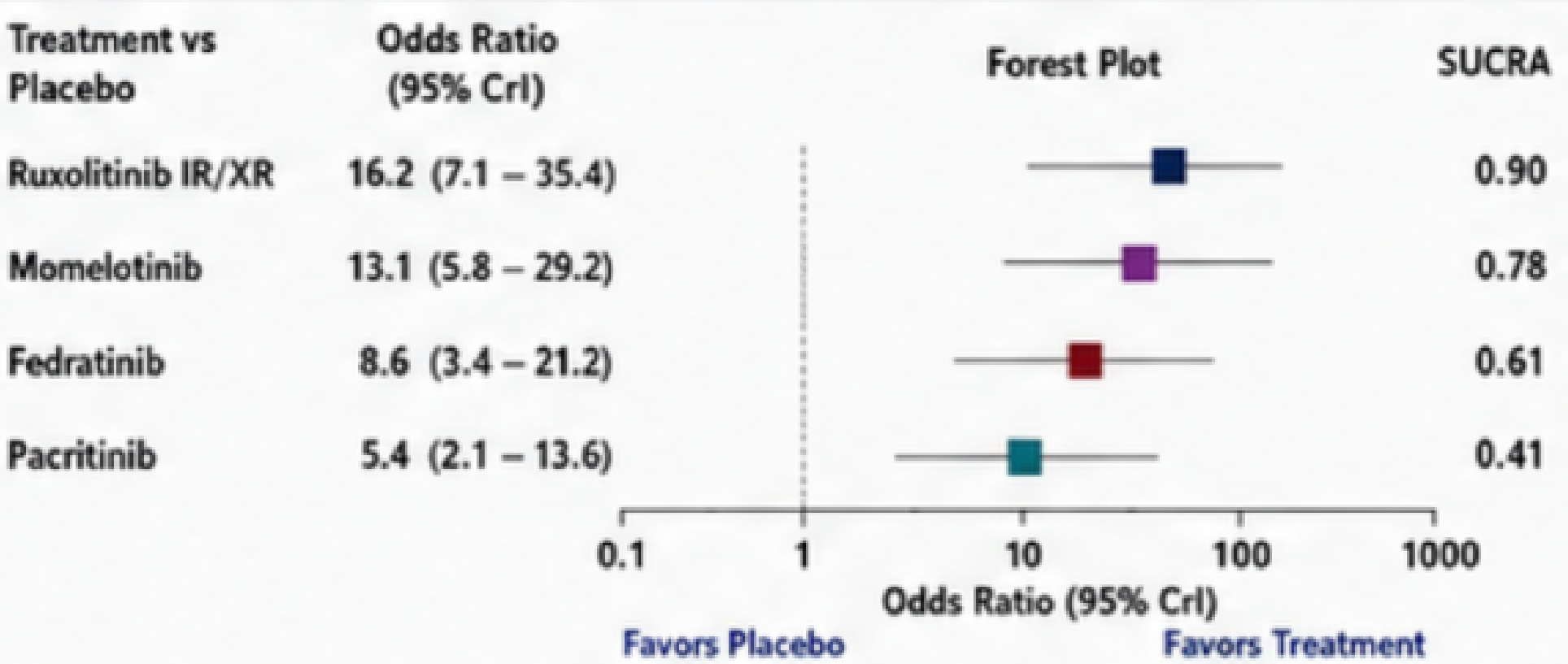
SVR35 at Week 24		TSS50	
Ruxolitinib IR/XR	0.95	Treattinitib IR/XR	0.90
Fedratinib	0.81	Momelotinib	0.78
Momelotinib	0.63	Fedratinib	0.61
Pacritinib	0.49	Pacritinib	0.41

RESULTS

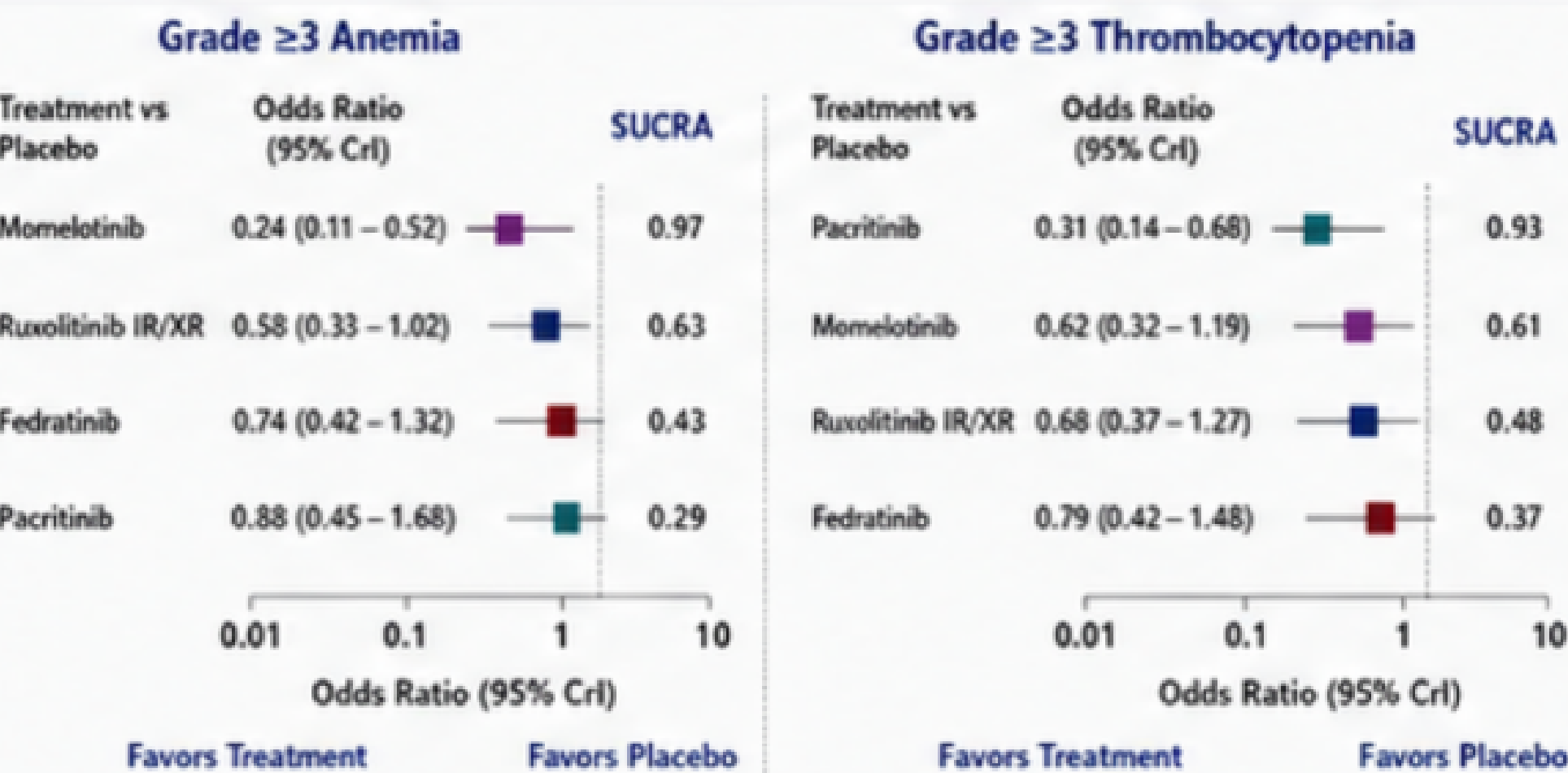
PRIMARY EFFICACY: Spleen Volume Reduction $\geq 35\%$ (SVR35) at Week 24



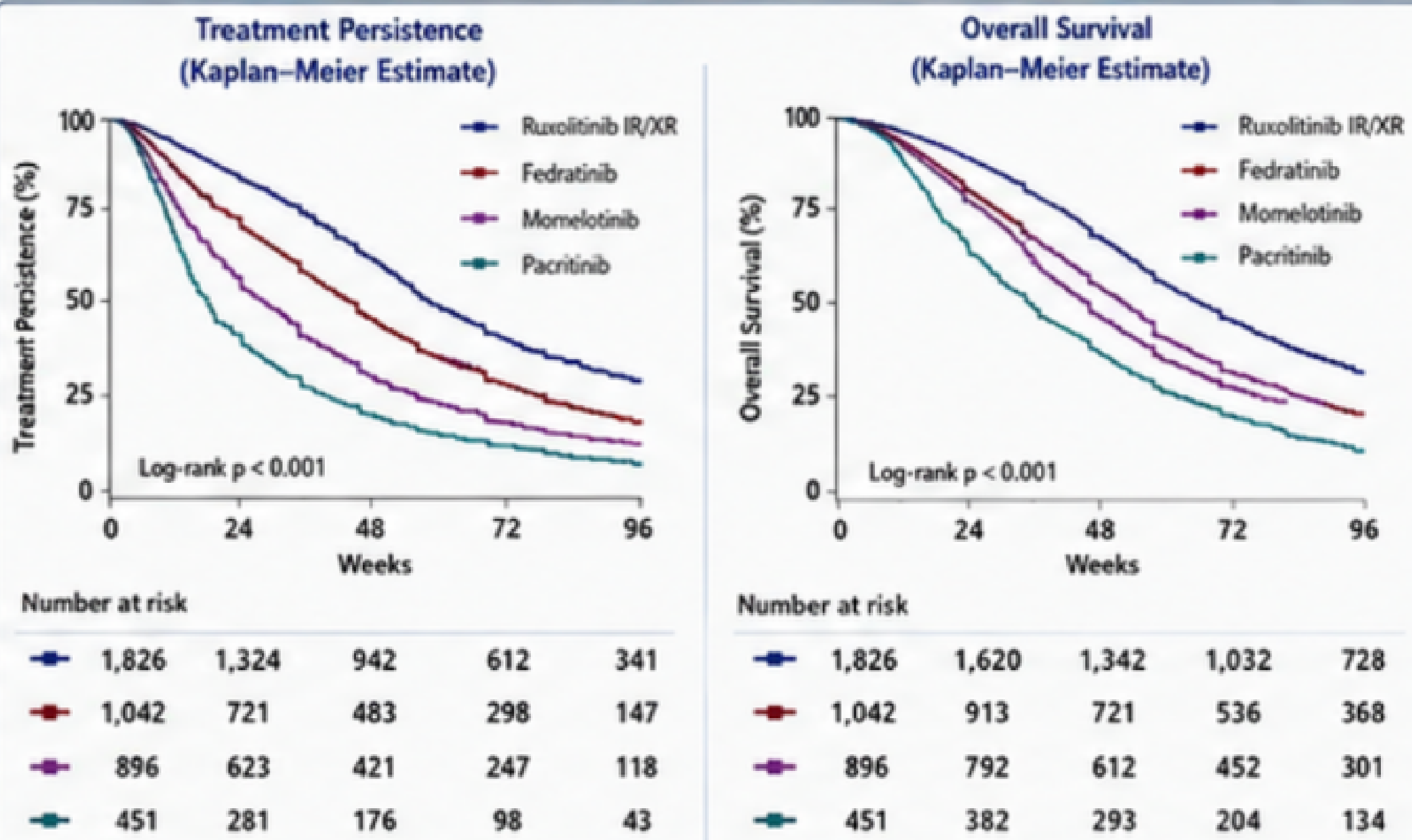
SYMPTOM RESPONSE: Total Symptom Score Reduction $\geq 50\%$ (TSS50)



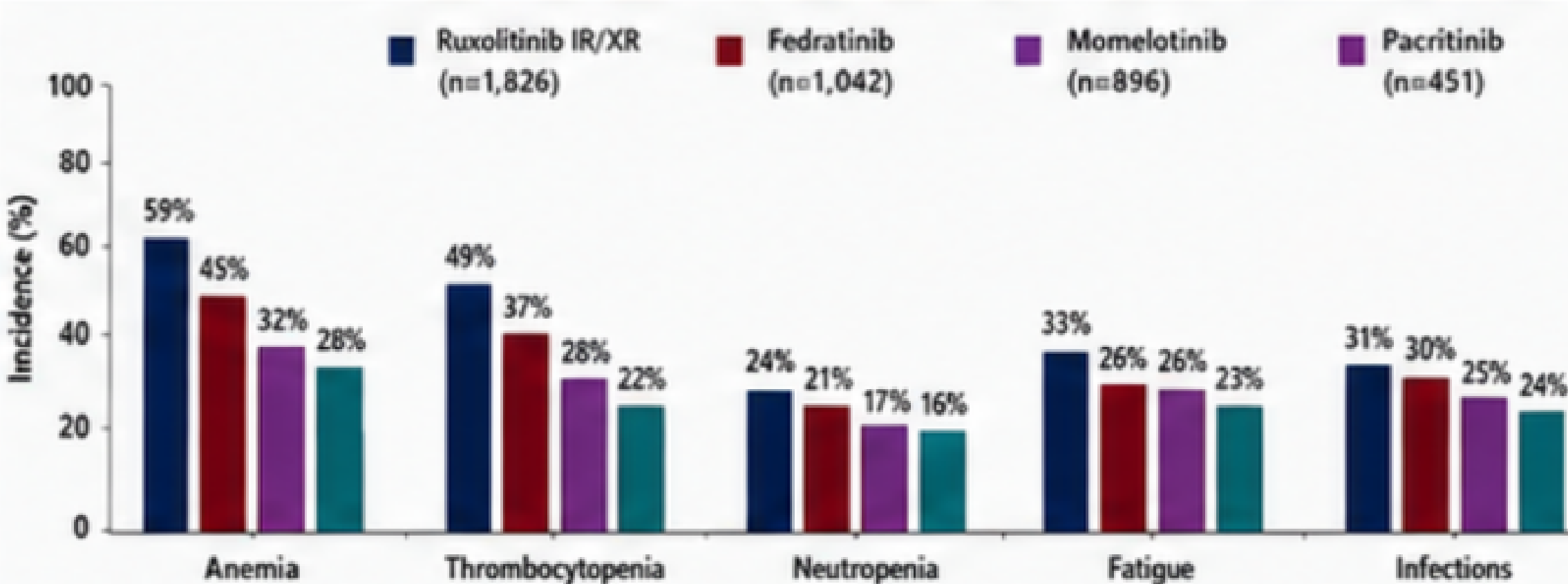
HEMATOLOGIC SAFETY (Grade ≥ 3 Adverse Events)



TREATMENT PERSISTENCE / SURVIVAL



TREATMENT-EMERGENT ADVERSE EVENTS (All Grades)



CONCLUSION

Ruxolitinib XR maintained superior efficacy and treatment persistence, while momelotinib and pacritinib demonstrated phenotype-specific safety advantages, supporting a personalized therapeutic approach in myelofibrosis, with overall low risk of bias across included trials using RoB 2.0.



CrI = Credible Interval; SUCRA = Surface Under the Cumulative Ranking Curve