Comparative Efficacy of Drug Therapies on Spleen Size and Symptom Reduction in Myelofibrosis: A Frequentist Network Meta-analysis

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INTRODUCTION

The therapeutic landscape of myelofibrosis (MF) has rapidly evolved with the development of novel JAK inhibitors and combination strategies. However, direct head-to-head comparisons among available and emerging therapies remain limited in JAK inhibitor–naïve and ruxolitinib-exposed patients. We performed a frequentist network meta-analysis (NMA) to compare spleen volume reduction ≥35% (SVR35) and total symptom reduction ≥50% (TSS50) among contemporary therapies.

AIM

- Compare contemporary MF therapies for SVR35.
- Compare total symptom score reduction ≥50% (TSS50).
- Use ruxolitinib as the reference in JAK inhibitor–naïve disease.
- Use best available therapy (BAT) as the reference after prior ruxolitinib exposure

METHOD

- PubMed and Embase search for randomized clinical trials from 2010–2026.
- JAK inhibitor–naïve: 10 RCTs; N=2,692.
- Prior ruxolitinib exposure: 5 RCTs; N=830.
- Active agents, placebo, and supportive care were eligible.
- Frequentist NMA performed in R using the netmeta package.
- Effects reported as odds ratios (ORs) with 95% confidence intervals.

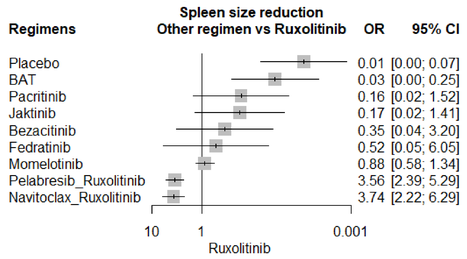
CONCLUSIONS

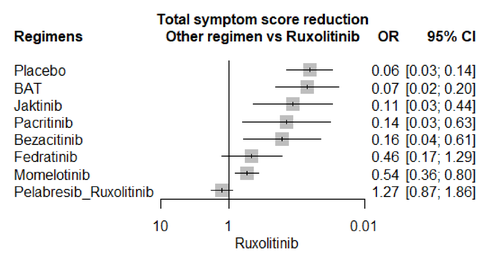
- Navitoclax + ruxolitinib and pelabresib + ruxolitinib showed the greatest spleen responses in JAK inhibitor–naïve MF.
- Ruxolitinib remained similar or superior to single-agent JAK inhibitors for spleen or symptom response.
- After prior ruxolitinib exposure, fedratinib, momelotinib, and pacritinib showed clinically meaningful activity versus BAT.
- Fedratinib was numerically the strongest option for SVR35 versus BAT.

RESULTS

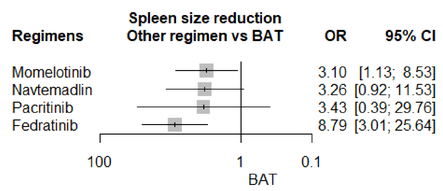
Compared with ruxolitinib alone, combination strategies demonstrated the highest probability of achieving SVR35 with an odds ratio (OR) of 3.74 (95%CI:2.22–6.29) with Navitoclax +ruxolitinib and 3.56 (95%CI:2.39–5.29) with pelabresib +ruxolitinib. Single-agent JAK inhibitors demonstrated variable efficacy similar to or worse than ruxolitinib with OR of 0.88 (95%CI:0.58–1.34) with momelotinib, 0.52 (95%CI:0.05–6.05) with fedratinib, 0.35 (95%CI:0.04–3.20) with bezacitinib, 0.17 (95%CI:0.02–1.41) jaktinib, and 0.16 (95%CI:0.02–1.52) with pacritinib. For TSS50, pelabresib plus ruxolitinib showed numerically improved symptom responses versus ruxolitinib with OR of 1.27 (95% CI 0.87–1.86). Placebo and BAT (best available therapy other than JAK inhibitors) arms consistently showed inferior

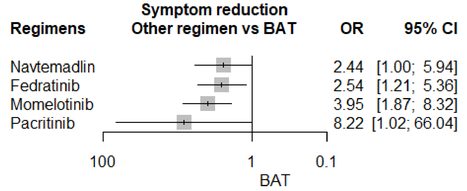
Ruxolitinib-naïve patients





Previously treated with ruxolitinib





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