JAK inhibitors vs Best Available Therapy for Myelofibrosis; A Meta-Analysis of Randomized Clinical Trials

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Introduction

Myelofibrosis (MF) is characterized by dysregulated JAK-STAT signaling, which is targeted by JAK inhibitors such as ruxolitinib and fedratinib, approved for MF treatment.

Aim

To evaluate clinical efficacy and safety profiles of JAK inhibitors against best available therapy (BAT) in primary and secondary myelofibrosis.

Objectives

To measure splenic volume reduction >35% at 24 weeks and TSS reduction >50% at 24 weeks in response to ruxolitinib, pacritinib, momelotinib and fedratinib when comparing with BAT.

Methods

- Meta-analysis conducted per PRISMA guidelines with systematic searches of PubMed, EMBASE, Cochrane, and ClinicalTrials.gov up to April 2024.
- Both dichotomous and continuous outcomes were pooled using RevMan 5.4 with 95% confidence intervals.
- Study heterogeneity evaluated by I^2 and χ^2 statistics.
- A p-value < 0.05 was considered statistically significant.

Results

Outcome	Effect Size 95% CI	p-value	I^2	Significant Improvement
Spleen Volume Reduction ≥35% at 24 weeks	OR = 5.81 (2.24 – 15.07)	<0.05	59%	Yes
TSS Reduction ≥50% at 24 weeks	OR = 2.35 (1.28 – 4.32)	<0.05	0%	Yes
Grade ≥3 Anemia	RR = 1.30 (1.01 – 1.67)	<0.05	0%	Yes
Grade ≥3 Thrombocytopenia	RR = 1.47 (1.05 – 2.04)	<0.05	0%	Yes
Diarrhea	RR = 3.37 (1.90 – 5.98)	<0.05	68%	Yes
Nausea	RR = 3.12 (1.84 – 5.29)	<0.05	43%	Yes
Pyrexia	RR = 1.42 (0.59 – 3.41)	NS	71%	No
Fatigue	RR = 1.04 (0.74 – 1.46)	NS	0%	No
Peripheral Edema	RR = 0.84 (0.62 – 1.15)	NS	0%	No

Table : Efficacy and Safety Outcomes of JAK Inhibitor vs Best Available Therapy in Myelofibrosis

Results

- **Key Endpoints:** JAK inhibitors (JAKi) significantly improved **spleen volume reduction ≥35%** (OR: 5.81) and **total symptom score (TSS) reduction ≥50% (OR: 2.35) at 24 weeks** compared to Best Available Therapy (BAT).
- **Safety Profile:** JAKi were associated with a higher risk of Grade ≥3 anemia (RR: 1.30), thrombocytopenia (RR: 1.47), diarrhea (RR: 3.37), and nausea (RR: 3.12) compared to BAT.
- **Other Adverse Events:** No significant difference was observed between JAKi and BAT for pyrexia, fatigue, or peripheral edema.

Summary

JAK inhibitors in myelofibrosis demonstrated superior efficacy over best available therapy, achieving meaningful clinical endpoints with manageable toxicities, setting a benchmark for future treatment strategies.

References

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