Ropeginterferon Alfa-2b in Polycythemia Vera: A PRISMA-compliant Systematic Review and Meta-Analysis

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Introduction

Ropeginterferon alfa-2b, a novel monopegylated interferon with improved pharmacokinetics, has emerged as a promising cytoreductive agent for managing Polycythemia Vera (PV). Despite increasing adoption, evidence synthesis of its efficacy and safety compared to standard care remains limited.

Aims

To evaluate the efficacy of Ropeginterferon alfa-2b in comparison to standard treatment options, including hydroxyurea and phlebotomy, in achieving complete hematologic response, partial molecular response, and reducing JAK2V617F allele burden in patients with PV.

Methods

A systematic search of four databases (PubMed, Scopus, Cochrane, and Embase) was conducted up to April 2025, following PRISMA 2020 guidelines. Randomized controlled trials (RCTs) comparing Ropeginterferon alfa-2b with standard therapies in PV patients were included. Meta-analyses were performed using random-effects models to derive odds ratios (OR) for dichotomous outcomes and mean differences (MD) for continuous outcomes. Sensitivity and subgroup analyses were conducted, and risk of bias was assessed using RoB 2.0.

Risk of bias (RoB 2.0): both included studies rated "some concerns" overall.

3	522	12
RCTS	PATIENTS	MONTHS

Results

Three RCTs comprising 522 patients were analyzed. Ropeginterferon alfa-2b showed no statistically significant advantage overall or over hydroxyurea for CHR, PMR, or JAK2 allele burden reduction. However, subgroup analyses revealed significant benefits over phlebotomy alone in all three outcomes.

Pooled Estimates

Outcome	Overall	vs Hydroxyurea
CHR (OR)	1.11 [0.47, 2.63]	0.74 [0.46, 1.20]
PMR (OR)	1.08 [0.40, 2.92]	0.73 [0.49, 1.08]
Allele burden (MD)	−9.13 [−29.22, 10.96]	−6.90 [−31.59, 17.80]

Included Trials

Trial	Comparator	Ropeg / Control
LOW PV	Phlebotomy + low-dose aspirin	64 / 63
PROUD PV	Hydroxyurea	127 / 127
CONTINUATION PV	Hydroxyurea / best available therapy	95 / 76

Outcomes Assessed

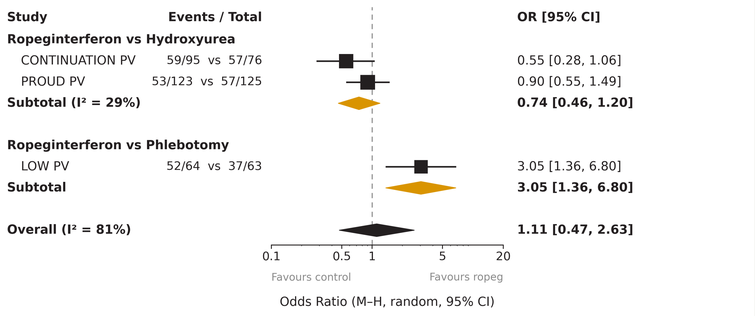
Complete hematological response (CHR)
Hematocrit ≤ 45% maintained without disease progression over 12 months

Partial molecular response (PMR)
≥ 20% reduction in JAK2V617F allele frequency from baseline at 12 months (ELN criteria)

JAK2V617F allele burden
Change in mean allele burden from baseline

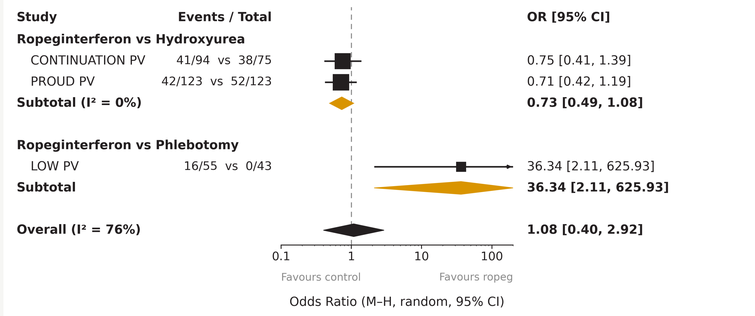
Complete Hematological Response at 12 Months

OR 3.05 vs phlebotomy alone
95% CI 1.36 – 6.80 · P = 0.007



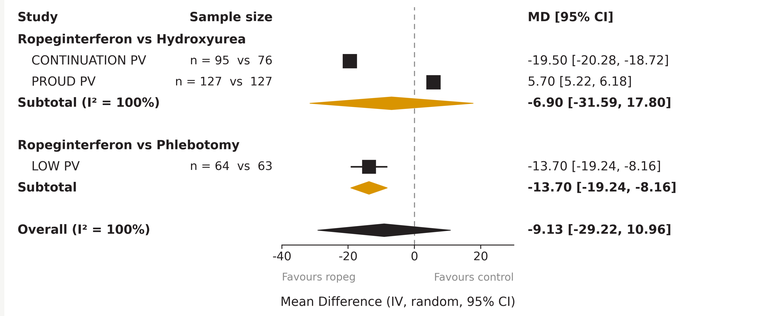
Partial Molecular Response at 12 Months

OR 36.34 vs phlebotomy alone
95% CI 2.11 – 625.93 · P = 0.01



Change in Mean JAK2V617F Allele Burden

MD −13.70 vs phlebotomy alone
95% CI −19.24 to −8.16 · P < 0.00001



Conclusion

Ropeginterferon alfa-2b demonstrates non-inferiority to hydroxyurea and superiority over phlebotomy in short-term efficacy for PV management. Its favorable molecular and hematologic outcomes support its role as a disease-modifying therapy, particularly in low-risk patients. However, larger and longer-term trials are needed to confirm these benefits across broader populations.