

Ropeginterferon Alfa-2b Shows Consistent Numerical Thrombotic Benefit Over Hydroxyurea Across All Endpoints in 285 Propensity-Matched Patients with Polycythemia Vera

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Background

• Polycythemia vera (PV) is a JAK2-driven myeloproliferative neoplasm with elevated risk of arterial and venous thromboembolism — the leading cause of morbidity and mortality

• Ropeginterferon alfa-2b (RPI) and hydroxyurea (HU) are both NCCN/ELN preferred first-line cytoreductive agents in high-risk PV

• RPI targets the JAK2-mutant clone and can induce molecular remission; HU provides non-selective myelosuppression without disease-modifying potential

• PROUD-PV¹ and CONTINUATION-PV² demonstrated superior molecular responses with RPI but were not powered for thrombotic endpoints

• No head-to-head real-world thrombotic or phlebotomy comparison exists between these two agents

Methods

Study Design:
Retrospective cohort study using the TriNetX Global Collaborative Network (172 healthcare organizations)

Population:
Adults with polycythemia vera (ICD-10: D45, ×2 within 3 months), initiating ropeginterferon alfa-2b or hydroxyurea as first cytoreductive agent on or after November 1, 2021

Exclusions:
Prior exposure to comparator agent, ruxolitinib, antecedent thromboembolism within 1 year, myelofibrosis, acute myeloid leukemia

Propensity Score Matching (1:1):
Age, sex, race, hypertension, diabetes mellitus, chronic kidney disease, ischemic heart disease, heart failure, COPD, anticoagulant use, antiplatelet use, platelet count, leukocyte count, HbA1c

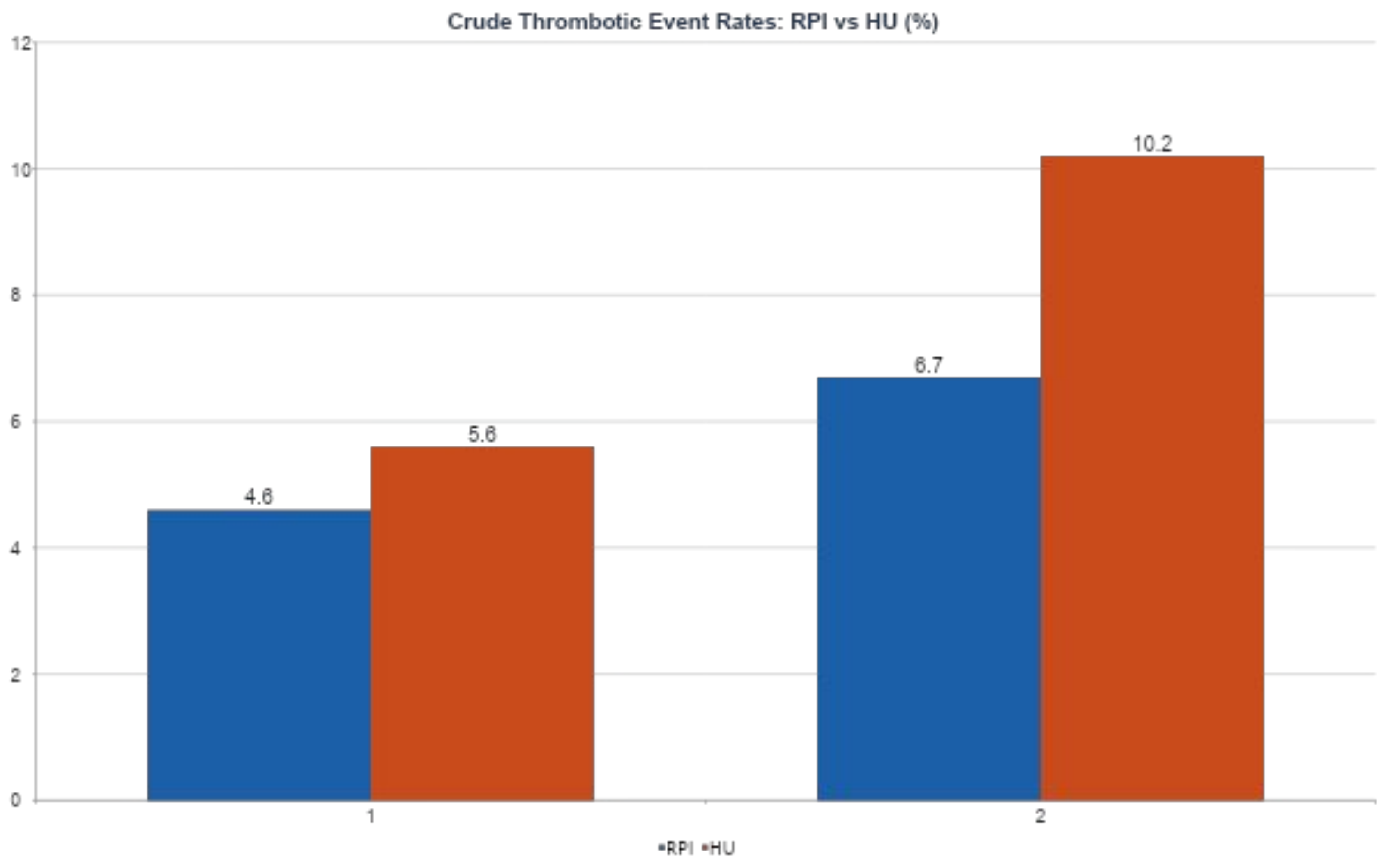
Outcomes (3-year window):
Venous thromboembolism (pulmonary embolism, portal vein thrombosis, venous embolism), composite thromboembolism (VTE, myocardial infarction, cerebral infarction, arterial embolism), phlebotomy frequency (CPT 99195)

Statistical Analysis:
Kaplan-Meier survival analysis, log-rank testing, hazard ratios, risk difference, independent samples t-test

Before Matching RPI n=311 · HU n=3,161	After Matching RPI n=285 · HU n=285
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Venous Thromboembolism (VTE)			Composite Thromboembolism (TE)			Phlebotomy Burden		
	RPI	HU		RPI	HU		RPI	HU
3-yr KM Free	94.31%	88.81%	3-yr KM Free	90.75%	82.40%	Mean Events	0.94	1.37
HR (95% CI)	0.76 (0.37–1.58)		HR (95% CI)	0.61 (0.34–1.08)		Pts with phlebotomy	72	85
p (log-rank)	0.461		p (log-rank)	0.086		p-value	0.052	



Propensity Score Matching

Variable	Pre-RPI (n=311)	Pre-HU (n=3,161)	p	Post-RPI (n=285)	Post-HU (n=285)	p
Age (median)	55	71	<0.001	57	56	0.711
Female	53.4%	50.5%	0.326	53.3%	52.3%	0.801
Hypertension	30.9%	51.1%	<0.001	31.6%	29.5%	0.585
Diabetes	7.4%	16.8%	<0.001	7.7%	7.0%	0.748
Ischemic HD	7.7%	19.0%	<0.001	8.1%	8.8%	0.763
CKD	3.2%	13.0%	<0.001	3.5%	4.2%	0.664
Heart Failure	3.2%	9.1%	<0.001	3.5%	3.5%	1.000

Channeling bias corrected after 1:1 propensity score matching

Discussion

• RPI associated with numerically lower VTE, composite TE, and phlebotomy burden vs HU across all endpoints

• Composite TE approached significance (p=0.086) with 8.35% absolute difference in 3-year thromboembolism-free survival

• Findings consistent with interferon-mediated JAK2-mutant clonal suppression — a mechanistic advantage not shared by hydroxyurea

• A prospective, thrombosis-powered head-to-head trial of RPI vs HU in high-risk PV is warranted

Limitations

• ICD-10 diagnosis only, no JAK2 confirmation

• Small RPI cohort (n=285), limited statistical power

• Short RPI follow-up, FDA approved November 2021

• Unmeasured confounding, hematocrit control, adherence unobservable

References

1. Gisslinger H, Klade C, Giorgio A, et al. Ropeginterferon alfa-2b versus standard therapy for polycythaemia vera (PROUD-PV and CONTINUATION-PV). Lancet Haematol. 2020;7(3):e196-e208.

2. Gisslinger H, Klade C, Giorgio A, et al. Final results from CONTINUATION-PV: ropeginterferon alfa-2b versus best available treatment in polycythemia vera. Haematologica. 2023;108(6):1519-1529.