

## INTRODUCTION

- Polycythemia Vera (PV) is a JAK2-mutated myeloproliferative neoplasm (MPN) associated with significant clinical, economic, and quality of life burden.<sup>1</sup>
- PV affects around 50/100,000 individuals, causing erythrocytosis, splenomegaly, and risks: thromboembolic events (TE; major cause of death), myelofibrosis (MF; 26% at 20 years), acute myeloid leukemia (AML) transformation.<sup>2</sup>
- Standard care (hydroxyurea [HU], phlebotomy) controls symptoms but lacks disease modification; ropeginterferon alfa-2b (a novel, site-specific mono-pegylated interferon) achieves deep molecular responses (66% JAK2 reduction at 6 years) and hematologic control without phlebotomy.<sup>3</sup>
- Long-term PROUD-PV/CONTINUATION-PV data (up to 7.5 years) show superior event-free survival vs HU.<sup>4</sup>
- Ropeginterferon alfa-2b yields 5-fold lower disease progression (MF/AML: 0.2 vs 1.0 per 100 patient-years) and comparable low TE rates vs best available therapy (BAT; 1.0 vs 1.2 per 100 patient-years).<sup>4</sup>
- Median JAK2V617F allele burden drops to 8.5% at 5 years (vs rebound to 44.4% BAT), with 54% <10%-potential for treatment discontinuation in early PV.<sup>4</sup>

## OBJECTIVE

- Calculate the absolute risk reduction (ARR) and number needed to treat (NNT) with ropeginterferon alfa-2b versus HU for TE, MF, AML from PROUD-PV/CONTINUATION-PV, and versus phlebotomy for TE in low-risk PV from Low-PV trial.
- Estimate the U.S. economic impact via cost avoidance per prevented event and per patient treated, assessing offset of PV complication spending.

## METHODS

### Step 1: Data extraction

- Six-year cumulative event rates per 100 patient-years were obtained from long-term PROUD-PV and CONTINUATION-PV trial publications, showing TE at 1.247% versus 1.002%, MF at 0.499% versus 0.200%, and AML at 0.499% versus 0.000% for HU versus ropeginterferon alfa-2b, respectively.<sup>4</sup>
- For low-risk PV, TE ARR versus phlebotomy was derived from randomized data of the Low-PV trial.<sup>5</sup>

### Step 2: Risk metrics calculation

- ARR was computed as the difference between the control group event rate and the ropeginterferon alfa-2b event rate, including 95% confidence intervals based on trial variance.
- NNT was determined as 1 divided by ARR.

### Step 3: Economic impact assessment

- Published US cost estimates per prevented event were applied, \$45,040 for TE, \$105,280 for MF, and \$280,236 for AML, to the ARR and NNT values, yielding potential cost avoidance both per prevented complication and per patient treated.<sup>6,7</sup>
- Analyses excluded discounting, drug acquisition costs, and quality-of-life utilities to focus purely on complication-related savings.

## Question

What is the absolute risk reduction (ARR)/number needed to treat (NNT) for ropeginterferon alfa-2b vs hydroxyurea (HU) or phlebotomy, and what cost savings might arise from averted complications in US PV care population?

## Study Methods

## Key Takeaways

### Data Extraction

- Extract 6-year cumulative event rates (TE, MF, AML)

### Analysis

- Calculate the ARR (event rate control with 95% CI)
- Calculate the NNT as 1/ARR

### Study Outcomes

- Calculate potential savings by multiplying avoided events by published US per-event costs (TE ~\$45k; MF ~\$105k; AML ~\$280k) for potential savings.

- Ropeginterferon alfa-2b reduces TE (ARR 0.245%), MF (0.298%), AML (0.499%) vs HU over 6 years; NNT 408/335/201.
- In low-risk PV, TE ARR 0.962% vs phlebotomy (NNT 104).
- Potential cost avoidance: ~\$110 per patient treated for TE, up to \$1,395 for AML vs HU. Supports use in high-risk PV to offset complication spending.

## RESULTS

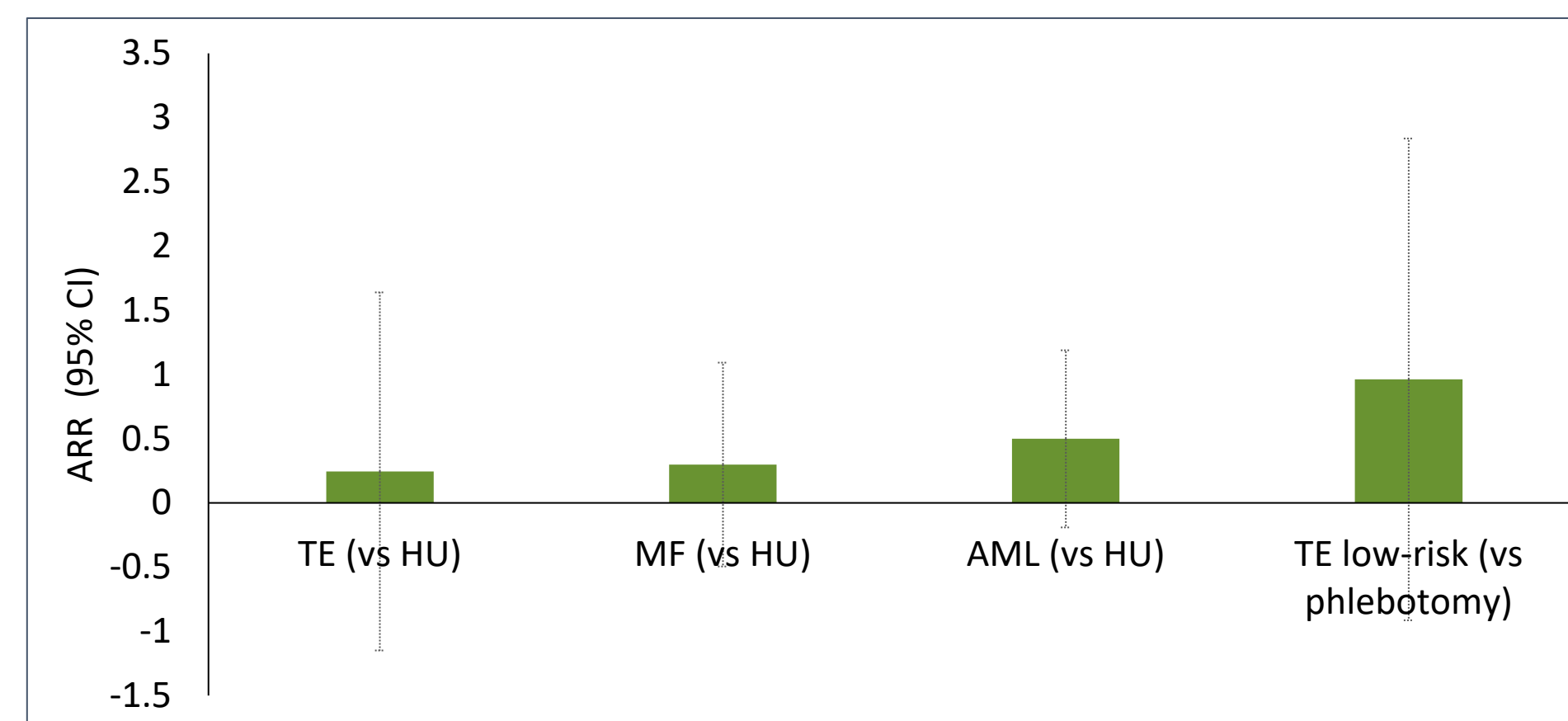
- Ropeginterferon alfa-2b demonstrated clinically meaningful ARR across all outcomes versus HU, with lowest NNT for AML prevention over 6 years (Table 1, Figure 1).
- In low-risk PV, TE risk reduction versus phlebotomy showed even more favorable NNT (Table 1).

**Table 1. Absolute risk reduction (ARR) and number needed to treat (NNT) with ropeginterferon alfa-2b versus hydroxyurea or phlebotomy**

Outcome	Control Rate (%)	Ropreg Rate (%)	ARR (95% CI), %	NNT
TE (vs HU)	1.247	1.002	0.245 (-1.149,1.639)	408
MF (vs HU)	0.499	0.200	0.298 (-0.495,1.092)	335
AML (vs HU)	0.499	0.000	0.499 (-0.191,1.188)	201
TE low-risk (vs phlebotomy)	-	-	0.962 (-0.914,2.837)	104

**Abbreviations:** AML: Acute myeloid leukemia; ARR: Absolute risk reduction; CI: Confidence interval; HU: Hydroxyurea; MF: Myelofibrosis; NNT: Number needed to treat; TE: Thromboembolic event.

**Figure 1. Absolute Risk Reduction for Ropeginterferon alfa-2b versus Comparators by Outcome**



**Abbreviations:** AML: Acute myeloid leukemia; ARR: Absolute risk reduction; CI: Confidence interval; HU: Hydroxyurea; MF: Myelofibrosis; TE: Thromboembolic event.

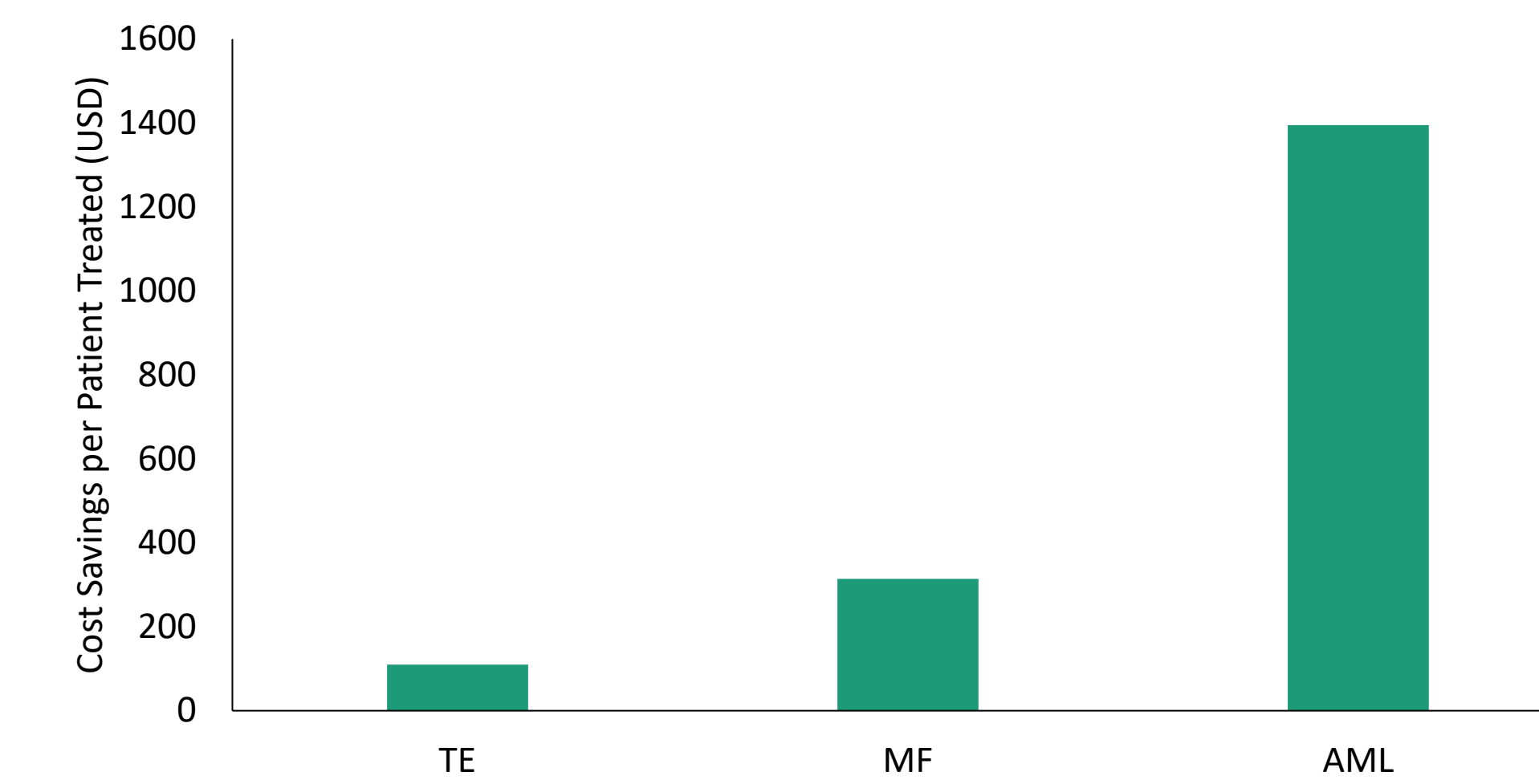
- Potential cost savings per patient treated (cost per NNT) were modest for TE but substantial for MF and AML, reflecting higher per-event costs (Table 2, Figure 2).
- Total complication avoidance could offset meaningful PV spending over extended horizons.

**Table 2. Cost Avoidance per Event and per NNT**

Event	Cost per Event (USD)	Cost Savings per NNT (USD)
TE	45,040	110
MF	105,280	314
AML	280,236	1,395

**Abbreviations:** AML: Acute myeloid leukemia; MF: Myelofibrosis; NNT: Number needed to treat; TE: Thromboembolic event.

**Figure 2. Potential Cost Savings per Number Needed to Treat by Outcome**



**Abbreviations:** AML: Acute myeloid leukemia; MF: Myelofibrosis; NNT: Number needed to treat; TE: Thromboembolic event.

## DISCUSSION

- Ropeginterferon alfa-2b's disease-modifying profile offers advantages over cytoreduction alone, with AML/MF savings potentially offsetting 10-20% of PV complication costs over 5+ years.
- Future patient-level simulations incorporating real-world adherence and longer horizons would strengthen economic case.

## LIMITATIONS

- Some ARR had 95% CIs crossing zero due to limited event numbers and trial power, reducing statistical precision.
- Per-event costs represent averages with wide ranges (e.g., TE \$24k-\$47k).
- Future analyses must consider drug acquisition costs to provide full economic picture, although here we focused purely on complication-related savings.
- Low-risk TE comparison used shorter-term Low-PV data versus 6-year high-risk data, limiting direct comparability.

## CONCLUSION

- Ropeginterferon alfa-2b reduces TE, MF, and AML risk versus HU (NNT 408/335/201) and TE versus phlebotomy in low-risk PV (NNT 104).
- Cost avoidance per patient treated ranges \$110-\$1,395, scaling meaningfully over time to support sustained use particularly in high-risk PV.
- These findings highlight the value of disease-modifying therapies in reducing PV's long-term clinical and economic burden.

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### Abbreviations:

AML: Acute myeloid leukemia; ARR: Absolute risk reduction; BAT: Best available therapy; CI: Confidence interval; HU: Hydroxyurea; JAK2: Janus kinase 2; MF: Myelofibrosis; MPN: Myeloproliferative neoplasm; NNT: Number needed to treat; PV: Polycythemia vera; TE: Thromboembolic event; US: United States.

### References:

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