PHASE 3 STUDY COMPARING ROPEGINTERFERON ALFA-2B WITH ANAGRELIDE AS SECOND-LINE TREATMENT FOR ESSENTIAL THROMBOCYTHEMIA: SURPASS-ET TRIAL

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Introduction

- ET is a clonal *BCR:ABL1*-negative MPN frequently associated with mutations in one or more MPN driver genes (*JAK2*, *CALR*, and *MPL*), and characterized by overproduction of platelets, increased risk of thrombosis or bleeding, and potential progression to MF and secondary AML.
- Current treatment approach for ET consists of non-specific cytoreductive therapies, predominantly hydroxyurea (first-line) and anagrelide. No new therapy has been approved for ET in the US since anagrelide in 1997.
- Ropeginterferon alfa-2b (ropeg) is a novel interferon-based therapy currently approved for the treatment of PV worldwide based on effective cytoreduction and direct anti-clonal impact[1-4].

Aim

To assess the safety and efficacy of ropeg, compared with anagrelide, in patients with high-risk ET with hydroxyurea-resistance or intolerance.

Design

SURPASS-ET (NCT04285086) is a randomized phase III study comparing ropeg to anagrelide in HU-intolerant/refractory ET. A total of 174 patients were enrolled. Ropeg was initiated at 250mcg, followed by 350mcg at Week 2 and 500mcg from Week 4 every 2 weeks if tolerated. The primary endpoint was the durable response rate at both months 9 and 12, according to the modified European Leukemia Net (ELN) criteria. Secondary endpoints included symptom improvement, hemorrhagic/thromboembolic events, spleen size, driver mutation allele burden, patient quality of life, and safety.

Results

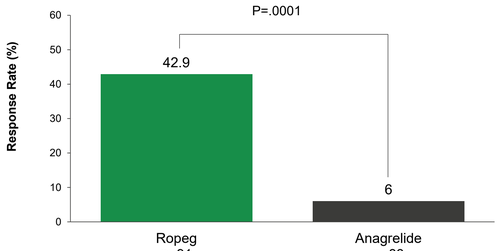
Baseline demographics and disease characteristics

	Ropeg n=91	Anagrelide n=83	P-value
Age, years, median (min, max)	61.0 (21, 80)	64.0 (20, 83)	0.5326
Sex, n (%)			0.8802
Female	47 (51.6)	44 (53.0)	
Male	44 (48.4)	39 (47.0)	
Spleen size–longitudinal diameter, median (min, max) — cm	13.10 (5.2, 16.3)	15.15 (9.2, 23.4)	0.0495
WBC count , median (min, max) — 10^9/L (central laboratory)	11.40 (7.2, 47.7)	11.60 (7.2, 75.9)	0.2447
Driver mutations, n (%)			
*JAK2*V617F positive	72 (79.1)	70 (84.3)	0.4358
CALR positive	11 (12.1)	10 (12.0)	1.000
MPL positive	1 (1.1)	1 (1.2)	1.000
Thrombosis history — no. (%)			0.3244
Yes	35 (38.5%)	26 (31.3%)	
No	56 (61.5%)	57 (68.7%)	

Primary endpoint: modified ELN response rate

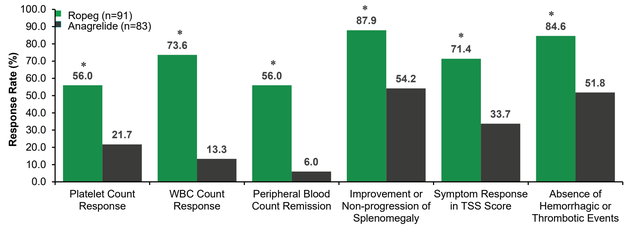
Significantly more participants in the ropeg arm achieved durable modified ELN criteria responses[a] at months 9 and 12, compared to those in the anagrelide arm

Modified ELN response criteria component endpoints:
- ≥10-point decrease in the MPN-SAF TSS for at least 12 weeks
- Normalization of peripheral blood counts for at least 12 weeks
- Absence of vascular events and disease progression
- Disappearance of bone marrow histological abnormalities



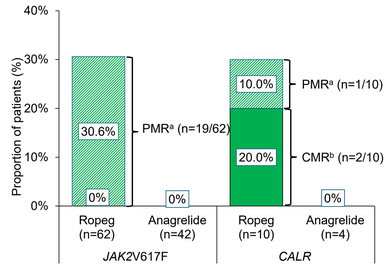
[a]Response defined as meeting the following criteria at months 9 and 12: hematologic control, spleen and symptom improvement or stability (MPN-SAF TSS), and no thrombotic/hemorrhagic events.
ELN, European Leukemia Net; MPN-SAF TSS, Myeloproliferative Neoplasms Symptom Assessment Form Total Symptom Score; n, number of participants.

Primary endpoint: response by individual ELN parameter



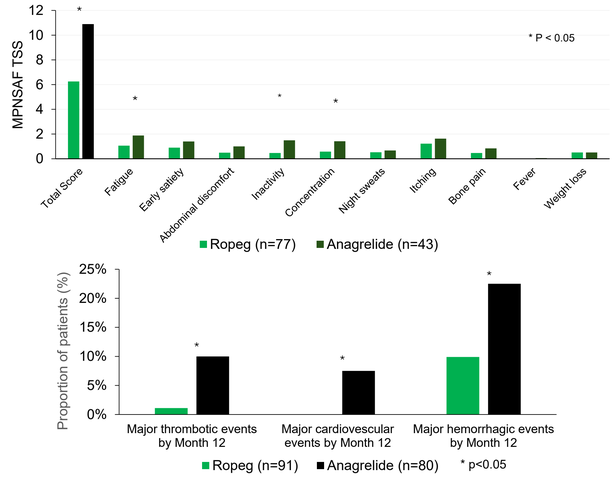
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ELN, European Leukemia Net; MPN-SAF TSS, Myeloproliferative Neoplasms Symptom Assessment Form Total Symptom Score; n, number of participants; WBC, white blood cell. * P < 0.0001.

Higher molecular response rates in terms of *JAK2*V617F and *CALR* allele reduction in the ropeg arm.



CMR, complete molecular response; PMR, partial molecular response.
[a]PMR is defined as reduction of ≥50% in burden from baseline in patients with <50% mutant allele burden at baseline or a reduction of ≥25% in burden from baseline in patients with >50% mutant allele burden at baseline (only applicable to patients with >10% baseline mutant allele burden).
[b]CMR is defined as reduction of any molecular abnormality to undetectable levels.

Significant reduction in symptoms and thrombotic/hemorrhagic events in the ropeg arm.



Lower rates of Grade ≥ 3 adverse events (AEs), serious AEs, and AE-related discontinuations in the ropeg arm.

Summary of Safety Results	Ropeg n=91	Anagrelide n=80
Any TEAE, n (%)	90 (98.9)	77 (96.3)
Grade ≥ 3 TEAE	21 (23.1)	27 (33.8)
Treatment-emergent SAE	13 (14.3)	24 (30.0)
AESI	25 (27.5)	35 (43.8)
TEAE leading to treatment discontinuation	5 (5.5)	16 (20.0)
AEs with fatal outcome	0	3 (3.8)

Conclusions

- Ropeg showed superior efficacy compared with anagrelide as second-line treatment in patients with high-risk ET
- Ropeg had a favorable safety profile compared to anagrelide
- Ropeg represents a potential new therapeutic option for patients with high-risk ET

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Acknowledgements

The authors would like to thank the people living with ET, their families, all investigators, study nurses, coordinators, and other participants involved in the SURPASS ET study.
SURPASS ET (NCT04285086) is sponsored by PharmaEssentia.

SOHO2025