EFFICACY AND MOLECULAR DYNAMICS OF ROPEGINTERFERON ALFA-2B IN HIGH-RISK ESSENTIAL THROMBOCYTHEMIA: TWO-YEAR RESULTS FROM THE PHASE 3 SURPASS-ET TRIAL

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INTRODUCTION

Essential thrombocythemia (ET) is a chronic myeloproliferative neoplasm with limited disease-modifying treatment options.[1,2] While hydroxyurea remains the standard first-line therapy, approximately 20% of patients develop resistance or intolerance.[3-5] Anagrelide, the only US FDA-approved therapy for ET since 1997, is limited by cardiovascular toxicity and an increased risk of bone marrow fibrosis.[6] The phase 3 SURPASS-ET trial core study previously demonstrated the superiority of ropeginterferon alfa-2b over anagrelide in achieving durable modified ELN responses at 12 months.[7] The long-term safety and efficacy of ropeg are being evaluated in an extension study.

AIM

To evaluate the long-term efficacy, safety, and durability of response with ropeginterferon alfa-2b compared with anagrelide through two years of treatment in the phase 3 SURPASS-ET extension study intended for patients completing the 52-week core study.

METHOD

SURPASS-ET is an open-label, randomized, active-controlled, multicenter study comparing ropeginterferon alfa-2b (ropeg) with anagrelide in patients with HU-resistant/intolerant ET and leukocytosis (WBC >10 × 10^9/L; Figure 1). In the extension part of the study, initiated after completion of the initial 52 weeks of core period, ropeg randomized patients continued on their ropeg treatment while those on anagrelide could transition to ropeg: no washout period, initial dose of 250 µg escalated to a target dose of 500 µg per the investigator. Efficacy outcomes, including ELN response, hematologic remission, and molecular response, were evaluated in the continuous-ropeg and transitioned-to-ropeg groups. The data cut-off date of the 2-year analysis was 2025-10-31.

CONCLUSIONS

- Early and continuous ropeg treatment provides durable hematologic and molecular benefits with favorable long-term tolerability in high-risk ET.
- Sustained JAK2V617FVAF reduction supports the disease-modifying potential of long-term ropeg therapy.
- Transition from anagrelide to ropeg improves hematologic control and reduces JAK2V617F allelic burden.
- Transition to ropeg is safe and well tolerated, with a safety profile comparable to that of continuous ropeg treatment. Long-term efficacy and safety analyses are ongoing.

RESULTS

Figure 1. Study design of SURPASS-ET trial

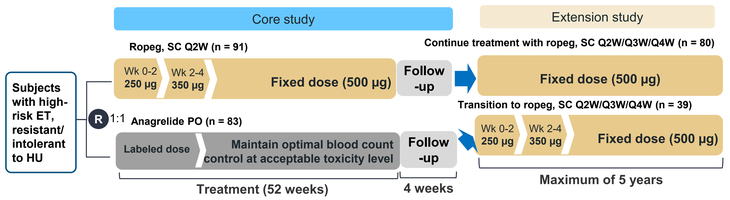
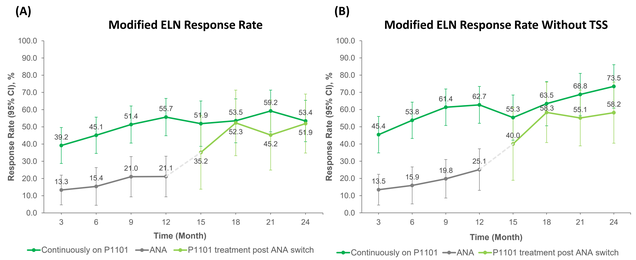


Table 1. Demographic and baseline characteristics at core study baseline in the extension safety analysis population

Characteristics	Continuously on ropeg (n=80)	Ropeg treatment post-ANA switch (n=39)
Age, median (min, max), years	60.0 (21, 80)	60.0 (20, 80)
Sex, female, n (%)	40 (50.0)	17 (43.6)
Race, n (%)		
Asian	76 (95.0)	39 (100.0)
White	4 (5.0)	0
Baseline MPN-SAF TSS ≥10, n (%)	37 (46.3)	17 (43.6)
Spleen size,[a] mean (SD), cm	12.2 (3.1)	15.3 (3.8)
Platelet count, mean (SD), ×10^9/L	996.5 (341.6)	933.6 (580.7)
WBC count, mean (SD), ×10^9/L	12.8 (5.8)	12.6 (4.1)
Presence of driver mutations, n (%)		
*JAK2*V617F	63 (78.8)	33 (84.6)
CALR	10 (12.5)	4 (10.3)
MPL	1 (1.3)	1 (2.6)
Triple negative	6 (7.5)	1 (2.6)

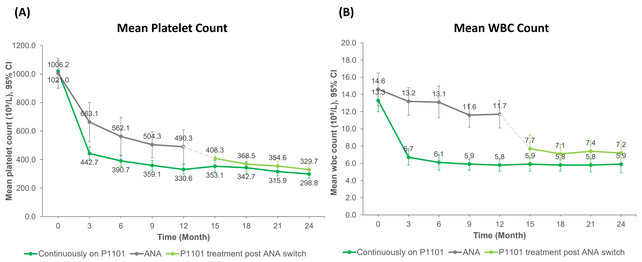
[a]Longitudinal diameter.
n, number of patients; MPN-SAF TSS, Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score; SD, standard deviation; WBC, white blood cell.

Figure 2. Modified ELN response rates increased over 2 years of ropeg treatment and following transition from anagrelide to ropeg



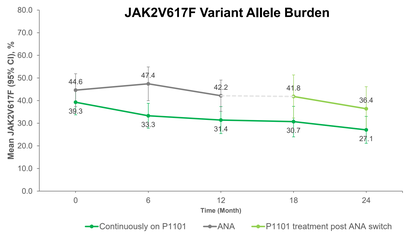
Note: (1) Patients in the control group switched from anagrelide to ropeg after completing the core study at Month 12.
(2) Multiple imputation method was used to estimate missing endpoint values.

Figure 3. Sustained hematologic responses over 2 years of ropeg treatment and normalization of platelet and WBC counts following transition from anagrelide to ropeg



Note: (1) Patients in the control group switched from anagrelide to ropeg after completing the core study at Month 12.
(2) Multiple imputation method was used to estimate missing endpoint values.

Figure 4. Continuous reduction in JAK2V617F allelic burden over 2 years of ropeg treatment and following transition from anagrelide to ropeg



Note: (1) Patients in the control group switched from anagrelide to ropeg after completing the core study at Month 12.
(2) Multiple imputation method was used to estimate missing endpoint values.

Table 2. AE profile for patients continually treated with ropeg in the extension study (N=80)

Any TEAE, n (%)						76 (95.0)
Grade ≥3 TEAE, n (%)						18 (22.5)
SAE, n (%)						14 (17.5)
AE of special interest, n (%)						16 (20.0)
Dose reductions due to TEAE, n (%)						24 (30.0)
TEAE leading to treatment discontinuation, n (%)						4 (5.0)
AE with fatal outcome, n (%)						1[a] (1.3)
Common AEs in the extension study (>10%)	**G1**	**G2**	**G3**	**G4**	**G5**	**Total**
Anaemia	20 (25.0)	8 (10.0)	1 (1.3)	0	0	29 (36.3)
Beta-2 microglobulin urine increased	24 (30.0)	0	0	0	0	24 (30.0)
Pruritus	12 (15.0)	5 (6.3)	0	0	0	17 (21.3)
Hepatic function abnormal	10 (12.5)	5 (6.3)	1 (1.3)	0	0	16 (20.0)
Pyrexia	9 (11.3)	5 (6.3)	0	0	0	14 (17.5)
Weight decreased	10 (12.5)	3 (3.8)	0	0	0	13 (16.3)
Alanine aminotransferase increased	7 (8.8)	3 (3.8)	0	0	0	10 (12.5)
White blood cell count decreased	3 (3.8)	7 (8.8)	0	0	0	10 (12.5)
Alopecia	10 (12.5)	0	0	0	0	10 (12.5)
Gamma-glutamyltransferase increased	9 (11.3)	0	0	0	0	9 (11.3)
Aspartate aminotransferase increased	9 (11.3)	0	0	0	0	9 (11.3)

Note: This table presents the AEs that occurred during the extension phase up to the data cut-off date (2025-10-31).
a. Acute myocardial infarction; unrelated to study drug

Table 3. Comparison of the AE profile during the 3-month periods before and after the transition from ANA to ropeg (N=39)

Before transition (ANA Treatment)						After transition (ropeg treatment)					
TEAE, n (%)	**G1**	**G2**	**G3**	**G4**	**G5**	**TEAE, n (%)**	**G1**	**G2**	**G3**	**G4**	**G5**
Anaemia	7 (17.9)	3 (7.7)	0	0	0	Anaemia	1 (2.6)	2 (5.1)	3 (7.7)	0	0
Palpitations	7 (17.9)	1 (2.6)	0	0	0	Pyrexia	2 (5.1)	4 (10.3)	0	0	0
Headache	7 (17.9)	0	0	0	0	Pruritus	4 (10.3)	1 (2.6)	0	0	0
Oedema peripheral	4 (10.3)	2 (5.1)	0	0	0	ALT increased	2 (5.1)	1 (2.6)	1 (2.6)	0	0
Pruritus	4 (10.3)	1 (2.6)	0	0	0	AST increased	1 (2.6)	0	2 (5.1)	0	0
Purpura	3 (7.7)	0	1 (2.6)	0	0	Neutrophil count decreased	0	1 (2.6)	0	1 (2.6)	0
GGT increased	2 (5.1)	2 (5.1)	0	0	0	Angina pectoris	0	0	1 (2.6)	0	0
Hypoaesthesia	1 (2.6)	1 (2.6)	1 (2.6)	0	0	Alcoholic liver disease	0	0	1 (2.6)	0	0
Hypertension	0	1 (2.6)	2 (5.1)	0	0	Herpes zoster	0	0	1 (2.6)	0	0
WBC count decreased	0	0	1 (2.6)	0	0	Cerebral infarction	0	0	1 (2.6)	0	0
Drug-induced liver injury	0	0	1 (2.6)	0	0	Leukopenia	0	0	1 (2.6)	0	0
Cerebral infarction	0	0	1 (2.6)	0	0						

Note: This table presents AEs occurring during the 3-month period before the last dose of anagrelide (left) and during the 3-month period after the transition from anagrelide to ropeg (right).
ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; WBC: White blood cell; G: Grade; GGT: Gamma-glutamyltransferase; TEAEs: Treatment-emergent adverse events

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CONTACT INFORMATION

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