Abstract: PB2850

Title: ROP-ET: A PROSPECTIVE PHASE III TRIAL INVESTIGATING THE EFFICACY AND SAFETY OF ROPEGINTERFERON ALFA-2B IN ESSENTIAL THROMBOCYTHEMIA PATIENTS WITH LIMITED TREATMENT OPTIONS

Abstract Type: Publication Only

Topic: Myeloproliferative neoplasms - Clinical

Background:

Commonly used approved treatments for Essential Thrombocythemia (ET), such as hydroxyurea (HU) and anagrelide (ANA), aim to normalize hematological parameters and reduce the thrombotic risk, but do not control malignant mutation-carrying clones and hence, have no impact on disease progression. A significant portion of patients with ET are unable to receive available therapies, whether due to treatment failures, contraindications, or other safety concerns and hence, these patients are left with no approved treatment alternatives.

Interferon-based therapies have emerged as promising disease-modifying agents for myeloproliferative neoplasms (MPNs), including ET. Ropeginterferon alfa-2b, a novel, monopegylated interferon alfa-2b with an extended administration interval was approved under the tradename BESREMi® in 2019 in Europe for the treatment of polycythemia vera (PV). Ropeginterferon alfa-2b not only provides robust hematological efficacy but also induces a sustained molecular response by reducing the mutant allele burden, offering a unique potential for disease modification in PV unlike any other treatments.

In patients with ET, interferons are commonly used off-label with an observed overall response rate exceeding 80% and with approximately 60% achieving complete hematologic remission (Bewersdorf et al 2021, Gu et al 2021). In addition, available evidence suggests a molecular response in up to 50% of patients (Gu et al 2021) and a significant improvement in myelofibrosis-free survival (Beauverd et al 2023), suggesting that, much like in PV, interferons, such as ropeginterferon alfa-2b, hold promise as a treatment option for ET.

Aims:

To assess the long-term safety and efficacy of ropeginterferon alfa-2b in ET patients with high need, i.e. patients with ET, who are unable to receive available cytoreductive therapies, whether due to intolerance or resistance, ineligibilities, or other safety concerns.

Methods:

The ROP-ET trial is a prospective, multicenter, single-arm phase III study that includes patients with ET who are intolerant or resistant to, and/or are ineligible for current therapies, such as hydroxyurea (HU), anagrelide (ANA), busulfan (BUS) and pipobroman, leaving these patients with limited treatment options. The primary endpoint is a composite response of hematologic parameters and disease-related symptoms, according to modified European LeukemiaNet (ELN) criteria. During the 3-year trial, secondary endpoints will include the assessment of allele burden, disease-related symptoms, vascular events, disease progression, and the safety profile of ropeginterferon alfa-2b. As an exploratory aspect of the study, patients have the option to participate in a sub-study focused on neutrophil extracellular traps (NETs) and inflammation marker testing with the aim to investigate the impact of ropeginterferon alfa-2b on these markers and their association with thrombotic events.

Results:

The study involves 36 sites in 10 countries in Europe. To date 16 patients have been recruited (8 men and 8 women) with the plan to enroll 117 patients. The mean and median age at recruitment was 60.8 years (SD: 13.5) and 63 years (range 38 to 85 years), respectively.

Summary/Conclusion:

No efficacy data are available for ropeginterferon alfa-2b in the planned ET study population and this study will provide new findings that may contribute to advancing the treatment landscape for ET patients with limited treatment alternatives.

This study is sponsored by AOP Health (EudraCT, 2023-505160-12-00).

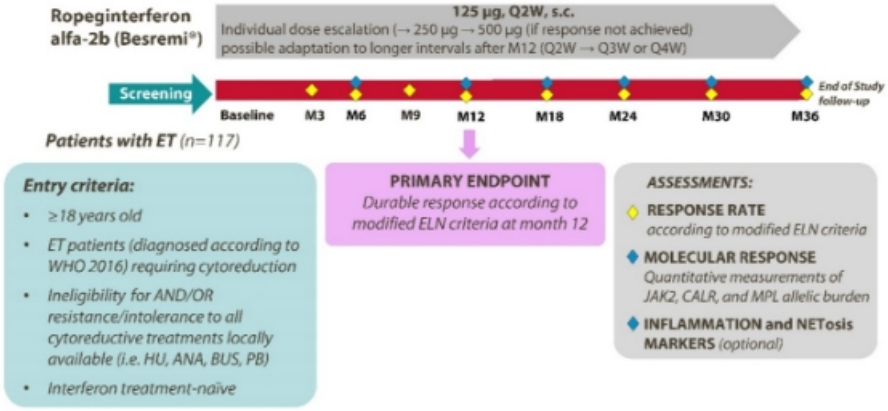

Figure 1. Study design ROP-ET study
ANA, Anagrelide; BUS, Busulfan; ET, Essential thrombocythemia; HU, Hydroxyurea; M, Month; PB, Pipobroman

Keywords: Essential Thrombocytemia, Phase III, Myeloproliferative disorder, Interferon-alpha