Essai Clinique

Généré le 02 mai 2024 à partir de

Titre	A Phase 3, Open-Label, Multicenter, Randomized, Active-controlled Study to Assess Pharmacokinetics and Compare the Efficacy, Safety, and Tolerability of P1101 vs Anagrelide as Second Line Therapy for Essential Thrombocythemia
Protocole ID	SURPASS ET
ClinicalTrials.gov ID	NCT04285086
Type(s) de cancer	NMP : Vaquez , Thrombocythémie essentielle, Métaplasie myéloide
Phase	Phase III
Type étude	Clinique
Médicament	P1101 versus anagrelide
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Statut	Actif en recrutement
Date d'activation	03-08-2022
But étude	This is a Phase 3 open-label, multicenter, randomized, active-controlled study designed to compare the efficacy and safety and tolerability of P1101 compared with ANA after 12 months of treatment as second-line therapy for subjects with ET who have had a suboptimal or failed response to HU. PharmaEssentia Corporation is developing a pegylated (PEG) IFN-α product, P1101, for the treatment of ET.Available clinical data and experience with P1101 in PV shows that the compound, with proper dose modifications, is effective in controlling disease in a significant proportion of subjects with ET. Further, its increased serum half-life presents distinct advantages for ET treatment over that of standard IFN-α and other available PEG IFN-α therapy. This pivotal Phase 3 study will establish the efficacy and safety of P1101 in ET subjects. The enrolled subjects will be randomized into two arms, the test arm is P1101, the control arm is ANA. The overall duration for each eligible patient is 14 months, including screening (1 month), treatment (12 months) and follow-up (1 month) period. Efficacy evaluations, safety assessments, and PK and immunogenicity evaluations of P1101 will be performed. Evaluation of efficacy will include clinical laboratory assessments, allelic burden measurements of CALR, JAK-2, and MPL, spleen size measurements, bone marrow sampling, EQ-5D-3L, and MPN-SAF TSS completion. Evaluation of safety will include assessing vital signs, clinical safety laboratory tests, physical examinations, ECG evaluation, heart ECHO, lung X-ray, ECOG performance status, ocular examination, and AEs.
Critères d'éligibilité	• Male or female subjects ≥18 years old • Subjects diagnosed with high-risk ET (either older than 60 years and JAK2V617-positive at screening, or having disease-related thrombosis or hemorrhage in the past), diagnosed according to the World Health Organization (WHO) 2016 criteria • Subjects have received prior HU for ET, while the washout between the last dose of HU and randomization should not be shorter than 14 days • Interferon treatment-naïve, or anti-P1101 binding antibody negative at screening and the washout between last dose of interferon and randomization should not be shorter than 14 days. • Documented resistance/intolerance to prior HU for ET, referencing modified ELN criteria (Barosi, et al, 2007), whereby at least one of the following criteria is met:Platelet count >600 x

	10^9/L at ≥2 g/day (or ≥2.5 g/day if subject body weight >80 kg) or maximally tolerated dose if <2 g/day after at least 3 months of HU, or Platelet count >400 x 10^9/L and WBC count <2.5 x 10^9/L at any dose and any duration of HU, or Platelet count >400 x 10^9/L and hemoglobin (HGB) <10 g/dL at any dose and any duration of HU, or Presence of HU-related toxicities at any dose and any duration of therapy (e.g., leg ulcers, mucocutaneous manifestations, pneumonitis, or HU-related fever), or Platelet count >450 x 10^9/L at any dose and any duration of HU. The actual dose and duration of HU must be recorded on the eCRF. Moreover, if patient received one dose of HU, the reason why subject was judged to be HU resistance/intolerance must be recorded on the eCRF. • Platelets >450 x 10^9/L at screening • WBC >10 x 10^9/L at screening • HGB ≥11 g/dL at screening for males and 10 g/dL at screening for females • Neutrophil count ≥1.0 x 10^9/L at screening • Adequate hepatic function defined as bilirubin ≤1.5 x upper limit normal (ULN), prothrombin time (PT) (international normalized ratio, INR) ≤1.5 x ULN, albumin >3.5 g/dL, alanine aminotransferase ≤2.0 x ULN, aspartate aminotransferase ≤2.0 x ULN at screening • Creatinine clearance ≥40 mL/min (by Cockcroft-Gault equation) • Males and females of childbearing potential, as well as all women <2 years after the onset of menopause, must agree to use an acceptable form of birth control until 28 days following the last dose of the study drug, and females must agree to not breastfeed during the study • Written informed consent obtained from the subject and ability for the subject to comply with the requirements of the study

Critères d'exclusion	• Any subject requiring a legally authorized representative
	• Any contraindications or hypersensitivity to IFN-α or ANA and their excipients
	• Known risk factors for QT-prolongation (e.g., congenital long QT, known history of acquired QT-prolongations). Medications that can prolong QTc and induce hypokalemia will not be allowed in the study.
	• Co-morbidity with severe or serious condition that, in the Investigator's opinion, would jeopardize the safety of the subject or their compliance with the protocol, including significant cardiac disease (including New York Heart Association Class III-IV congestive heart failure and clinically significant arrhythmias) and pulmonary hypertension
	• History of major organ transplantation
	• Pregnant or lactating females
	• Subjects with any other significant medical conditions that, in the opinion of the Investigator, would compromise the results of the study or may impair compliance with the requirements of the protocol, including but not limited to:
	  • Documented autoimmune disease at screening or in the history (e.g., thyroid dysfunction, hepatitis, idiopathic thrombocytopenic purpura, scleroderma, psoriasis, or any arthritis of autoimmune origin)
	  • Clinically relevant pulmonary infiltrates, pneumonia, and pneumonitis at screening that, in the Investigator's opinion, would jeopardize the safety of the subject or their compliance with the protocol
	  • Infections with systemic manifestations (e.g., bacterial, fungal, or human immunodeficiency virus [HIV], except hepatitis B [HBV] and/or hepatitis C [HCV], at screening)
	  • Evidence of severe retinopathy (e.g., cytomegalovirus retinitis, macular degeneration) or clinically relevant ophthalmological disorder (due to diabetes mellitus or hypertension)
	  • History or presence of clinically relevant depression, or previous suicide attempts or at any risk of suicide at screening, in the judgement of the Investigator
	  • History or presence of clinically significant neurodegenerative diseases
	  • History of any malignancy within 5 years (except Stage 0 chronic lymphocytic leukemia, basal cell, squamous cell, and superficial melanoma)
	  • History of alcohol or drug abuse within the last year
	  • History or evidence of any other MPN
	• Use of any investigational drug <4 weeks prior to the first dose of study drug or not recovered from effects of prior administration of any investigational agent
	• Subjects with documented ANA resistance or intolerance (see Appendix 8 for definition).