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A Single-arm Multicenter Study to Assess the Efficacy, Safety, and Tolerability of Ropeginterferon alfa-2b-njft (P1101) in North American Adults With Essential Thrombocythemia

EXCEED ET
ESSENTIAL THROMBOCYTHEMIA

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CONTEXT

- ET is a chronic MPN subtype caused by specific driver mutations with subsequent clonal expansion of neoplastic cells. It leads to thrombocytosis (and, in certain cases, leukocytosis) and is associated with a higher risk of thrombosis and hemorrhage as well as transformation to MF and/or AML.[1-3]
- Among US adults participating in a SEER Study conducted from 2002 to 2016, the estimated incidence rates for ET ranged from 0.7-2.5 per 100,000 person years,[3,4] with a five-year mortality rate of 19.2%.[4]
- Ideal therapeutic approaches should achieve adequate control of platelets and WBC, reduce the risk of thrombo-hemorrhagic complications, and prevent progression to post-ET myelofibrosis or secondary AML.[2]
- Low-dose aspirin with HU is typically given as first-line therapy in high-risk patients.[2] However, HU can be poorly tolerated and at least 20% of ET patients become HU-intolerant or -resistant, resulting in inadequate control of their disease.[5] In ET, HU-resistance may precede complications, disease progression, transformation, or death.[5]
- There exists a paucity of prospective clinical trial data, as well as an unmet medical need to guide the management of ET in patients who are cytoreduction-naive and those who are HU-resistant or -intolerant.
- Ropeginterferon-alfa-2b-njft (P1101) is a next-generation monopegylated IFN alfa-2b, developed specifically to treat MPNs, including ET.
- The objective of the EXCEED ET (NCT05482971) Study is to assess the efficacy, safety, and tolerability of ropeginterferon alfa-2b-njft (P1101) in adults with ET who live in the United States or Canada.

AML, acute myeloid leukemia; ET, essential thrombocythemia; HU, hydroxyurea; IFN, interferon; MF, myelofibrosis; MPN, myeloproliferative neoplasm; SEER, Surveillance, Epidemiology, and End User Results; WBC, white blood cell.

EXCEED ET STUDY STATUS

ENROLLMENT UPDATE

- Estimated enrollment is 64 patients
- Approximately 20-25 clinical sites

ClinicalTrials.gov

STUDY SITE LOCATIONS



64 Patients

25 Clinical Sites

EXCEEDET.com US Clinical Trial Site

DESIGN

EXCEED ET is a Phase 2b, single arm, multicenter trial, the aim of which is to evaluate the efficacy, safety, and tolerability of ropeginterferon alfa-2b-njft (P1101) for the treatment of adult patients with ET. Ropeginterferon alfa-2b-njft (P1101) will be administered SC Q2W at the starting dose of 250 mcg (Week 0), 350 mcg (Week 2), and target optimal dose of 500 mcg (Week 4). Dose adjustment to prior dose will be allowed if triggered by safety or tolerability concerns. Patient visits will be scheduled every 14 days (±3 days) during the core 12-month study period. Telephone visits will be permitted once a patient reaches the core treatment phase and has verified the ability to self-administer the treatment and has shown stable blood counts with no clinically meaningful toxicity or ET-related event in the acute phase.

The total duration of the study is approximately 15 months including a 28-day screening period, a 4-week titration period, a 12-month core treatment phase, and a 28-day follow-up phase (**Figure 1**). For patients deriving a benefit from therapy, a subsequent extension phase will continue to supply ropeginterferon alfa-2b-njft (P1101) until an alternative source is available.

MAJOR INCLUSION CRITERIA

- Diagnosed with ET according to WHO 2016 criteria
- Cytoreductive treatment-naive, or pre-exposed to HU and/or ANA
- IFN treatment naive
- Platelet count >450 × 10^9/L at screening

KEY EXCLUSION CRITERIA

- Pregnant or lactating females
- Documented autoimmune disease
- History or presence of clinically significant depression or neurological disease
- Clinically significant medical conditions
- Presence of more than one driver mutation (eg, V617F JAK2 and CALR, CALR and MPL, V617F JAK2 and MPL)

Figure 1. Study Design



ANA, anagrelide; CALR, calreticulin gene; ET, essential thrombocythemia; HU, hydroxyurea; IFN, interferon; MPL, myeloproliferative leukemia virus oncogene; Q2W, every 2 weeks; SC, subcutaneous; V617F JAK2, V617F mutation Janus associated kinase 2; WHO, World Health Organization.

MAIN OUTCOMES MEASURES

PRIMARY EFFICACY ENDPONT

The primary endpoint is a durable response rate

- Peripheral blood count remission (platelets ≤400 x 10^9/L and WBC <10 x 10^9/L) for at least 80% of the bi-weekly measurements for a consecutive 32 weeks during the core treatment period between Week 4 and Week 56

SECONDARY EFFICACY ENDPOINTS

- Clinical response as defined by the Modified ELN Criteria
- Hematological response, defined as peripheral blood count remission (platelets ≤400 x 10^9/L and WBC <10 x 10^9/L)
- Durable response at quarterly intervals both during the 13-month active treatment study period and the extension phase
- Response rates based separately on the individual components of the ELN clinical response definition
- Response rates based on peripheral blood count remission, no signs of progressive disease, and absence of any hemorrhagic or thrombotic events
- Occurrence of thromboembolic events
- Time to first peripheral blood count remission response
- Duration of peripheral blood count remission response
- Disease progression to post-ET MF and secondary AML
- Change of CALR, MPL, and JAK-2 allelic burden over time

EXPLORATORY ENDPOINTS:

- Symptomatic improvement assessed by the 10-item MPN-SAF TSS and quality of life by EQ-5D-3L
- Bone marrow (optional) histological remission defined as the disappearance of megakaryocyte hyperplasia and absence of > grade 1 reticulin fibrosis

SAFETY ENDPOINTS

- AEs according to CTCAE v5.0 and AEs of special interest (eg, cardiovascular events, hemorrhagic, TEs, and psychiatric events)
- Other safety data, including ECOG performance status, vital signs, ECGs, ECHOs, clinical laboratory tests, physical examinations, chest X-rays, and ocular examinations will be summarized

PPK AND E-R ANALYSES ENDPOINTS

- PK parameters will be derived using PPK analysis, and the relationship between exposure and efficacy and safety endpoints will be examined using E-R analysis

IMMUNOGENICITY ENDPOINTS

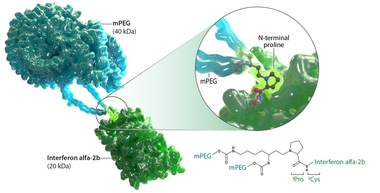
- Proportion of patients who are ADA positive and negative
- Presence of neutralizing antibodies to ropeginterferon alfa-2b-njft (P1101)

ADA, antidrug antibody; AE, adverse event; AML, acute myeloid leukemia; CALR, calreticulin gene; CTCAE, Common Terminology Criteria for Adverse Events; ECOG, Eastern Cooperative Oncology Group; ECG, electrocardiogram; ECHO, echocardiogram; ELN, European Leukemia Network; EQ-5D-3L, EuroQOL 5 dimensions 3 level version questionnaire; E-R, exposure-response; ET, essential thrombocythemia; JAK-2, Janus kinase-2; MF, myelofibrosis; MPL, myeloproliferative leukemia; MPN-SAF TSS, Myeloproliferative Neoplasm Symptom Assessment Form Total Symptom Score; PK, pharmacokinetic; PPK, population pharmacokinetics; TE, thrombotic events; WBC, white blood cell.

P1101

- P1101 is a monopegylated interferon alfa-2b[6] (**Figure 2**)
- It is a PEG recombinant manufactured analogue of native IFN-α, with improved PK properties due to proprietary, innovative PEGylation technology[6]
- Specifically engineered as only 1 single isoform, it is anticipated a reduced dosing frequency will be possible[6]

Figure 2. P1101 Structure



Cys, cysteine; IFN-α, interferon-α; mPEG, monopegylated; PEG, pegylated; PK, pharmacokinetic; Pro, proline.

SUMMARY

- Ropeginterferon alfa-2b-njft (P1101) is currently being investigated in patients with ET
- No pivotal prospective clinical trial data exist to guide management of ET patients who are HU-resistant or -intolerant. Treatment options are limited; several second-line treatment options are associated with increased risk of disease transformation
- The EXCEED ET Study is a Phase 2b, single arm, multicenter trial, the aim of which is to evaluate the efficacy, safety, and tolerability of ropeginterferon alfa-2b-njft (P1101) for the treatment of adult patients with ET
- Ropeginterferon alfa-2b-njft (P1101) could represent an important addition to the therapeutic landscape

ET, essential thrombocythemia; HU, hydroxyurea.

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DISCLOSURES

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