Abstract Submission

33. Bleeding disorders (congenital and acquired)

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EFFICACY AND SAFETY OF EFGARTIGIMOD PH20 SUBCUTANEOUS IN ADULT PATIENTS WITH PRIMARY IMMUNE THROMBOCYTOPENIA: ADVANCE SC, A GLOBAL PHASE 3 CLINICAL TRIAL IN PROGRESS

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Background: Primary immune thrombocytopenia (ITP) is an acquired autoimmune bleeding disorder characterized by a low platelet count, increased risk of bleeding and fatigue. Immunoglobulin G (IgG) autoantibodies directed against platelet surface antigens can be detected in most patients with ITP. These autoantibodies accelerate platelet clearance, can inhibit platelet production, and may impair platelet function. IgG homeostasis is regulated by the neonatal Fc receptor (FcRn). Efgartigimod, a human IgG1 antibody Fc-fragment, is a natural ligand of the FcRn engineered to competitively bind to FcRn and prevent the recycling of endogenous IgG. In a Phase 2 trial in 38 patients with primary ITP, efgartigimod 5 mg/kg or 10 mg/kg administered in 4 weekly IV infusions was well tolerated compared to placebo (Newland AC. *Am J Hematol*. 2020;95:178-187. NCT03102593). Efgartigimod induced a rapid reduction of total IgG levels (up to 63.7% mean change from baseline), which was associated with clinically relevant increases in platelet counts (38% vs 0% achieved ≥50×10^9/L for at least 10 cumulative days), and a reduced proportion of patients with bleeding. These data warrant further evaluation of FcRn antagonism as a novel therapeutic approach in ITP. A subcutaneous (SC) formulation (efgartigimod PH20) has been developed to offer additional flexibility and convenience for patients.

Aims: ADVANCE SC, a Phase 3, multicenter, randomized, double-blinded, placebo-controlled trial (NCT04687072), will evaluate the efficacy and safety of efgartigimod PH20 in adults with persistent or chronic ITP.

Methods: Eligible patients must have a mean platelet count <30×10^9/L over a minimum of 3 qualifying platelet evaluations and have received at least 2 prior ITP treatments or 1 prior and 1 concurrent treatment, with response to at least one. Patients will enter a 24-week treatment period and receive SC treatment with either efgartigimod (fixed dose of 1,000 mg) co-formulated with PH20 (recombinant human hyaluronidase PH20, an enzyme used to increase the dispersion and absorption of co-administered substances when administered SC) or matching placebo (randomization 2:1). Permitted concurrent ITP treatments include corticosteroids, oral immunosuppressants, dapsone/danazol, fostamatinib and/or oral TPO-RAs. Efgartigimod PH20 or placebo PH20 will be given weekly from visits 1 to 4 and then either weekly or every other week from visits 5 to 16, as determined by platelet counts. Dosing schedule will be fixed from visits 17 to 24. The primary endpoint is the proportion of patients with a sustained platelet count response defined as

platelet counts of ≥50×10^9/L for at least 4 of the 6 visits between study weeks 19 and 24 (study visits 20 to 25). Secondary endpoints include overall platelet count response, safety and tolerability, bleeding severity, use of rescue therapy, quality of life and patient-reported outcome measures, and the immunogenicity and pharmacokinetic/pharmacodynamic effects of efgartigimod PH20. Efficacy analyses will be performed on the full analysis set, consisting of all randomized patients. Safety will be assessed in all patients who receive ≥1 dose of study treatment.
Results: ADVANCE SC recruitment is ongoing with a target of approximately 117 patients with chronic ITP and up to 39 patients with persistent ITP across approximately 170 sites in Asia-Pacific, Europe, Japan, Latin America, Middle East, Africa and USA.
Summary/Conclusion: Trial participants will be eligible for continuation into ADVANCE SC$^+$, a long-term open-label extension trial.

Keywords: Bleeding disorder, Clinical trial, Fc receptor, Immune thrombocytopenia (ITP)