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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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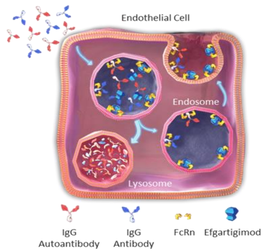
BACKGROUND

Efgartigimod: A Neonatal Fc Receptor (FcRn) Antagonist[1-3]



- Efgartigimod is a human immunoglobulin G1 (IgG1) Fc fragment with proprietary ABDEG™ mutations engineered for increased affinity for the FcRn
- It blocks FcRn, outcompeting endogenous IgG binding, preventing recycling of IgG and thereby decreasing serum IgG concentration
- FcRn blockade also leads to rapid decrease in circulating autoantibodies that may effectively treat IgG-mediated autoimmune diseases
- Efgartigimod is an investigational drug proposed for the treatment of IgG-mediated autoimmune disease
- The ongoing ADVANCE trial is evaluating intravenous efgartigimod 10 mg/kg; ADVANCE SC is a companion trial evaluating subcutaneous efgartigimod 1000 mg
- PH20 SC (Halozyme Therapeutics, San Diego, CA, USA) increases dispersion and absorption of co-administered drugs

Primary Immune Thrombocytopenia (ITP): An IgG-Mediated Autoimmune Disease[4-6]

- ITP is an acquired autoimmune bleeding disorder characterized by a low platelet count, increased risk of bleeding, and decreased quality of life
- IgG autoantibodies targeting platelet surface antigens are detected in most patients with ITP
- Autoantibodies accelerate platelet clearance, can inhibit platelet production, and may impair platelet function
- Splenectomy remains the only treatment that provides sustained remission off therapy for ≥1 year for a high proportion of patients

PHASE 2 RESULTS SUPPORT THE RATIONALE FOR THERAPEUTIC IGG DEPLETION IN PRIMARY ITP[7]

- In a randomized, double-blinded, placebo-controlled phase 2 trial in patients with ITP (NCT03102593), intravenous infusion of efgartigimod demonstrated a favorable safety and tolerability profile, consistent with previous studies
- Selective IgG reduction was observed within a few days in efgartigimod-treated groups, without impacting levels of other Ig isotypes
- A platelet count ≥100×10^9/L at any time was achieved by 46.2% and 38.5% of patients receiving efgartigimod 5 mg/kg or 10 mg/kg versus 8.3% of patients receiving placebo
- The proportion of patients with bleeding decreased in the efgartigimod-treated group, from 46.2% at baseline to a minimum of 7.7% at day 64, compared with 33.3% at baseline to a minimum of 25.0% at day 50 for the placebo group

KEY ELIGIBILITY CRITERIA

Inclusion criteria

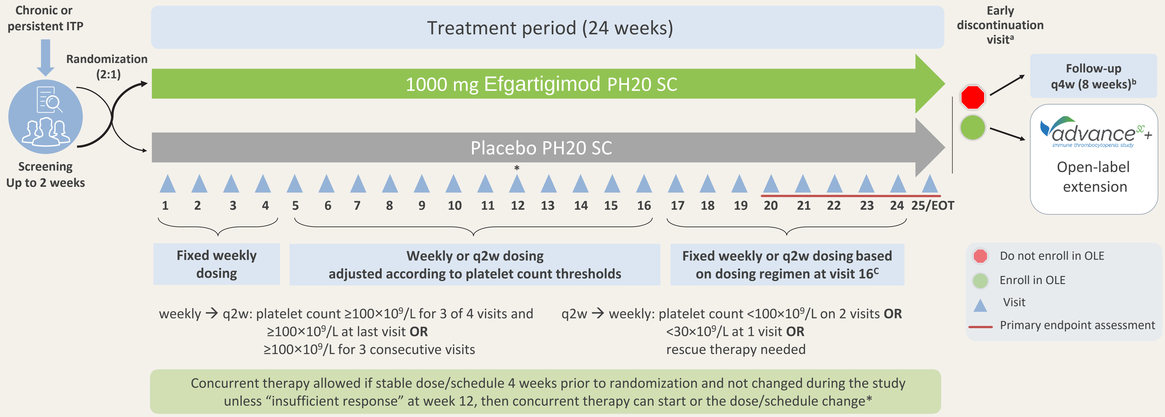
- Confirmed diagnosis of primary ITP ≥3 months; no known etiology for thrombocytopenia
- Mean platelet count <30×10^9/L from 3 qualifying counts within preceding 3 months
- Response to a prior ITP therapy (other than thrombopoietin receptor agonists)
- At least 2 prior ITP treatments or 1 prior and 1 concurrent ITP treatment; stable in dose and frequency ≥4 weeks before randomization

Exclusion criteria

- Secondary ITP/thrombocytopenia associated with another condition
- Use of anticoagulants, romiplostim, transfusions, Ig, or plasmapheresis (PLEX) within 4 weeks prior to randomization
- Undergone splenectomy <4 weeks prior to randomization
- Use of an investigational product with 3 months or 5 half-lives (whichever is longer) or monoclonal antibody or Fc fusion proteins within 6 months of first efgartigimod dose
- History of malignancy (no recurrence ≥3 years before first dose), uncontrolled hypertension, history of thrombotic or embolic event, history of coagulopathy or hereditary thrombocytopenia, uncontrolled infection, active viral infection (hepatitis B virus, hepatitis C virus, HIV), alcohol or drug abuse, other known autoimmune disease

ADVANCE SC (ARGX-113-2004) Trial Design

Subcutaneous Efgartigimod Phase 3, Multicenter, Randomized, Double-blind, Placebo-controlled Trial in Primary ITP



Concurrent therapy allowed if stable dose/schedule 4 weeks prior to randomization and not changed during the study unless "insufficient response" at week 12, then concurrent therapy can start or the dose/schedule change*

EOT = end of treatment; ITP = immune thrombocytopenia; IV = intravenous; OLE = open-label extension; PH20 = recombinant human hyaluronidase PH20; q2w = every 2 weeks; q4w = every 4 weeks.
*As of week 12, the start or an increase in the dose and/or schedule of permitted concurrent ITP therapy is allowed for participants who have an "insufficient response" (i.e., no platelet count of ≥30×10^9/L in any of the visits during the last 4 weeks. These participants will be considered as "non-responders" for the primary endpoint analysis.
[a]Early discontinuation visit should be performed on the day of early discontinuation.
[b]Patients who complete the 24-week study period but do not roll over into the OLE trial or patients who discontinue early but do not withdraw consent will complete an 8-week follow-up period consisting of 2 q4w visits.
[c]Dosing regimen at visit 16 or the dosing regimen at the last visit at which drug was administered.

PHASE 3 ADVANCE CLINICAL TRIAL PRIMARY ENDPOINT

Proportion of patients with a sustained platelet count response, defined as platelet counts of ≥50×10^9/L for ≥4 of 6 visits between weeks 19 and 24 (corresponding to visits 20–25/EOT)

SECONDARY AND ADDITIONAL ENDPOINTS

- Overall platelet count response
- Safety and tolerability
- Incidence and severity of bleeding events
- Use of rescue treatment and changes in concurrent ITP therapy
- QoL (SF-36) and PRO (FACIT-Fatigue, FACT-Th6) measures
- Immunogenicity
- Pharmacokinetics and pharmacodynamics

EOT = end of treatment; FACIT = Functional Assessment of Chronic Illness Therapy Fatigue Scale; FACT-Th6 = Functional Assessment of Cancer Therapy –Thrombocytopenia 6 Item Version; ITP = immune thrombocytopenia; PRO = patient-reported outcome; QoL = quality of life; SF-36 = 36-Item Short-Form Survey.

Recruitment targets (ongoing)
117 patients with chronic primary ITP
≤39 patients with persistent primary ITP
170 sites in Asia-Pacific, Europe, Japan, Latin America, Middle East, Africa, and USA
ClinicalTrials.gov: NCT04687072 and NCT04812925

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DISCLOSURES AND ACKNOWLEDGMENTS

CMB: Honoraria: Alexion, argenx, Apellis, Sanofi. **VM:** Advisory: Amgen, Novartis, Sobi; Research Grants: Grifols, Rigel. **SJ:** Advisory Board Panel: argenx, Dova, Sanofi; Speaker Bureau: GBT, Novartis; CME Course Speaker: Clinical Viewpoints, Plexus Communication; Board Member: Sickle Cell Disease Association of Illinois. **SB:** Stock and other ownership interests: Fort Wayne Medical Oncology & Hematology, Lutheran Hospital; Honoraria: Alexion Pharmaceuticals, AstraZeneca, Bayer, Bristol-Myers Squibb, Castle Biosciences, Lilly; Advisory: Alexion Pharmaceuticals, Amgen, argenx, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Janssen Oncology, Kite Pharma; Speakers Bureau: Alexion Pharmaceuticals; Research Grants: AbbVie, Alexion Pharmaceuticals, Amgen, argenx, AstraZeneca/MedImmune, Bristol-Myers Squibb, Genentech/Roche, Janssen Oncology, Lilly, Merck, Nektar, Novartis, Sanofi, Syndax, TG Therapeutics; Travel Expenses: Alexion Pharmaceuticals, Bristol-Myers Squibb, Genentech/Roche, Lilly, Janssen Oncology. **ENO:** Consultancy: BMS; Advisory Board: Alexion, Amgen, BMS, Novartis. **WP, AH, KDB, DG:** Employees of argenx. **YM:** Consultant: argenx, Kyowa Kirin, UCB, Zenyaku Kogyo; Honoraria: Alexion, Chugai, Pfizer, Sanofi. **WG:** Advisory Boards: Amgen, Bristol-Myers Squibb, Novartis, Principia, Sanofi; Lecture Honoraria: Amgen, Bayer, Bristol-Myers Squibb, Novartis; Research Grants: Bayer, Bristol-Myers Squibb/Pfizer.

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