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Transition From Intravenous Immunoglobulin to Efgartigimod PH20 SC in Participants With Chronic Inflammatory Demyelinating Polyneuropathy: A Phase 4 Study in Progress

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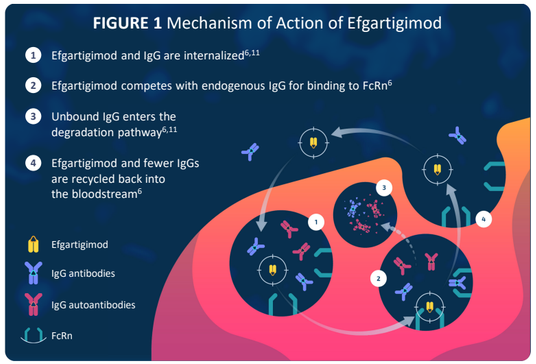
BACKGROUND

Efgartigimod Blocks FcRn and Reduces IgG Levels

- CIDP is an autoimmune, inflammatory, demyelinating neuropathy resulting in distal/proximal weakness and/or sensory deficits, with a high treatment burden[1–4]
- FcRn recycles IgG antibodies, saving them from lysosomal degradation and resulting in IgG antibodies having the longest half-life and being the most abundant of all Ig[5–7]
- Efgartigimod is an IgG1 antibody Fc fragment engineered for increased affinity for FcRn compared to endogenous IgG, and is uniquely composed of the only part of the IgG antibody that normally binds FcR[6]
- Efgartigimod selectively reduces IgG by blocking FcRn-mediated IgG recycling without impacting antibody production, reducing albumin levels, or affecting other parts of the immune system[6,8] (**Figure 1**)

Efgartigimod PH20 SC is a coformulation of efgartigimod and rHuPH20, which allows for rapid (30–90s single injection) SC administration[9,10]

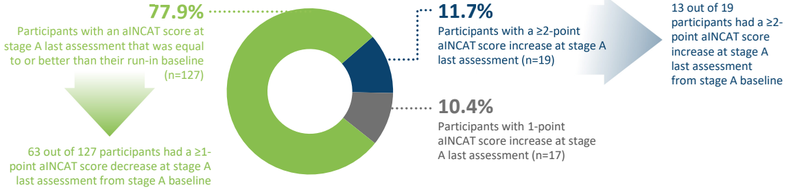
FIGURE 1 Mechanism of Action of Efgartigimod



Study Rationale

- In the ADHERE study (NCT04281472), efgartigimod PH20 SC demonstrated a significant, clinically meaningful benefit in participants with CIDP, regardless of prior CIDP therapy[12]
- Participants who received CIDP treatment within 6 months of entering ADHERE were required to withdraw these treatments and show disease worsening during a treatment-free run-in period before receiving efgartigimod PH20 SC for ≤12 weeks (stage A)[12]
- The frequency of aINCAT score changes from run-in baseline to stage A last assessment in the ADHERE Trial is shown in **Figure 2**
  - 63 out of 127 participants had a ≥1-point aINCAT score decrease at stage A last assessment from stage A baseline
- In the ADHERE trial, 38.7% (63/163) of participants had a ≥1-point aINCAT score decrease at stage A last assessment from stage A baseline
- Disease worsening before starting efgartigimod treatment was specific to the ADHERE trial design and not be part of clinical practice
- Research on the transition from IVIg to efgartigimod PH20 SC without disease worsening is needed to improve clinical practice
- This phase 4 study will assess the transition to efgartigimod PH20 SC treatment one week after the last IVIg infusion in adults with CIDP (**Figure 3**). Initiating treatment with efgartigimod PH20 SC 1 week after the last IVIg infusion was selected as:
  - Delay between the last IVIg infusion and the beginning of efgartigimod PH20 SC treatment could increase the chance of patients experiencing disease worsening
  - Switching from IVIg to efgartigimod PH20 SC too early can be considered a waste of IVIg, or may interfere with a perceived benefit of IVIg
  - Bulk of IVIg exposure occurs in the first week after infusion, with total IgG levels initially peaking after infusion and then declining by 50% within 2–4 days[13]
  - Assuming pathogenic IgG levels follow total IgG levels, reduction of pathogenic IgG levels occurs mostly during first week after IVIg infusion
  - Preclinical interaction studies showed efgartigimod rapidly reduced IgG when administered 3 days after IVIg

FIGURE 2 Frequency of aINCAT Score Changes From Run-in Baseline to Stage A Last Assessment in the ADHERE Trial



STUDY DESIGN

Screening (≤3 Weeks)

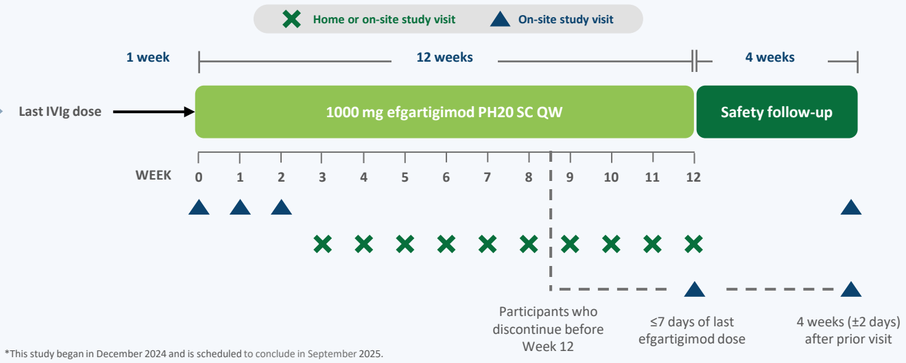
KEY INCLUSION CRITERIA

- ≥18 years old at the time of consent
- CIDP or possible CIDP diagnosis according to criteria from EFNS/PNS[2]
- Being treated with IVIg (0.5–2 g/kg) every 3–6 weeks, on a stable dose and dosing interval for ≥3 doses at the time of screening
- If receiving oral corticosteroids, treatment must have been at a dosage of ≤20 mg/day (or ≤40 mg every other day) at a stable dose for ≥1 month before screening
- Nonsteroidal immunosuppressive therapy allowed if received at a stable dose for ≥3 months before screening

KEY EXCLUSION CRITERIA

- Medical condition interfering with CIDP assessment or putting the participant at risk
- History of malignancy unless considered cured by adequate treatment with no evidence of recurrence for ≥3 years
- History of myelopathy or evidence of central demyelination
- Pregnancy or lactating state
- Total IgG concentration <4 g/L
- Treatment with SCIg
- Anti-CD20 or anti-CD-19 antibody received <6 months before screening, mAb (other than anti-CD20 or anti-CD19), PLEX and live or live-attenuated vaccine received <4 weeks before screening

FIGURE 3 Phase 4, Open-label, Single-Group, Multicenter Study (NCT06637072) in ~25 Participants With CIDP*



*This study began in December 2024 and is scheduled to conclude in September 2025.

Primary Endpoint

Proportion of participants who begin treatment with efgartigimod PH20 SC within one week after stopping IVIg therapy and are still receiving efgartigimod PH20 SC at the end of the 12-week treatment period

Secondary Endpoints

Patient-Reported Outcomes and Treatment Satisfaction

Actual values and changes from baseline in EQ-5D-5L, PGI-C, PGI-S, and TSQM-9 over time

Safety & Tolerability

Adverse events (incidence and severity), laboratory test results, vital sign measurements, and electrocardiogram results

KEY TAKEAWAY

This phase 4 study will evaluate the transition to efgartigimod PH20 SC one week after the last IVIg infusion in patients with CIDP

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ABBREVIATIONS

aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIDP, chronic inflammatory demyelinating polyneuropathy; EQ-5D-5L, EuroQol 5-dimension 5-level; EFNS, European Federation of Neurological Societies; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; Ig, immunoglobulin; IVIg, intravenous immunoglobulin; mAb, monoclonal antibody; PGI-C, Patient Global Impression of Change; PGI-S, Patient Global Impression of Severity; PLEX, plasma exchange; PNS, Peripheral Nerve Society; QW, once weekly; rHuPH20, and recombinant human hyaluronidase PH20; SC, subcutaneous; SCIg, subcutaneous immunoglobulin; TSQM-9, Treatment Satisfaction Questionnaire for Medication – abbreviated 9-item version.

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SCAN ME