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Efgartigimod in Pretreated CIDP With Persistent Disease Activity or Progressive/Relapsing Active Disease: ADHERE Analysis

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BACKGROUND

Efgartigimod Blocks FcRn and Reduces IgG Levels

- CIDP is a severe autoimmune peripheral neuropathy characterized by progressive or relapsing muscle weakness and sensory disturbance and is associated with a high treatment burden[1–5]
- Efgartigimod is an IgG1 antibody Fc fragment engineered for increased affinity for FcRn compared with endogenous IgG, and is uniquely composed of the only part of the IgG antibody that normally binds FcRn[6–8]
- 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[6–9]

Efgartigimod PH20 SC is a coformulation of efgartigimod and rHuPH20, which allows for rapid (30–90 s single injection) SC administration[10,11]

- In the ADHERE trial (**Figure 1**), efgartigimod PH20 SC reduced the risk of relapse and led to clinically meaningful improvements in functional ability, daily activity, or grip strength versus placebo, and was well tolerated in participants with CIDP[12]

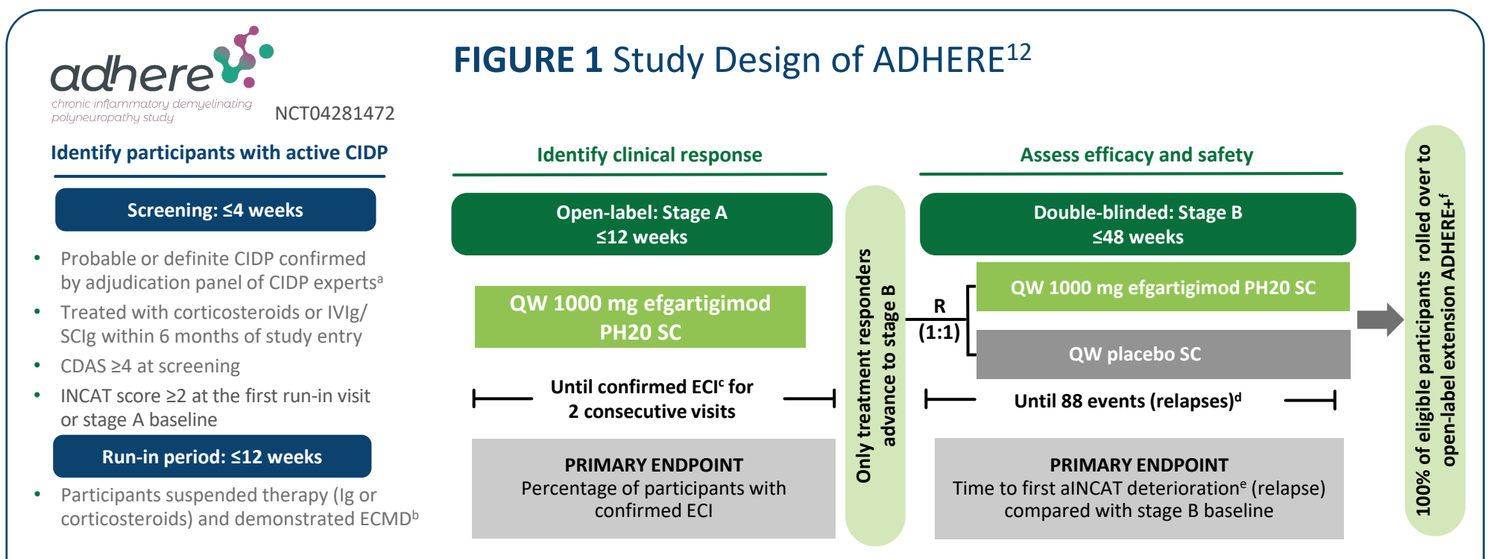
OBJECTIVE AND METHODS

Objective

This prespecified analysis explored a subgroup who received corticosteroids or Ig treatment for CIDP and had persistent disease activity or progressive/relapsing active disease (CDAS ≥4)

Methods

FIGURE 1 Study Design of ADHERE[12]



[a]According to 2010 criteria of the European Federation of Neurological Societies/Peripheral Nerve Society (Van den Bergh PYK, et al. *Eur J Neurol.* 2010), progressing or relapsing forms. [b]ECMD: an aINCAT increase of ≥1 point, an I-RODS decrease of ≥4 points (centile metric), or a grip strength decrease of ≥8 kPa. [c]ECI: a clinical improvement on the parameters that the participant worsened in during run-in (≥4-point increase in I-RODS and/or ≥8 kPa increase in mean grip strength) or clinical improvement (≥1-point decrease) in INCAT. ECI was confirmed after these criteria were met after 4 injections and 2 consecutive visits. [d]The primary endpoint was assessed once 88 total relapses or events were achieved in stage B and was based on the HR for the time to first aINCAT deterioration (ie, relapse). [e]aINCAT deterioration was defined as, compared with stage B baseline, a ≥1-point increase in aINCAT score confirmed at a consecutive visit after the first 1-point increase in aINCAT score, or a ≥2-point increase observed at a single visit. [f]All (101/101) eligible subgroup participants entered ADHERE+ (OLE; NCT04280718).

RESULTS

Participants

- Of 322 participants enrolled in stage A of the ADHERE trial, 139 had pretreated, persistent disease. Participants excluded from this analysis (n=183) were either off treatment or had a CDAS score of 2–3 at screening
- Baseline characteristics were generally similar to those in the overall ADHERE population,[12] except for the percentage of patients with unstable disease and with prior treatment, which were higher in this subgroup, by definition (**Table 1**)

Efgartigimod PH20 SC Demonstrated Clinical Benefits

- Most participants responded to efgartigimod PH20 SC (stage A) and reduced rate of relapse was observed (stage B) (**Figure 2**)
- Improvements in various efficacy endpoints at last assessment in both stages in this subgroup (**Table 2**) were similar to those of the overall population enrolled in the ADHERE trial[12]

Safety and Tolerability

- Safety and tolerability in this subgroup (**Table 3**) were generally similar to those of the overall population enrolled in the ADHERE trial[12]

TABLE 1 Baseline Characteristics

	Open-Label Stage A	Double-Blinded Stage B	
	Efgartigimod PH20 SC (N=139)	Efgartigimod PH20 SC (N=48)	Placebo SC (N=47)
Characteristics assessed at screening baseline			
Age, years, mean (SD)	52.6 (13.9)	54.2 (12.4)	49.2 (14.6)
Sex, male, n (%)	88 (63.3)	30 (62.5)	32 (68.1)
Time since diagnosis, years, mean (SD)	4.4 (5.5)	3.1 (4.3)	3.6 (4.0)
Typical CIDP diagnosis, n (%)	113 (81.3)	44 (91.7)	40 (85.1)
Unstable active disease (CDAS: 5), n (%)	118 (84.9)	40 (83.3)	43 (91.5)
Prior treatment (within past 6 months), n (%)			
Corticosteroids	37 (26.6)	15 (31.3)	17 (36.2)
Immunoglobulins (IVIg, SCIg)	102 (73.4)	33 (68.8)	30 (63.8)
Scores assessed at the beginning of each stage			
INCAT score, mean (SD)[a]	4.9 (1.9)	3.3 (1.7)	3.0 (1.6)
I-RODS score, mean (SD)[a]	37.5 (16.0)	52.3 (18.6)	53.6 (16.2)
Grip strength (dominant hand), kPa, mean (SD)[b]	34.4 (25.5)	50.2 (25.3)	59.4 (27.4)

[a]Lower scores represent improvement on INCAT, while higher scores represent improvement for I-RODS. [b]Nondominant scores were similar.

TABLE 2 Clinical Efficacy Endpoints

	Open-Label Stage A	Double-Blinded Stage B	
	Efgartigimod PH20 SC (N=139)	Efgartigimod PH20 SC (N=48)	Placebo SC (N=47)
Change from stage A or B baseline to respective stage A or B last assessment,[a] mean (SE)			
aINCAT score[b]	–1.0 (0.16)	0.0 (0.16)	1.5 (0.30)
I-RODS score[c]	9.1 (1.45)	1.3 (1.56)	–13.5 (3.14)
Grip strength (dominant hand), kPa	14.0 (1.66)	2.4 (1.98)	–14.3 (3.10)
Total MRC sum score[d]	3.9 (0.75)	–0.5 (0.71)	–5.7 (1.64)
TUG test score,[e] seconds	–4.1 (1.08)	0.6 (0.46)	2.9 (0.98)

[a]Last assessment in stage A or B was defined as the last nonmissing post-baseline value in the respective stage. [b]Higher aINCAT score indicates worsening of disease. [c]Lower I-RODS score indicates worsening of disease. [d]Lower total MRC sum score indicates greater muscle weakness. [e]Higher TUG test score indicates reduced functional mobility.

FIGURE 2A Open-Label Stage A: Percentage of Participants With Confirmed ECI

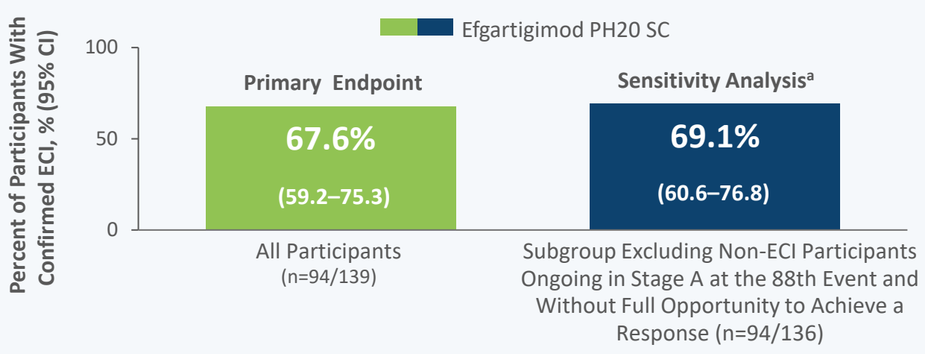
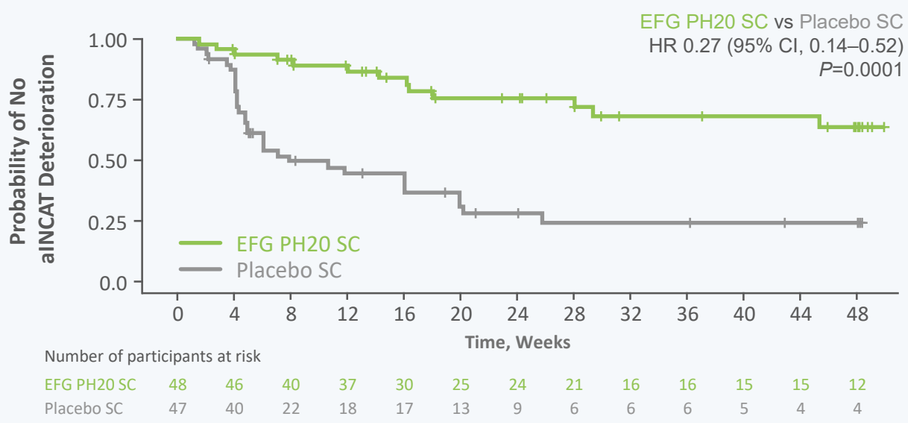


FIGURE 2B Double-Blinded Stage B: Time-to-First aINCAT Deterioration[b] Compared With Stage B Baseline



27.1% relapsed with efgartigimod PH20 SC versus **68.1% with** placebo (HR: 0.269,[c] *P*=0.0001), corresponding to a **73.1% lower rate of relapse** with efgartigimod PH20 SC

[a]Prespecified. [b]Defined as the number of days from first dose in stage B to the first occurrence of aINCAT deterioration compared with stage B baseline. [c]HR was obtained from a Cox proportional hazard model with treatment as a fixed effect, and stratified by prior CIDP therapy and aINCAT score during stage A.

TABLE 3 Safety and Tolerability

n (%) [event rate][a]	Open-Label Stage A	Double-Blinded Stage B	
	Efgartigimod PH20 SC (N=139; PYFU=18.7)	Efgartigimod PH20 SC (N=48; PYFU=24.2)	Placebo SC (N=47; PYFU=12.9)
Any TEAE	92 (66.2) [14.48]	36 (75.0) [4.58]	27 (57.4) [5.18]
Any SAE	7 (5.0) [0.54]	1 (2.1) [0.04]	4 (8.5) [0.46]
Any injection site reactions	27 (19.4) [2.25]	8 (16.7) [0.54]	3 (6.4) [0.23]
Discontinued due to TEAEs[b]	8 (5.8) [0.43]	0	1 (2.1) [0.08]
Deaths[c]	2 (1.4) [0.11]	0	1 (2.1) [0.08]
Most common TEAEs (≥5% of participants in either group)			
Injection site erythema	12 (8.6) [0.75]	3 (6.3) [0.12]	0
CIDP	7 (5.0) [0.48]	1 (2.1) [0.04]	1 (2.1) [0.08]
Arthralgia	4 (2.9) [0.21]	3 (6.3) [0.12]	2 (4.3) [0.16]
Nasopharyngitis	3 (2.2) [0.16]	5 (10.4) [0.21]	0
Upper respiratory tract infection	3 (2.2) [0.16]	2 (4.2) [0.12]	5 (10.6) [0.39]
COVID-19	2 (1.4) [0.11]	9 (18.8) [0.41]	4 (8.5) [0.31]
Influenza-like illness	1 (0.7) [0.05]	3 (6.3) [0.12]	0

[a]Event rates were calculated as the number of events divided by the PYFU. [b]TEAEs (Preferred Terms) leading to efgartigimod PH20 SC discontinuation were: cardiac arrest (n=1), muscular weakness (n=1), and CIDP (n=6) in ADHERE stage A; pneumonia (n=1) in ADHERE stage B placebo SC. [c]2 deaths (cardiac arrest and deterioration of CIDP) in stage A were considered not related to efgartigimod PH20 SC by the investigator; 1 death (pneumonia) in the placebo arm of stage B was considered treatment related by the investigator.

KEY TAKEAWAYS

Efgartigimod PH20 SC induced and maintained a therapeutic effect in pretreated participants with CIDP with persistent disease activity or progressive/relapsing active disease

- 67.6% showed confirmed evidence of clinical improvement (stage A)
- 73.1% reduced rate of relapse compared with placebo (stage B)
- Improvements in stage A in diverse efficacy outcomes were maintained with efgartigimod PH20 SC in stage B but (partially) lost with placebo

Weekly efgartigimod PH20 SC was well tolerated, with most TEAEs being mild to moderate

Efficacy and safety results in this subgroup were generally aligned with those observed in the overall population included in the ADHERE trial

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ABBREVIATIONS

AE, adverse event; aINCAT, adjusted INCAT; CDAS, chronic inflammatory demyelinating polyradiculoneuropathy disease activity status; CI, confidence interval; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; COVID-19, coronavirus disease 2019; ECI, evidence of clinical improvement; ECMD, evidence of clinically meaningful deterioration; EFG, efgartigimod; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; HR, hazard ratio; Ig, immunoglobulin; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-Built Overall Disability Scale; IVIg, intravenous immunoglobulin; MRC, Medical Research Council; OLE, open-label extension; PYFU, participant years of follow-up; rHuPH20, recombinant human hyaluronidase PH20; QW, once weekly; R, randomization; SAE, serious adverse event; SC, subcutaneous; SCIg, subcutaneous immunoglobulin; SD, standard deviation; SE, standard error; TEAE, treatment-emergent adverse event; TUG, Timed Up and Go.

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