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Impact of Prior Chronic Inflammatory Demyelinating Polyradiculoneuropathy Treatments in the ADHERE Trial: *Post Hoc* Analyses

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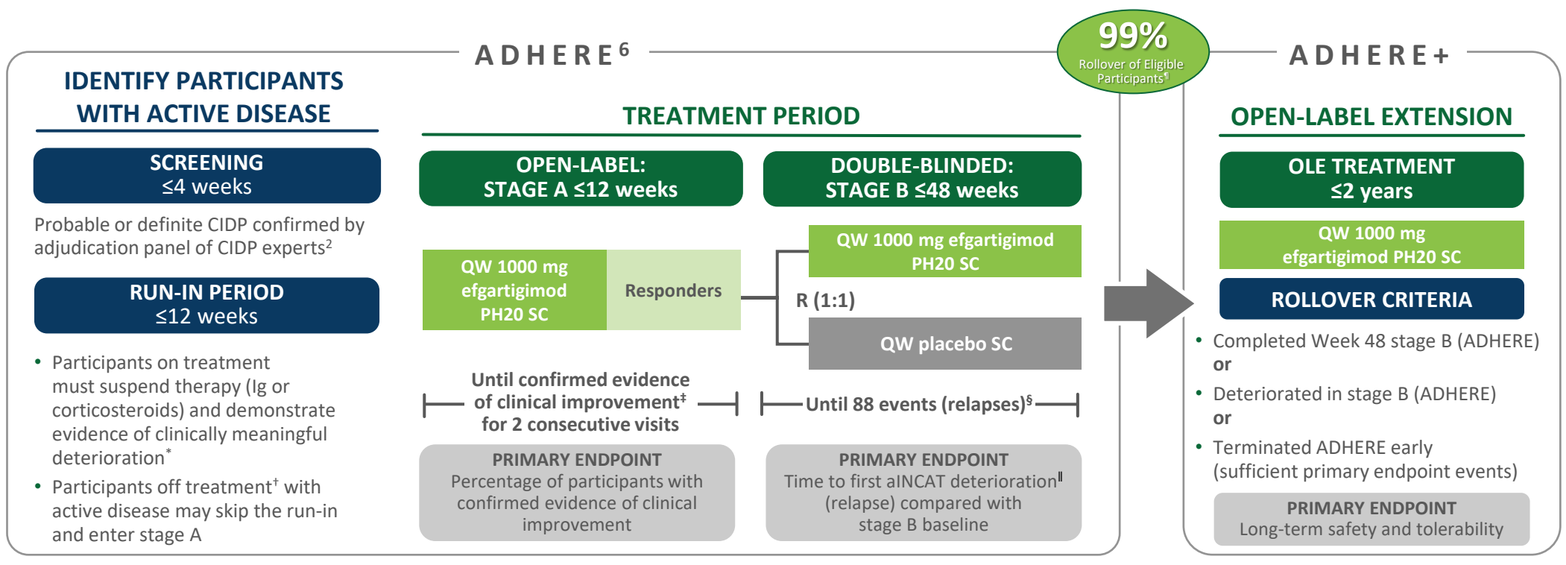
BACKGROUND

- CIDP is a rare, severe, progressive immune-mediated disease leading to disability due to proximal and/or distal weakness and sensory disturbance[1,2]
- Efgartigimod is a human IgG antibody Fc fragment that blocks the neonatal Fc receptor[3]
- Efgartigimod outcompetes endogenous IgG, decreases IgG recycling, promotes lysosomal degradation of IgG, and reduces IgG levels without impacting IgG production[3–8]
- In the ADHERE trial (NCT04281472), efgartigimod PH20 SC (co-formulated with recombinant human hyaluronidase PH20)[9] reduced relapse risk, including in those who received prior treatment, and was well tolerated in participants with CIDP[6]

OBJECTIVE

- In this *post hoc* analysis, we report outcomes with efgartigimod PH20 SC by prior treatment received for CIDP

METHODS



*ECMD was defined as an aINCAT increase of ≥1 points, an I-RODS decrease of ≥4 points (centile metric), or a grip strength decrease of ≥8 kPa. †Off treatment was defined as participants who had never received CIDP treatment (treatment naïve) or who had not received CIDP treatment (corticosteroids, IVIg, or SCIg) within 6 months of trial entry. ‡ECI was defined as 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. §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). ‖aINCAT deterioration was defined as a ≥1-point increase in aINCAT score compared with stage B baseline, which was confirmed at a consecutive visit after the first 1-point increase in aINCAT or not confirmed for participants with ≥2-point increase in aINCAT compared with stage B baseline. ¶n=228/229. 229 participants enrolled in ADHERE+, including 3 participants who inadvertently rolled over without meeting per-protocol inclusion criteria. The safety population for ADHERE+ included 228 participants who received ≥1 dose of efgartigimod PH20 SC in the OLE, as 1 participant discontinued before receiving the first dose of efgartigimod PH20 SC.

RESULTS

Baseline Characteristics

- 322 participants entered stage A:
  - 63 (19.6%) had received prior corticosteroids
  - 165 (51.2%) had received prior IVIg/SCIg
  - 94 (29.2%) were off treatment before entry into ADHERE
- Mean time since diagnosis was similar in the corticosteroids and off treatment subgroups (3.8 and 3.9 years), and longer in the IVIg/SCIg subgroup (5.8 years) (**Table 1**)
- Other characteristics were similar across subgroups

TABLE 1 Baseline Disease Characteristics by Prior CIDP Treatment in Stage A

	Corticosteroids (N=63)	IVIg/SCIg (N=165)	Off Treatment (N=94)
Characteristics assessed at baseline screening			
Time since diagnosis, mean (SD), years	3.8 (4.8)	5.8 (6.8)	3.9 (5.4)
CIDP type, n (%)			
Typical	54 (85.7)	131 (79.4)	83 (88.3)
Atypical	9 (14.3)	34 (20.6)	11 (11.7)
CIDP Disease Activity Status Score, n (%)			
2	0	1 (0.6)	5 (5.3)
3	26 (41.3)	62 (37.6)	8 (8.5)
4	3 (4.8)	18 (10.9)	2 (2.1)
5	34 (54.0)	84 (50.9)	79 (84.0)
Scores assessed at stage A baseline			
Total INCAT Disability Score, mean (SD)	4.6 (1.8)	4.6 (1.7)	4.8 (1.6)
I-RODS score, mean (SD)	40.0 (15.8)	40.3 (14.9)	39.7 (13.7)
Grip strength (kPa), mean (SD)			
Dominant hand	40.2 (25.8)	36.8 (24.8)	40.2 (21.8)
Nondominant hand	40.0 (23.9)	37.9 (26.3)	40.2 (22.5)

- Participants in the efgartigimod PH20 SC and placebo arms were stratified to enter Stage B by most recent prior treatment and aINCAT score change during Stage A (**Table 2**)

TABLE 2 Prior CIDP Treatment in Stage B

	Efgartigimod PH20 SC (N=111)	Placebo (N=110)	Total (N=221)
Prior CIDP therapy, n (%)			
Corticosteroids	24 (21.6)	23 (20.9)	47 (21.3)
IVIg/SCIg	48 (43.2)	48 (43.6)	96 (43.4)
Off treatment	39 (35.1)	39 (35.5)	78 (35.3)

- 19 participants in the IVIg/SCIg subgroup experienced the adverse event of CIDP worsening (n=17), muscle weakness (n=1), or quadriparesis (n=1); of these, 17 recovered, 1 partially recovered and 1 died during follow-up (deemed unlikely related to treatment)
- Study discontinuation rates were higher in the prior IVIg/SCIg subgroup than in the prior corticosteroid or off treatment subgroups
  - A quarter of these IVIg/SCIg participants received <4 efgartigimod PH20 SC injections (minimum treatment required to achieve maximal IgG reduction) (**Table 3**)
  - Not all participants who withdrew from stage A experienced deterioration on aINCAT (**Table 3, Figure 1**)

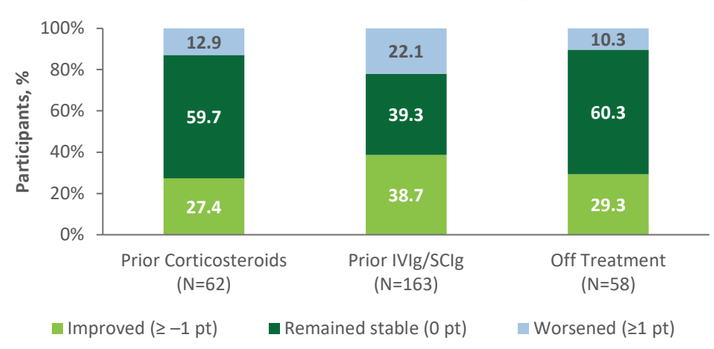
TABLE 3 Reasons for Study/Treatment Discontinuation by Prior CIDP Medication

	Corticosteroid (N=63)	IVIg/SCIg (N=165)	Off Treatment (N=94)
Participants who discontinued stage A treatment	8 (12.7)	55 (33.3)	8 (8.5)
Adverse event	2 (3.2)	18 (10.9)	0
Death	0	1 (0.6)	0
Lack of efficacy	3 (4.8)	21 (12.7)	4 (4.3)
Lost to follow-up	0	1 (0.6)	1 (1.1)
Noncompliance with study drug	1 (1.6)	0	0
Physician decision	0	1 (0.6)	0
Prohibited medications	0	2 (1.2)	0
Withdrawal by subject	1 (1.6)	8 (4.8)	1 (1.1)
Other	1 (1.6)	3 (1.8)	2 (2.1)
Participants with all events required for primary analysis achieved	4 (6.3)	11 (6.7)	7 (7.4)
Participants who completed stage A treatment	51 (81.0)	99 (60.0)	79 (84.0)
Participants who received <4 injections and discontinued from the trial	2 (3.2)	42 (25.5)	3 (3.2)
All events required for primary analysis achieved	0	4 (2.4)	3 (3.2)
Any other reason	2 (3.2)	38 (23.0)	0
Adverse event	1 (1.6)	15 (9.1)	0
Death	0	1 (0.6)	0
Lack of efficacy before end of stage A	1 (1.6)	12 (7.3)	0
Lost to follow-up	0	1 (0.6)	0
Noncompliance with study drug	0	0	0
Physician decision	0	1 (0.6)	0
Prohibited medications	0	1 (0.6)	0
Withdrawal by subject	0	5 (3.0)	0
Other	0	2 (1.2)	0

Efficacy

- All patients in ADHERE had to show deterioration (≥1 point on aINCAT, ≥4 points on centile metrics I-RODS, or ≥8 kPa on MGS) during a treatment-free run-in period and were already on a path of deterioration before starting efgartigimod in stage A. The percentage of patients with ≥1-point worsening on aINCAT from run-in baseline to stage A baseline (period capturing treatment withdrawal phase of the study) was 37.1% for prior corticosteroids, 41.7% for prior IVIg/SCIg, and 39.7% for the off-treatment group
- At stage A last assessment, the percentage of patients with a ≥1-point worsening on aINCAT compared with run-in baseline was lower than at stage A baseline in all prior treatment groups (**Figure 1**)
- Stage A ECI response rates were 77.8% for corticosteroids, 58.8% for IVIg/SCIg, and 72.3% for off treatment. At stage A last assessment, the majority of patients in all groups had equal or better aINCAT scores compared with run-in baseline (**Figure 1**)
- During stage B, further improvement was observed. In the prior IVIg/SCIg-treated participants randomized to efgartigimod, 34/49 (69.4%) improved ≥1 aINCAT point and 20/49 (40.8%) ≥2 aINCAT points at stage B best improvement compared with run-in baseline

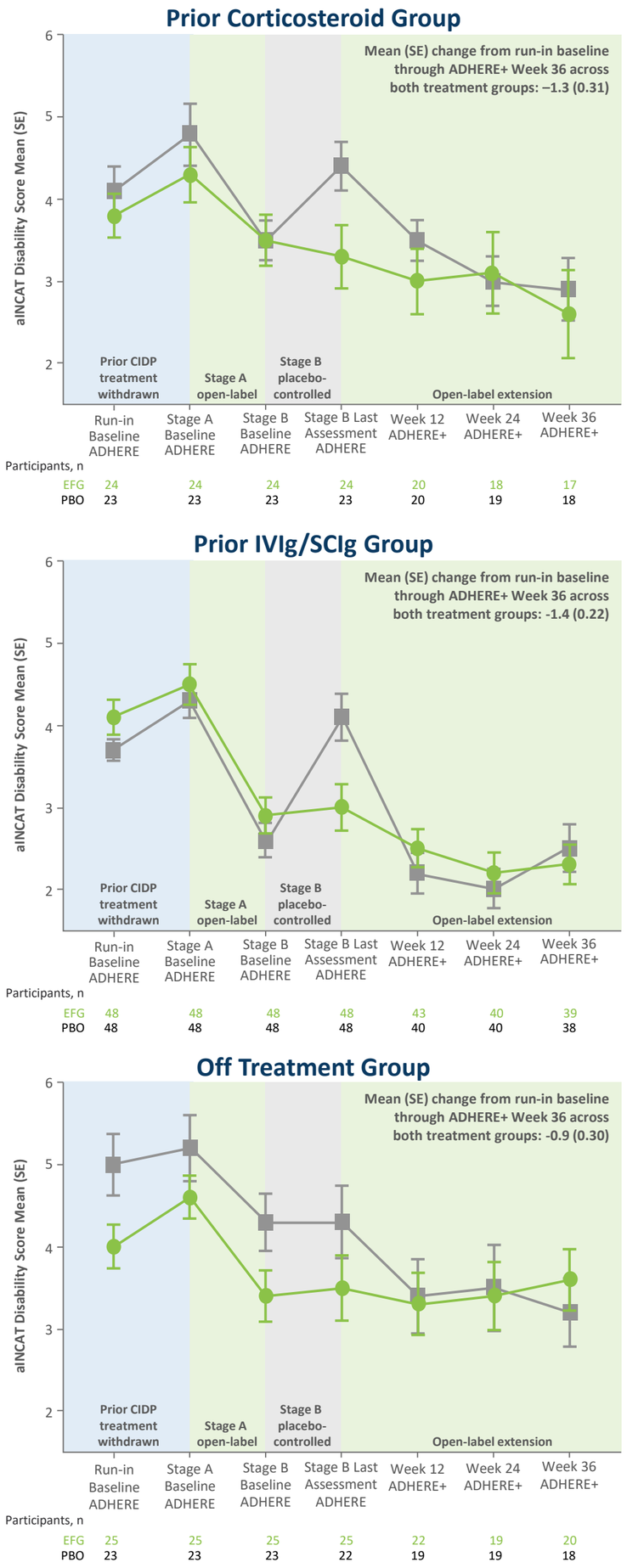
FIGURE 1 Change in aINCAT Scores From Run-In Baseline* to Stage A Last Assessment by Prior CIDP Medication Subgroups



* At stage A last assessment, 1.6% (corticosteroids), 16.0% (IVIg/SCIg), and 1.7% (off treatment) worsened ≥1 point on aINCAT compared with stage A baseline.

- Across all prior treatment subgroups, efgartigimod PH20 SC improved aINCAT scores through Week 36 of ADHERE+. These improvements corresponded with time on efgartigimod PH20 SC treatment (**Figure 2**)

FIGURE 2 Longitudinal Efficacy* by Prior CIDP Treatment Groups in Stage A Responders



*Based on aINCAT Scores in the mITT population. 1-point difference in aINCAT is the minimal clinically important difference. †Efgartigimod-efgartigimod-efgartigimod. ‡Efgartigimod-withdrawal placebo-efgartigimod.

KEY TAKEAWAYS

The potential impact of efgartigimod PH20 SC treatment or withdrawal of IVIg on deterioration in stage A cannot be conclusively determined due to the ADHERE study design. A study (NCT06637072) investigating transition from IVIg to efgartigimod PH20 SC without disease worsening is ongoing

In all prior treatment groups, the majority of patients improved and responded to efgartigimod in stage A. Though the proportion of participants discontinuing the study/treatment was higher among those who received prior IVIg/SCIg versus those who received prior corticosteroids or were off treatment, the prior IVIg/SCIg subgroup had the highest proportion of aINCAT improvement in stage A with efgartigimod and demonstrated the greatest aINCAT improvement by Week 36 ADHERE+

In stage A responders, efgartigimod PH20 SC demonstrated aINCAT improvement through Week 36 of ADHERE+ regardless of prior treatment status. Mean change from run-in baseline through ADHERE+ Week 36 improved regardless of prior CIDP treatment (corticosteroids, –1.3; IVIg/SCIg, –1.4; off treatment, –0.9)

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ABBREVIATIONS

aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CI, confidence interval; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; ECI, evidence of clinical improvement; ECMD, evidence of clinically meaningful deterioration; EFG, efgartigiomod PH20; Fc, fragment crystallizable; HR, hazard ratio; IgG, immunoglobulin G; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-Built Overall Disability Scale; IVIg, intravenous immunoglobulin; MGS, mean grip strength; mITT, modified intention-to-treat; OLE, open-label extension; PBO, placebo; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SCIg, subcutaneous immunoglobulin; SE, standard error.

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