025

Treatment Impact of Efgartigimod PH20 SC on I-RODS Daily Activity Assessment in Patients With Chronic Inflammatory Demyelinating Polyneuropathy: Post Hoc Analysis of the Registrational ADHERE Study

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BACKGROUND

- CIDP is a rare, severe, progressive immune-mediated disease leading to disability due to proximal/distal weakness and sensory disturbance[1,2]
- Efgartigimod is a human IgG1 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[3–6] (**Figure 1**)
- Efgartigimod PH20 SC is a coformulation of efgartigimod and PH20 that allows for rapid (30–90s single injection) SC administration of larger volumes[7]

FIGURE 1 Efgartigimod Mechanism of Action

- In the randomized, double-blinded, placebo-controlled ADHERE trial (NCT04281472), efgartigimod PH20 SC demonstrated a significant, clinically meaningful benefit in participants with CIDP, regardless of prior CIDP therapy[6]
- I-RODS is a 24-item participant-reported scale with each item representing a common daily activity or social participation that ranges from very easy to very difficult, with higher scores indicating less disability[9]
- In this post hoc analysis of ADHERE, we report changes in total and individual items of I-RODS

METHODS

- The study design of the ADHERE trial has been reported previously[6]
- The run-in baseline period for ADHERE involved withdrawal of standard treatments for CIDP (ie, off treatment) for ≤12-weeks to identify which participants had active disease
- Participants with active disease received open-label, weekly efgartigimod PH20 SC 1000 mg (stage A)
- Participants who entered Stage B were randomized (1:1) to weekly efgartigimod PH20 SC 1000 mg or placebo for ≤48 weeks
- Participants completed the I-RODS weekly in stage A and every 4 weeks in stage B

Participants

- 322 participants entered stage A (open-label, weekly efgartigimod PH20 SC 1000 mg)
- 221 participants (111 efgartigimod PH20 SC, 110 placebo) were randomized and treated for ≤48 weeks in stage B
- Mean I-RODS score was 40.1 at stage A baseline and 53.6 (efgartigimod PH20 SC) and 51.2 (placebo) at stage B baseline (**Table 1**)
- 191/221 (86.4%) participants had assessments at run-in, stage A, and stage B baselines

TABLE 1 ADHERE Baseline Characteristics

	Open-Label Stage A	Double-Blinded Stage B	
	Efgartigimod PH20 SC (N=322)	Efgartigimod PH20 SC (N=111)	Placebo SC (N=110)
Age, y, mean (SD)	54.0 (13.9)	54.5 (13.2)	51.3 (14.5)
Sex, male, n (%)	208 (64.6)	73 (65.8)	69 (62.7)
Time since diagnosis, y, mean (SD)	4.9 (6.1)	3.7 (4.4)	3.8 (4.7)
Typical CIDP diagnosis, n (%)	268 (83.2)	97 (87.4)	95 (86.4)
Unstable active disease (CDAS: 5), n (%)	197 (61.2)	74 (66.6)	76 (69.1)
Prior treatment (within the past 6 months), n (%)			
Corticosteroids	63 (19.6)	24 (21.6)	23 (20.9)
Immunoglobulins (IVIg, SCIg)	165 (51.2)	48 (43.2)	48 (43.6)
Off treatment[a]	94 (29.2)	39 (35.1)	39 (35.5)
aINCAT score, mean (SD)[b,c]	4.6 (1.7)	3.1 (1.5)	3.3 (1.6)
I-RODS score, mean (SD)[b,c]	40.1 (14.7)	53.6 (17.9)	51.2 (15.4)
Grip strength (dominant hand), kPa, mean (SD)[b,d]	38.5 (24.2)	54.9 (23.6)	58.0 (25.1)

[a]Off treatment was defined as participants who had discontinued treatment ≥6 months before study entry or without previous treatment. [b]Clinical assessments were performed at the beginning of each stage. [c]Lower scores represent improvement on aINCAT, while higher scores represent improvement for I-RODS. [d]Grip strength scores in nondominant hand were similar.

Change in I-RODS Centile Metric Score

- At stage B baseline, the mean (SE) change in I-RODS centile metric score compared with run-in baseline was 3.5 (0.98). At Stage B last assessment, these scores were 5.7 (1.88) and -4.9 (1.82) for participants who received efgartigimod and placebo, respectively
- At stage B baseline, 36/97 (37.1%) and 34/92 (37.0%) participants randomized to efgartigimod or placebo, respectively, had ≥4-point improvement in I-RODS centile metric score compared with run-in. At stage B last assessment, a similar number of participants in the efgartigimod group (37/97; 38.1%) had this improvement, while it was lower in the placebo group (24/92; 26.1%)

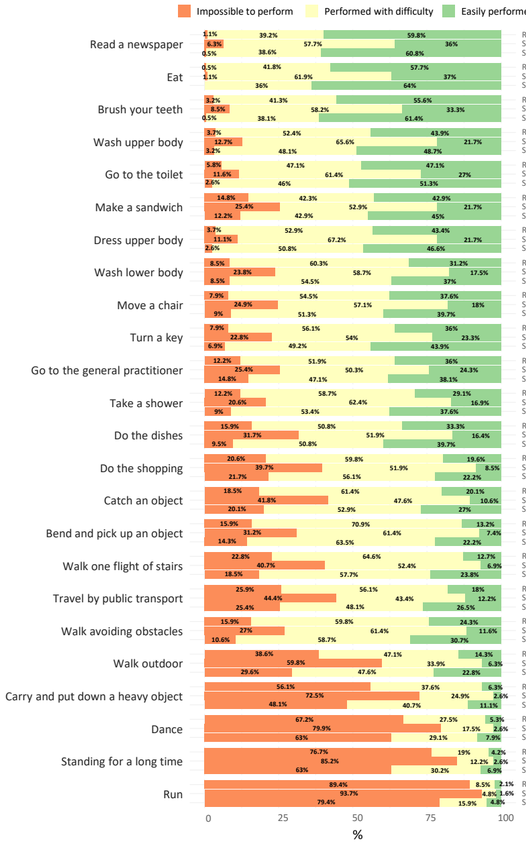
Change in individual I-RODS items

- The tasks become more difficult to perform between run-in baseline and stage A baseline, and improvements were observed across all 24 items from run-in and stage A baselines to stage A last assessment (**Figure 2A**)
- Separation of efgartigimod PH20 SC from placebo was noted for all 24 individual I-RODS items at stage B last assessment (**Figure 2B**)
- Maintenance or further improvement in efficacy was observed for participants randomized to efgartigimod PH20 SC on all 24 I-RODS items (**Figure 2B**); a loss of efficacy was observed in patients randomized to placebo on all 24 items
- In addition to improvements with efgartigimod PH20 SC in the easy-to-perform tasks, improvements were also seen in the more difficult tasks (**Figures 2A** and **2B**)
  - The tasks increase in difficulty from top to bottom across the graphs

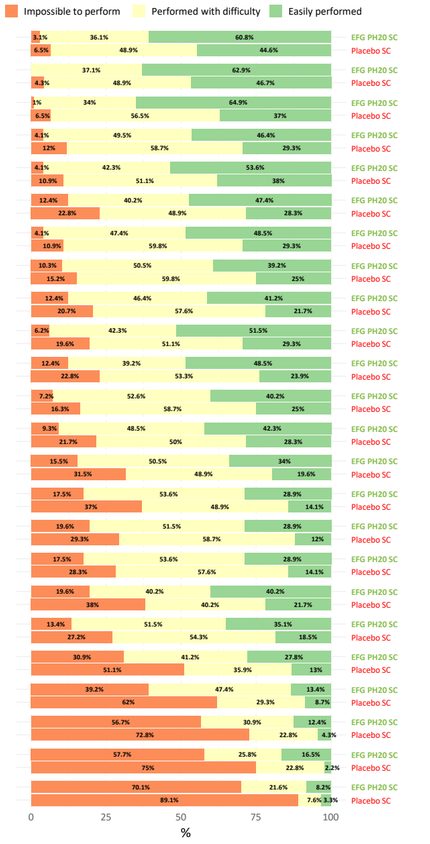
RESULTS

FIGURE 2

A Response to Individual I-RODS Questions at Run-in Baseline, Stage A Baseline and Stage A Last Assessment



B Response to Individual I-RODS Questions at Stage B Last assessment



KEY TAKEAWAYS

- Efgartigimod PH20 SC resulted in clinically meaningful improvements in functional ability compared with placebo, as evidenced by change from baseline in the I-RODS centile metric score
- A higher proportion of participants receiving efgartigimod PH20 SC (38.1%) vs placebo (26.1%) experienced ≥4-point improvement in I-RODS centile metric score at stage B last assessment
- Improvements with efgartigimod PH20 SC vs placebo were also seen across individual I-RODS items
- Improvements in I-RODS items following treatment with efgartigimod PH20 SC may potentially reflect enhanced quality of life in patients with CIDP, which could be evaluated in future studies

Presented at the American Academy of Neurology (AAN) Annual Meeting 2025; April 5–9, 2025; San Diego, CA, USA

ABBREVIATIONS

aINCAT: adjusted Inflammatory Neuropathy Cause and Treatment; CDAS: CIDP disease activity status; CIDP: chronic inflammatory demyelinating polyneuropathy; EFG: efgartigimod; IgG: immunoglobulin G; I-RODS: Inflammatory Rasch-built Overall Disability Scale; IVIg: intravenous immunoglobulin; kPa: kilopascal; PH20: recombinant human hyaluronidase PH20; PRO: patient-reported outcomes; RI: run-in; SC: subcutaneous; SCIg: subcutaneous immunoglobulin; SD: standard deviation; SE: standard error; y: year.

DISCLOSURES AND ACKNOWLEDGMENTS

JAA: Akcea, Alexion, Alnylam Pharmaceuticals, Annexon, argenx, CSL Behring, Grifols, Immunovant, Immupharma, Johnson & Johnson, Pfizer, Takeda Pharmaceuticals; **JL**: argenx, Janssen, Novartis, Pfizer, Sanofi; **MS**: argenx, Bayer, Biogen Idec, Biotest, CSL Behring, Genzyme, Grifols, Immunovant, Kedrion, Merck, Novartis, Octapharma, PPTA, Roche, Sanofi-Aventis, TEVA, UCB; **IM**: argenx, CSL Behring, J&J, LFB, Novartis, Octapharma, Talecris; **KGG**: Alexion, Amgen, argenx, UCB, Xeris Pharmaceuticals; **SK**: Alexion, argenx, CSL Behring, Takeda Pharmaceuticals; **GL**: Biogen, Chromocell, CSL Behring, Home Biosciences, Janssen, Lilly, Sangamo Therapeutics, Vertex Pharmaceuticals, Zambon; **LQ**: Annexon Biosciences, Alnylam Pharmaceuticals, argenx, Avilar Therapeutics, Biogen, CIBERER, CSL Behring, Dianthus, Fundació La Marató, GBS-CIDP Foundation International, Grifols, Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), Janssen, LFB, Lundbeck, Merck, Novartis, Octapharma, Roche, Sanofi, UCB; **NS**: Alnylam Pharmaceuticals, Takeda Pharmaceuticals; **CK**: Alpine, Alexion, Alnylam Pharmaceuticals, Annexon, argenx, Astra Zeneca, Biogen, Corino, CSL Behring, Genentech, Ionis, Neuroderm, Novo Nordisk, Pfizer, Sanofi, UCB, Takeda Pharmaceuticals, Zai Lab; **TS**: Alexion, Alnylam Pharmaceuticals, argenx, Bayer Vital, Biogen, Bristol Myers Squibb, Celgene, Centogene, CSL Behring, Euroimmun, Grifols, Hexal AG, Horizon, Janssen-Cilag, Merck Serono, Novartis, Pfizer, Roche, Sanofi, Siemens, Swedish Orphan Biovitrum, Teva, Viatris; **SR**: Annexon, argenx, the Beijing Association of Holistic and Integrated Medicine, British Medical Association, CSL Behring, Dianthus, Excemed, Fresenius, GBS/CIDP Foundation International, Guillain-Barré syndrome and Related Inflammatory Neuropathies (GAIN) charity, Hansa Biopharma, the Irish Institute of Clinical Neuroscience, Medical Research Council (UK), National Institute of Health Research, the Pathological Society of Great Britain Ireland, Peripheral Nerve Society, Takeda Pharmaceuticals, UCB, the University of Oxford's John Fell Fund, Wellcome Trust; **AEL**: Alnylam Pharmaceuticals, argenx, CSL Behring, Grifols, LFB, Pfizer, Sanofi; **JTG, GI, ADR, BVH**: Employees of argenx; **RY**: Alnylam Pharmaceuticals Japan, CSL Behring, FP Pharm Co, Japan Tobacco Inc, Kyowa Kirin, Ono Pharmaceutical Co Ltd, Takeda Pharmaceuticals; **PVD**: Annexon Biosciences, argenx, Grifols, Hansa Biopharma, Octapharma, Prinses Beatrix Spierfonds, Roche, Sanofi, Sanquin, Takeda Pharmaceuticals; **RAL**: Alexion, Annexon Biosciences, argenx, Boehringer Ingelheim, CSL Behring, Dianthus, GBS/CIDP Foundation International, Grifols, Immunovant, Johnson & Johnson, Medscape, Nervosave, Novartis, Nuvig, Peripheral Nerve Society, Sanofi, Seismic, Takeda Pharmaceuticals. This study was sponsored by argenx. Medical writing support was provided by Envision Pharma Group and funded by argenx. The authors gratefully acknowledge the trial participants and investigators involved.

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