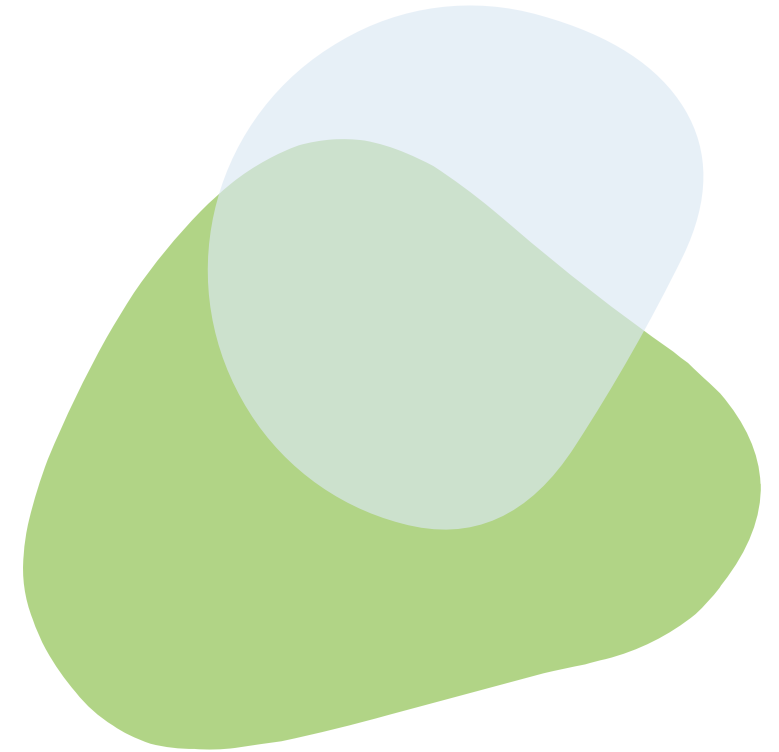


Efficacy, Safety, and Tolerability of Efgartigimod in Patients With Chronic Inflammatory Demyelinating Polyneuropathy: Results From the ADHERE Trial



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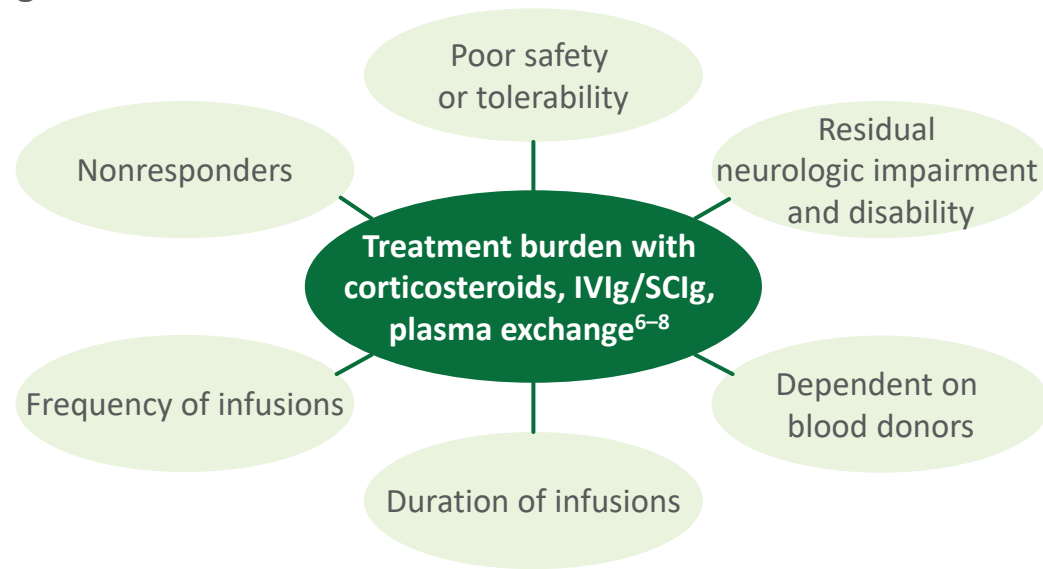
| | |
|--|---|
| Jeffrey A. Allen | Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, argenx , CSL Behring, Grifols, Immunovant, ImmuPharma, Johnson & Johnson, Pfizer, Takeda |
| Ivana Basta | Actavis, Dianthus Therapeutics, Mylan, Pfizer, Salveo Pharma |
| Christian Eggers | argenx , Biogen, GlaxoSmithKline, UCB |
| Kelly G. Gwathmey | Alexion, argenx , UCB, Xeris Pharmaceuticals |
| Channa Hewamadduma | argenx , Biogen, Lupin, Roche, UCB |
| Satoshi Kuwabara | Alexion, argenx , CSL Behring, Takeda |
| Frank Leypoldt | Alexion, Bayer, Biogen, Fresenius Kabi, Grifols, Merck, Novartis, Roche, Teva Pharmaceuticals |
| Marta Lipowska | argenx , CSL Behring, Kedrion, Medison Pharma/Alnylam, Pfizer, Sanofi, Sobi, Takeda |
| Murray Lowe Anissa Tse | Employees of argenx at the time of the study |
| Giuseppe Lauria | Biogen, Chromocell, CSL Behring, Home Biosciences, Janssen, Lilly, Sangamo Therapeutics, Vertex Pharmaceuticals, Zambon |
| Luis Querol | Annexon Biosciences, Alnylam, argenx , Avilar Therapeutics, Biogen, CIBERER, CSL Behring, Dianthus Therapeutics, 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 Genzyme, UCB |
| Niraja Suresh | Alnylam, Takeda |
| Pieter A. van Doorn | Annexon Biosciences, argenx , Grifols, Hansa Biopharma, Immunic Therapeutics, Octapharma, Prinses Beatrix Spierfonds, Roche, Sanofi, Sanquin |
| Richard A. Lewis | Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, argenx , Boehringer Ingelheim, CSL Behring, GBS/CIDP Foundation International, Grifols, Johnson & Johnson, Medscape, MGFA, Novartis, Peripheral Nerve Society, Pfizer, Roche, Sanofi, Takeda |
| Jeffrey T. Guptill Erik Hofman Peter Ulrichs Benjamin Van Hoorick | Employees of argenx |
| Yessar Hussain Jie Lin Ting Chang Ryo Yamasaki | Nothing to declare |

Efgartigimod is an investigational drug. Efgartigimod has not been approved as safe or effective by the FDA for use in CIDP

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CIDP is a Severe and Debilitating Immune-Mediated Polyneuropathy¹⁻⁴

- CIDP is an **autoimmune, inflammatory, demyelinating neuropathy** resulting in distal/proximal weakness and/or sensory deficits, with a high treatment burden^{1,5}



- Evidence supports **a role for pathogenic IgGs** in the pathogenesis of CIDP, although in most patients a specific antibody is not detectable^{2,9-11}
- **Efgartigimod** is a human IgG1 Fc fragment that outcompetes endogenous IgG, preventing recycling, and promoting lysosomal degradation of IgG, **without impacting IgG production**¹²⁻¹⁷
- **Efgartigimod PH20 SC** is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for **rapid (30–90s single injection)** SC administration of larger volumes^{18,19}

Efgartigimod has been shown to **reduce IgG antibody levels** in healthy volunteers and patients with other autoimmune diseases^{12,14-17}

CIDP, chronic inflammatory demyelinating polyneuropathy; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin; PH20, recombinant human hyaluronidase PH20; s, second; SC, subcutaneous; SCIg, subcutaneous immunoglobulin.

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ADHERE (NCT04281472): A Multicenter, Multi-Stage, Randomized-Withdrawal, Double-Blinded, Placebo-Controlled Trial of Efgartigimod in CIDP

IDENTIFY PATIENTS WITH ACTIVE DISEASE

SCREENING

- Diagnosis of probable or definite CIDP confirmed by adjudication panel of CIDP experts¹
- Current CIDP treatment:
 - Corticosteroids
 - IVIg/SCIg
 - Off treatment: treatment discontinued ≥ 6 months before study entry or without previous treatment

RUN-IN PERIOD

≤ 12 weeks

- Participants on treatment must suspend therapy and demonstrate evidence of clinically meaningful deterioration^a
- Patients off treatment with active disease may skip the run-in and enter stage A

TREATMENT PERIOD

OPEN-LABEL STAGE A

1000 mg efgartigimod PH20 SC weekly

Responders

DOUBLE-BLINDED STAGE B

1000 mg efgartigimod PH20 SC weekly

Placebo PH20 SC weekly

≤ 12 weeks

≤ 48 weeks

Until ECI^b for 2 consecutive visits

Until 88 events (relapses)^c

PRIMARY ENDPOINT

Percentage of participants with evidence of clinical improvement

PRIMARY ENDPOINT

Time to first aINCAT deterioration^d (relapse) compared with stage B baseline

aINCAT, adjusted INCAT; CIDP, chronic inflammatory demyelinating polyneuropathy; ECI, evidence of clinical improvement; ECMD, evidence of clinically meaningful deterioration; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-built Overall Disability Scale; IVIg, intravenous immunoglobulin; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SCIg, subcutaneous immunoglobulin.

^aECMD was defined as an aINCAT increase of ≥ 1 points, an I-RODS decrease of ≥ 4 points, or a grip strength decrease of ≥ 8 kPa. ^bECI was defined as an improvement (≥ 1 -point decrease) in aINCAT score compared with stage A baseline score. For non-off-treatment participants who had no change in aINCAT score and deteriorated on I-RODS and/or grip strength during the run-in period, ECI was defined as an increase of ≥ 4 points in I-RODS and/or an increase of ≥ 8 kPa in grip strength during stage A, or improvement in aINCAT. ^cThe primary endpoint was assessed once 88 total relapses or events were achieved in stage B and was based on the hazard ratio for the time to first aINCAT deterioration (ie, relapse). ^daINCAT deterioration was defined as an increase of ≥ 1 points in aINCAT score compared with stage B baseline.

1. Van den Bergh PYK, et al. *Eur J Neurol*. 2010;17(3):356–63.

Baseline Characteristics Were Similar Between Stages A and B and Well Balanced Between Treatment Groups

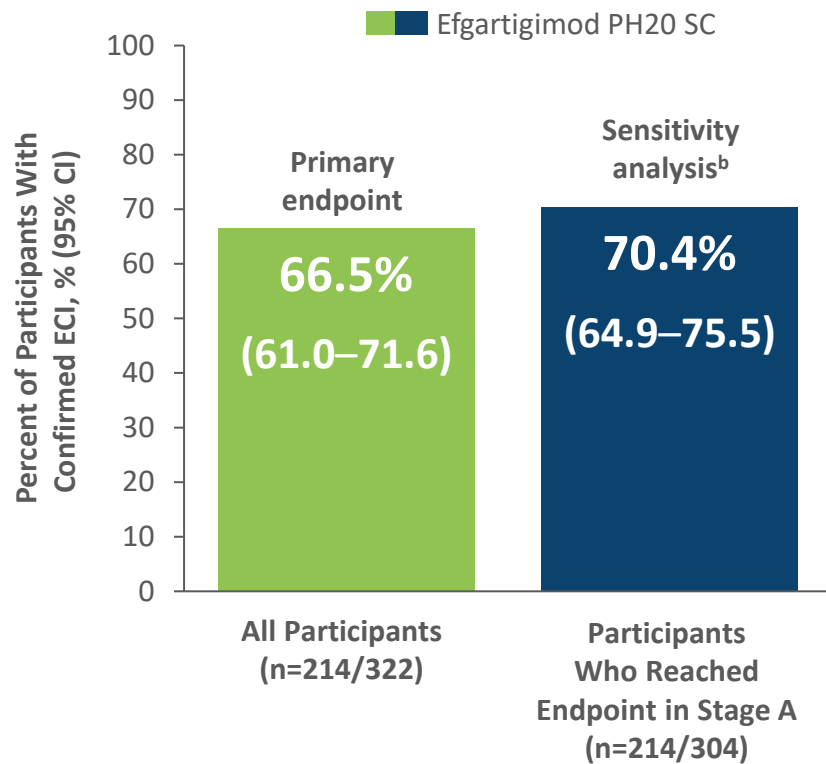
| | Open-Label Stage A | Double-Blinded Stage B | |
|--|------------------------------|------------------------------|-----------------|
| | Efgartigimod PH20 SC (N=322) | Efgartigimod PH20 SC (N=111) | Placebo (N=110) |
| Age, y, mean (SD) | 54.0 (13.9) | 54.5 (13.2) | 51.3 (14.5) |
| Sex, male, n (%) | 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 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) |

aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CDAS, CIDP disease activity status; CIDP, chronic inflammatory demyelinating polyneuropathy; I-RODS, Inflammatory Rasch-built Overall Disability Scale; IVIg, intravenous immunoglobulin; kPa, kilopascal; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SCIg, subcutaneous immunoglobulin; SD, standard deviation; y, year.

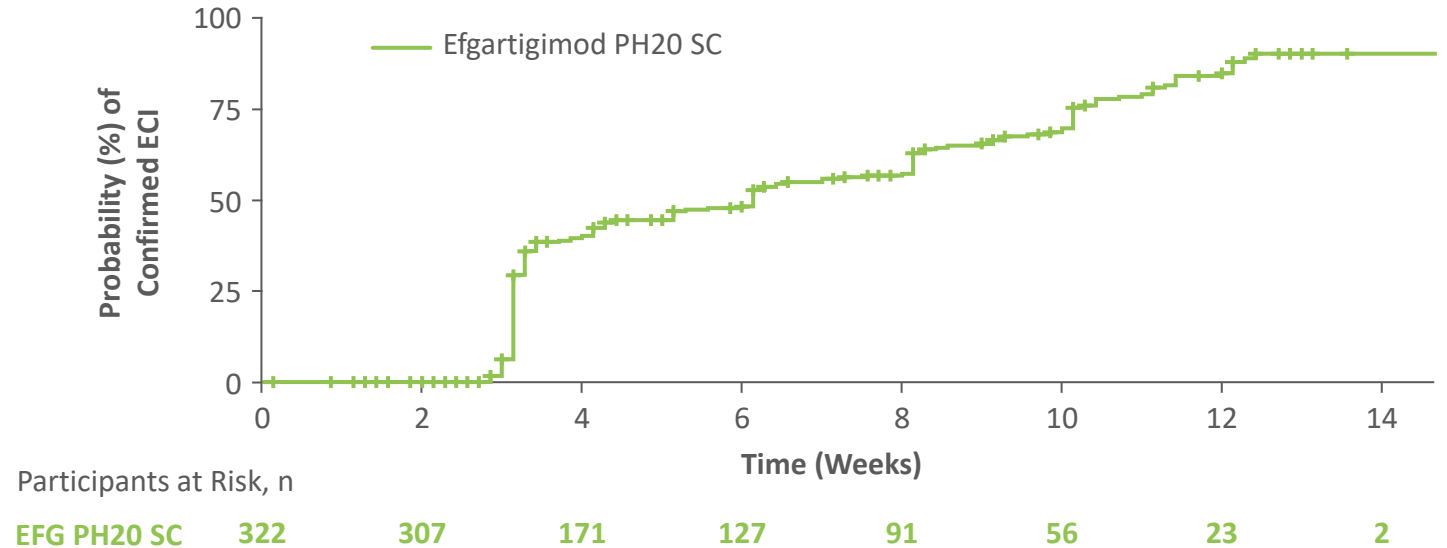
^aOff treatment was defined as participants who had discontinued treatment ≥6 months before study entry or without previous treatment. ^bClinical assessments were performed at the beginning of each stage. ^cLower scores represent improvement on aINCAT, while higher scores represent improvement for I-RODS. ^dNondominant scores were similar.

Efgartigimod Was Clinically Effective: 66.5% of Participants Demonstrated Clinical Improvement in Stage A

Open-Label Stage A:
Percent of Participants With Confirmed ECI^a



Open-Label Stage A: Secondary Endpoint
Time to Initial Confirmed ECI^a



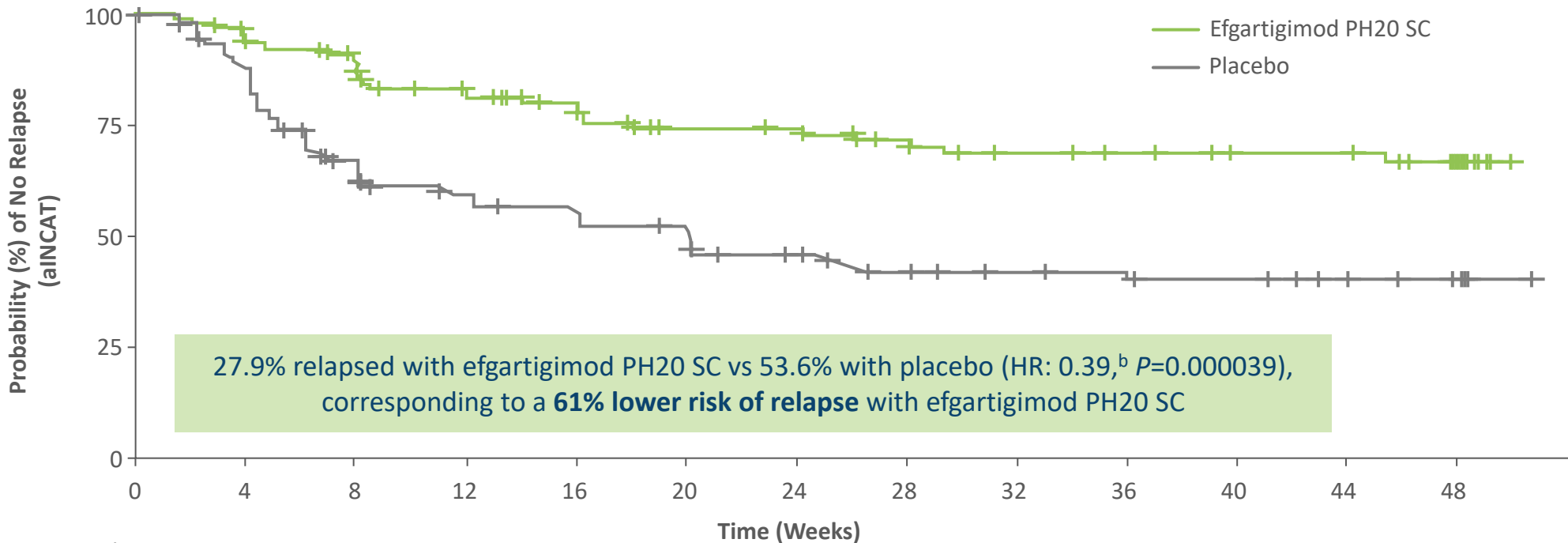
Rapid onset of clinically meaningful improvement with efgartigimod:
39.8% (128/322) of participants demonstrated ECI by Week 4
Week 4 was the earliest time point at which the ECI criteria could have been met

aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CI, confidence interval; CIDP, chronic inflammatory demyelinating polyneuropathy; ECI, evidence of clinical improvement; I-RODS, Inflammatory Rasch-built Overall Disability Scale; kPa, kilopascal; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous.

^aECI was defined as an improvement (≥ 1 -point decrease) in aINCAT score compared with stage A baseline score. For non-off-treatment participants who had no change in aINCAT score and deteriorated on I-RODS and/or grip strength during the run-in period, ECI was defined as an increase of ≥ 4 points in I-RODS and/or an increase of ≥ 8 kPa in grip strength during stage A or improvement in aINCAT. ^bPrespecified sensitivity analysis excluded participants who were ongoing in stage A at the time of study completion (after the 88th event had occurred) and did not have the full opportunity to achieve a response.

Efgartigimod Significantly Reduced the Risk of Relapse by 61% Compared With Placebo in Stage B

Double-Blinded Stage B: Primary Endpoint
Time to First aINCAT Deterioration^a Compared With Stage B Baseline



Participants at Risk, n

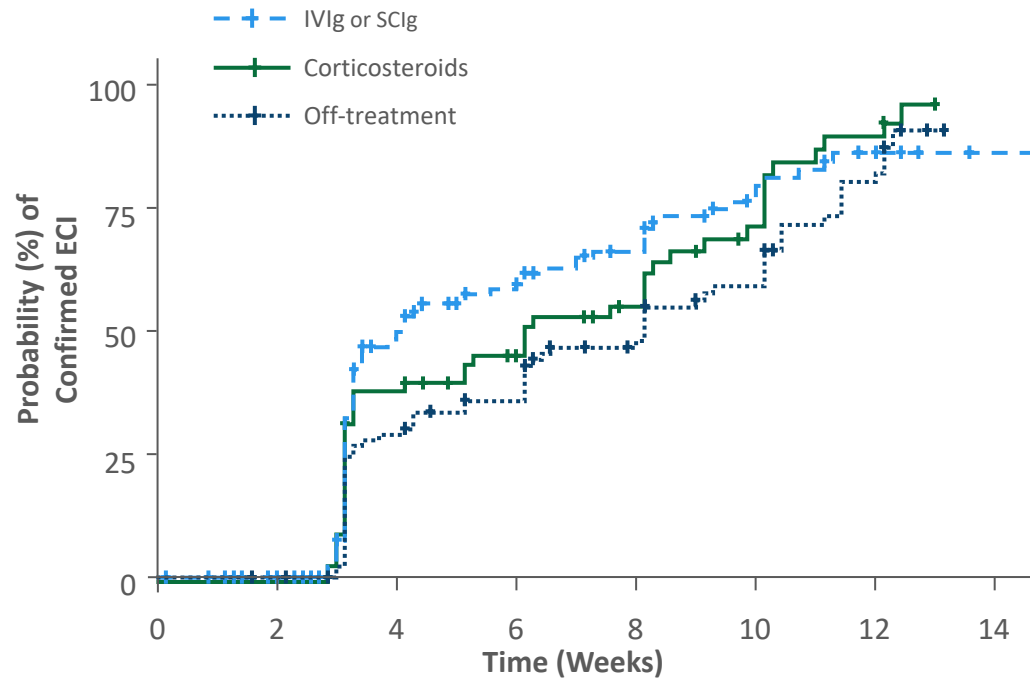
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|--------------------|------------|------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| EFG PH20 SC | 111 | 107 | 93 | 80 | 68 | 56 | 55 | 48 | 42 | 40 | 36 | 36 | 28 |
| Placebo | 110 | 94 | 67 | 55 | 51 | 47 | 38 | 31 | 28 | 26 | 24 | 21 | 16 |

aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIDP, chronic inflammatory demyelinating polyneuropathy; HR, hazard ratio; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous.

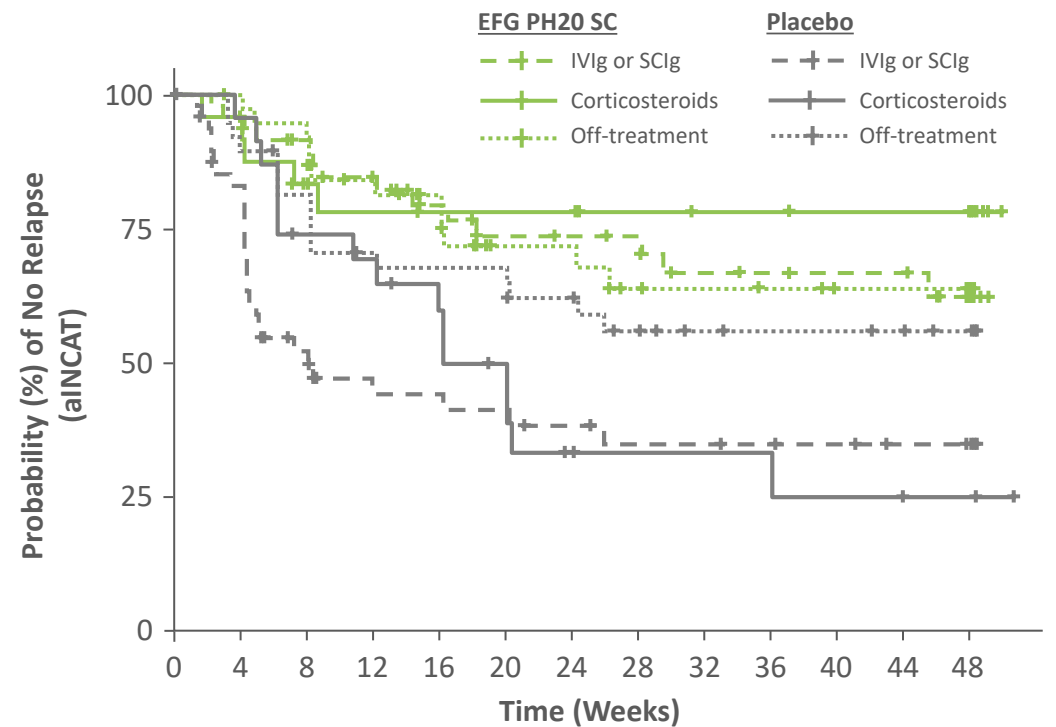
^aThe time to first aINCAT deterioration was defined as the number of days from first dose in stage B to the first occurrence of an increase of ≥ 1 points on the aINCAT score compared with stage B baseline. ^bThe HR was obtained from a Cox proportional hazard model with treatment as a fixed effect, and the model was stratified by prior CIDP therapy and aINCAT score during stage A.

Clinical Benefit Was Demonstrated Across Multiple Efficacy Measures, Regardless of Prior CIDP Treatment

Open-Label Stage A: Secondary Endpoint
Time to Initial Confirmed ECI by Prior Treatment^a



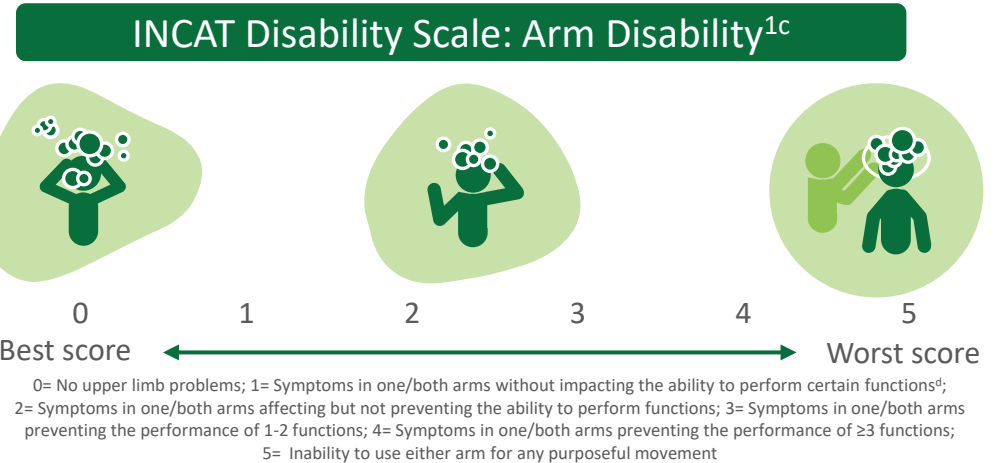
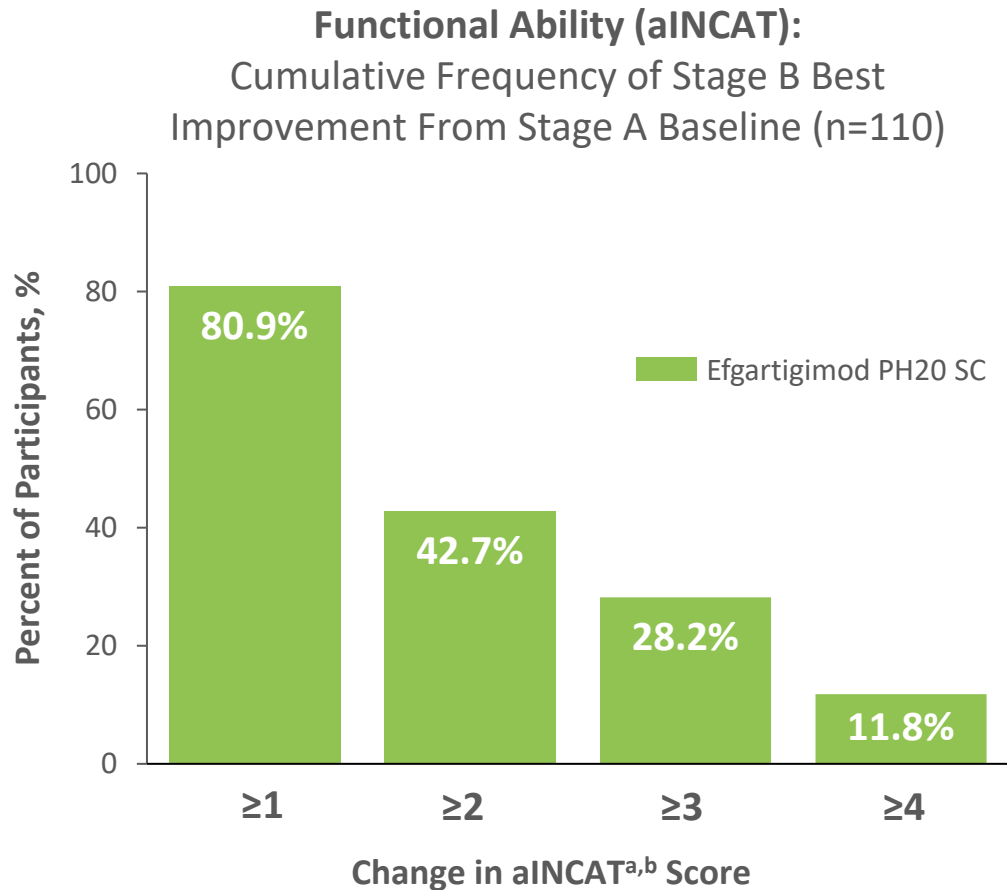
Double-Blinded Stage B: Primary Endpoint
Time to First aINCAT Deterioration^b Compared With Stage B Baseline
by Prior Treatment



aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIDP, chronic inflammatory demyelinating polyneuropathy; ECI, evidence of clinical improvement; EFG, efgartigimod; I-RODS, Inflammatory Rasch-built Overall Disability Scale; IVIg, intravenous immunoglobulin; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous; SCIg, subcutaneous immunoglobulin.

^aECI was defined as an improvement (≥ 1 -point decrease) in aINCAT score compared with stage A baseline score. For non-'off-treatment' participants who had no change in aINCAT score and deteriorated on I-RODS and/or grip strength during the run-in period, ECI was defined as an increase of ≥ 4 points in I-RODS and/or an increase of ≥ 8 kPa in grip strength during stage A or improvement in aINCAT. ^bThe time to first aINCAT deterioration was defined as the number of days from first dose in stage B to the first occurrence of an increase of ≥ 1 points on the aINCAT score compared with stage B baseline.

Efgartigimod-Treated Participants Experienced Deep and Clinically Meaningful Improvements in Functional Ability



aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; INCAT, Inflammatory Neuropathy Cause and Treatment; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous.

^aMean stage A baseline aINCAT score was 4.5. Some participants could not improve beyond a certain level due to their baseline aINCAT score, ie, participants with an aINCAT baseline score of 2 or 3 could not reach improvements of 3 or 4, respectively.

^bFor the aINCAT score, changes in the function of the upper limbs from 0 (normal) to 1 (minor symptoms) or vice versa were not recorded as deterioration or improvement, because these changes were not considered clinically significant.

^cThe INCAT disability score¹ is a 10-point scale that assesses activity limitations of arms and legs; both are scored separately from 0–5, with 0 representing no functional impairment and 5 representing inability to make any purposeful movement.

^dFunctions include: doing all zips and buttons, washing or brushing hair, using a knife and fork together, and handling small coins.

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Efgartigimod Was Well Tolerated and Most TEAEs Were Mild or Moderate in Severity

| | Open-Label Stage A | Double-Blinded Stage B | |
|---|--|--|-------------------------------|
| n (%) | Efgartigimod PH20 SC (N=322; PYFU=46.9) | Efgartigimod PH20 SC (N=111; PYFU=56.7) | Placebo (N=110; PYFU=42.1) |
| Participant with event | | | |
| Any TEAE | 204 (63.4) | 71 (64.0) | 62 (56.4) |
| Any SAE | 21 (6.5) | 6 (5.4) | 6 (5.5) |
| Injection site reactions | 62 (19.3) | 16 (14.4) | 7 (6.4) |
| Discontinued due to AEs ^a | 22 (6.8) | 3 (2.7) | 1 (0.9) |
| Deaths ^b | 2 (0.6) | 0 (0) | 1 (0.9) |
| Most common TEAEs (≥5% of participants in any group) | | | |
| Injection site erythema | 33 (10.2) | 6 (5.4) | 0 (0) |
| CIDP | 17 (5.3) | 1 (0.9) | 1 (0.9) |
| Headache | 16 (5.0) | 4 (3.6) | 2 (1.8) |
| Upper respiratory tract infection | 11 (3.4) | 2 (1.8) | 11 (10.0) |
| COVID-19 | 6 (1.9) | 19 (17.1) | 14 (12.7) |
| Injection site bruising | 4 (1.2) | 6 (5.4) | 1 (0.9) |

AE, adverse event; CIDP, chronic inflammatory demyelinating polyneuropathy; COVID-19, coronavirus disease 2019; PH20, recombinant human hyaluronidase PH20; PYFU, participants years of follow-up; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event.

^aTEAEs grouped under Preferred Terms leading to efgartigimod PH20 SC discontinuation were Cardiac arrest (n=1), Injection site rash (n=1), COVID-19 (n=1), COVID-19 pneumonia (n=1), Muscular weakness (n=1), CIDP (n=15), Quadriparesis (n=1), and Pruritus (n=1) in stage A; COVID-19 pneumonia (n=1), Prostate cancer (n=1), and Transitional cell carcinoma (n=1) in stage B efgartigimod PH20 SC; and Pneumonia (n=1) in stage B placebo SC. ^bTwo deaths (cardiac arrest and deterioration of CIDP) in stage A were considered not related to efgartigimod PH20 SC by the investigator; one death (pneumonia) in the placebo arm of stage B was considered treatment related by the investigator.

Conclusions

- ADHERE, the largest randomized, controlled trial of any CIDP treatment to date, supports a key role for IgG autoantibodies in CIDP pathology
- Regardless of prior CIDP therapy, participants treated with efgartigimod PH20 SC demonstrated clinical benefits:
 - Evidence of rapid clinical improvement (stage A)
 - Maintained clinical response to treatment (stage B)
 - 61% reduced risk of relapse compared with placebo (stage B)
- Weekly efgartigimod PH20 SC was well tolerated and demonstrated a consistent safety profile with prior clinical trials in other autoimmune diseases^{1–4}
- A single, rapid (30–90s) injection of weekly efgartigimod PH20 SC may provide a new therapeutic option to reduce treatment burden in patients with CIDP