Impact of Efgartigimod PH20 SC on Autoimmunity Biomarkers in the ADHERE Trial: Exploratory Analyses

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Disclosure

- Jérôme Joël Devaux, Clémence Roué, and Jérémie El Bechir have no actual or potential conflict of interest in relation to this presentation.

- Benjamin Van Hoorick, Erik Hofman and Geoffrey Istas are employees of argenx

- CIDP is an **autoimmune** peripheral neuropathy characterized by **progressive or relapsing muscle weakness and sensory disturbance** and associated with a **high treatment burden**[1–5]
- Although the exact pathophysiology of CIDP is yet to be fully understood, **IgG autoantibodies** play a key role in **demyelination**[6–9]
- **Efgartigimod PH20 SC** is a coformulation of efgartigimod and (rHuPH20, which allows for **rapid (30–90s single injection)** SC administration[10,11]

Demyelination Due to IgG Autoantibodies

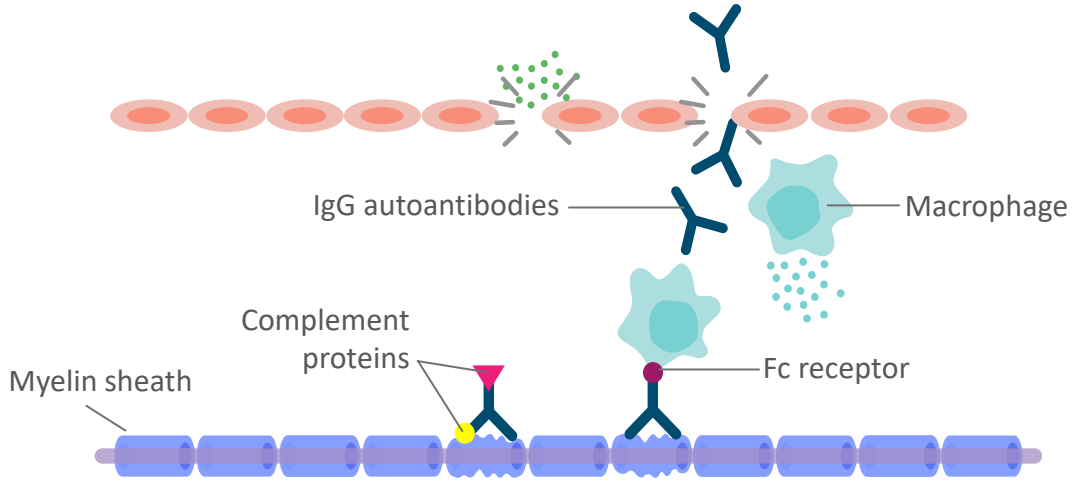
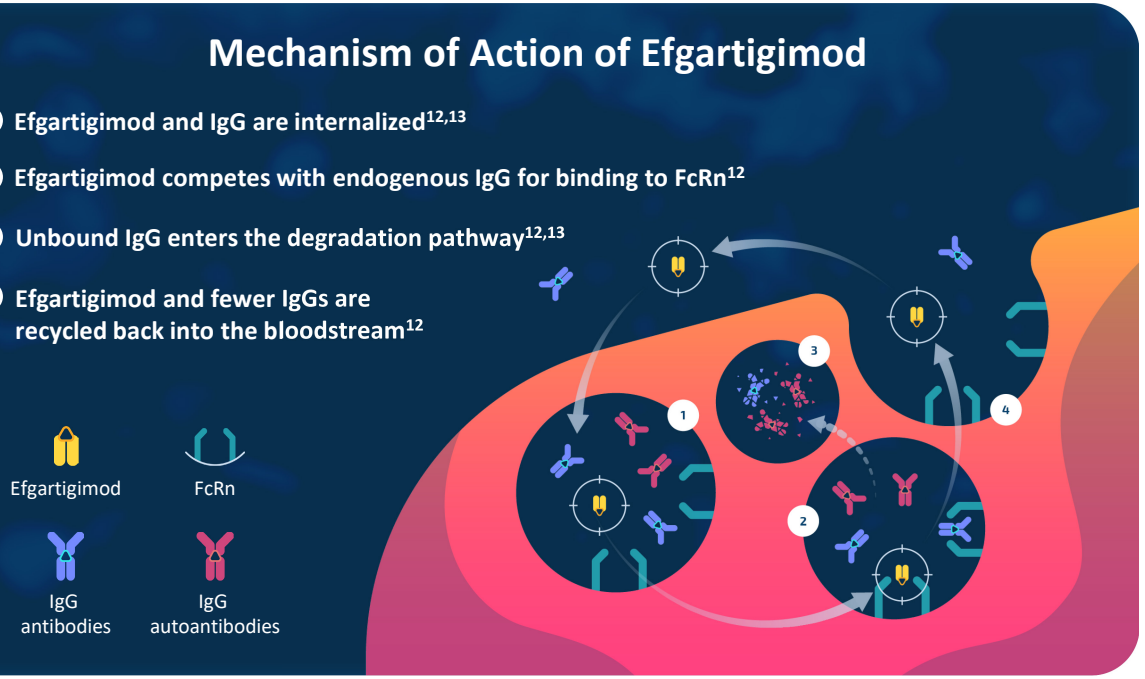


Image adapted from CIDP Progress by argenx (2024). Demyelination due to IgG autoantibodies. https://cidpprogress.com/emerging-evidence?id=935962952. Accessed March 12, 2025.

Mechanism of Action of Efgartigimod

1. Efgartigimod and IgG are internalized[12,13]
2. Efgartigimod competes with endogenous IgG for binding to FcRn[12]
3. Unbound IgG enters the degradation pathway[12,13]
4. Efgartigimod and fewer IgGs are recycled back into the bloodstream[12]

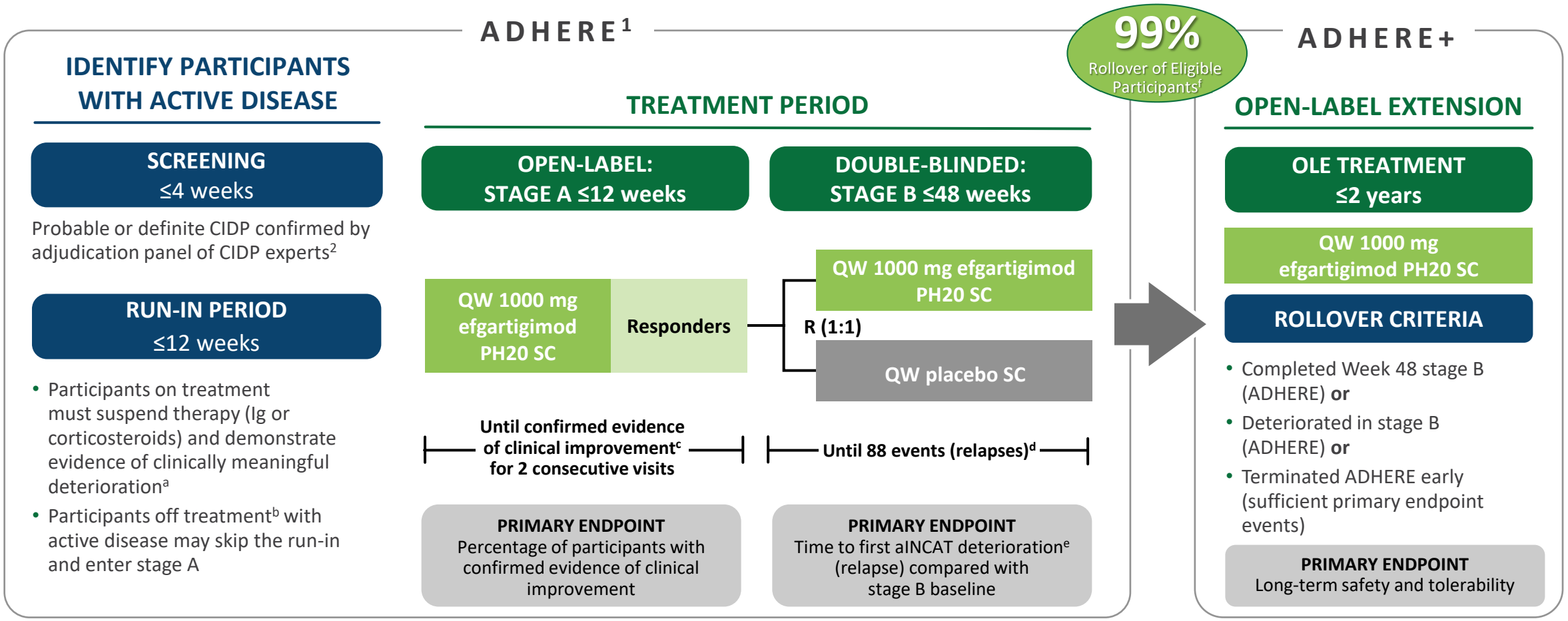


Efgartigimod has been shown to **reduce IgG antibody levels** in healthy volunteers and patients with other autoimmune diseases[13–18]

CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; IgG, immunoglobulin G; PH20, recombinant human hyaluronidase PH20; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous.

1. Cox ZC, et al. *Clin Geriatr Med.* 2021;37(2):327–45. 2. Van den Bergh PYK, et al. *Eur J Neurol.* 2021;28(11):3556–83. 3. Brun S, et al. *Immuno.* 2022;2(1):118–31. 4. Bus SRM, et al. *J Neurol.* 2022;269(2):945–55. 5. Gorson KC. *Ther Adv Neurol Disord.* 2012;5(6):359–73. 6. Querol LA, et al. *Neurotherapeutics.* 2022;19(3):864–73. 7. Yan WX, et al. *Ann Neurol.* 2000;47(6):765–75. 8. Dziadkowiak E, et al. *Int J Mol Sci.* 2021;23(1):179. 9. Koike H, et al. *Neurol Ther.* 2020;9(2):213–27. 10. Locke KW, et al. *Drug Deliv.* 2019;26(1):98–106. 11. VYVGART HYTRULO. Prescribing information. argenx; 2024. https://www.argenx.com/product/vyvgart-hytrulo-prescribing-information.pdf. Accessed March 12, 2025. 12. Ulrichts P, et al. *J Clin Invest.* 2018;128(10):4372–86. 13. Sesarman A, et al. *Cell Mol Life Sci.* 2010;67(15):2533–50. 14. Vaccaro C, et al. *Nat Biotech.* 2005;23(10):1283–8. 15. Howard JF Jr, et al. *Lancet Neurol.* 2021;20(7):526–36. 16. Goebeler M, et al. *Br J Dermatol.* 2022;186(3):429–39. 17. Broome CM, et al. *Lancet.* 2023;402(10413):1648–59. 18. Howard JF Jr, et al. *Front Neurol.* 2024;14:1284444.

Efgartigimod in CIDP: Study Designs of ADHERE and ADHERE+

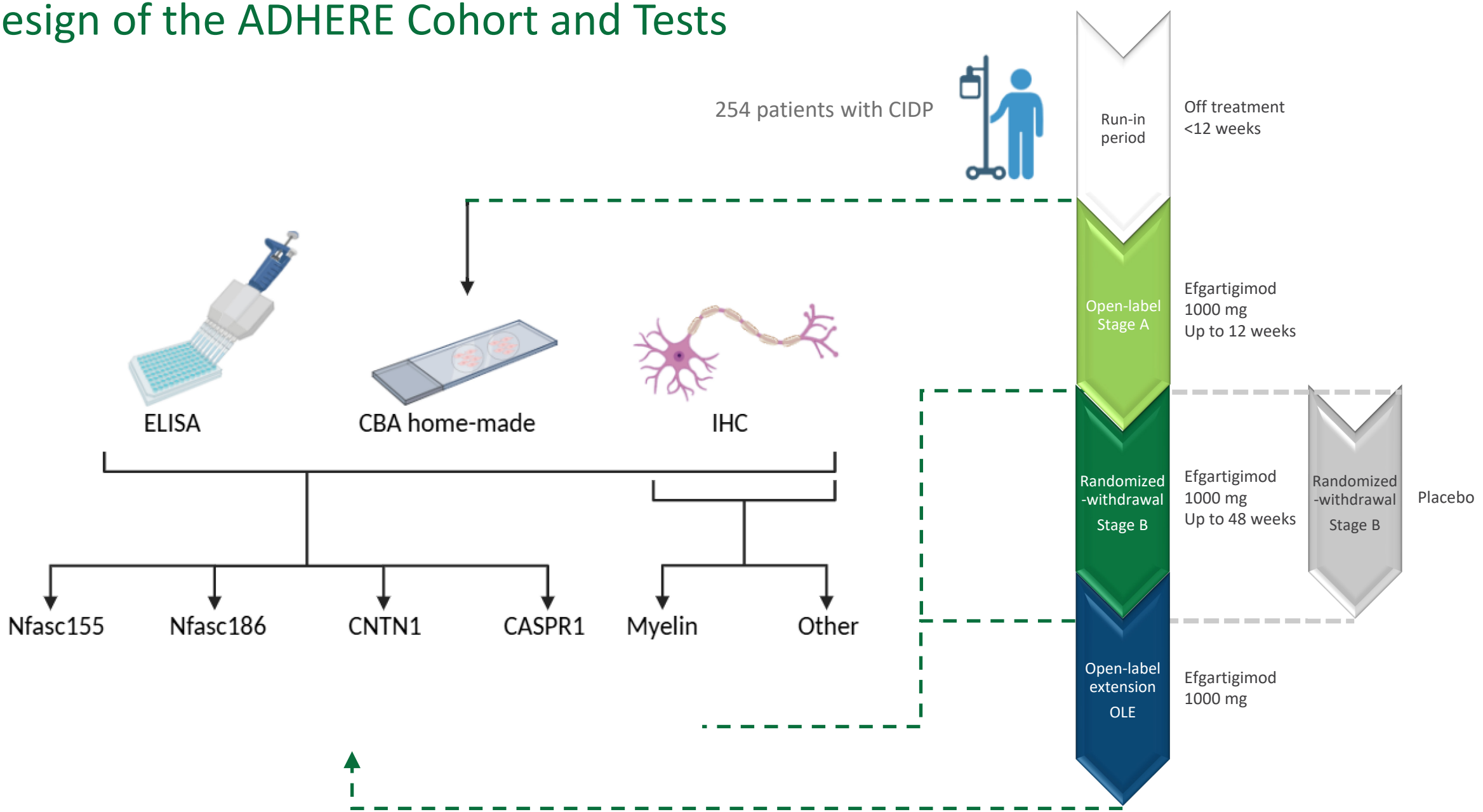


aINCAT, adjusted Inflammatory Neuropathy Cause and Treatment; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; ECI, evidence of clinical improvement; ECMD, evidence of clinically meaningful deterioration; HR, hazard ratio; Ig, immunoglobulin; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-Built Overall Disability Scale; IVIg, intravenous immunoglobulin; OLE, open-label extension; PH20, recombinant human hyaluronidase PH20; QW, once weekly; R, randomization; SC, subcutaneous; SCIg, subcutaneous immunoglobulin.

[a]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. [b]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. [c]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 four injections and two 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 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. [f]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.

1. Allen JA, et al. *Lancet Neurol.* 2024;23(10):1013–24. 2. Van den Bergh PYK, et al. *Eur J Neurol.* 2010;17(3):356–63.

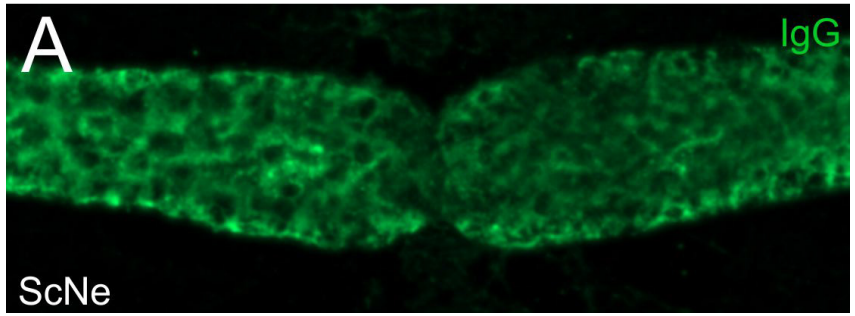
Design of the ADHERE Cohort and Tests



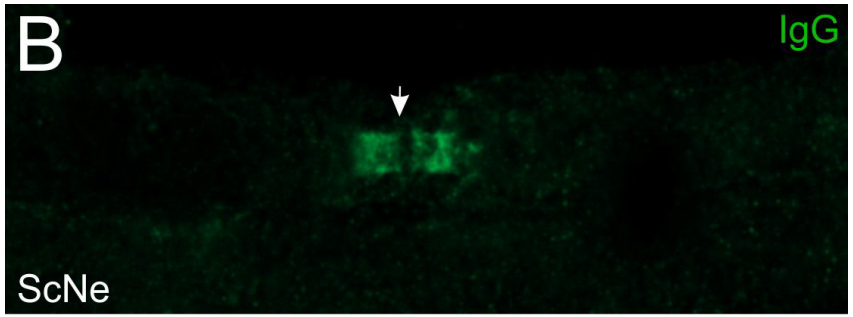
CASPR1, contactin-associated protein-1; CBA, cell-based assay; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CNTN1, contactin-1; ELISA, enzyme-linked immuno-sorbent assay; IHC, immunohistochemistry; Nfasc, neurofascin.

Prevalence of AN and Myelin Reactivity in the ADHERE Cohort

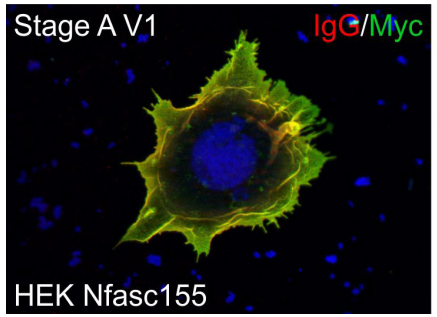
(56/254)



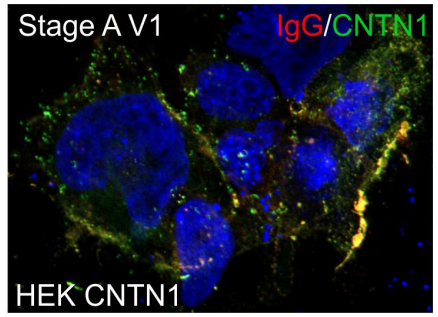
utoimmune nodopathy: 4% (10/254)



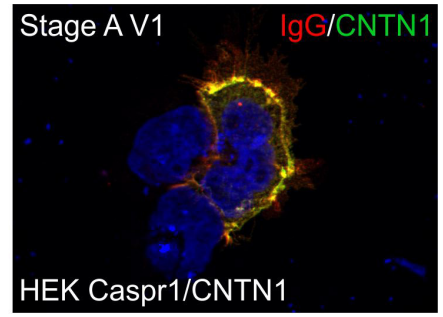
Nfasc155 (n=8)



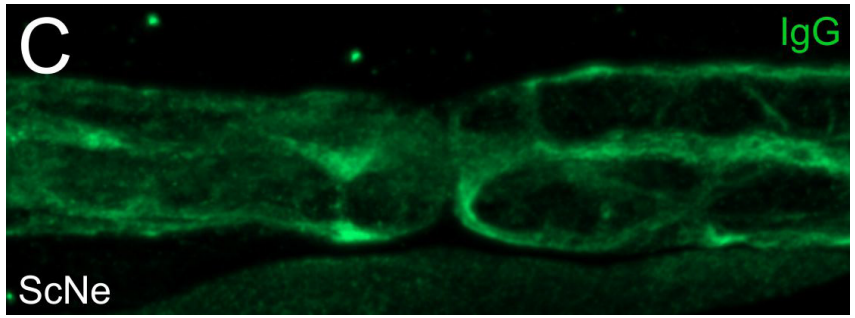
CNTN1 (n=1)



CASPR1 (n=1)

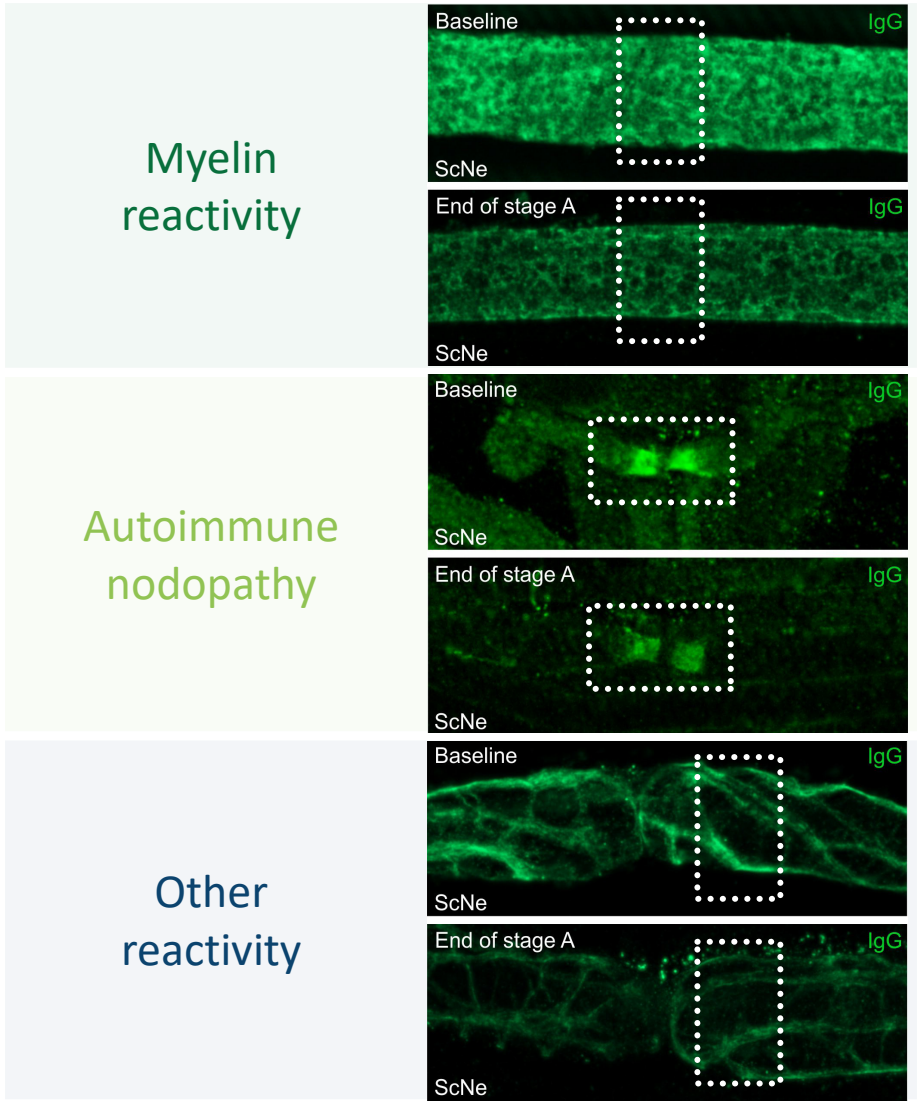


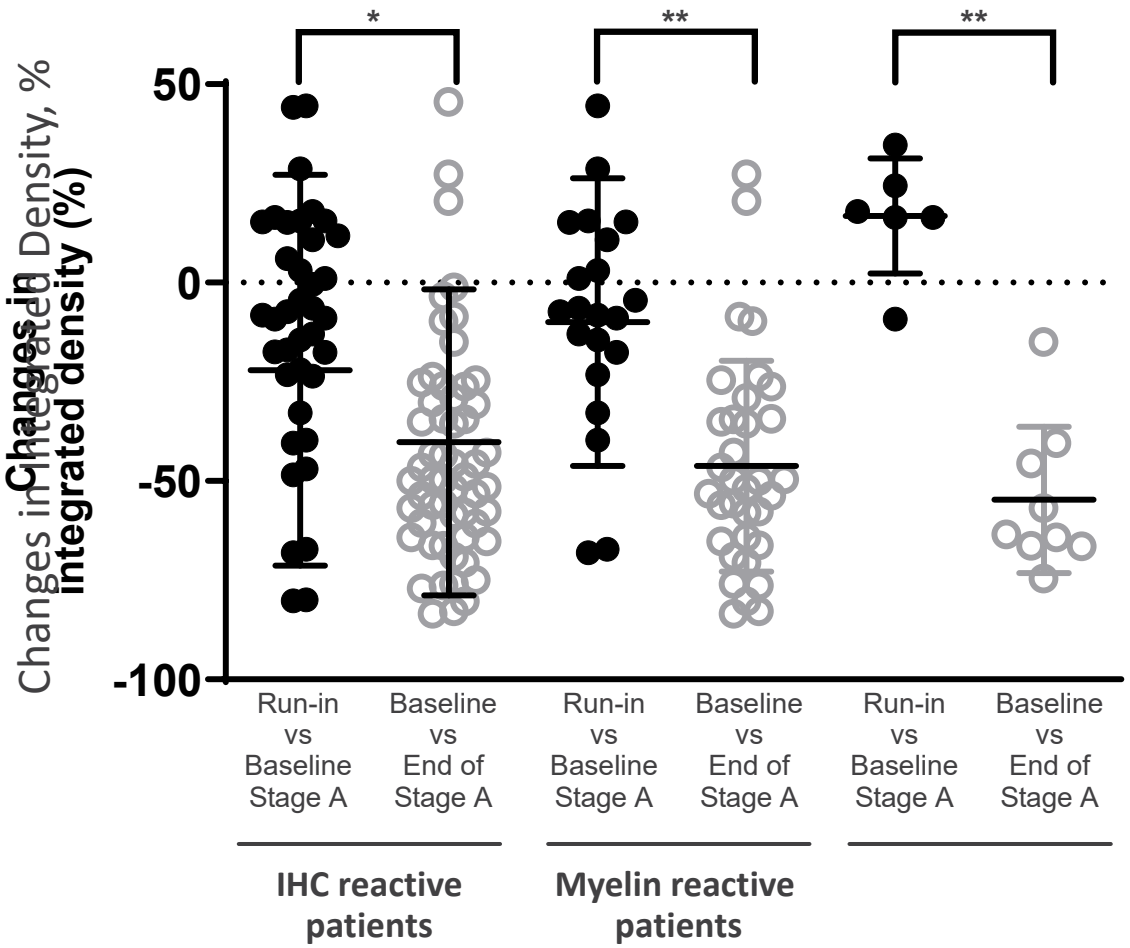
Other reactivity: 11% (28/254)



AN, autoimmune nodopathy; CASPR1, contactin-associated protein-1; CBA, cell-based assay; CNTN1, contactin-1; IgG, immunoglobulin G; HEK, human embryonic kidney; IHC, immunohistochemistry; Myc, anti-Myc tag antibody; Nfasc, neurofascin; ScNe, sciatic nerve.

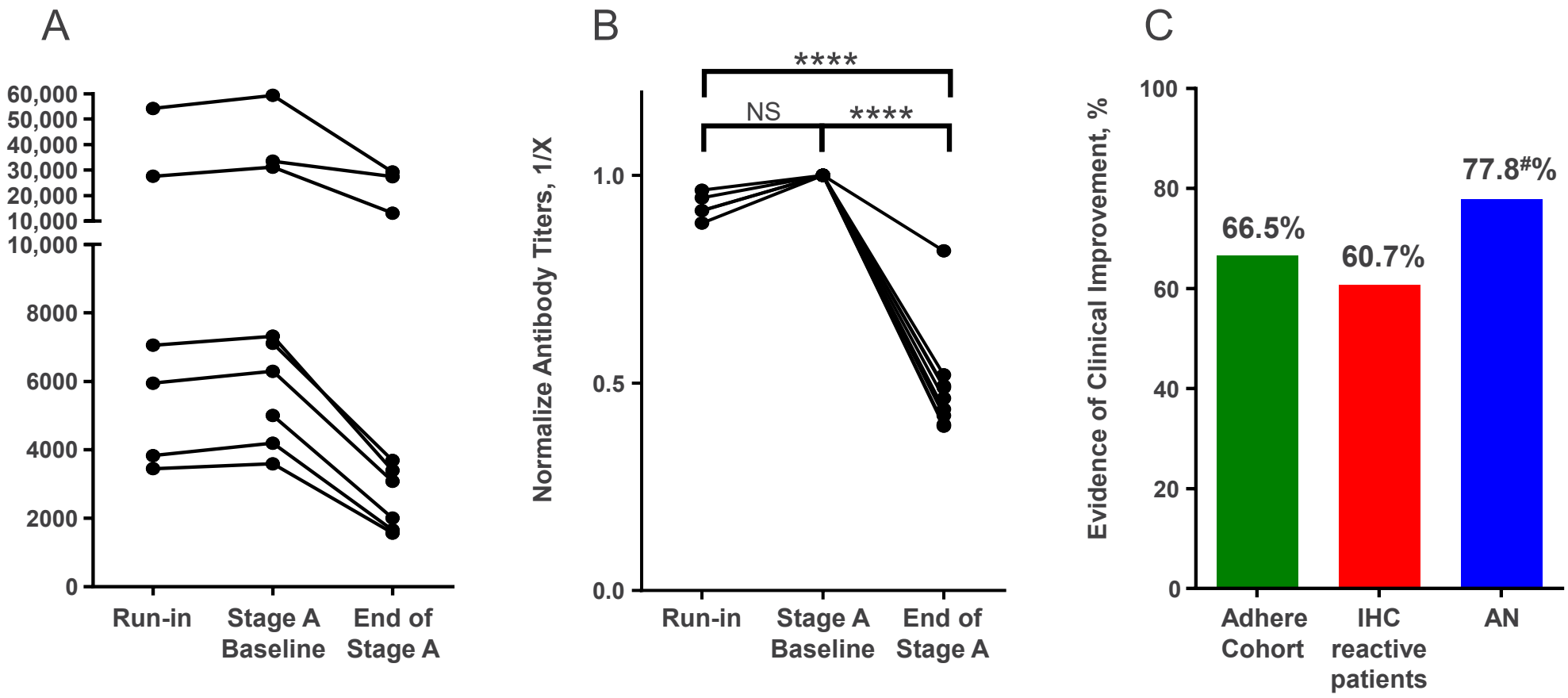
Efgartigimod Decreases IgG Reactivity in Patients With CIDP and AN in Stage A





AN, autoimmune nodopathy; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; IHC, immunohistochemistry; ScNe, sciatic nerve; *p<0,05; **p<0,005.

Efgartigimod Lowers IgG Titers Against Paranodal Proteins



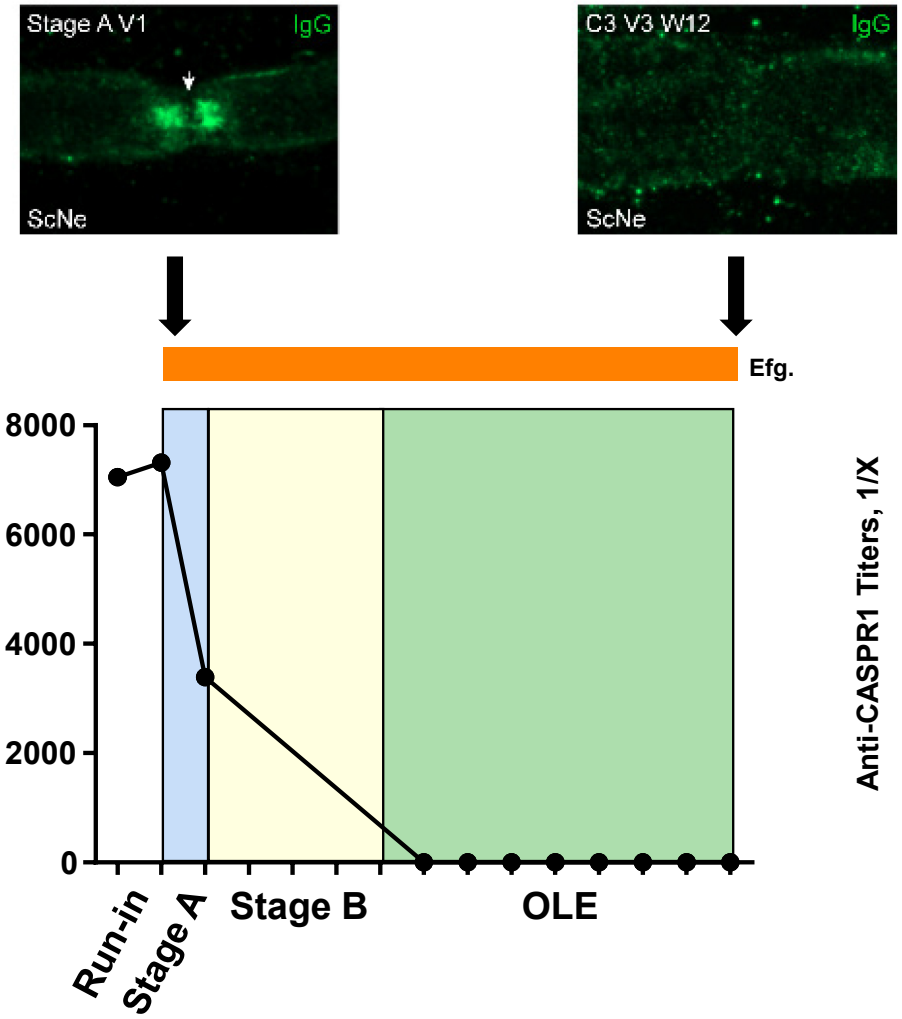
Out of 10 autoimmune nodopathy:

- 8 were followed during stage B (placebo-controlled part)
- 6 were followed during OLE (open-label extension)

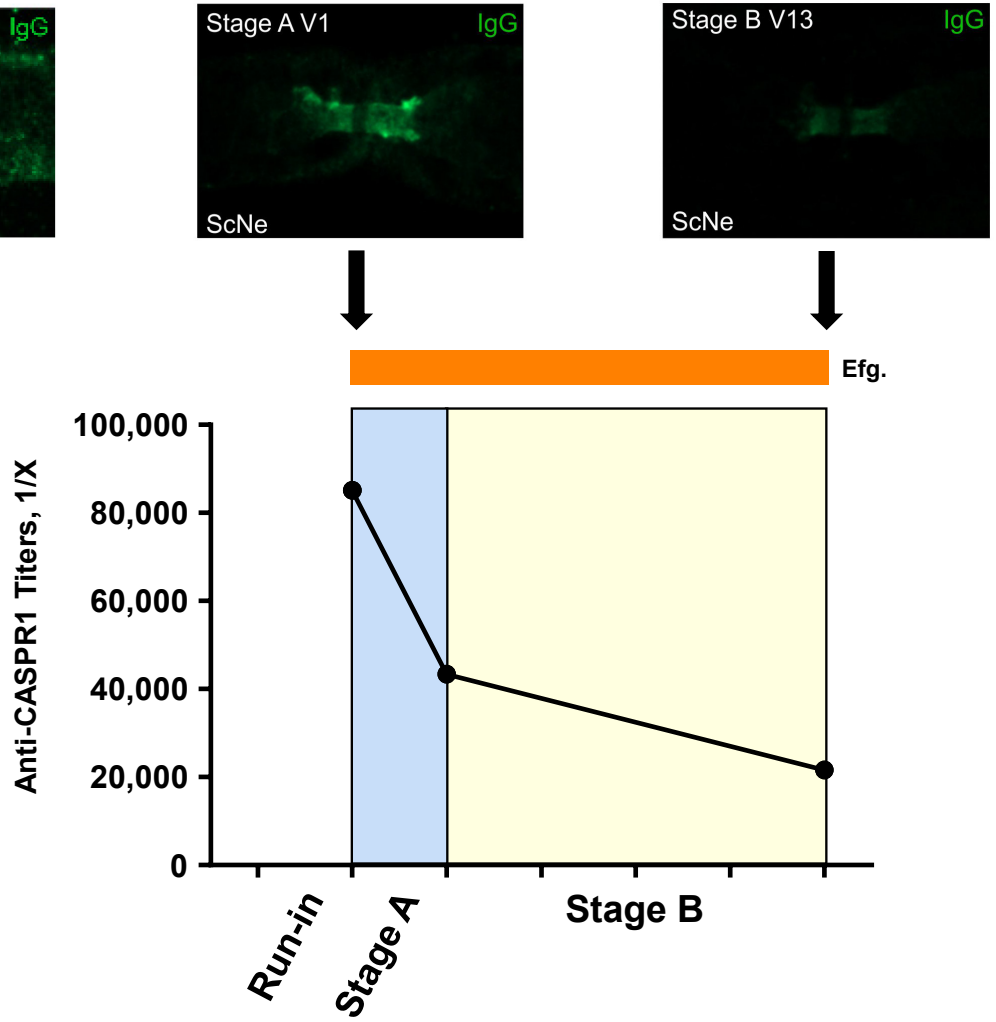
AN, autoimmune nodopathy; CASPR1, contactin-associated protein-1; CNTN1, contactin-1; IgG, immunoglobulin G; IHC, immunohistochemistry; Nfasc, neurofascin; NS, not significant. **** p<0,01; # n=9 patients, one patient was not treated at Stage A

Anti-CNTN1 IgG Levels Were Undetectable in One Patient After Receiving Efgartigimod

30 – CNTN1 (IgG4) Efgartigimod



32 – CASPR1 (IgG4) Efgartigimod

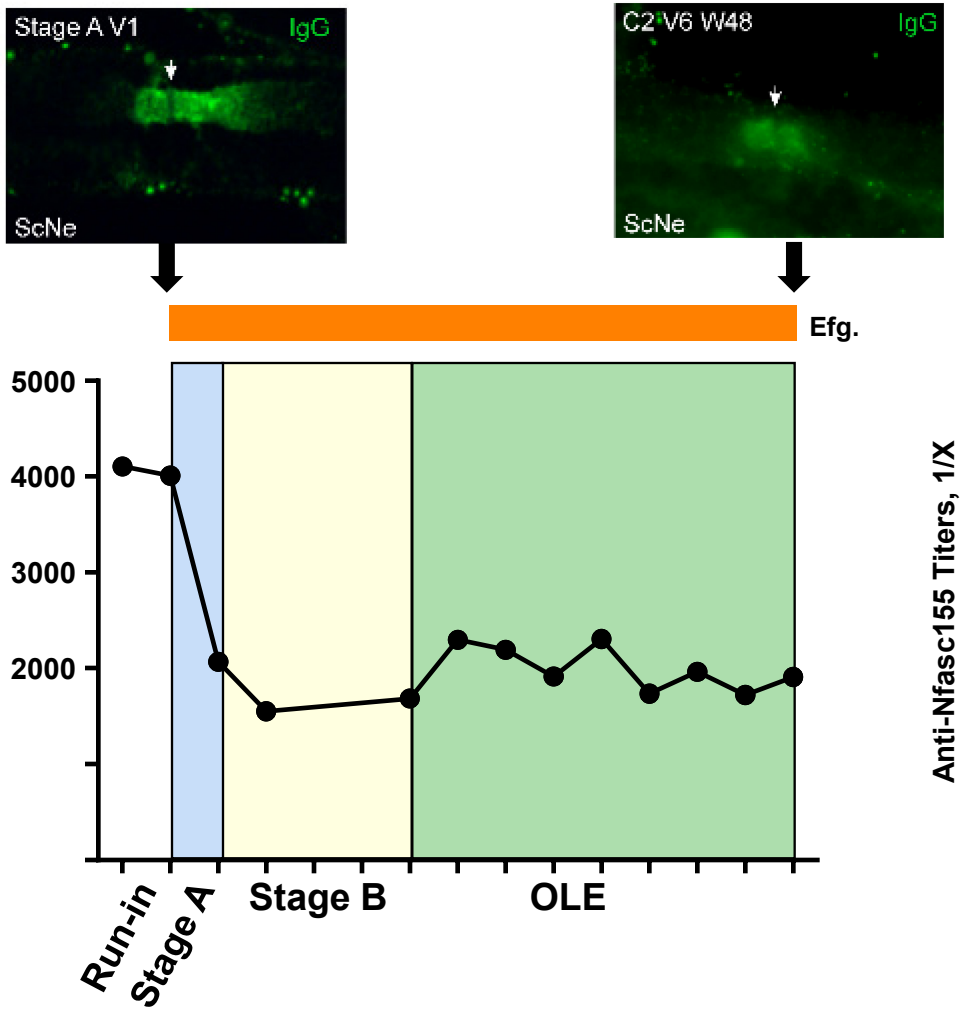


CASPR1, contactin-associated protein-1; CNTN1, contactin-1; Efg, efgartigimod; ELISA, enzyme-linked immuno-sorbent assay; IgG, immunoglobulin G; Nfasc, neurofascin; ScNe, sciatic nerve; W, week.

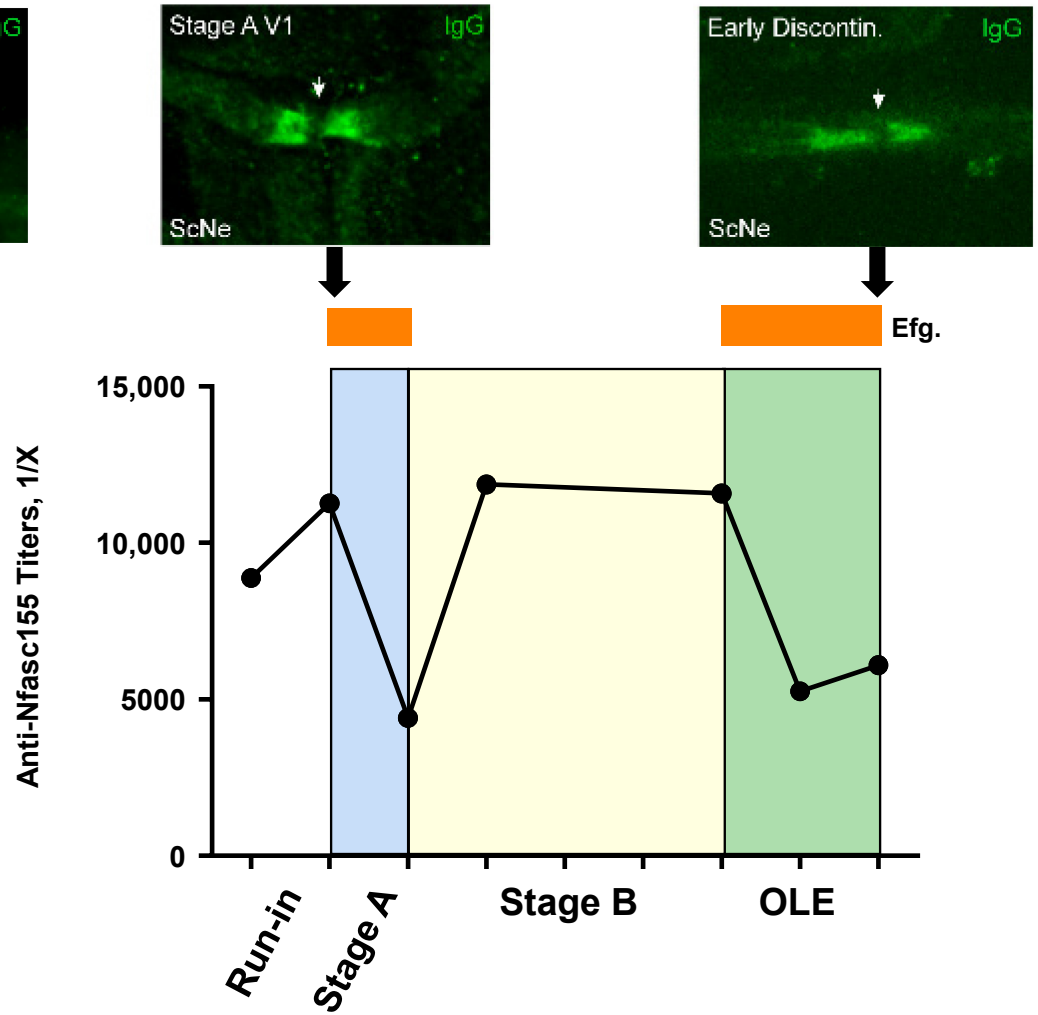
Measurements in OLE was done every 12 weeks

Efgartigimod Lowers Anti-Nfasc155 IgG4 Titers

Participant 6 – Nfasc155 (IgG4) Efgartigimod



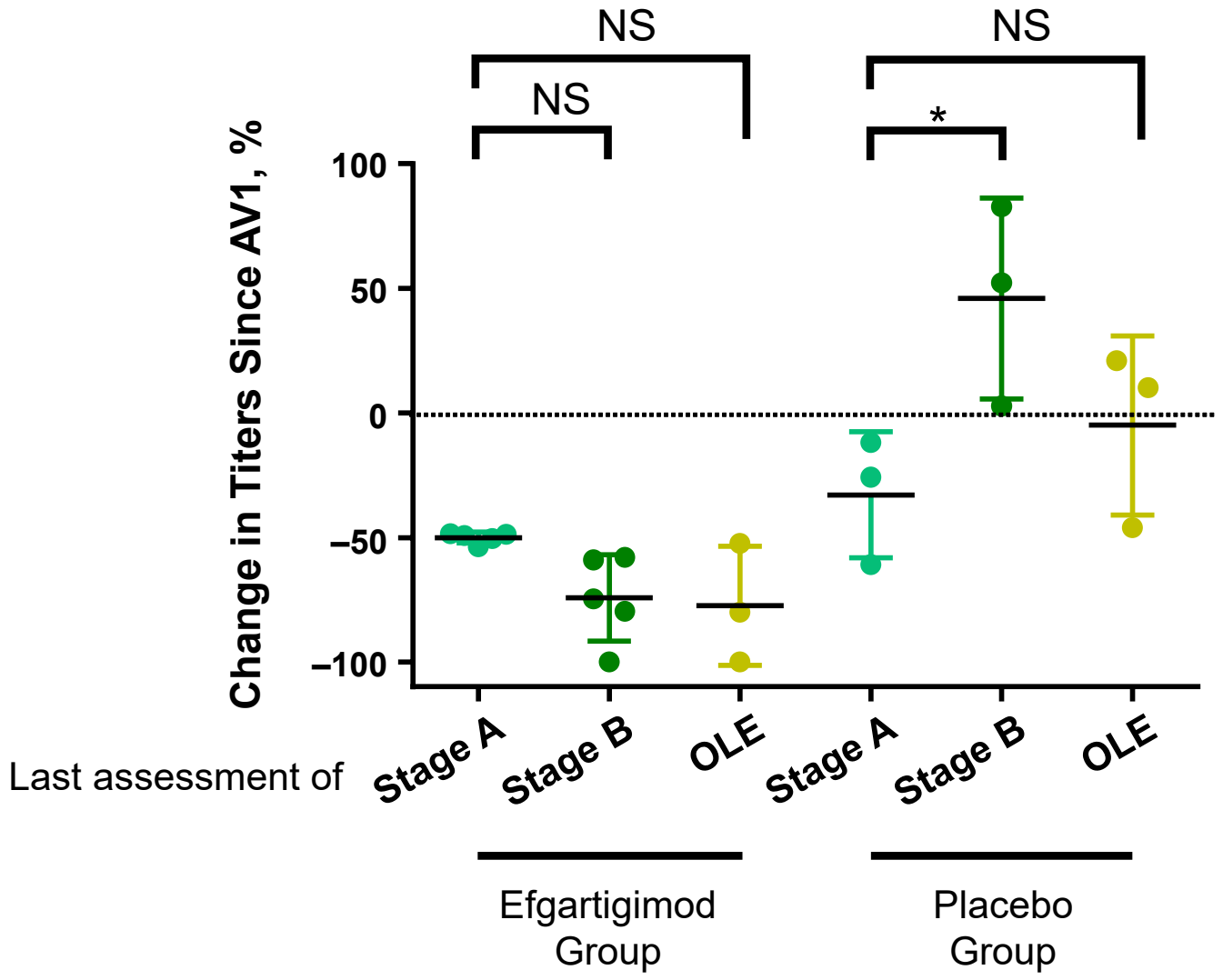
Participant 162 – Nfasc155 (IgG4) Placebo

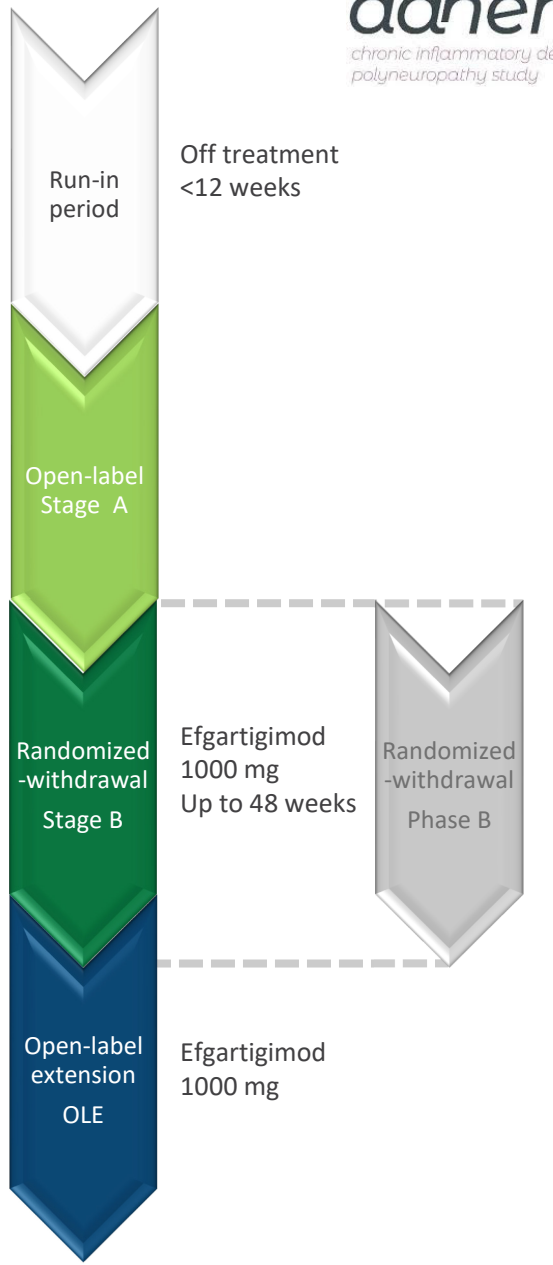


CASPR1, contactin-associated protein-1; Efg, efgartigimod; ELISA, enzyme-linked immuno-sorbent assay; IgG, immunoglobulin G; Nfasc, neurofascin; ScNe, sciatic nerve; W, week.

Measurements in OLE was done every 12 weeks

Efgartigimod Lowers Anti-Node/Paranode IgG4 Titers





IgG, immunoglobulin G; NS, not significant; OLE, open label extension; * p<0,05.

Conclusions

- The prevalence of AN (4 %) and IgG myelin reactivity (22 %) in the ADHERE cohort is similar to that described in published studies[1-3]
- Efgartigimod decreases IgG reactivity in patients with CIDP and AN in Stage A
- Anti-CNTN1 IgG levels were undetectable in one Patient after receiving efgartigimod
- Autoantibodies also Target unknown myelin antigens in CIDP
- Efgartigimod decreases the levels of anti-myelin autoantibodies

AN, autoimmune nodopathy; CIDP, chronic inflammatory demyelinating polyradiculoneuropathy; CNTN1, contactin-1; IgG, immunoglobulin G.

1. Cortese A et al. Neurol Neuroimmunol Neuroinflamm 2020; 7(1). 2. Davies AJ et al. J Clin Med 2020; 9(7). 3. Vallat JM et al. Eur J Neurol 2020; 27(4): 692-701.

Acknowledgments

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Geoffrey Istas

Anneleen Remmerie

ADHERE Study Group

Number (%) Patients in Each Group

OPTION A

Group	N (%)
All subjects tested	254 (100.0)
IHC reactivity	109 (42.9)
No IHC reactivity	145 (57.1)
IgM reactivity	17 (6.7)
IgG reactivity	58 (22.8)
Target identified by ELISA	12 (4.7)
Target identified by CBA	10 (3.9)

Denominator is ALL patients tested
(not all tested patients were treated in stage A)

CBA, cell-based assay; ELISA, enzyme-linked immuno-sorbent assay; IgG, immunoglobulin G; IgM, immunoglobulin M; IHC, immunohistochemistry.