421

Empasiprubart in Multifocal Motor Neuropathy: Exploratory Analyses of the Phase 2 ARDA Study

W. Ludo van der Pol,[1] Daniëlle Krijgsman,[2] Luis Querol,[3,4] Emma K. Persson,[5] Sofie Rutjens,[5] Stéphanie Cadour,[5] Tine Casneuf,[5] Kim Dijkxhoorn,[2] Lauri M. Bloemenkamp,[1,6] Elisabeth de Zeeuw,[2] Miodrag Vujcic,[5] Inge Van de Walle[5]

[1]University Medical Center Utrecht, Utrecht, the Netherlands; [2]Center for Translational Immunology, University Medical Center Utrecht, Utrecht, the Netherlands; [3]Neuromuscular Diseases Unit, Hospital de La Santa Creu I Sant Pau, Universitat Autònoma de Barcelona, Barcelona, Spain; [4]Centro De Investigación Biomédica en Red en Enfermedades Raras (CIBERER), Madrid, Spain; [5]argenx, Ghent, Belgium; [6]University Medical Center Utrecht Brain Center, Utrecht University, Utrecht, the Netherlands

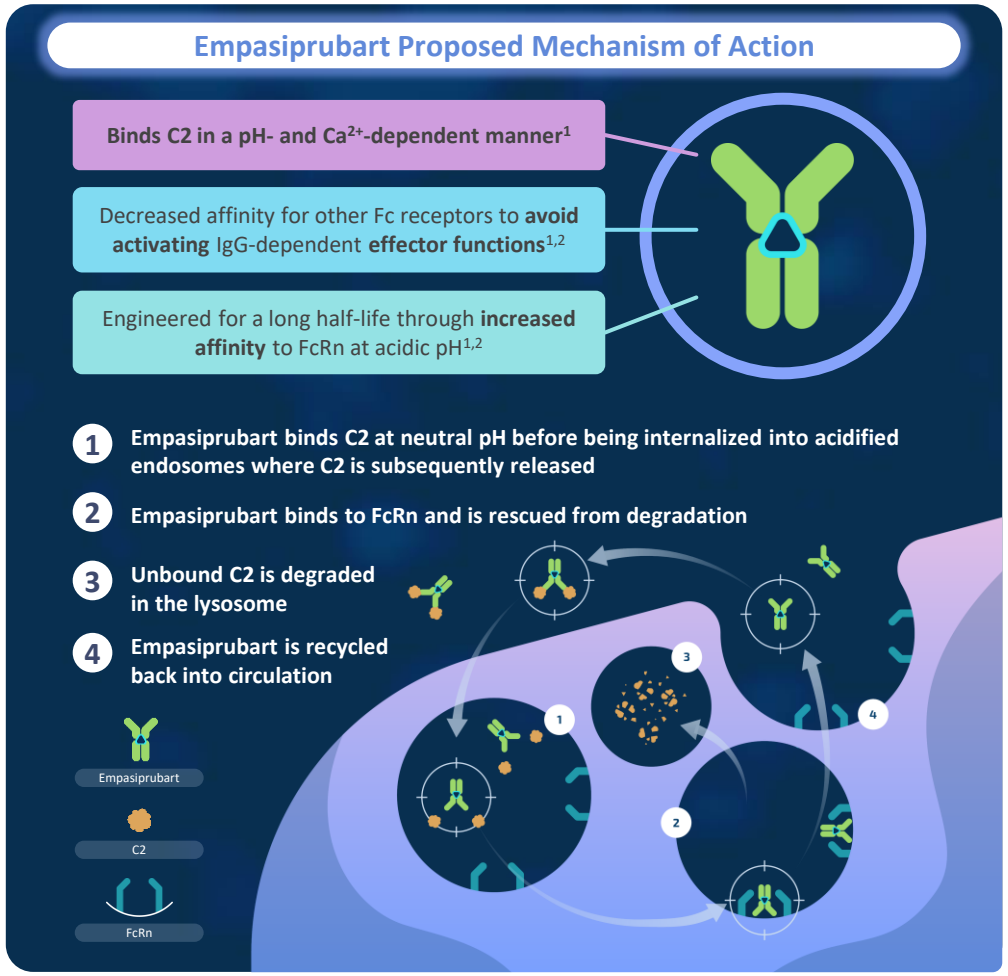
DISCLOSURES AND ACKNOWLEDGMENTS

WLvdP: argenx, Biogen, Biohaven, NMD, Novartis, Roche, Scholar Rock, Takeda; **DK:** Nothing to declare; **LQ:** Alnylam, Annexon, argenx, Avilar, Biogen, CIBERER, Fundació La Marató, CSL Behring, Dianthus, 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; **EKP:** Employee: argenx; **SR:** Employee: argenx; **SC:** Employee: PPD, part of Thermo Fisher Scientific; Consultant: argenx; **TC:** Employee: argenx; **KD:** Nothing to declare; **LMB:** Nothing to declare; **EdZ:** Nothing to declare; **MV:** Employee: argenx; **IVdW:** Employee: argenx.

This study was sponsored by argenx. Medical writing support was provided by Envision Pharma Group, funded by argenx. The authors gratefully acknowledge the trial participants and investigators involved in this study.

Presented at the 2025 Peripheral Nerve Society (PNS) Annual Meeting; May 17–20, 2025; Edinburgh, Scotland

Evaluation of Empasiprubart, a C2-targeting Monoclonal Antibody, on Biomarkers in the Phase 2 ARDA Study



Objective

To investigate the effect of empasiprubart on anti-ganglioside GM1 status, treatment response by GM1 status, and complement inhibitory effect of empasiprubart assessed by an *in vitro* iPSC motor neuron model in the phase 2 ARDA study (NCT05225675) in adults with MMN

SCAN ME

for details of the ARDA clinical trial

In Vitro iPSC Motor Neuron Model

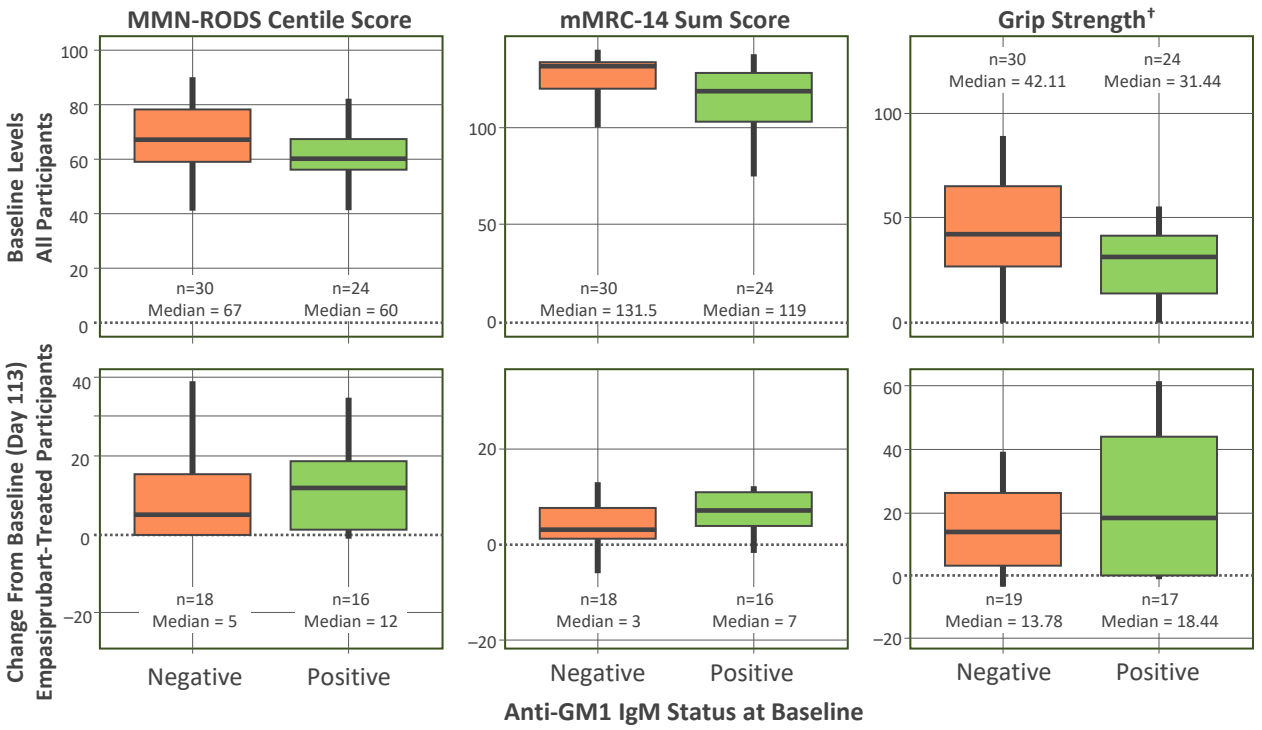
*Negative control sample was a complement active serum pre-incubated with 10 mM EDTA to correct for nonspecific background C3 fixation.

C, complement component; Ca^{2+}, calcium ion; EDTA, ethylenediaminetetraacetic acid; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; GM1, monosialotetrahexosylganglioside; Ig, immunoglobulin; iPSC, induced pluripotent stem cell; MMN, multifocal motor neuropathy; MN, motor neuropathy.

1. Van de Walle I, et al. *J Allergy Clin Immunol*. 2021;147:1420–9. **2.** Vaccaro C, et al. *Proc Natl Acad Sci*. 2006;103:18709–14.

Efficacy of Empasiprubart by Anti-GM1 Status and Its Impact on C3 Fixation

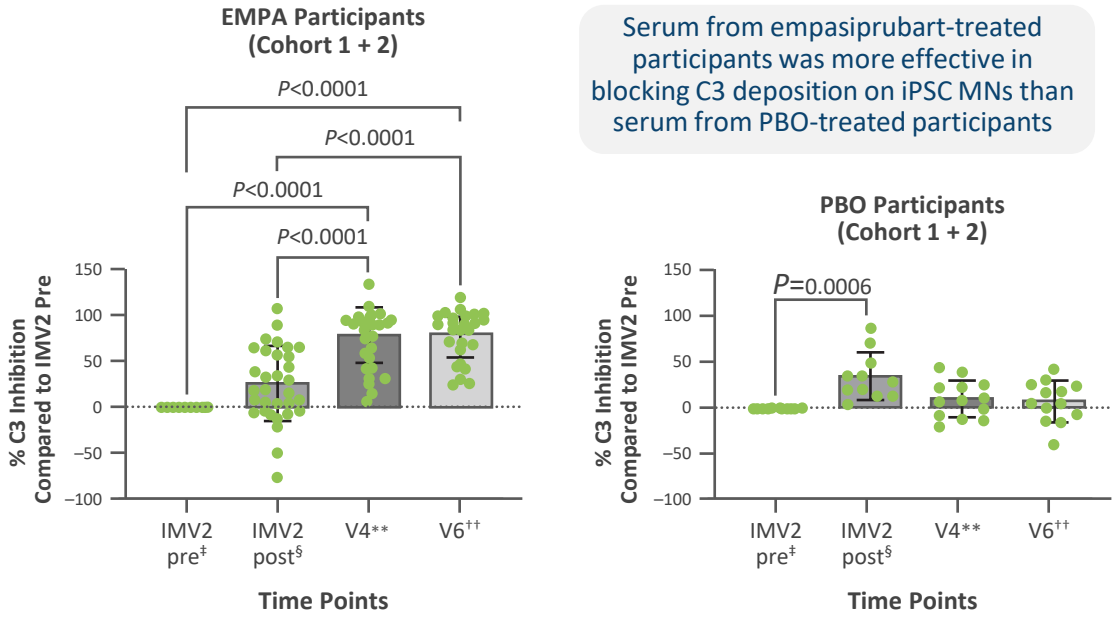
Baseline and Change from Baseline at Last Assessment* by Anti-GM1 Status



Symptoms were slightly more severe at baseline in anti-GM1 positive participants

Anti-GM1 status did not determine the response to empasiprubart treatment at Day 113

Inhibition of C3 Fixation



Serum from empasiprubart-treated participants was more effective in blocking C3 deposition on iPSC MNs than serum from PBO-treated participants

>90% ARDA participant serum samples showed C3 complement deposition to iPSCs despite ~40% giving a positive anti-GM1 ELISA result

Empasiprubart-treated participants demonstrated a decrease in C3 deposition, in alignment with positive clinical outcome in this treatment group

A reduction in C3 fixation was linked with clinical improvement (grip strength, MMN-RODS, mMRC-14 sum score)

ELISA, enzyme-linked immunosorbent assay; EMPA, empasiprubart; IMV, IVIg monitoring visit; iPSC, induced pluripotent stem cell; IVIg, intravenous immunoglobulin; MMN-RODS, Rasch-Built Overall Disability Scale for Multifocal Motor Neuropathy; mMRC-14, modified Medical Research Council-14; PBO, placebo; V, visit.

*Last assessment during the double-blinded treatment period. †3-day moving average; most affected hand. ‡IMV2 pre samples were taken prior to IVIg cycle 2 during the IVIg monitoring period. §IMV2 post samples were taken after IVIg cycle 2 during the IVIg monitoring period. **V4, visit 4 (Day 15); ††V6, visit 6 (Day 29).

Conclusions

421

- ARDA is the largest interventional study conducted in MMN to date (n=54)
- Anti-GM1 status did not impact response to empasiprubart, suggesting empasiprubart may be effective regardless of anti-GM1 status
- In an *in vitro* iPSC motor neuron model, empasiprubart-treated participants demonstrated a decrease in C3 deposition, in alignment with positive clinical outcome in this treatment group

Scan for Poster 421 and More Details