EPR-250

Empasiprubart (ARGX-117) in Multifocal Motor Neuropathy: Initial Safety and Efficacy Data of the Phase 2 ARDA Study

Luis Querol,[1] W. Ludo van der Pol,[2] Stojan Peric,[3] Yessar Hussain,[4] Stephanie Cadour,[5] Inge Van de Walle,[5] Emma Persson,[5] Iris Van Hoomissen,[5] Oleksandr Mashchenko,[5] Miodrag Vujcic,[5] Olivier Van de Steen,[5] Jeffrey A. Allen[6]

[1]Hospital de la Santa Creu i Sant Pau, Neuromuscular Disorders Unit, Barcelona, Spain; [2]Department of Neurology and Neurosurgery, University Medical Center Utrecht, Utrecht, The Netherlands; [3]University of Belgrade, Faculty of Medicine, Neurology Clinic, University Clinical Center of Serbia, Belgrade, Serbia; [4]Austin Neuromuscular Center, Austin, TX, USA; [5]argenx, Ghent, Belgium; [6]University of Minnesota, Department of Neurology, Minneapolis, MN, USA

Presented at the 10th Congress of the European Academy of Neurology (EAN); June 29–July 2, 2024; Helsinki, Finland

Disclosures and Acknowledgements

Luis Querol	Alnylam, Annexon Biosciences, **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
W. Ludo van der Pol	**argenx**, Biogen, Novartis Gene Therapies, Roche, Takeda
Stojan Peric	ADOC, **argenx**, Berlin Chemie Menarini, Dianthus Therapeutics, Kedrion, Medis, Mylan, Octapharma, Pfizer, Remedica, Roche, Salveo, Sanofi Genzyme, Teva Actavis, Viatris, Worwag
Yessar Hussain	Nothing to declare
Inge Van de Walle **Emma Persson** **Iris Van Hoomissen**	Employees of **argenx**
Olivier Van de Steen	Consultant for **argenx**
Stephanie Cadour **Oleksandr Mashchenko** **Miodrag Vujcic**	Consultants for **argenx** and PPD
Jeffrey A. Allen	Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, **argenx**, CSL Behring, Grifols, Immunovant, ImmuPharma, Johnson & Johnson, Pfizer, Takeda

We thank the patients participating in this study and their caregivers, physicians, nurses, staff at study sites, and staff involved in data collection and analyses.
This study was funded by argenx. Medical writing support was provided by Envision Pharma Group and funded by argenx

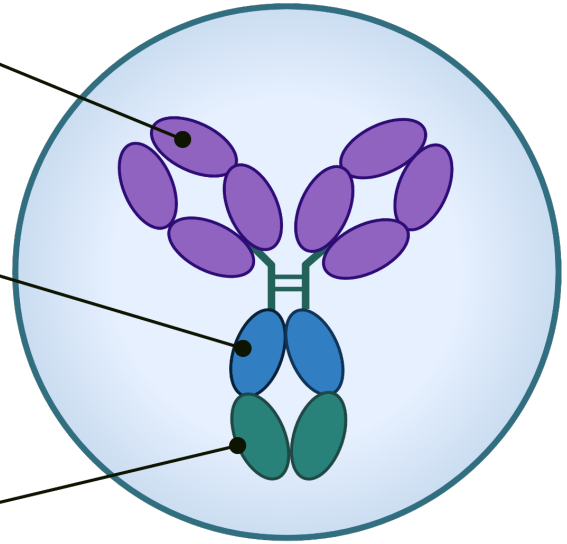
Empasiprubart is an investigational agent. Empasiprubart is not currently approved by the US Food and Drug Administration or European Medicines Agency for any use, and its safety and efficacy have not been established

Empasiprubart is a first-in-class, humanized, monoclonal antibody that specifically binds to C2[1,2]

Binds C2 in a pH- and Ca^{2+}-dependent manner[1]

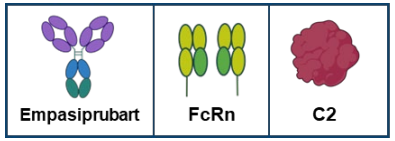
Decreased affinity for other Fc receptors to **avoid activating** IgG-dependent **effector functions**[1,2]

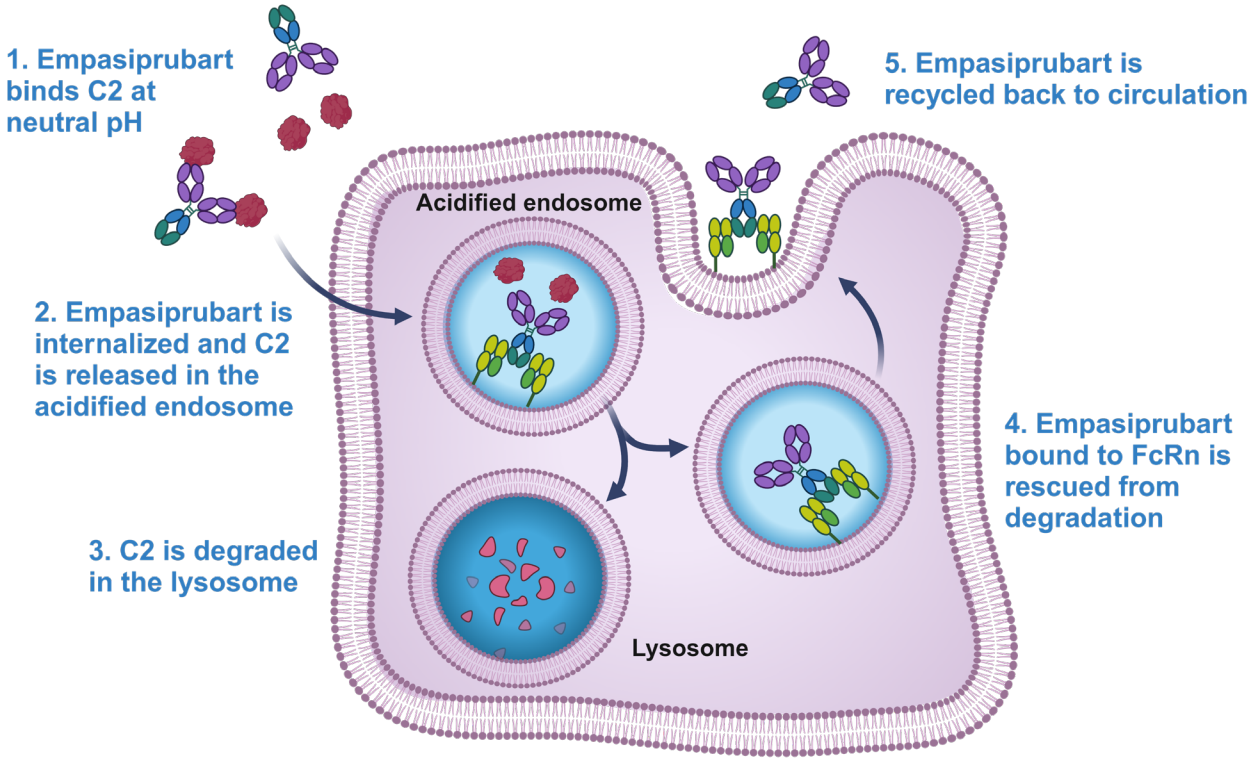
Engineered for a long half-life through **increased affinity** to FcRn at acidic pH[1,2]



Empasiprubart

Proposed MoA of Empasiprubart[1]





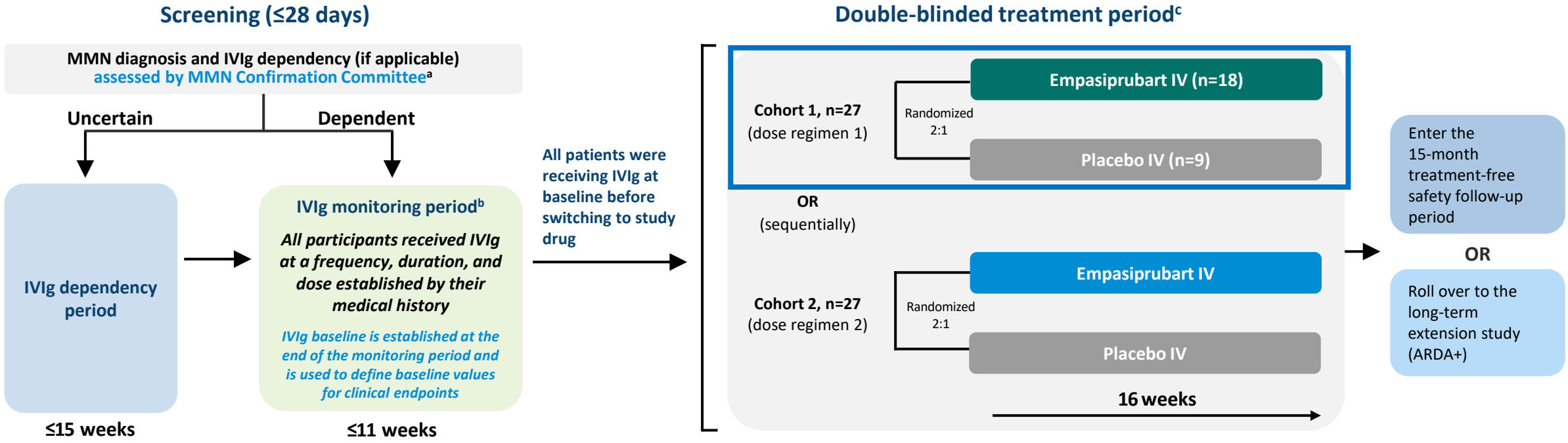
C2, complement component 2; Ca^{2+}, calcium ion; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; IgG, immunoglobulin G; MoA, mechanism of action.

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.

ARDA: Phase 2, randomized, double-blinded, placebo-controlled, parallel-group trial in MMN[1,2]

arda Multifocal Motor Neuropathy Study

NCT05225675



Primary endpoint | Safety outcomes based on AE monitoring and other safety assessments (clinical laboratory tests)

Secondary and additional endpoints

- Time to first retreatment with IVIg
- Evaluation of efficacy measures
- Evaluation of productivity, treatment satisfaction, and QoL measures
- Evaluation of PK, PD, and immunogenicity

AE, adverse event; IV, intravenous; IVIg, intravenous immunoglobulin; MMN, multifocal motor neuropathy; PD, pharmacodynamics; PK, pharmacokinetics; QoL, quality of life.

[a]Vaccinations were required. IVIg dependency parameters and vaccination requirements are summarized in the key inclusion criteria, full details provided at https://www.clinicaltrials.gov/study/NCT05225675. [b]The length of the monitoring period will depend on an individual's IVIg dose frequency: dosed every 2 weeks–up to 35 days monitoring, dosed every 3 weeks–49 days monitoring, dosed every 4 weeks–63 days monitoring, dosed every 5 weeks–77 days monitoring. [c]Double-blinded treatment period will begin 7 days after final IVIg administration during the monitoring period. Participants will be retreated with IVIg if there is a clinically meaningful deterioration in muscle strength and/or motor function.

1. ClinicalTrials.gov identifier: NCT05225675. https://www.clinicaltrials.gov/study/NCT05225675. Accessed June 2024. **2**. van der Pol, WL, et al. Presented at NMSG Annual Scientific Meeting; September 22–24, 2023; Orlando, FL.

Empasiprubart was generally well tolerated, with most AEs mild or moderate in severity

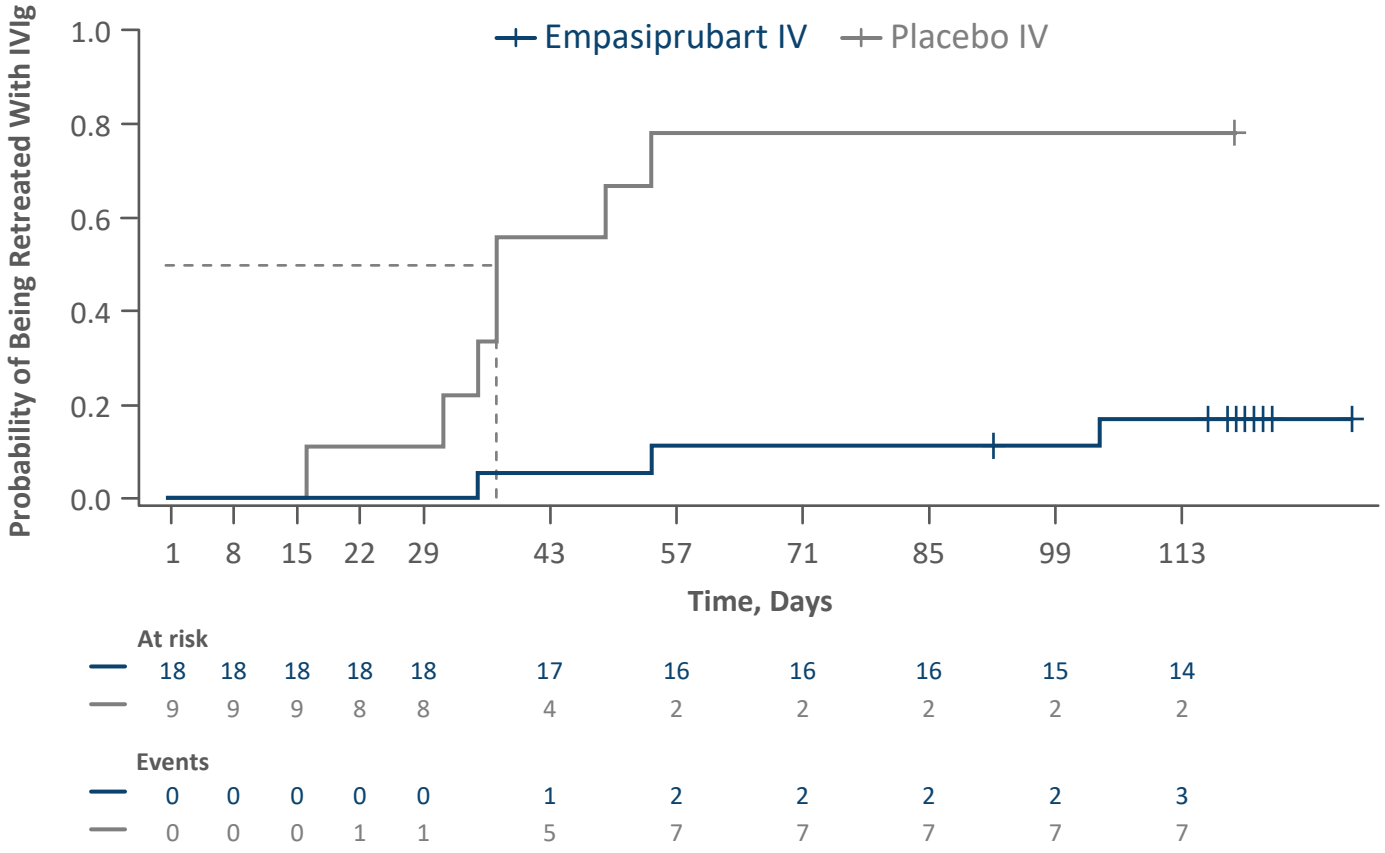
	Empasiprubart (n=18; PYFU=5.55)		Placebo (n=9; PYFU=2.62)	
	n (%)	Events	n (%)	Events
Participant with event				
Any AE[a]	14 (77.8)	33	5 (55.6)	14
Any SAE	2 (11.1)[b]	2	0 (0.0)	0
Procedure-related AEs	2 (11.1)	2	0 (0.0)	0
Discontinued due to AEs	1 (5.6)[c]	1	0 (0.0)	0
Any grade ≥3 AEs	2 (11.1)	2	0 (0.0)	0
AEs of special interest (severe infections)[d]	1 (5.6)[e]	1	0 (0.0)	0
Deaths	0 (0.0)	0	0 (0.0)	0
Most common AEs (≥2 participants in any group)				
Headache	5 (27.8)	6	1 (11.1)	1
Urinary tract infection	2 (11.1)	2	0 (0.0)	0

AE, adverse event; PYFU, participants years of follow-up; SAE, serious adverse event.

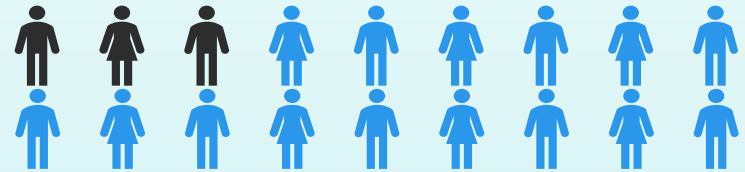
[a]AEs were predominantly mild or moderate in severity. [b]SAEs: Pneumonia grade 3 (not related) and acute coronary syndrome grade 4 (considered treatment-related by the investigators).[c]One patient discontinued due to grade 4 acute coronary syndrome. [d]AEs of special interest were defined as severe infection events (grade ≥3). [e]Severe infection: Pneumonia grade 3 (not related).

Empasiprubart reduced the risk of IVIg retreatment by 91% compared with placebo

Time to First Retreatment[a] With IVIg (days)



Participants retreated with IVIg:



Empasiprubart: 16.7% (**3 out of 18**)

Placebo: 77.8% (**7 out of 9**)

HR: 0.09 (95% CI: 0.02–0.44)

Participants were retreated with IVIg during the DBTP if there was a clinically meaningful deterioration in muscle strength and/or motor function, defined as:

A >30% decline in the grip strength of either hand observed for ≥2 consecutive days

and/or

A decline of ≥2 points on the mMRC-10 sum score compared with the day of randomization

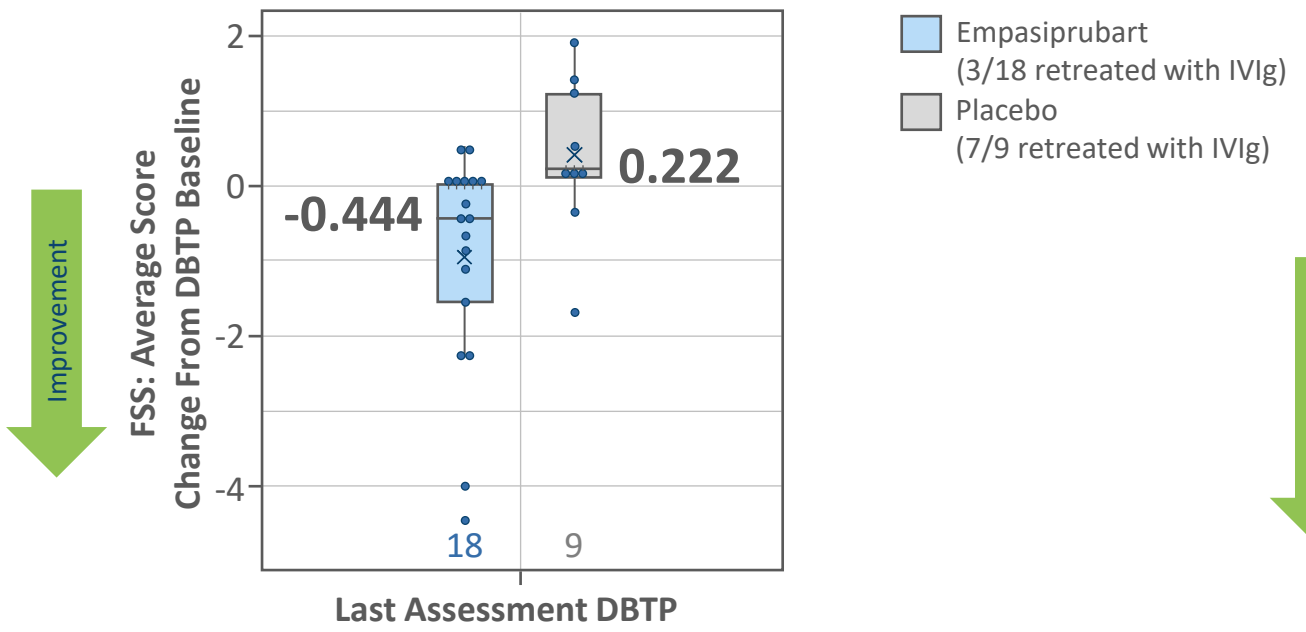
However, based on their clinical judgment, the investigator may have chosen to not retreat the participant with IVIg

CI, confidence interval; DBTP, double-blinded treatment period; HR, hazard ratio; IV, intravenous; IVIg, intravenous immunoglobulin; mMRC-10, modified Medical Research Council-10.

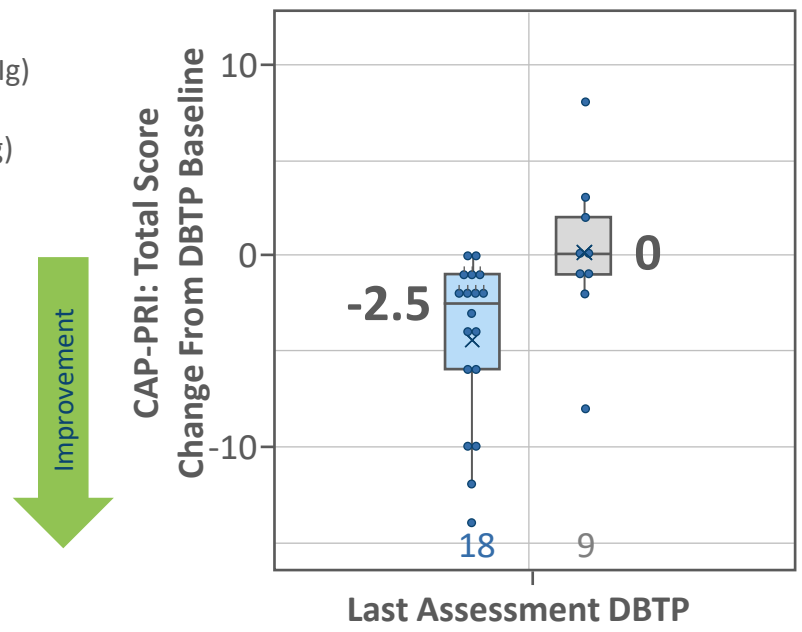
[a]Time to first treatment with IVIg is defined as the time from last IVIg administration before randomization (including unscheduled visits) up to the first IVIg retreatment during the DBTP.

Empasiprubart improved fatigue levels and disease-specific QoL compared with placebo

Change From Baseline[a] FSS Average Score[b] by Treatment Group at Last Assessment During Treatment Period



Change From Baseline[a] CAP-PRI Total Score by Treatment Group at Last Assessment During Treatment Period



In participants with MMN, empasiprubart reduced fatigue severity and improved health-related QoL and functional disability measures as reported by the patients

CAP-PRI, Chronic Acquired Polyneuropathy Patient-Reported Index; DBTP, double-blinded treatment period; FFS, 9-item Fatigue Severity Scale; IVIg, intravenous immunoglobulin; MMN, multifocal motor neuropathy; QoL, quality of life.

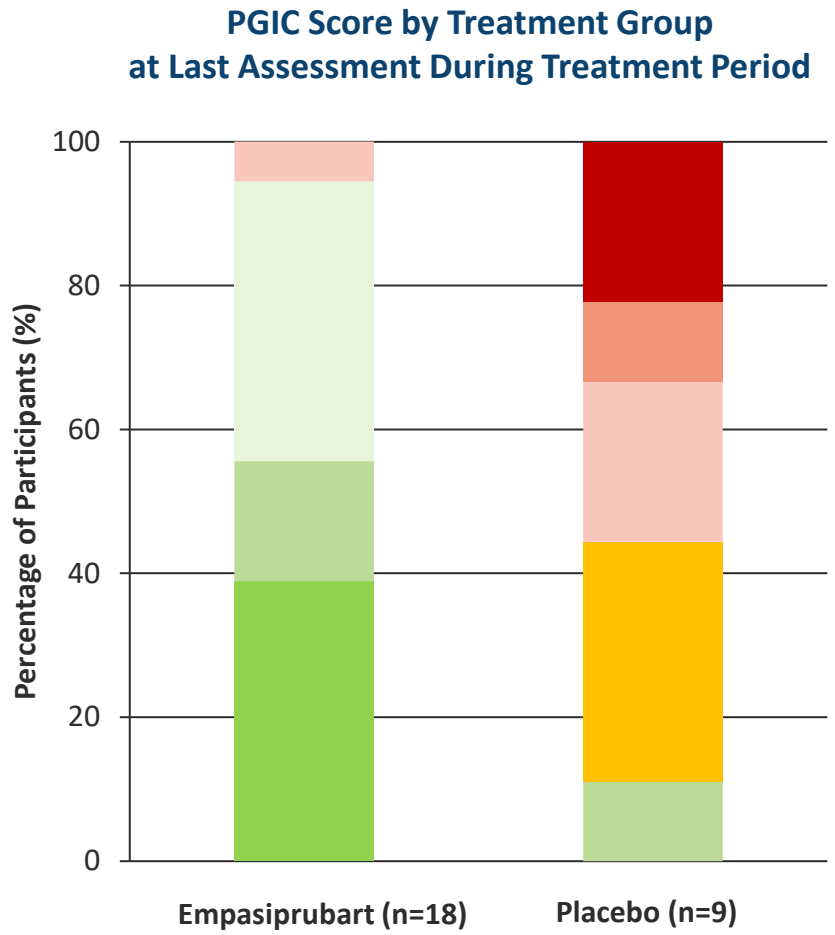
[a]Baseline values established following IVIg monitoring period and prior to initiation of the DBTP. [b]The FSS consists of 9 items to measure the respondent's fatigue symptoms over the past week. Each item is rated on a scale from 1 (completely disagree) to 7 (completely agree). The final score is an average of the 9 items and ranges from 0 to 7.

A greater proportion of empasiprubart-treated participants reported symptom improvement compared with placebo

Patient Global Impression of Change Score

"How much has your condition (MMN) changed as compared to the time you received the first treatment in this trial?"

- Very much improved
- Much improved
- Minimally improved
- No change
- Minimally worse
- Much worse
- Very much worse



In 17 out of 18 participants with MMN, empasiprubart led to self-reported improvement in their condition

DBTP, double-blinded treatment period; IVIg, intravenous immunoglobulin; MMN, multifocal motor neuropathy; PGIC, Patient Global Impression of Change.

Conclusions

ARDA is the largest interventional study conducted in MMN to date; we report data for the 27 participants who received empasiprubart (n=18) or placebo (n=9) in cohort 1 of the ARDA study

Empasiprubart was generally well tolerated, with most AEs being mild or moderate in severity

Compared with placebo, treatment with empasiprubart:

- Reduced the risk of IVIg retreatment by 91% (HR: 0.09 [95% CI: 0.02–0.44])
- Improved disease-specific QoL and functional disability measures
- Improved self-reported condition

Early efficacy and safety results from cohort 1 of the ARDA trial support proof of concept of empasiprubart in MMN and pave the way for a phase 3 trial in this patient population

AE, adverse event; CI, confidence interval; HR, hazard ratio; IVIg, intravenous immunoglobulin; MMN, multifocal motor neuropathy; QoL, quality of life.