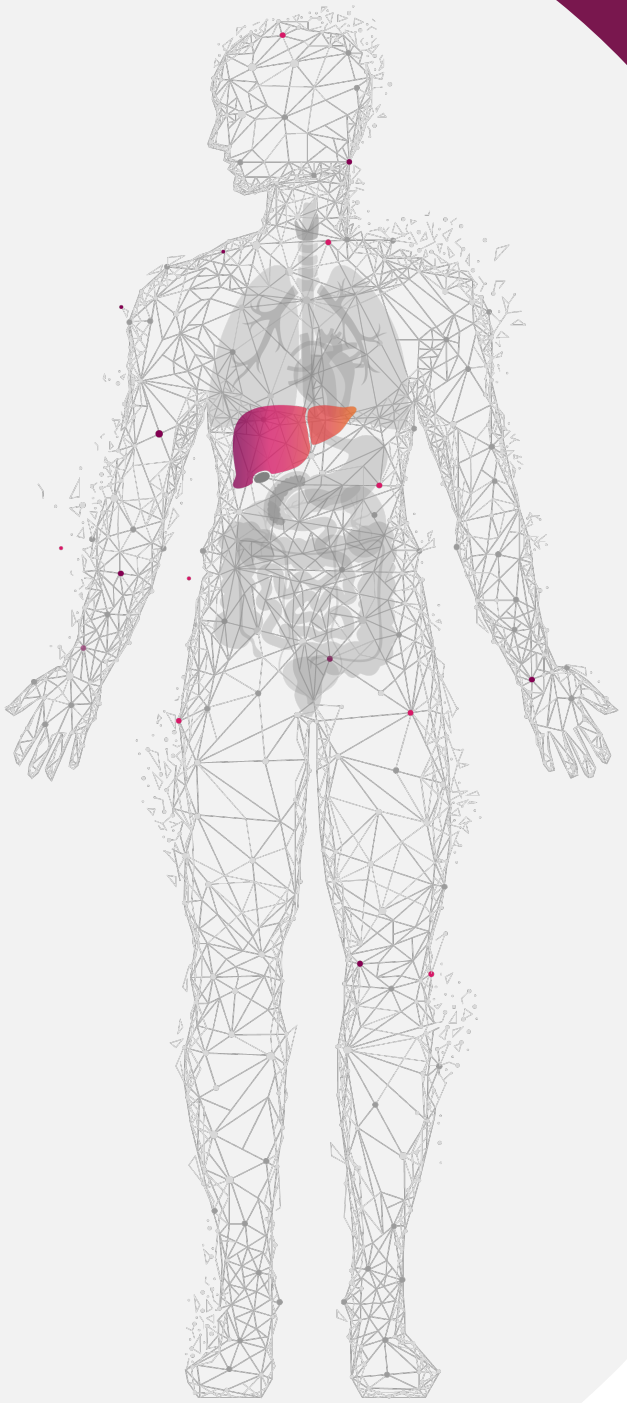

Eplontersen in hereditary ATTR-polyneuropathy: Week 66 final analysis of the phase 3 NEURO-TTRansform study

Sami Khella, Wilson Marques Jr, Noel R. Dasgupta, Chi-Chao Chao, Yeşim Parman, Marcondes Cavalcante França Jr, Yuh-Cherng Guo, Jonas Wixner, Long-Sun Ro, Cristian R. Calandra, Pedro Kowacs, John L. Berk, Laura Obici, Fabio A. Barroso, Markus Weiler, Isabel Conceição, Shiangtung W. Jung, Gustavo Buchele, Michela Brambatti, Steven G. Hughes, Eugene Schneider, Nicholas J. Viney, Ahmad Masri, Morie R. Gertz, Yukio Ando, Julian D. Gillmore, P. James B. Dyck, Márcia Waddington Cruz, Teresa Coelho

Presented at the American Academy of Neurology Annual Meeting; Boston, Massachusetts; April 22-27, 2023

Presenting Author's Disclosures

Sami Khella, MD

University of Pennsylvania School of Medicine,
Philadelphia, Pennsylvania, USA

- Consultant to Ionis, Alnylam, SOBI, Pfizer, and Eidos

Please see poster and QR code for full author details.

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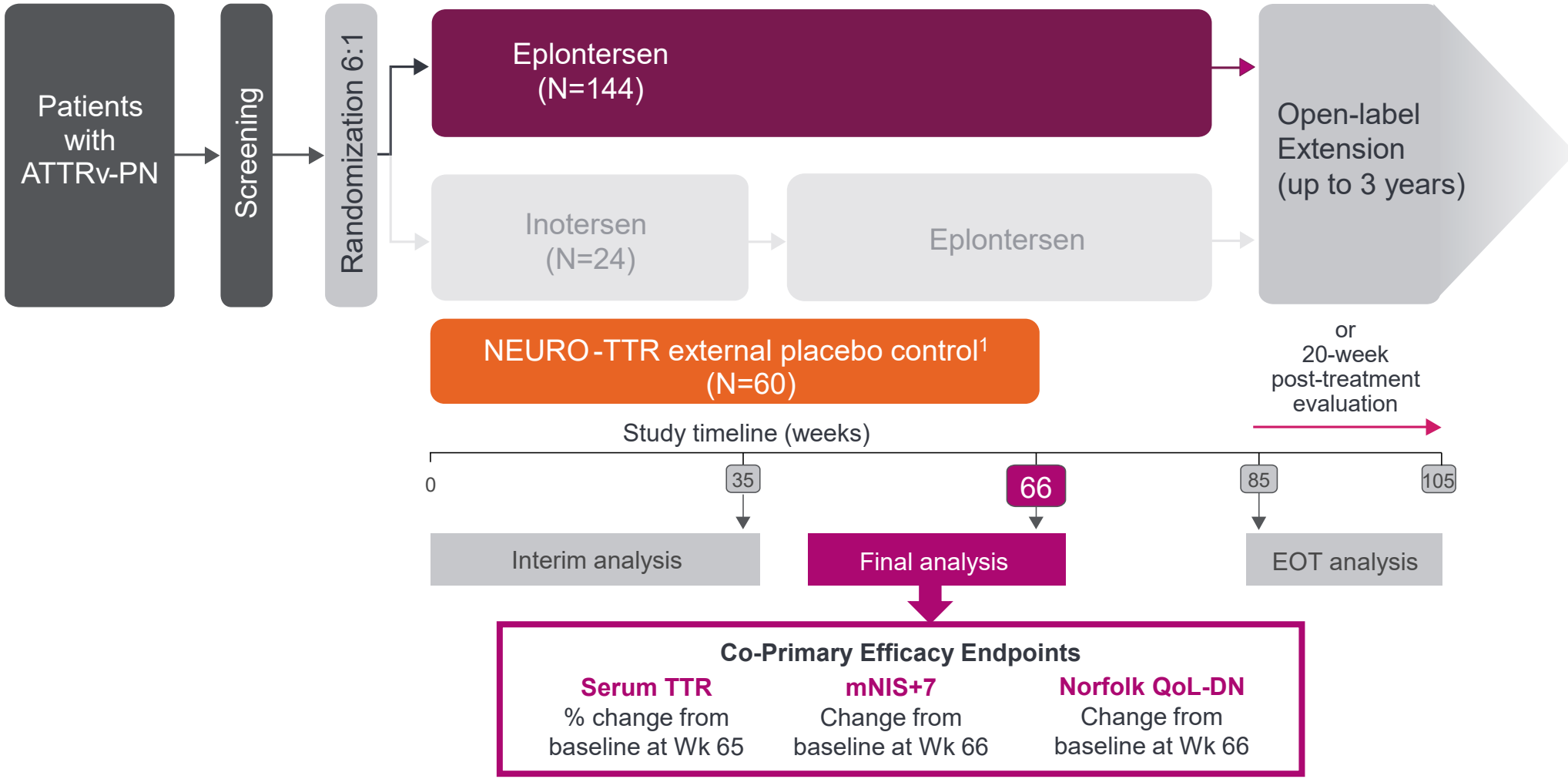
NEURO-TTRansform Study Design



- The external placebo control from NEURO-TTR[1] was appropriate because of similar eligibility criteria and endpoints
- Baseline demographics and clinical characteristics were generally well balanced between eplontersen and external placebo control

[1]Benson et al, *N Engl J Med* (2018) 379:22-31.
Figure adapted from Coelho et al, *Neurol Ther* (2021) 10:375-89.

Please see poster and QR code for additional details.

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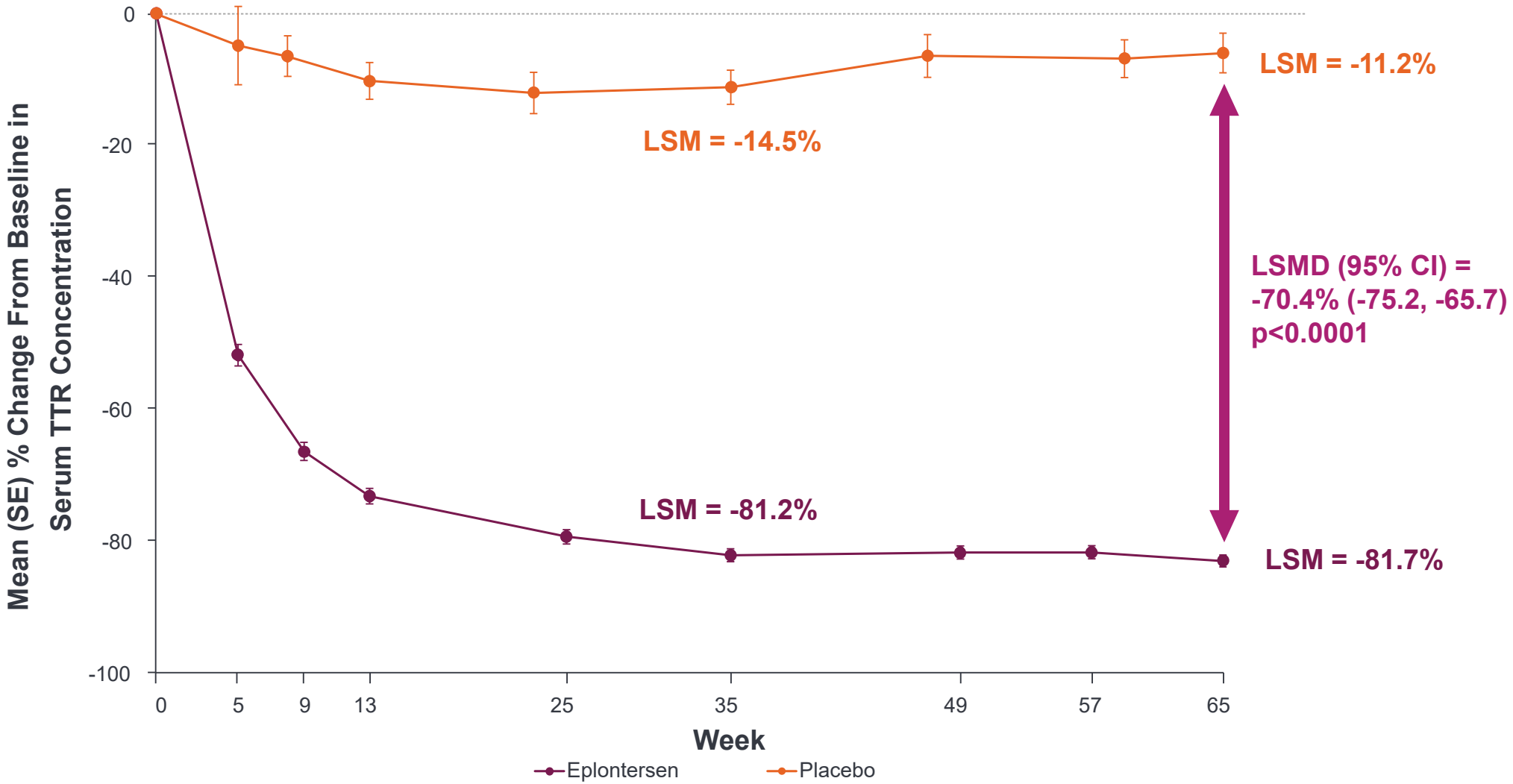
Significant and Sustained Reduction in TTR Concentration From Baseline With Eplontersen Compared With Placebo



The statistical analysis of percent change from baseline is based on a mixed effects model with repeated measures (MMRM) adjusted by propensity score weights with fixed categorical effects for treatment, time, treatment-by-time interaction, disease stage, V30M variant, previous treatment, and fixed covariates for the baseline value and the baseline-by-time interaction.

Please see poster and QR code for additional details.

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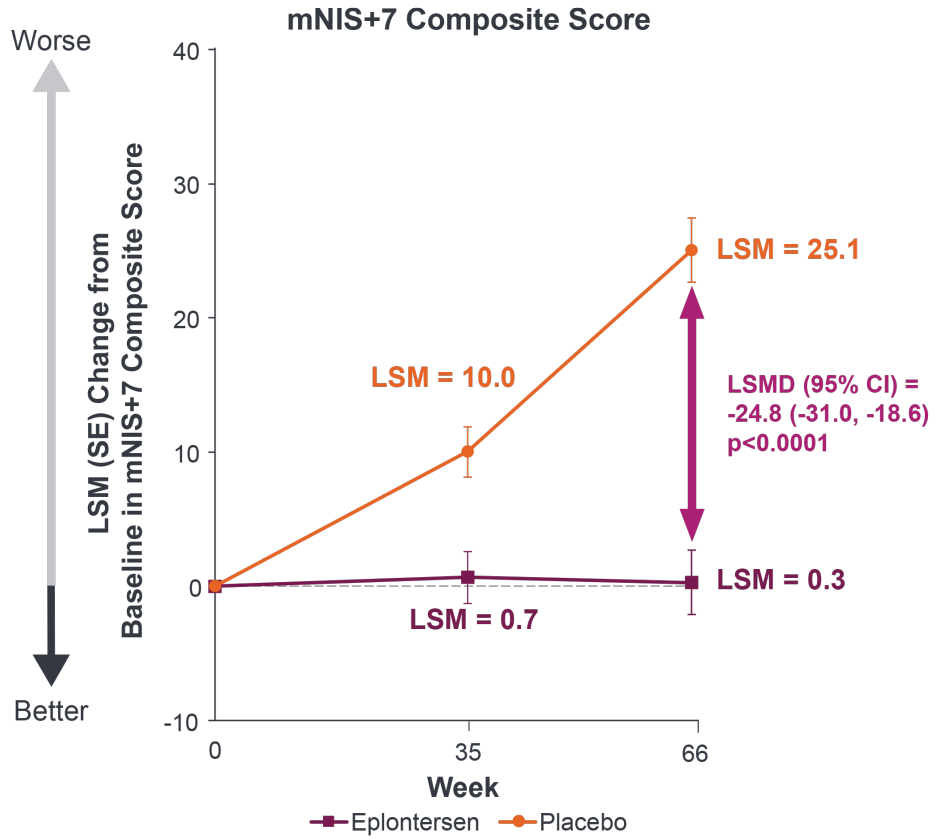
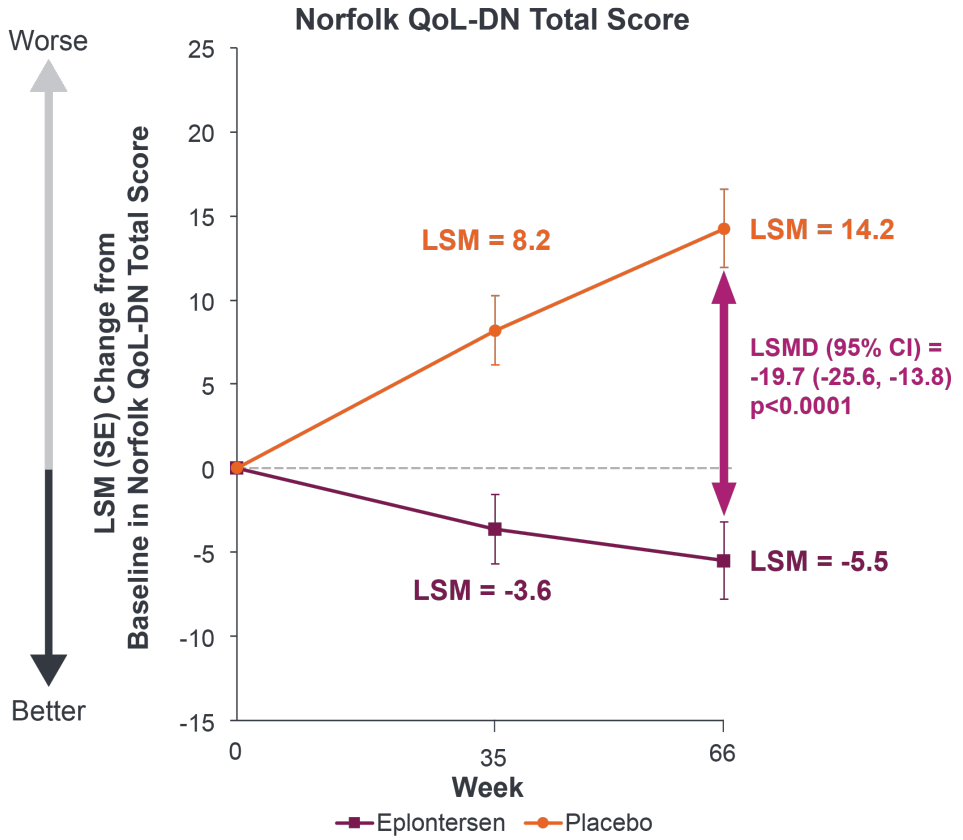
Eplontersen Halted Progression of Neuropathy Impairment and Significantly Improved Quality of Life vs Placebo at Week 66





Final Analysis

- Eplontersen treatment effect was consistent across prespecified subgroups as well as for mNIS+7 components and Norfolk QoL-DN domains at Week 66
- Eplontersen resulted in statistically significant improvements in all secondary endpoints at Week 66 compared with placebo

The statistical analysis of change from baseline is based on a mixed effects model with repeated measures (MMRM) adjusted by propensity score weights with fixed categorical effects for treatment, time, treatment-by-time interaction, disease stage, V30M variant, previous treatment, and fixed covariates for the baseline value and the baseline-by-time interaction.

Please see poster and QR code for additional details.

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Eplontersen was Well Tolerated and Demonstrated an Acceptable Safety Profile at Week 66

- Eplontersen and placebo had comparable incidences of TEAEs, including those related to study drug and leading to treatment discontinuation
- No TEAEs of special interest led to study drug discontinuation
- No SAEs were related to study drug
- 2 deaths occurred in the eplontersen group prior to the interim analysis, both related to known sequelae of ATTR amyloidosis[1-5] and neither assessed as study drug–related

Incidence, n (%)	Placebo	Eplontersen
N	60	144
Any TEAE	60 (100)	140 (97.2)
Related to study drug	23 (38.3)	53 (36.8)
Leading to study drug discontinuation	2 (3.3)	5 (3.5)
TEAE of special interest	12 (20.0)	41 (28.5)
Ocular events potentially related to Vit A deficiency	9 (15.0)	39 (27.1)
Thrombocytopenia	1 (1.7)	3 (2.1)
Glomerulonephritis	2 (3.3)	0
Other TEAE of interest	47 (78.3)	87 (60.4)
Any serious TEAE	12 (20.0)	21 (14.6)
Related to study drug	1 (1.7)	0
Fatal TEAE	0	2 (1.4)
Related to study drug	0	0

[1]Cavallaro et al, *Neurology* (2016) 87:750-1; [2]Yamada et al, *Prog Mol Biol Transl Sci* (2012) 107:41-78; [3]Yamashita et al, *Neurology* (2008) 70:123-8; [4]Ellie et al, *Neurology* (2001) 57:135-7; [5]Porcari et al, *Cardiovasc Res* (2023) 118:3517-35.

Please see poster and QR code for additional details.

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Conclusions

- In patients with ATTRv-PN, eplontersen treatment resulted in clinically and statistically significant benefits through Week 66 compared with placebo
  - Sustained reduction in serum TTR concentration
  - Halted progression of neuropathy impairment
  - Improved patient quality of life
- These findings are further supported by statistically significant improvements in all secondary endpoints at Week 66 compared with placebo
- Eplontersen was well tolerated and demonstrated an acceptable safety profile
- Long-term safety and tolerability data are being assessed in the open-label extension study

Please see poster and QR code for additional details.

Acknowledgements

- Study Participants and Caregivers
- Study Investigators:
  - Ahmad Masri
  - Aikaterini Papagianni
  - Anna Mazzeo
  - Barbara Distad
  - Chi-Chao Chao
  - Conrado Jose Estol
  - Cristian Ricardo Calandra
  - David Adams
  - Davide Pareyson
  - Edward John Gane
  - Eleni Zamba-Papanicolaou
  - Fabio Adrian Barroso
  - Ioannis Zaganas
  - Isabel Conceição
  - John Berk
- Ionis Pharmaceuticals, Inc.
  - Jonas Wixner
  - Juan Gonzalez Moreno
  - Julie Khoury
  - Kon-Ping Lin
  - Laura Piera Obici
  - Long-Sun Ro
  - Lucia Galan Davila
  - Marcelo Francisco Rugiero
  - Márcia Waddington Cruz
  - Marco Luigetti
  - Marcondes Cavalcante França Jr
  - Markus Weiler
  - Mazen Dimachkie
  - Merrilee Needham
  - Merrill Benson
- AstraZeneca
  - Michael Polydefkis
  - Michelle Mezei
  - Morie Gertz
  - Morton Scheinberg
  - Noel Dasgupta
  - Pascal Cintas
  - Pedro Kowacs
  - Rebecca Traub
  - Sami Khella
  - Shahram Attarian
  - Teresa Coelho
  - Thomas Brannagan III
  - Vera Bril
  - Wilson Marques Jr
  - Yeşim Parman
  - Yuh-Cherng Guo

Eplontersen, also known as IONIS-TTR-L_{Rx} and AKCEA-TTR-L_{Rx}. This study was sponsored by Ionis Pharmaceuticals, Inc., Carlsbad, CA, USA.
Medical writing and editorial support were provided by Peloton Advantage, LLC, an OPEN Health company, and funded by Ionis Pharmaceuticals, Inc.

Eplontersen is an investigational drug and has not been approved by the FDA, EMA, or any other regulatory agency.

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