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A phase 3 randomized study evaluating sialic acid extended-release for GNE myopathy

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Cite as: *Neurology*® 2019;92:e2109-e2117. doi:10.1212/WNL.0000000000006932

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Study objective

To investigate the efficacy of aceneuramic acid extended-release (Ace-ER) in patients with GNE myopathy.

Summary results

Ace-ER does not improve muscle strength or function in patients with GNE myopathy.

Classification of evidence

Class I.

What is known and what this paper adds

A phase 2 trial provided evidence that Ace-ER stabilizes upper extremity strength in patients with GNE myopathy. However, this phase 3 trial shows that Ace-ER does not prevent muscle strength deterioration in patients with GNE myopathy.

Participants and setting

This study recruited 89 patients with GNE myopathy through 13 sites in Bulgaria, Canada, France, Israel, Italy, the UK, and the US. These participants were 18–55 years old and could walk ≥200 meters in a 6-minute walk test at baseline.

Design, size, and duration

This phase 3, double-blind trial randomized participants 1:1 with sex-stratification into Ace-ER (6 g/d; n = 45) and placebo (n = 44) groups. Pills were taken orally thrice daily for 48 weeks. This study calculated Upper Extremity Composite (UEC) muscle strength scores at baseline and every 8 weeks thereafter for 48 weeks A generalized estimating equation model was used for data analysis.

Primary outcome measures

The primary outcome was the comparison between the Ace-ER and placebo group in change from baseline in UEC score at 48 weeks.

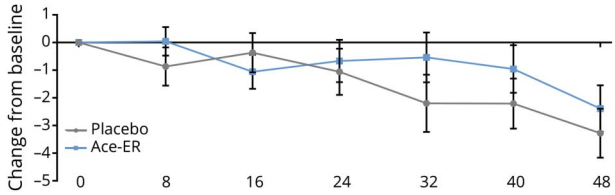
Main results and the role of chance

The Ace-ER and placebo groups had similar change from baseline UEC scores at 48 weeks (−2.25 vs −2.99 kg; $p = 0.5387$).

Harms

There were 2 serious adverse events (SAEs) in the Ace-ER group and 1 in the placebo group. All SAEs were resolved and only 1 SAE in Ace-ER was considered possibly treatment-related. The most common adverse events were mild-to-moderate gastrointestinal events.

Figure Change from baseline UEC score over the study period in the Ace-ER (blue) and placebo (gray) groups



Bias, confounding, and other reasons for caution

This study's 48-week duration might have been too short to observe treatment benefits. Compared to the phase 2 study and possibly accounting for the differing results, the phase 3 study was larger, more heterogeneous, and comprised of participants with less disease severity at baseline.

Generalizability to other populations

This study's large sample size and international nature favor the generalizability of the results.

Study funding/potential competing interests

This study was funded by Ultragenyx Pharmaceutical Inc. Some authors report receiving support for research projects and clinical trials from various healthcare companies, including Ultragenyx Pharmaceutical Inc.; consulting for various healthcare companies; serving on advisory boards for various healthcare companies, including Ultragenyx Pharmaceutical Inc.; and being Ultragenyx Pharmaceutical Inc. employees and stockholders. Dr. Tarnopolsky is the Chief Executive Officer of Exerkine Corporation. Go to Neurology.org/N for full disclosures.

Trial registration number

NCT02377921 on ClinicalTrials.gov and 2014-005432-33 in the EU Register.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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Neurology 2019;92;e2109-e2117 Published Online before print January 25, 2019
DOI 10.1212/WNL.0000000000006932