Randomized trial of L-serine in patients with hereditary sensory and autonomic neuropathy type 1

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Cite as: Neurology® 2019;92:e359-e370. doi:10.1212/WNL.0000000000006811

Study objective
To assess the safety and efficacy of L-serine in patients with hereditary sensory and autonomic neuropathy type 1 (HSAN1).

Summary results
L-Serine is safe for patients with HSAN1 and potentially effective at slowing disease progression.

Classification of evidence
Class I.

What is known and what this paper adds
HSAN1 most commonly results from SPTLC1 and SPTLC2 mutations that reduce the affinity of the serine palmitoyltransferase enzyme for L-serine resulting in the formation of neurotoxic 1-deoxysphingolipids. This study provides evidence that treatment with L-serine reduces 1-deoxysphingolipid formation and is safe in patients with HSAN1.

Participants and setting
This study enrolled 18 patients (67% female; mean age, 47.8 ± 14.0 years) with SPTLC1 mutation-related HSAN1 and signs of peripheral neuropathy. Enrolment occurred through the Massachusetts General Hospital and the University of Massachusetts Hospital between August 2013 and April 2014.

Design, size, and duration
This double-blind study used permuted-block randomization for 1:1 allocation of participants to L-serine (400 mg/kg daily) and placebo groups. Study drugs were administered as powders in aqueous solution. The Charcot-Marie-Tooth Neuropathy Score version 2 (CMTNS), on which higher scores reflect greater neuropathy severity, was used to evaluate participants at baseline and follow-up assessments.

Primary outcome measures
The primary outcomes were from-baseline CMTNS changes at the 48-week follow-up timepoint.

Main results and the role of chance
The study completion rates were 100% and 78% for the L-serine and placebo groups, respectively. Relative to the placebo group, the L-serine group experienced a CMTNS decline over 48 weeks (−1.5 units; 95% confidence interval, −2.8 to −0.1; p = 0.03).

Harms
No serious adverse events were noted.

Bias, confounding, and other reasons for caution
This study had a small sample size. Validated HSAN1-specific outcome measures are unavailable.

Generalizability to other populations
This study was conducted through only 2 centers in a single US state. This may limit the generalizability of this study’s results.

Study funding/potential competing interests
This study was funded by the Deater Foundation, the Food and Drug Administration, the NIH, the European Commission, the Swiss National Foundation, the Hurka Foundation, and the Rare Disease Initiative Zurich. Some authors report receiving research support, committee appointments, and consulting fees from various healthcare companies. Go to Neurology.org/N for full disclosures.

Trial registration number
NCT01733407 on ClinicalTrials.gov.

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:e359-e370 Published Online before print January 9, 2019
DOI 10.1212/WNL.0000000000006811

This information is current as of January 9, 2019

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