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Nusinersen in later-onset spinal muscular atrophy

Long-term results from the phase 1/2 studies

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Study objective and summary result

This analysis of data from the phase 1/2 studies investigated the therapeutic efficacy of intrathecal nusinersen in children with later-onset spinal muscular atrophy (SMA), and it found that nusinersen improves motor function in such patients.

Classification of evidence

Class IV.

What is known and what this paper adds

Clinical trials have found that nusinersen is effective for children with infantile-onset SMA or later-onset SMA. This study provides further evidence for the long-term efficacy of nusinersen and a time-dependent effect in an extended age range of children with later-onset SMA.

Participants and setting

This study analyzed data from 28 children (54% male; mean baseline age, 7.1 ± 4.7 years) with later-onset SMA who first received nusinersen in the ISIS-396443-CS2 (CS2) study and were eligible to participate in the ISIS-396443-CS12 (CS12) extension study ~7–13 months later. These studies were conducted through 4 centers in the US between October 2012 and January 2017.

Design, size, and duration

In the phase 1b/2a CS2 study, the participants received 2–3 intrathecal nusinersen doses of 3–12 mg over 85 days. In the CS12 study, they received 4 intrathecal nusinersen doses of 12 mg over 533 days. Motor functions were assessed with the Hammersmith Functional Motor Scale–Expanded (HFMSE), the Upper Limb Module (ULM), and the 6-Minute Walk Test (6MWT).

Primary outcome measures

The primary outcomes were from-baseline changes in HFMSE, ULM, and 6MWT scores by day 1,150.

Main results and the role of chance

The participants experienced from-baseline improvements in HFMSE, ULM, and 6MWT scores by day 1,150.

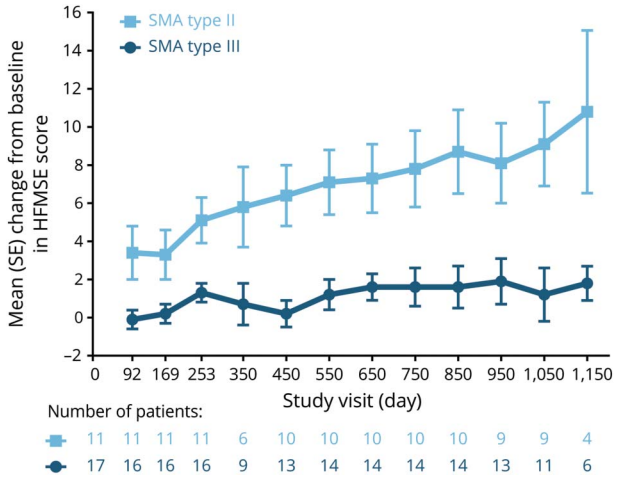
Harms

No serious adverse events that were considered nusinersen-related occurred.

Bias, confounding, and other reasons for caution

The CS2 and CS12 studies were open-labeled and had small sample sizes.

Figure Changes in HFMSE scores in participants with SMA Type II or III



Performance differences between phenotypes may have been influenced by baseline scores as participants with SMA type II had a lower mean ± SE baseline HFMSE score (21.3 ± 2.9) vs participants with SMA type III (48.9 ± 3.0; maximum total HFMSE score = 66).

Generalizability to other populations

This study's reliance on data from the US may limit the international generalizability of the results.

Study funding/potential competing interests

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Trial registration number

NCT01703988 (CS2) and NCT02052791 (CS12) 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.

