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MOTOR NEURON DISEASE

Benefits of nusinersen extend to later-onset SMA

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Children with later-onset spinal muscular atrophy (SMA) can benefit from treatment with the antisense oligonucleotide drug nusinersen, according to the results of the CHERISH trial, which were recently published in *The New England Journal of Medicine*. The findings complement those of a previous trial, ENDEAR, which demonstrated improvements in motor function after nusinersen treatment in children with infantile-onset SMA.

SMA is a motor neuron disease caused by mutations in *SMN1*, which encodes the survival motor neuron protein (SMN). Nusinersen works by promoting production of SMN by the paralogous gene *SMN2*, thereby compensating for the loss of *SMN1* function.

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The phase III CHERISH trial included 126 children aged 2–9 years with later-onset SMA, which is defined as symptom onset after 6 months of age. The children were randomly assigned in a 2:1 ratio to receive intrathecal injections of nusinersen or undergo a sham procedure on days 1, 29 and 85 of the trial. The Hammersmith Functional Motor Scale — Expanded (HFMSE) was used to assess motor function at baseline and at 3-month intervals over a 15-month period.

On average, the children who received nusinersen showed significant improvements in HFMSE scores over the course of the trial. By contrast, despite an initial increase in HFMSE scores, motor function declined over the 15-month period in the control group. Nusinersen seemed to be particularly effective in younger children and in those who received the treatment soon after symptom onset, suggesting that early intervention is crucial.

Most importantly, the improvements in motor function were considered to be clinically relevant. "Persons with later-onset SMA and their caregivers indicated that stabilization of their current state would meet their therapeutic expectations and represent a clinically meaningful response," write the investigators. "In this trial, as in the ENDEAR trial for infantile-onset SMA … we found that nusinersen had the capacity to produce meaningful changes in the clinical course of SMA."

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ORIGINAL ARTICLE Mercuri, E. et al. Nusinersen versus sham control in later-onset spinal muscular atrophy. *N. Engl. J. Med.* **378**, 625–635 (2018)
FURTHER READING Finkel, R. S. et al. Nusinersen versus sham control in infantile-onset spinal muscular atrophy. *N. Engl. J. Med.* **377**, 1723–1732 (2017) | Groen, E. J. et al. Advances in therapy for spinal muscular atrophy: promises and challenges. *Nat. Rev. Neurol.* https://doi.org/10.1038/nrneurol.2018.4 (2018)