Defining the effect of medical treatment on respiratory needs in patients with Type 1 spinal muscular atrophy

To the Editor:

We read with interest the article by Sansone et al.[1] We would like to offer 2 comments on this timely and pertinent study.

First, among patients <7 months of age at baseline, none had improved respiratory function, 25% remained stable, 58% required further ventilatory assistance, and 17% died. These data are striking because they are not concordant with the data from motor function studies, which show a significant increase in survival and an overall improvement of motor function in patients treated with nusinersen compared with a sham procedure.[2] This finding implies that improved motor function is neither the surrogate of respiratory function on its own, nor the only reason for improved survival.

In the older groups, most children remained stable, but the majority were already assisted by some level of respiratory support. The authors argue that "being stable" from a respiratory perspective, points to an actual effect of the treatment. However, at baseline most children had already initiated respiratory assistance with a mechanical in-exsufflator. A comparison with and without a mechanical in-exsufflator is not possible. Natural history studies do not have detailed information about proactive respiratory care.[3,4] Thus, a comparison of the authors' data with these studies provides an incomplete view of respiratory prognosis. It is well-known that extubation and prolonged survival are possible with noninvasive interventions.[5,6]

Researchers may be unable to study this effect, because respiratory care by experienced specialists and proactive care have become standards of care and randomizing patients would be questioned from the ethics aspect.[7] Because the modality and hours of ventilation are highly dependent on proactive respiratory care, better surrogates for respiratory function should be studied in the future cohorts. Vital capacity can be a good surrogate since it correlates with disease severity and prognosis in spinal muscular atrophy.[8]

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Reply

To the Editor:

We are grateful to Yetimakman et al for their comment and the opportunity to clarify a few points related to our study reporting respiratory function in patients with spinal muscular atrophy (SMA) treated with nusinersen. Yetimakman et al rightly point out that none of the children in the younger age group (<7 months) improved. Three patients in this age group continued spontaneous breathing at 10 months, and one-quarter remained stable. Although we agree that respiratory data have a different pattern compared with motor function, which often improves, we believe that stabilization of respiratory function in this age group should not be underestimated. Natural history studies in young infants with SMA type 1 show a clear progressive decline in respiratory function, and stabilization over 12 months is unexpected. We appreciate, however, that this is a topic that should be addressed with families when discussing treatment options.