# Onasemnogene abeparvovec preserves bulbar function in infants with presymptomatic spinal muscular atrophy: a *post-hoc* analysis of the SPR1NT trial

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## ARTICLE INFO

## ABSTRACT

Bulbar function in spinal muscular atrophy has been defined as the ability to meet nutritional needs by mouth while maintaining airway protection and communicate verbally. The effects of disease-modifying treatment on bulbar function are not clear. A multidisciplinary team conducted *post-hoc* analyses of phase 3 SPR1NT trial data to evaluate bulbar function of infants at risk for spinal muscular atrophy who received one-time gene replacement therapy (onasemnogene abeparvovec) before symptom onset. Three endpoints represented adequate bulbar function in SPR1NT: (1) absence of physiologic swallowing impairment, (2) full oral nutrition, and (3) absence of adverse events indicating pulmonary instability. Communication was not assessed in SPR1NT. We descriptively assessed numbers/percentages of children who achieved each endpoint and all three collectively. SPR1NT included infants <6 postnatal weeks with two ($n = 14$) or three ($n = 15$) copies of the *survival motor neuron 2* gene. At study end (18 [two-copy cohort] or 24 [three-copy cohort] months of age), 100% (29/29) of patients swallowed normally, achieved full oral nutrition, maintained pulmonary stability, and achieved the composite endpoint. When administered to infants before clinical symptom onset, onasemnogene abeparvovec allowed children at risk for spinal muscular atrophy to achieve milestones within published normal ranges of development and preserve bulbar function.

## 1. Introduction

Spinal muscular atrophy (SMA) is a neurodegenerative disease that results in motor neuron loss because of biallelic mutations of the *survival motor neuron 1* (*SMN1*) gene. *SMN1* directs the production of the ubiquitously expressed SMN protein, which is essential for the development and maintenance of motor neurons in the brainstem and spine [1]. The loss of SMN protein leads to severe, progressive muscle weakness and atrophy [2,3]. The *survival motor neuron 2* (*SMN2*) gene functions as a partial backup to *SMN1*, and the severity of SMA correlates inversely with the number of *SMN2* gene copies [4–6].

SMA type 1 is a very severe, and the most common, phenotype of SMA, with symptoms usually appearing within the first 6

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**Table 1**
Composite definition and assessment of bulbar function in SMA.

| Bulbar function is integrity within cranial nerves that enables an individual to: | Swallow food and liquids without functional deficits | Meet nutritional needs by mouth | Maintain pulmonary stability | Establish verbal communication skills[a] |
|---|---|---|---|---|
| **Represented by:** | Absence of clinician-identified (clinical or fluoroscopic) markers of swallowing impairment | Full oral nutrition | Absence of aspiration-induced morbidities because of compromised airway protection | Ability of a child to vocalize at least two different, distinct vowel sounds |
| **Defined by:** | Any finding of "functional swallow," "normal swallow," or "safe for swallow" | A lack of non-oral nutrition support and receiving 76–100% of nutrition via oral intake | No occurrence of aspiration or aspiration pneumonia | Achievement of item #6 or above on the Bayley Scales of Infant and Toddler Development, 3rd Edition, Expressive Communication subtest [37] |

SMA, spinal muscular atrophy.

[a] Communication was not assessed in SPR1NT.

months of life. Most children with SMA type 1 have two copies of *SMN2* [7,8]. Without treatment, patients with SMA type 1 are not able to sit independently and usually do not survive without requiring permanent ventilation by 2 years of age [9,10]. Infants with SMA type 1 frequently require nutritional and ventilatory support [10,11]. Patients with three or four copies of *SMN2* usually have SMA types 2 or 3, respectively, which have later onsets and less severe presentations than SMA type 1 [12–15]. Patients with SMA types 2 or 3 usually develop respiratory, musculoskeletal, and feeding problems, but the severity and frequency of the symptoms, as well as the age of onset, vary considerably among patients [12–16]. Expressive verbal communication is variably affected in SMA because of global motor impairment, particularly for patients with the most severe presentation of the disease [11,17].

Ventilatory, nutritional, and verbal communication deficits observed in SMA are caused by impairments in bulbar motor neurons, which control muscles required for mouth opening, chewing, swallowing, and speaking [11,17,18]. In SMA, these muscles progressively weaken, and deficits in the related life-sustaining functions can lead to choking, malnutrition, chest infections, and death [12,18–23]. In addition to improved motor function, a goal of disease-modifying treatment (DMT) for SMA is the improvement and maintenance of bulbar function. However, limited data exist on the ability of DMTs to achieve this goal.

Onasemnogene abeparvovec is a one-time, intravenously administered gene replacement therapy that delivers a functional human *SMN* gene to restore expression of full-length SMN protein [24,25]. Clinical trials demonstrated improved survival and motor function, as well as achievement of milestones such as sitting without support, standing alone, and walking alone, after administration of onasemnogene abeparvovec for infants with SMA type 1 [26–28]. Trials of onasemnogene abeparvovec for children with other types of SMA and/or more than two copies of *SMN2* are currently ongoing or awaiting publication of results [29–32]. SPR1NT was the first clinical trial of onasemnogene abeparvovec conducted in presymptomatic children younger than 6 weeks old with two or three copies of *SMN2*. When onasemnogene abeparvovec was administered before the onset of SMA symptoms, children achieved milestones consistent with children without SMA of the same age [33,34]. Data are limited regarding the impact of onasemnogene abeparvovec on bulbar function [35], especially when it is administered before the onset of SMA symptoms.

A multidisciplinary team of academics and Novartis Gene Therapies, Inc., SMA experts on deglutition, respiratory function, physical therapy, nutrition, neurology, clinical statistics, and cell and tissue engineering conducted *post-hoc* analyses of data from the phase 3 SPR1NT trial [33,34] to evaluate bulbar function for children at risk for SMA who received onasemnogene abeparvovec before symptom onset.

## 2. Materials and methods

In a previous analysis [36], we defined bulbar function as integrity within cranial nerves that enables an individual to meet nutritional needs by mouth without pulmonary instability and to demonstrate verbal communication abilities. We chose four endpoints from an available clinical trial data set to represent key components of bulbar function: (1) absence of clinician-identified (clinical or fluoroscopic) markers of physiologic swallowing impairment, (2) achievement of full oral nutrition (defined as not requiring a feeding tube for nutrition support and receiving 76–100% of nutrition via oral intake), (3) absence of adverse events relating to pulmonary stability (i.e., aspiration or aspiration pneumonia), and (4) ability to vocalize at least two different, distinct vowel sounds, which was defined as achievement of item #6 or above on the Bayley Scales of Infant and Toddler Development, 3rd Edition, Expressive Communication subtest [37] (Table 1). For this *post-hoc* analysis of SPR1NT, we assessed the available endpoints representing bulbar function — swallowing, nutrition intake, and airway protection — individually and together as a composite endpoint. Communication was not evaluated as part of the SPR1NT protocol, and, therefore, these data were not available for inclusion in this analysis.

SPR1NT was conducted in accordance with the Declaration of Helsinki, International Council for Harmonisation/Good Clinical Practice guidelines and applicable regulatory requirements (for example, those relating to informed consent and the protection of human patients in biomedical research). The study was approved by institutional review boards at all participating institutions and written informed consent was obtained from all parents/legal guardians of patients enrolled in SPR1NT.

Data from the two cohorts of the SPR1NT phase 3 clinical trial were pooled for these *post-hoc* analyses. Details of the study design, patient populations, and results have been published [33,34]. Briefly, SPR1NT was a multicenter, single-arm trial that investigated the safety and efficacy of onasemnogene abeparvovec for children with biallelic *SMN1* mutations who were younger than 6 postnatal weeks at the time of gene therapy administration. Children included in SPR1NT had either two ($n = 14$) or three copies ($n = 15$) of *SMN2* and were asymptomatic at the time of onasemnogene abeparvovec administration. All children received the therapeutic dose of onasemnogene abeparvovec of $1.1 \times 10^{14}$ vector genomes/kg. Children with two copies of *SMN2* were

followed until 18 months of age, and those with three copies were followed until 24 months of age.

Swallowing was evaluated at screening and formal swallowing tests were performed every 6 months starting at Month 6 and at the end of the study when children reached 18 (two-copy cohort) or 24 (three-copy cohort) months of age according to the study protocol. Swallowing was assessed by a clinical bedside examination or a fluoroscopic examination according to standard practice and clinician decision at each study site. The choice of test varied between study sites and practitioners based on local standard practices, and information on the method used was not collected under the study protocols and was, therefore, not available for this analysis. Because the goal of this analysis was to evaluate bulbar function and not specific physiologic integrity, as well as the fact that "normal" fluoroscopic results are not clearly delineated in infants, any finding of "functional swallow," "normal swallow," or "safe for swallow" was categorized as an absence of swallowing impairment (or normal swallow) for this analysis.

The need for nutrition support and the percentage of nutrition received via oral intake were assessed via parent report or provider observation at the end-of-study visit. A lack of non-oral nutrition support (i.e., enteral nutrition via feeding tube or parenteral nutrition) and receiving 76–100% of nutrition via oral intake together represented maximum oral nutrition for this analysis.

Information on adverse events was collected at every study visit beginning at screening through the end of the study. We considered adverse events of aspiration or aspiration pneumonia as evidence of poor airway protection. A lack of these adverse events was considered evidence of the ability to maintain pulmonary stability.

We assessed numbers and percentages of children who achieved each endpoint, as well as all three evaluable endpoints as a composite endpoint. Performance at the last evaluated time point was used to judge achievement of individual and composite bulbar function outcomes. Analyses were descriptive only, and no hypothesis was considered for this *post-hoc* analysis. Categorical variables are described as numbers and percentages. Continuous variables are described as mean and median with corresponding standard deviation (SD) and range.

## 3. Results

### 3.1. Patient disposition

Most of the children included in the SPR1NT study (28/29 [96.6%]) were identified as being at risk for SMA via confirmation of biallelic deletions of *SMN1* based on prenatal testing or newborn screening. The remaining patient (1/29 [3.4%]) was identified to be at risk for SMA via testing for a reason other than prenatal testing or newborn screening. All 29 children in the original SPR1NT study were included in the *post-hoc* analyses of the three outcomes pertaining to bulbar function. Children had two (*n* = 14) or three (*n* = 15) copies of *SMN2*. In the two-copy cohort, the mean (SD; median [range]) age (evaluated in 9 of 14 children) at SMA diagnosis was 7.2 (4.8; 8.0 [1-14]) days and the mean age at administration of onasemnogene abeparvovec was 20.6 (7.9; 21.0 [8-34]) days. In the three-copy cohort, the mean age (evaluated in 14 of 15 children) at diagnosis was 9.9 (7.7; 8.0 [2-26]) days and the mean age at administration was 28.7 (11.7; 32.0 [9-43]) days. Overall, onasemnogene abeparvovec demonstrated a favorable safety profile, and no serious adverse events were considered related to treatment according to the investigators.

**Table 2**
Individual and composite endpoints achieved at end of study in SPR1NT.

| Endpoint | Patients (N = 29), n (%) |
| --- | --- |
| Normal swallow | 29 (100) |
| Full oral nutrition | 29 (100) |
| Able to maintain pulmonary stability | 29 (100) |
| Composite endpoint | 29 (100) |

### 3.2. Individual endpoints

At baseline, no child had experienced clinical signs or symptoms that were, in the opinion of the investigators, strongly suggestive of SMA (e.g., tongue fasciculation, hypotonia, areflexia). No investigator identified physiologic swallowing impairment, all children received age-appropriate full oral nutrition, and no children had a history of pulmonary instability.

At the last evaluated time point (18 months, *n* = 14; 24 months, *n* = 15), 100% (29/29) of the children had evidence of a normal swallow. In addition, 100% (29/29) of the children received full oral nutrition and did not require non-oral nutrition support. None of the children reported any occurrence of aspiration or aspiration pneumonia, indicating that 100% (29/29) of the children maintained airway protection during the study (Table 2).

### 3.3. Composite endpoint

Overall, 100% (29/29) of the children achieved the composite endpoint of being able to swallow normally, receiving full oral nutrition, and demonstrating pulmonary stability (Table 2).

## 4. Discussion

These *post-hoc* analyses indicate that children treated with onasemnogene abeparvovec before the onset of SMA symptoms were able to swallow and meet nutritional needs orally while maintaining pulmonary stability. These findings demonstrate a substantial clinical benefit that is not observed in the natural history of SMA. Children in SPR1NT achieved motor milestones consistent with children without SMA [33,34], and data from this *post-hoc* analysis indicate that onasemnogene abeparvovec could preserve not only motor function but bulbar function as well.

A prior *post-hoc* analysis of bulbar function from pooled phase 1 (START [26]) and phase 3 (STR1VE-US [27] and STR1VE-EU [28]) studies evaluated patients with SMA type 1 who received onasemnogene abeparvovec after the onset of SMA symptoms [36]. All four endpoints representing bulbar function (normal swallow, full oral nutrition, pulmonary stability, and expressive verbal communication [in START and STR1VE-US only]) were assessed. Most of the 65 children included in the analysis achieved and maintained bulbar function, but no individual outcome was achieved by 100% of children. A majority of those with data available for all four endpoints (75% [15/20]) achieved the composite endpoint representing preserved bulbar function [36].

While components of bulbar function in SMA are routinely evaluated in clinical practice, until recently, no standard, comprehensive definition of bulbar function existed, and bulbar function endpoints are not consistently measured with objective scales specific for SMA. To date, most clinical studies of bulbar function in SMA have included patients with SMA types 2 or 3, with ages ranging from childhood to adulthood [20,38–41], and studies of bulbar function of very young patients and those with SMA type 1 are lacking. Patients with SMA consistently suffer dysphagia and mastication problems, though the frequency of oropharyngeal manifestations of SMA is unclear, since definitions

**Table 3**

Clinical trials of presymptomatic DMT administration/initiation for SMA reporting endpoints representing bulbar function.

| DMT | Study/Description | Patient population | Bulbar function components evaluated | | | | Findings |
|---|---|---|---|---|---|---|---|
| | | | Swallowing | Nutrition | Pulmonary stability | Communication | |
| Onasemnogene abeparvovec | SPR1NT [33,34] / *Post-hoc* analysis of clinical trial data | 29 children with two (*n* = 14) or three (*n* = 15) copies of *SMN2* who were followed until 18 or 24 months old, respectively | √ | √ | √ | | 100% of children achieved all components, including composite endpoint, representing bulbar function |
| Nusinersen | NURTURE [46] / Component of bulbar function assessed as secondary endpoint in a clinical trial | 25 children with two (*n* = 15) or three (*n* = 10) copies of *SMN2* | √ | | | | Interim data indicated that swallowing ability was maintained in 92% (23/25) of children (13 with two *SMN2* copies, 10 with three copies) after more than 2 years of treatment The remaining two children (both with two copies of *SMN2*) required full-time tube feeding |
| Risdiplam | RAINBOWFISH [47,48] / Components of bulbar function assessed as secondary endpoints in clinical trial | Preliminary report included seven children with at least two copies of *SMN2* who were treated for more than 12 months | √ | √ | | | All children (7/7) maintained feeding and swallowing abilities and were able to feed exclusively by mouth after 12 months of treatment |

DMT, disease-modifying treatment; SMA, spinal muscular atrophy; *SMN2, survival motor neuron 2* gene.

of bulbar function vary across studies and reports provided by patients are subjective. Our previous *post-hoc* analysis of bulbar function was the first to comprehensively investigate expressive verbal communication and deglutition elements of bulbar function after administration of onasemnogene abeparvovec and the first to offer an objective, multiple-component definition of bulbar function in SMA [36]. Although we could not evaluate the children's achievement of all components of bulbar function in this investigation because communication was not evaluated in SPR1NT, the achievement of the deglutition and respiratory components of bulbar function offers a striking contrast to natural history and good prognostic value for the integrity of cranial nerves controlling verbal communication.

In addition to onasemnogene abeparvovec, two other DMTs are approved for the treatment of SMA, both of which increase the production of SMN protein via modified *SMN2* splicing: nusinersen, an intrathecally administered antisense oligonucleotide, and risdiplam, an oral small-molecule drug [42]. Few studies have investigated components of bulbar function following treatment with nusinersen or risdiplam, and among those that have, it is difficult to compare bulbar function outcomes due to differences in patient populations, tools used to assess components of bulbar function, and the timing of DMT initiation relative to symptom onset (Tables 3 **and** 4).

The ENDEAR (nusinersen) [43] and FIREFISH (risdiplam) [44] clinical trials evaluated DMT initiation after the onset of SMA symptoms (Table 3). The ENDEAR study included 80 infants with two copies of *SMN2* who initiated nusinersen at an average age of 163 days. Of these, 51% (41/80) had swallowing or feeding difficulties and 9% (7/80) required a feeding tube at the time of treatment initiation. After 13 months of therapy, 11% (9/80) of patients had dysphagia, but the specific attributes of this diagnosis were not listed, and the number of patients requiring tube feeding was not reported [19,43,45]. The FIREFISH study included 41 infants with SMA type 1 aged 1–7 months with two copies of *SMN2*. At baseline, 95% (39/41) were able to swallow, and 85% (35/41) were able to feed orally (80% [33/41] received oral nutrition exclusively). After 24 months of risdiplam treatment, 88% (36/41) maintained the ability to swallow, and 85% (35/41) maintained the

ability to receive at least some oral nutrition (71% [29/41] received oral nutrition exclusively) [44]. Overall, impairments in at least some components of bulbar function were evident after initiation of nusinersen and risdiplam in patients with symptomatic SMA. This is consistent with the results of our previous *post-hoc* analysis in which bulbar function was preserved in a majority of the 65 children with symptomatic SMA type 1 and two copies of *SMN2* who received onasemnogene abeparvovec, but among whom no outcome was achieved by 100% of children [36]. These findings are not consistent with those of the current SPR1NT analysis, in which all children achieved all endpoints representing bulbar function.

The NURTURE (nusinersen) [46] and RAINBOWFISH (risdiplam) [47] clinical trials have reported bulbar function outcomes following initiation of DMT prior to the onset of SMA symptoms in infants younger than 6 weeks of age (Table 4). An interim report from the NURTURE study included 25 children with two (*n* = 15) or three (*n* = 10) copies of *SMN2*. After more than 2 years of treatment with nusinersen and a median (range) age of 3.8 (2.8–4.8) years, 92% (23/25) of children (two *SMN2* copies, *n* = 13; three *SMN2* copies, *n* = 10) maintained the ability to swallow, as measured by the Hammersmith Infant Neurological Examination. The remaining two children (8%) required full-time tube feeding [48]. An early report from the ongoing RAINBOWFISH study revealed that seven infants (two *SMN2* copies, *n* = 4; three *SMN2* copies, *n* = 2; atypical number of *SMN2* copies falling between three and four, *n* = 1) who were treated with risdiplam for more than 12 months (range, 12.2–22.8 months) have maintained feeding and swallowing abilities, as measured by the Parent Assessment of Swallowing Ability [47]. Compared with DMT initiation after the onset of SMA symptoms, DMT initiation before symptom onset appears to indicate a greater percentage of children with preserved bulbar function, which is in line with our current *post-hoc* analysis.

To date, no trials of head-to-head comparisons of the effects of DMTs on bulbar function have been conducted. The studies of bulbar function with DMTs for SMA included small patient populations and used different scales to evaluate only deglutition components of bulbar function, making comparisons difficult. Future investigations comparing differences in bulbar outcomes for

**Table 4**

Clinical trials of symptomatic DMT administration/initiation for SMA reporting endpoints representing bulbar function.

| DMT | Study/Description | Patient population | Bulbar function components evaluated | | | | Findings |
| | | | Swallowing | Nutrition | Pulmonary stability | Communication | |
|---|---|---|---|---|---|---|---|
| Onasemnogene abeparvovec | START [26], STR1VE-US [27], STR1VE-EU [28] / *Post-hoc* analysis of pooled data from three clinical trials | 65 children with SMA type 1 and two copies of *SMN2* who were followed until 18 (STR1VE-US and STR1VE-EU) or 24 (START) months old | √ | √ | √ | √ | No outcome was achieved by 100% of children 75% (15/20) of children achieved composite endpoint representing preserved bulbar function |
| Nusinersen | ENDEAR [43,45] / Components of bulbar function assessed as secondary endpoints in a clinical trial | 80 children with two copies of *SMN2* | √ | √ | | | At baseline, 51% (41/80) of infants had swallowing and feeding difficulties, and 9% (7/80) required tube feeding After nusinersen, 11% (9/80) of patients had dysphagia |
| Risdiplam | FIREFISH [44] / Components of bulbar function assessed as exploratory endpoints in a clinical trial | 41 children with SMA type 1 and two copies of *SMN2* who were followed for 24 months | √ | √ | | | 88% (36/41) maintained the ability to swallow and feed orally, and 85% (35/41) maintained the ability to receive at least some oral nutrition |

DMT, disease-modifying treatment; SMA, spinal muscular atrophy; *SMN2, survival motor neuron 2* gene.

patients who receive DMTs at similar stages of disease progression are critical to fully understand the therapeutic effects.

Treatment advances have shifted the prognosis of SMA from likely fatal in severe phenotypes to long-term survival with motor and functional benefits, but responses to DMTs are heterogeneous. It is unclear if differences reported in outcomes, including those representing bulbar function, are a result of differences in the DMT itself, the timing of administration, or other factors. Patient age at the time of treatment, which is closely correlated to symptom onset, disease duration, and extent of motor neuron loss, has been correlated to improved response to treatment [49]. Our analysis supports these findings, with infants who had not experienced SMA symptom onset and were younger than 6 weeks of age at the time of onasemnogene abeparvovec administration achieving milestones within published ranges of normal development.

The impact of SMA is substantial for children and for their caregivers, and near-universal bulbar function impairment is expected. Patients and families are faced not only with physical limitations and morbidity and mortality risks but also social and communication-related limitations, emotional stress, limited independence, and poor health-related quality of life [50–54]. However, SMA can now be detected early, even before symptom onset, thanks to newborn screening programs [55,56]. According to the most recent data available, as of February 2023, 48 states in the United States screen for SMA at birth, accounting for 99% of newborns screened [57]; worldwide, as of 2021, only 2% of newborns were screened, but many countries are increasingly implementing or planning widespread newborn screening programs [55,58].

One challenge to establishing clear, standardized definitions and terminology related to bulbar function in SMA is that the causes of bulbar dysfunction are not entirely clear. Swallowing and feeding impairments, pulmonary instability due to risk of aspiration, and expressive verbal communication difficulties are likely due to a variety of causes, including bulbar muscle weakness [19,24,25,38,59,60]. Multifaceted physiology underscores the need for multidisciplinary assessment and management of SMA in general and in bulbar function specifically. Nutrition, swallowing, airway protection, and verbal communication are important in the management of patients with SMA, and specific, comprehensive

measures of bulbar function should be established and consistently applied across the care continuum to guide clinical decision-making.

Our findings are limited by the small number of children included in this analysis, as well as the fact that this was a *post-hoc* rather than *a-priori* analysis. The data available for evaluation were also limited, as communication was not assessed in SPR1NT but is an important component of bulbar function that must be considered in comprehensive definitions and assessments. Further, we used a definition of bulbar function that was established by a team of multidisciplinary experts for a previous *post-hoc* analysis and endpoints that were chosen based on available data from pooled clinical trials. Other surrogate endpoints representing bulbar function may be considered in other populations and settings. In addition, swallowing assessments were not standardized within the protocol and varied among institutions and practitioners. Larger, prospective studies using standardized, age-based assessments are needed to assess the durability of bulbar function for infants at risk for SMA who receive onasemnogene abeparvovec before symptom onset. Ongoing real-world studies and registries, as well as long-term follow-up studies of SPR1NT and earlier clinical trials of onasemnogene abeparvovec, will help clarify the clinical benefits of this DMT for SMA.

## 5. Conclusions

This *post-hoc* analysis demonstrates that children at risk for SMA treated with onasemnogene abeparvovec before the onset of symptoms met all the components of the composite endpoint representing the successful preservation of bulbar function, which included no evidence of swallowing impairment, achievement of full oral nutrition, and no evidence of aspiration or aspiration pneumonia. Communication was not assessed in the study. When compared with a prior *post-hoc* analysis of patients with symptomatic SMA, a greater percentage of children who received treatment before symptom onset achieved endpoints representing bulbar function compared with patients who received treatment after symptom onset. Together, these findings demonstrate that children who received onasemnogene abeparvovec before the onset of SMA symptoms achieved bulbar function, in

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addition to motor milestones [33,34], consistent with typically developing children. Early intervention with onasemnogene abeparvovec during the presymptomatic phase of SMA, along with multidisciplinary management, allows achievement of motor gains and somatic growth, as well as preservation of bulbar function [61].

## Author contributions

All authors participated in the design, conduct, and analysis of the study, and manuscript development, and approved the final manuscript for submission.

## Declaration of Competing Interest

**Richard D. Shell** has been a paid speaker for Novartis Gene Therapies. **Katlyn E. McGrattan** has received research grants from the National Institutes of Health, National Institute of Child Health and Human Development, National Institute of Environmental Health Sciences, 1R41HD104305-01 on "A novel non-invasive method of aspiration detection in preterm infants (Ongoing)." In addition, she is a consultant for Novartis Gene Therapies, Biogen, and Roche. **Rebecca Hurst-Davis** is a Cure SMA Medical Advisory Council member. **Sally Dunaway Young** is an advisory board member/consultant for Biogen, Cure SMA, Genentech/Roche, and Scholar Rock, and receives grant support from Novartis Gene Therapies, Inc., Biogen, Cure SMA, Genentech/Roche, Genzyme, Minoryx, PTC Therapeutics, and Scholar Rock. **Giovanni Baranello** has received speaker and consulting fees from Biogen, Novartis Gene Therapies, Inc. (AveXis), and Roche, and has worked as a principal investigator of SMA studies sponsored by Novartis Gene Therapies, Inc., and Roche. **Arseniy Lavrov, Eamonn O'Brien, Shiri Wallach, Nicole LaMarca,** and **Sandra P. Reyna** are employees of Novartis Gene Therapies and hold stock/other equities. **Basil T. Darras** has served as an *ad-hoc* scientific advisory board member for Audentes, AveXis/Novartis Gene Therapies, Biogen, Pfizer, Sarepta, Roche/Genentech, and Vertex; as a steering committee chair and member for the Roche FIREFISH and Biogen ASCEND studies, respectively, and data and safety monitoring board member for Amicus Inc.; he has no financial interests in these companies. He has received research support from the National Institutes of Health/National Institute of Neurological Disorders and Stroke, the Slaney Family Fund for SMA, the Spinal Muscular Atrophy Foundation, CureSMA, and Summit and Working on Walking Fund and has received grants from Ionis Pharmaceuticals, Inc., for the ENDEAR, CHERISH, CS2/CS12 studies; from Biogen for CS11; and from Novartis Gene Therapies, Inc., Sarepta Pharmaceuticals, Novartis, PTC Therapeutics, Roche, Scholar Rock, and Fibrogen. He has also received royalties for books and online publications from Elsevier and UpToDate, Inc.

## Data availability

Novartis is committed to sharing clinical trial data with external researchers and has been doing so voluntarily since 2014. Novartis was the third member to join ClinicalStudyDataRequest.com (CSDR), which is the first data sharing consortium of clinical study sponsors and funders. CSDR is a leader in the data sharing community

inspired to drive scientific innovation and improve medical care by facilitating access to patient-level data from clinical studies. More information is available at https://www.novartisclinicaltrials.com/TrialConnectWeb/voluntarydataviewmore.nov

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