Real-World Outcomes and Health Care Resource Utilization of Onasemnogene Abeparvovec for US Patients with Spinal Muscular Atrophy Type 2 Aged ≥6 Months: Results of a Retrospective Chart Review Study

PCR262

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Introduction

- SMA is a rare, genetic, progressive neuromuscular disorder caused by biallelic deletion or mutation of the *SMN1* gene. The phenotypic presentation of SMA ranges from profound weakness at birth to milder, more slowly progressive symptoms with adult onset, but all types of SMA are debilitating if untreated.[1–4]
- Patients with SMA type 2 experience relatively rapid neuromuscular decline until 13 years of age and more gradual decline through adulthood. Patients with SMA type 2 can sit independently but do not stand or walk.[4–6]
- The *SMN2* gene functions as a partial backup gene to *SMN1*, and the severity of SMA correlates inversely with the polymorphic number of *SMN2* gene copies.[7–9] Typically, patients with SMA type 1 have two copies of *SMN2*, and patients with SMA type 2 have three copies.[4–6]
- Three DMTs are currently available for SMA:
  - *SMN2* gene splicing modifiers, including risdiplam, an oral small-molecule drug, and nusinersen, an intrathecally administered ASO[10]
  - Onasemnogene abeparvovec, a one-time gene replacement therapy that delivers a fully functional copy of the human *SMN* gene[11,12]
- Clinical trials of DMTs have demonstrated improved survival, gains in motor function, and achievement of motor milestones for patients with SMA[13–21]
  - Almost all patients included in clinical trials of onasemnogene abeparvovec have been younger than 6 months old, and none had received a prior DMT[22,23]
  - In a real-world setting, patients may be older than 6 months at the time of treatment or they may receive multiple DMTs
- Real-world data on outcomes and HCRU for patients with SMA type 2 treated with DMTs are lacking

Objective

- We sought to describe real-world outcomes and HCRU for patients in the United States with SMA type 2 aged ≥6 months at the time of treatment with onasemnogene abeparvovec monotherapy or switching to onasemnogene abeparvovec from nusinersen

Methods

- We conducted a retrospective chart review of patients who had SMA type 2 and were treated with onasemnogene abeparvovec at age 6 months or older or initiated nusinersen between the ages of 6 months and 5 years
- Data were collected from providers actively treating patients in the United States
- The index date was the date of onasemnogene abeparvovec initiation. Patient characteristics and outcomes were summarized descriptively for patients with available data at or before the index date and with ≥1 follow-up visit. HCRU (inpatient admissions, emergency room visits, and consultation visits) was summarized per patient-year (PPY).
- All analyses were descriptive and no statistical comparisons between groups were performed. Missing or incomplete data were not included in the calculations.

Results

Patients

- The chart review included 10 patients (nine who received onasemnogene abeparvovec monotherapy and one who switched to onasemnogene abeparvovec after initial treatment with nusinersen) (**Table 1**)
- All patients (100%) had three copies of *SMN2*
- On the index date, six (66.7%) patients receiving onasemnogene abeparvovec monotherapy and the patient (100%) who switched to onasemnogene abeparvovec weighed ≥8.5 kg (**Table 1**)
- The onasemnogene abeparvovec monotherapy group had a mean (±SD) age of 13.0±4.8 months, and the patient who switched to onasemnogene abeparvovec was 22.0 months old at the time of onasemnogene abeparvovec initiation (**Table 1**)

Table 1. Demographics and baseline clinical characteristics

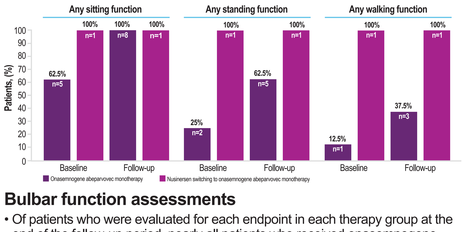
Characteristic	Onasemnogene abeparvovec monotherapy (n=9)	Switched to onasemnogene abeparvovec from nusinersen (n=1)
Sex, n (%)		
Female	4 (44.4)	0
Male	5 (55.6)	1 (100)
Missing	0	0
Race/ethnicity, n (%)		
Asian	1 (11.1)	0
Black or African American	1 (11.1)	0
Hispanic or Latino	0	0
White	7 (77.8)	1 (100)
Missing	0	0
Gestational age at birth, n (%)		
33–35 weeks	2 (28.6)	0
>35 weeks	5 (71.4)	1 (100)
Missing/N	2/9 (22.2)	0
Age at SMA diagnosis, months		
Mean (SD)	10.7 (6.6)	0 (–)
Median	13.0	N/A
IQR	9.0–14.0	N/A
Range	0.0–18.0	N/A
Age at treatment initiation with onasemnogene abeparvovec, months		
Mean (SD)	13.0 (4.8)	22.0 (–)
Median	14.0	N/A
IQR	11.0–15.0	N/A
Range	6.0–20.0	N/A
Weight ranges at treatment initiation with onasemnogene abeparvovec, kg		
<8.5	3 (33.3)	0
≥8.5 to <13	5 (55.6)	0
≥13	1 (11.1)	1 (100)
Missing	0	0
Weight at treatment initiation with onasemnogene abeparvovec, kg		
Mean (SD)	9.5 (2.1)	15.0 (–)
Median	9.5	N/A
IQR	8.0–9.8	N/A
Range	7.0–13.8	N/A

IQR, interquartile range; N/A, not applicable; SMA, spinal muscular atrophy.

Motor milestone and motor function assessments

- Eight of the nine patients in the onasemnogene montherapy group and the patient who switched to onasemnogene abeparvovec had data on motor milestones and were included in the analysis
- Improvement and/or maintenance of motor milestones was achieved by all patients in the analysis (**Figure 1**). All patients evaluated in each treatment group were able to sit, five patients (63%) in the onasemnogene abeparvovec monotherapy group and the patient (100%) who switched to onasemnogene abeparvovec were able to stand, and three patients (38%) in the onasemnogene abeparvovec monotherapy group and the patient (100%) who switched to onasemnogene abeparvovec were able to walk.
- Mean time to initial improvement in any motor milestone (±SE) was 1.9±0.5 months for patients receiving onasemnogene abeparvovec monotherapy. The patient who switched from nusinersen to onasemnogene abeparvovec maintained achieved motor function improvements.

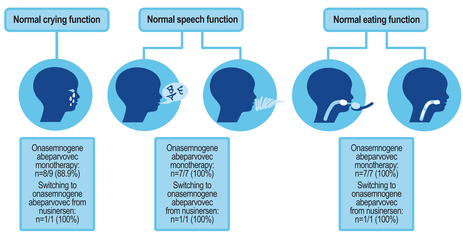
Figure 1. Motor milestones at baseline versus follow-up



Bulbar function assessments

- Of patients who were evaluated for each endpoint in each therapy group at the end of the follow-up period, nearly all patients who received onasemnogene abeparvovec monotherapy or switched to onasemnogene abeparvovec following nusinersen maintained a normal cry function (88.9% [n=8/9] and 100% [n=1/1], respectively), maintained speech function (100% [n=7/7] and 100% [n=1/1], respectively), and maintained any eating function (100% [n=7/7] and 100% [n=1/1], respectively) (**Figure 2**)

Figure 2. Bulbar function status at the end of the follow-up period



HCRU assessments

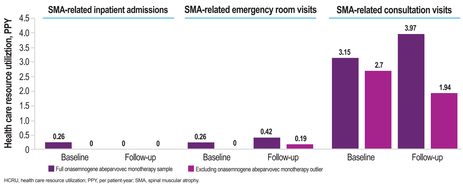
- The rate of inpatient admissions was reduced after treatment with onasemnogene abeparvovec monotherapy and the rate of SMA-related consultations was reduced after switching to onasemnogene abeparvovec (**Table 2**)
- A slight increase in emergency room visits and SMA-related consultations was observed for patients treated with onasemnogene abeparvovec monotherapy; however, the patient group was very small, and these findings were influenced by a single patient. When the outlier was removed from the analysis, SMA-related consultations decreased (**Figure 3**).

Table 2. HCRU at baseline and during follow-up

	SMA-related inpatient admissions (PPY)		SMA-related emergency room visits (PPY)		SMA-related consultation visits (PPY)	
Treatment group	Baseline	Follow-up	Baseline	Follow-up	Baseline	Follow-up
Onasemnogene abeparvovec monotherapy	0.26	0	0.26	0.42	3.15	3.97
Onasemnogene abeparvovec after nusinersen	0	0	0	0	3.24	0

HCRU, health care resource utilization; PPY, per patient-year; SMA, spinal muscular atrophy.

Figure 3. Sensitivity analysis of HCRU at baseline and during follow-up for patients receiving onasemnogene abeparvovec monotherapy



HCRU, health care resource utilization; PPY, per patient-year; SMA, spinal muscular atrophy.

Limitations

- Only a small number of patients was included in the treatment groups and data completeness was variable across charts
- Results are descriptive and do not account for differences in patient characteristics or other potential confounders
- The duration of baseline and follow-up periods was variable across patients; however, rates were standardized PPY to account for this variation

Conclusions

- Patients with SMA type 2 improved or maintained function across multiple outcomes after receiving onasemnogene abeparvovec, with rapid onset of therapeutic effect
  - Approximately two-thirds of patients were able to stand and one-third of patients were able to walk after receiving onasemnogene abeparvovec. These milestones are not typically achieved by patients with SMA type 2.
  - The mean time to motor function improvements was less than 2 months after onasemnogene abeparvovec administration
  - Nearly all patients were able to communicate and eat. These bulbar functions are typically impaired in patients with SMA.
- Patients also experienced reductions in the rate of inpatient admissions, with no admissions reported after receiving onasemnogene abeparvovec as monotherapy or after switching to onasemnogene abeparvovec after initial nusinersen

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Abbreviations

ASO, antisense oligonucleotide; *DMT*, *disease-modifying treatment*; *HCRU*, health care resource utilization; SMA, spinal muscular atrophy; *SMN1*, *survival motor neuron 1 gene*; *SMN2*, *survival motor neuron 2* gene.

Acknowledgments and Disclosures

This study was funded by Novartis Gene Therapies, Inc.

Editorial support was provided by Jennifer Gibson, PharmD, of Kay Square Scientific, Newtown Square, PA. This support was funded by Novartis Gene Therapies, Inc.

Disclosures: MY, **MG**, and **AA** are employees of Analysis Group, Inc., which has received consulting fees from Novartis Gene Therapies, Inc., for this research. **OD**, **WT**, **NL**, **AP**, and **SPR** are employees of Novartis Gene Therapies, Inc., and own Novartis stock or other equities.