

Real-World Treatment Patterns and Outcomes in Patients With Spinal Muscular Atrophy Collected From the RESTORE Registry

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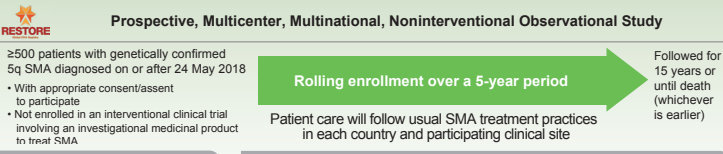
OBJECTIVE

The purpose of the RESTORE Registry is to assess long-term outcomes in patients diagnosed with SMA. Here we report initial data from the RESTORE Registry, including cohort clinical characteristics, treatments received, and limited outcomes from patients with available data

INTRODUCTION

- SMA is caused by deletion or mutation of the *SMN1* gene, and is associated with loss of both voluntary motor function and bulbar function essential for breathing and swallowing¹
- Although two therapies are currently FDA approved for treating SMA (nusinersen and onasemnogene aberaparovoc),^{2,3} real-world data on treatment outcomes are limited – particularly for patients who switch treatments

STUDY DESIGN (NCT04174157)⁴



STUDY OBJECTIVES

- Primary objective is to assess contemporary SMA treatments, including effectiveness, short- and long-term safety, and overall patient survival
- Secondary objectives include the assessment of HCRU, caregiver burden, and changes in patient functional independence over time

ENROLLMENT SOURCES

- Individual *de novo* clinical sites
- Existing SMA consortia (eg, iSMAC,^{5,6} Treat-NMD,^{7,8} Cure SMA,⁹ SMARtCARE¹¹)
- MAP: 14 patients from the US MAP cohort and 9 patients from the single-patient IND program are included in the RESTORE Registry. The US MAP provided onasemnogene aberaparovoc (formerly AVXS-101) access to eligible patients with a genetic diagnosis of SMA, which ended with US FDA approval of onasemnogene aberaparovoc
- Expanded access program
- Post-marketing surveillance (required follow-up)

- The RESTORE Registry captures data from patients who have received multiple therapies or have switched from one active therapy to another

RESULTS

- 67 patients were enrolled in the RESTORE Registry between Sep 2018 and 31 Jan 2020; all from *de novo* clinical sites in the United States
- Information on treatment regimen was available for 56 of the 67 enrolled patients; here we present initial data on this subgroup

DEMOGRAPHICS AND CLINICAL CHARACTERISTICS

Characteristic	Treatment-Evaluable Patients (N=56) n (%)
Gender	
Female	49 (87.5)*
Male	29 (59.2)
	20 (40.8)
SMN2 copy number	
1	53 (94.6)*
2	2 (3.6)
3	30 (56.6)
4	15 (28.3)
>4	6 (11.3)
	0
SMA type	
Presymptomatic	56 (100)*
I	5 (8.9)
II	38 (67.8)
III	8 (14.3)
	5 (8.9)
SMA function status	
Non-sitter	56 (100)*
Sitter	40 (71.4)
Standing	12 (21.4)
Walker	0
	4 (7.1)
Age at first treatment	
0–6 months	43 (76.8)*
>6–24 months	26 (60.5)
>24 months	12 (27.9)
	5 (11.6)

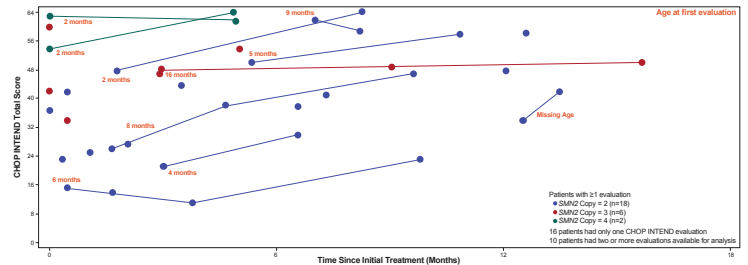
*Percentage based on eligible patients, n/N (%).

SMA Symptoms at Diagnosis – Treated Patients

Symptom, n (%)	Treatment Received					All treated patients (N=56)
	Onasemnogene aberaparovoc → nusinersen (n=2)	Nusinersen → onasemnogene aberaparovoc (n=17)	Nusinersen → onasemnogene aberaparovoc → nusinersen (n=8)	Onasemnogene aberaparovoc only (n=18)	Nusinersen only (n=11)	
Patients with Symptoms, n	2	16	8	15	10	51
Hypotonia	1 (50.0)	12 (75.0)	8 (100.0)	13 (86.7)	7 (70.0)	41 (80.4)
Limb weakness	2 (100.0)	13 (81.3)	7 (87.5)	11 (73.3)	9 (90.0)	42 (82.4)
Pneumonia or respiratory symptoms	2 (100.0)	10 (62.5)	5 (62.5)	5 (33.3)	1 (10.0)	23 (45.1)
Tongue fasciculations	0	10 (62.5)	3 (37.5)	6 (40.0)	0	19 (37.3)
Developmental delay	1 (50.0)	8 (50.0)	5 (62.5)	8 (53.3)	5 (50.0)	27 (52.9)
Constipation	1 (50.0)	5 (31.3)	4 (50.0)	2 (13.3)	4 (40.0)	16 (31.4)
Swallowing or feeding difficulties	1 (50.0)	12 (75.0)	7 (87.5)	8 (53.3)	1 (10.0)	29 (56.9)
Other	0	0	0	0	2 (20.0)	2 (3.9)

FUNCTIONAL ASSESSMENTS

CHOP INTEND Scores Among 26 Patients with Evaluations by Time Since Treatment and SMN2 Copy Number



SAFETY

Treatment-Emergent Adverse Events by Treatment

Adverse event, n (%)	Patients Receiving >1 Active Therapy				Patients Receiving Monotherapy (n=4)	Total (n=39)
	Onasemnogene aberaparovoc → nusinersen (n=1)	Nusinersen → onasemnogene aberaparovoc (n=14)	Nusinersen → onasemnogene aberaparovoc → nusinersen (n=8)	Onasemnogene aberaparovoc only (n=12)		
≥1 treatment-emergent adverse event (any grade)	1 (100)	11 (78.6)	8 (100)	10 (83.3)	2 (50)	32 (82.1)
Serious adverse events	1 (100)	4 (28.6)	5 (62.5)	4 (33.3)	1 (25)	15 (38.5)
Serious and related adverse events*	0	3 (21.4)	2 (25)	1 (8.3)	0	6 (15.4)
Adverse events of special interest to onasemnogene aberaparovoc						
Hepatotoxicity*	0	8 (57.1)	6 (75)	6 (50)	0	20 (51.3)
Thrombocytopenia*	0	3 (21.4)	0	1 (8.3)	0	4 (10.3)
Cardiac adverse events*	1 (100)	3 (21.4)	3 (37.5)	2 (16.7)	0	9 (23.1)

*For patients who received >1 therapy, relatedness could be due to either medicinal product and was not specified by the reporter. *Primarily transient transaminase elevations. *Primarily isolated decrease in platelet count without clinical evidence of bleeding events. *Cardiac adverse events include bradycardia, Torsionade, cardiac arrest, thrombotic microangiopathy, and hepatopathy, at least 1 blood and lymphatic system-related adverse event and 1 event of hepatopathy were misclassified as cardiac and will be corrected.

- At the time of this report, adverse event data were reported for 39 of 56 patients with known treatment regimens
- Among these 39 patients, 32 (82.1%) reported ≥1 adverse event

LIMITATIONS

Limitations of this analysis include a small number of patients overall and for each treatment regimen; short, variable duration of follow-up; and variable completeness of data across study sites at time of analysis. Ceiling effect and potential inconsistency in CHOP INTEND evaluations across study sites may both complicate analyses of these data. Finally, since only adverse events that occur after enrollment are recorded, adverse events occurring soon after initiation of treatment may not be captured.

SUMMARY

The current enrollment in the RESTORE Registry reflects a range of SMA patient types and treatment regimens

- Patients continue to be enrolled, and the registry continues to expand globally throughout North America, Latin America, Europe, Asia Pacific, and the Middle East

Most patients with >1 CHOP INTEND evaluation achieved higher scores over the follow-up period

Based on limited data available, adverse event experience of onasemnogene aberaparovoc observed in the RESTORE Registry is consistent with experience in clinical trials for SMA

No new safety signals were identified among patients treated with onasemnogene aberaparovoc or among those who switched treatments

ABBREVIATIONS: CHOP INTEND, Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; FDA, Food and Drug Administration; HCRU, healthcare resource utilization; IND, investigational new drug; iSMAC, International Spinal Muscular Atrophy Consortium; MAP, managed access program; NMD, neuromuscular disorders; SMA, spinal muscular atrophy; SMN, survival motor neuron; US, United States.

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