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

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 swallowing.
- Although two therapies are currently FDA approved for treating SMA (nusinersen and onasemnogene abeparvovec), real-world data on treatment outcomes are limited – particularly for patients who switch treatments.

STUDY DESIGN (NCT04174157)*
Prospective, Multicenter, Multinational, Noninterventional Observational Study

ENROLLMENT SOURCES
- 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 HCRI, caregiver burden, and changes in patient functional independence over time.

STUDY OBJECTIVES
- Individual de novo clinical sites
- Existing SMA consortia (eg, iSMAC, Treat-NMD, Cure SMA, SMN CARE*1)
- MAP: >14 patients fromthe US MAP cohort and 9 patients from the single-patient IND program are included in the RESTORE Registry. The US MAP provided onasemnogene abeparvovec (formerly RGX-101) access to eligible patients with a genetic diagnosis of SMA, which ended with US FDA approval of onasemnogene abeparvovec.
- Expanded access program
- Post-marketing surveillance (required follow-up)

The RESTORE Registry captures data from patients who have received multiple therapies initially and may switch to another

RESULTS
- 67 patients were enrolled in the RESTORE Registry between Sep 2018 and Jan 2021; all 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

- Study participants were >=500 patients with genetically confirmed SMA.

- STUDY DESIGN (NCT04174157)*

- Prospective, Multicenter, Multinational, Noninterventional Observational Study

- Rolling enrollment over a 5-year period

- Patient care will follow usual SMA treatment practices in each country and participating clinical site

- Followed for at least 15 years or until death (whichever is earlier)

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

SAFETY
- Treatment-Emergent Adverse Events by Treatment

- All adverse events reported for 39 of 56 patients with known treatment regimens
- Among these 39 patients, 32 (82%) reported at least one 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. Ceil effect and potential inconsistency in CHOPEMAD/MADEMAD evaluating across study sites may both complicate analyses of these data. Finally, since 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, 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 abeparvovec 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 abeparvovec or among those who switched treatments.

ABBREVIATIONS: CHOPEMAD/MAD, Multi-center Observational Study of SMA Patients Enrolled in a Clinical Trial: MAD Global Registry. MAD Global Registry is part of MAD International with the objective of investigating real-world outcomes and novel therapies for individuals with SMA; CHOP INTEND, Children’s Hospital of Philadelphia Infant姿 in plem 4 rare diseases; HCRI, Hospital Center of Reference for SMA; HDQ, Human Development Quotient; iSMAC, International Spinal Muscular Atrophy Consortium; IND, Investigational New Drug; IOM, Institute of Medicine; NCT, National Clinical Trial; NMD, neuromuscular disorder; SMA, spinal muscular atrophy; SMN2, survival motor neuron 2; SMN2, survival motor neuron 2 copy number; TIMA, Trial of Individuals with Muscular Dystrophy; TREAT-NMD, Treatment and Research in Rare Neurological Diseases (TREAT-NMD); USFDA, U.S. Food and Drug Administration.


- All the data of this report, adverse event data were reported for 36 of 56 patients with known treatment regimens
- Among these 39 patients, 32 (82%) reported at least one adverse event

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