Real-world treatment with risdiplam in adults with SMA: A multicenter study

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Background

- Risdiplam (EVRYSDI®) is a centrally and peripherally distributed oral *SMN2* pre-mRNA splicing modifier that increases the levels of functional SMN protein.[1,2]
  - Risdiplam has been approved for the treatment of patients with SMA in more than 90 countries worldwide.[3*]
- Although there is a body of literature on the use of risdiplam in adult patients from clinical trials, including SUNFISH (NCT02908685; 2–25 years)[4,5] and JEWELFISH (NCT03032172; 1–60 years)[6], real-world evidence on adult patients receiving risdiplam is limited.
- Adults with SMA currently account for >35% of the SMA population worldwide; this proportion will grow as new treatments support survival into adulthood.[7]
- Here we present the design of a retrospective, non-interventional cohort study that aims to increase understanding of the characteristics, treatment patterns and clinical outcomes of patients aged ≥25 years treated with risdiplam.

*Risdiplam has been approved for the treatment of pediatric and adult patients with SMA by the FDA and for patients aged ≥2 months with a clinical diagnosis of Type 1, 2 or 3 SMA or with one to four copies of *SMN2* by the EC.[8,9]

Selection criteria

- Diagnosed with SMA
- Risdiplam treatment first received at age ≥25 years*
- At least two visits to the clinic for SMA-related care
- At least 12 months between the first and last visit†

*After drug authorization or prior to drug authorization but provided via an expanded access program. †The first visit occurring on or after initiation of risdiplam and the last visit occurring on or before the date of data abstraction.

Data collection and analysis

- Medical record data will be abstracted from the histories of eligible patients managed for SMA at each participating site. All medical information available in the patient's record at the participating site will be eligible for review by the site's abstraction team.
- A maximum of 70 patient records are expected from at least three sites across the US depending on participating sites and number of eligible records at each site.
- Data will be descriptive in nature and summarized using univariate statistics, including mean, standard deviation, minimum, maximum, and median for continuous variables and frequency distributions for categorical variables.
- Results will be presented overall and by relevant subgroups i.e., previously treated, ambulant or non–ambulant, *SMN2* copy number, disease onset and disease severity.
- This study is explorative and statistical comparisons between subgroups for the purpose of hypothesis testing are not within the scope of this study.

Study feasibility

- As part of the assessment for site feasibility we assessed the measures that clinicians use for their patients in real–world clinical practice.
- Outcome measures for this study were then selected based on the responses from the sites to reflect the current clinical practice.

Pilot test

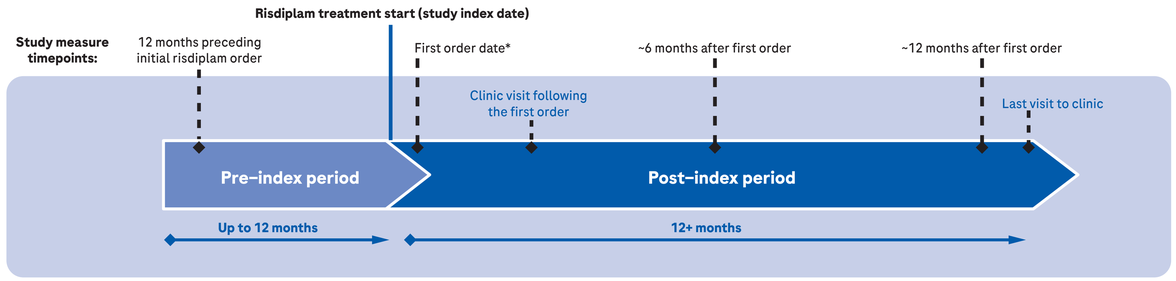
- Prior to the start of data collection, two identified study sites will be contacted to obtain ethics clearance and pilot test the electronic data capture form.
- Pilot testing will include full abstraction of up to two patient records by each site using the most current version of the electronic data capture form.
- A pilot feedback guide will be provided to the sites to be used during pilot interviews.

Participating sites

- Site enrollment is currently open.
- For more information on how to participate in this study, please contact guittari.carol-jean@gene.com

Study design

- A real-world retrospective, non–interventional cohort study of patients with a confirmed diagnosis of SMA who received treatment with risdiplam at age ≥25 years



- Patients will have differing durations of follow-up (minimum of 1 year) and, where appropriate, study measures may be standardized (e.g. monthly/annually).

Outcome measures

Patient demographics

- Age (≥25 years)
- Sex
- Race/ethnicity

SMA-related healthcare resource utilization

- Inpatient stays
- Outpatient office visits
- Number of days treated with modality

Clinical, genetic and disease-specific characteristics

- Age at diagnosis
- SMA type
- *SMN2* copy number
- Motor function

Clinical outcome measures

- Physiotherapy-based scale assessments: HFMSE, RULM, 6MWT, MFM
- Mortality
- Respiratory function

SMA pharmacologic treatment characteristics

- Agents used
- Duration of therapy
- Dose modification(s)
- Reason(s) for discontinuation/ dose reduction

Other treatment modalities

- Orthopedic surgery
- Physical therapy
- Mechanical ventilation
- Cough assist and other assistive devices
- Other medical appliances

Limitations

- Data captured will be limited to information available in the medical records held by the physicians at the participating sites. Study results will be based solely on the population included in this study. As sites are not randomly chosen, the results will not be generalizable to all adult patients ≥25 years of age with SMA.
- Treatment patterns, disease monitoring and HCRU patterns may reflect site-specific protocols. Multiple sites will, however, be included in this study to mitigate these effects.

Conclusions

- This study is expected to provide real-world data on adults with SMA who are aged ≥25 years and have been treated with risdiplam, including disease-specific and other relevant clinical and genetic characteristics and treatment patterns.
- This will fulfill a critical need for descriptive information about the diagnosis, treatment, management and outcomes for this population.

Abbreviations

6MWT, 6–minute walking test; EC, European Commission; FDA, US Food and Drug Administration; HCRU, Health Care Resource Utilisation; HFMSE, Hammersmith Functional Motor Scale Expanded; MFM, Motor Function Measure; mRNA, messenger ribonucleic acid; RULM, Revised Upper Limb Module; SMA, spinal muscular atrophy; SMN, survival of motor neuron; US, United States.

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