NOVARTIS

COAV101A1CZ01R Study Results Abstract for Public Disclosure

Title

Real-World Evidence of Clinical Use of Available Treatments for Pediatric Patients with Spinal Muscular Atrophy (SMA): A Multi-Site Retrospective Analysis Based on REaDY registry

Keywords

Spinal muscular atrophy (SMA), real-world evidence, retrospective study, patient registry, disease-modifying therapy (DMT)

Rationale and background

Spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disease caused by mutations in the *SMN1* gene, leading to progressive muscle weakness and paralysis. The introduction of three causative therapies—nusinersen, onasemnogene abeparvovec, and risdiplam—has dramatically changed the disease course, offering improved survival and function. Early treatment, especially in presymptomatic patients, is now possible due to newborn screening programs. However, new disease phenotypes and management questions have emerged, highlighting the need for real-world data to better predict outcomes and guide clinical practice. This study aims to provide real-world evidence on treatment patterns and clinical outcomes for pediatric SMA patients in the Czech and Slovak Republics, using data from the REaDY registry.

Research question and objectives

The study aims to:

- Describe demographics of patients in Czech and Slovak Republic including the stratification based on the birth date (birth before vs after May 2017)
- Monitor the response to first DMT selection.
- Understand the relationship between diagnostic markers and disease progression.
- Assess outcomes in patients treated with DMTs versus untreated patients.
- Develop recommendations for improved patient management.
- Identify predictors of treatment outcomes and assess quality of life in SMA patients.

Study design

This is a local, retrospective, non-interventional, multicenter registry data analysis. The study evaluates secondary data from pediatric SMA patients enrolled in the REaDY registry by 13 March 2025. Patients were divided into two cohorts: those who received at least one DMT (Cohort A) and those who did not (Cohort B). Baseline characteristics were assessed at the index date (start of treatment or enrolment examination), and outcomes were analyzed in the post-index period.

Setting

The study was conducted using retrospective data from the REaDY registry, which systematically collects real-world data on SMA patients in Czech and Slovak specialist centers. The analysis includes all pediatric patients (≤18 years) with genetically confirmed SMA and informed consent, enrolled by 13 March 2025.

Subjects and study size

A total of 406 patients were enrolled in the registry, with 213 pediatric patients (155 from Czech sites, 58 from Slovak sites) included in the analysis. Inclusion required genetically confirmed SMA, informed consent, and a known clinical examination at the index date. The study aimed to include all eligible patients; no formal sample size calculation was performed.

Variables and data sources

Primary endpoints included demographic and baseline clinical characteristics (age, sex, SMA type, genetic mutation, *SMN2* copy number, screening status, and clinical parameters). Secondary endpoints included changes in physiotherapeutic, feeding, and pulmonary function, and quality of life during follow-up. Data were sourced from the REaDY registry and managed using the CLADE-IS electronic data capture system.

Statistical methods

Categorical variables were described by absolute and relative frequencies; numerical variables by mean, standard deviation, median, range, and interquartile range. Changes in outcomes were analyzed using Wilcoxon paired tests. Regression models with random effects (linear mixed effects models) were used for physiotherapeutic outcomes, and Cox proportional hazards models for feeding and pulmonary function. No data imputation or sensitivity analyses were performed.

Results

Of the 213 pediatric patients analyzed, 191 received DMTs and 22 were untreated. The majority had SMA type I or II. Time from symptom onset to diagnosis improved after the introduction of first causal therapy and newborn screening. Treated patients showed therapeutic benefit, with improvements or stabilization in motor function depending on SMA type. However, deterioration in ventilation and feeding function was still observed, particularly in SMA type I and II. Quality of life generally stabilized under treatment. The real incidence of pediatric SMA was estimated at 7–10 per 100,000 newborns.

Discussion

This real-world registry study demonstrates the positive impact of DMTs on pediatric SMA outcomes in the Czech and Slovak Republics. Early diagnosis and treatment, especially following introduction of the first causal treatment and newborn screening, have improved patient trajectories. However, challenges remain including ongoing risks of functional decline. For optimal patient management, nutritional monitoring is essential. The main limitations of this study include missing or incomplete registry data. Comprehensive, regularly updated registries are crucial for real-world evidence interpretations.

Conclusion

SMA remains predominantly a pediatric condition in the Czech and Slovak Republics. While DMTs have improved outcomes, risks of motor, feeding, and ventilation deterioration persist. Newborn screening and nutritional monitoring are critical. The study identified limitations of the data in this registry (in particular, missing unfilled values for some important parameters). Therefore, it is important to verify and complement the conclusions of this study from other real-world data sources.