Use Case Highlighting Opportunities and Challenges of Registries for Regulatory Decision-making

Industry Perspective
Simon Bennett
Director Regulatory Policy

Biogen

Introduction

First treatment for Spinal Muscular Atrophy (SMA) in the EU was authorised in 2017.

Registrational clinical trials focussed on a relatively homogenous patient population which was highly selected and consisted of infants and children.

- Whilst controlled clinical trials demonstrated the positive benefit risk balance of the product in patients, further data collection/analysis would be able to expand understanding of the product in the wider patient population and address evidence gaps that were acceptable at the time of the marketing authorisation.

Goal:

- To support a rare disease registry approach for SMA with multiple partners which enables collection of high-quality real world data (RWD).
  - To meet the key needs of the SMA community, healthcare providers, researchers, regulators, payors, and industry.
  - To gather robust information on clinical outcomes, characterize SMA natural course and evolving phenotypes, and improve understanding of approved and emerging treatments in a real world setting.

Key Considerations

Supporting a global, collaborative network of SMA registries.

- Establish collaborations with multiple SMA registries to utilize existing observational data.
- Strengthen the capabilities of external registries to fulfill the research needs of multiple stakeholders.
- Consensus-building with organizations to collect new data fields as needed.

Since 2017, work has been undertaken with registry partners to:

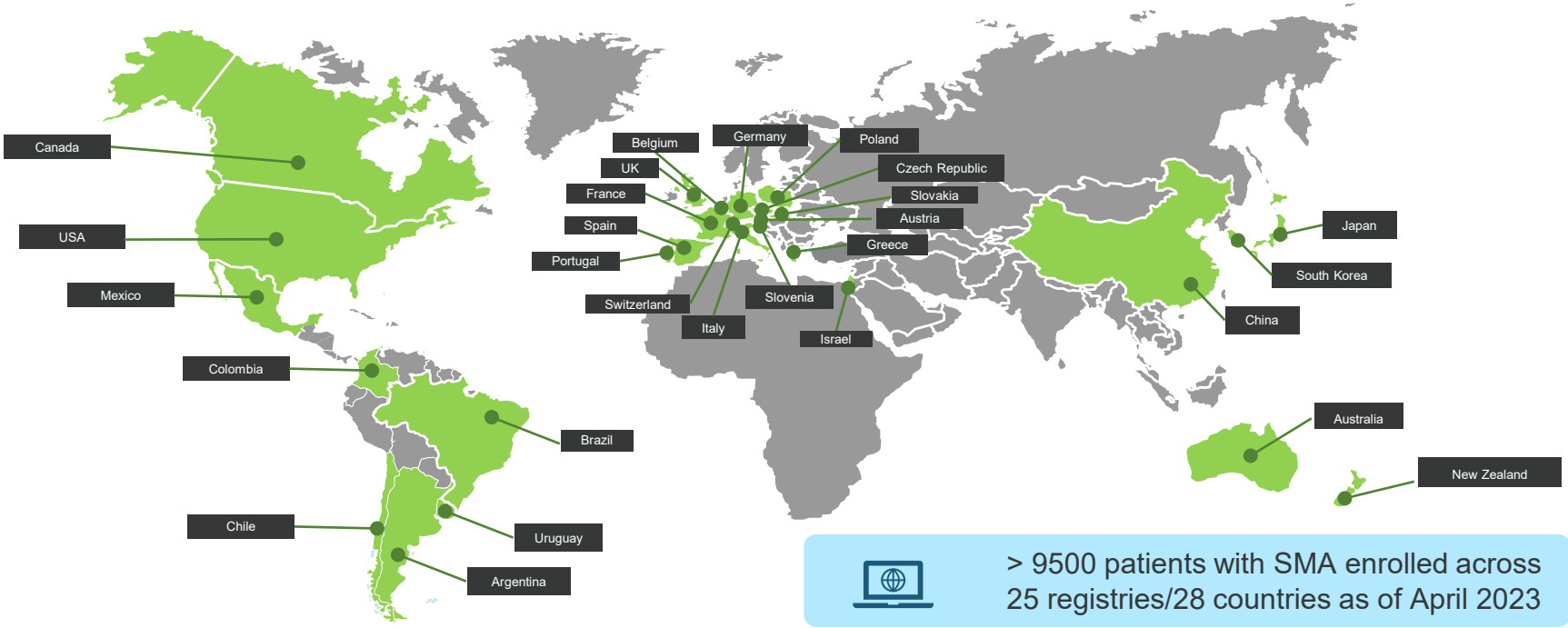
- Improve the capacity and capability of registries to collect reliable patient-level data.
- Standardize data across clinician-entered registries to an international aligned core data set (TREAT-NMD).
- Provide financial support to implement data collection and ensure sustainability.

Model has evolved in time to accommodate country-specific payer needs for which some *de novo* registries were initiated (e.g., Germany).

The aligned data set includes key information on patient demographics, clinical characteristics, medical history, functional outcomes, hospitalizations, and treatments.

Biogen-supported SMA disease-registry status in 2023

- **Biogen has partnered with 25 registries in 28 countries, enrolling > 9500 individuals as of April 2023.**
- **Global registry data collection includes Europe, Northern and Latin America, Asia, and Oceania.**

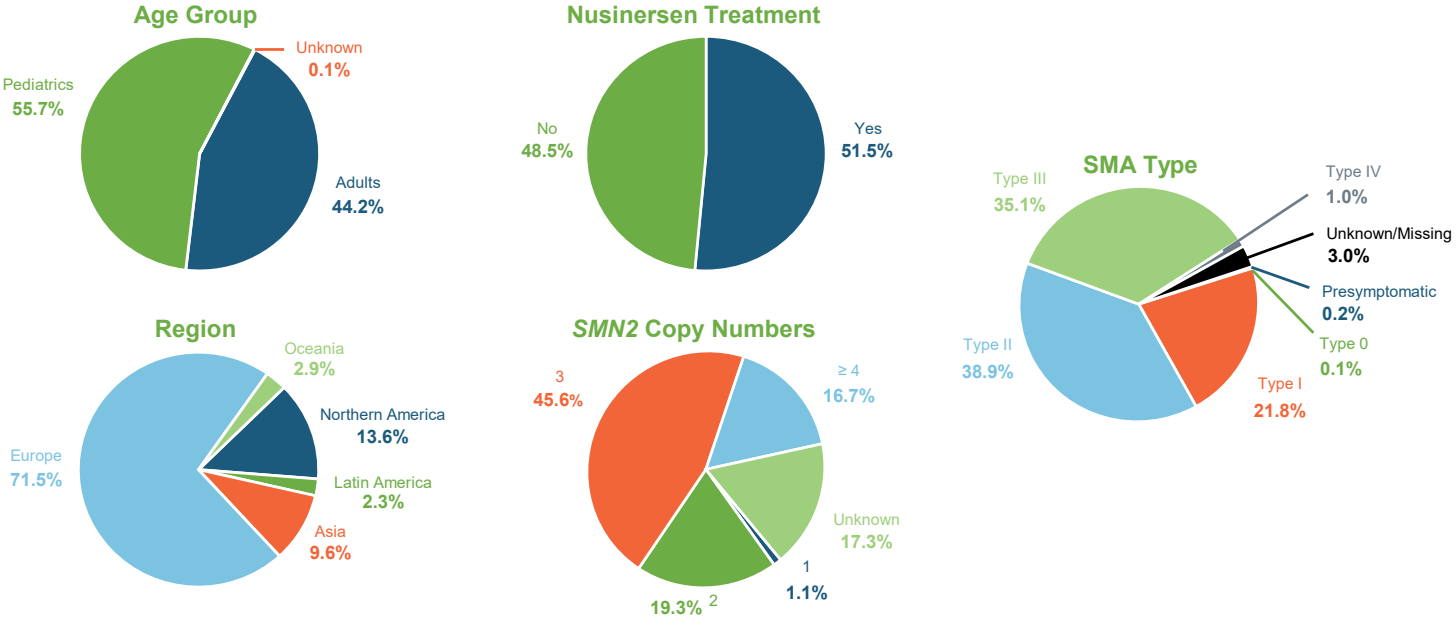


Ref: A Global Disease Registry Strategy for Generating Real-world Evidence in Spinal Muscular Atrophy: Overview and Recent Progress; Paradis AD et al. 15th Euro Paediatric Neuro Soc (EPNS) Conference; June 20-24, 2023

SMA Registries Enrolled Diverse RW Patient Population

Providing Insights on SMA Natural History and Effectiveness/Safety of SMA Tx

- **Approximately 40% of enrolled patients were adults, who have been historically underrepresented in SMA clinical trials.**
- **The majority of patients had SMA Type I, II, or III.**
- **Findings from registries in Europe (Italy, Spain, Germany, Belgium) have been included in regulatory and reimbursement submissions to inform treatment value in specific populations including adults.**



Patient characteristics obtained from 22 registries. The definition of adults varied among registries with minimum age ranging from ≥ 17 to 20 years.
Classification of region was based on the United Nations geoscheme.

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Key Learnings to Carry Forward

Data quality and consistency varies between different registries within the same disease area.

Registries need to be fit for use to address specific questions.

- Some may be used to answer specific questions from regulators and other stakeholders e.g., expanded patient populations in SMA.
- Others may be used to define general trends about patients, treatment and natural history of the disease.

Significant work often involved to ensure that data from registries are suitable for decision making by different stakeholders.

- Evaluating data collection process, data quality, registry expansion, initiating and reviewing contracts, discussions with other stakeholders and companies.
  - In some cases, actual data quality vs expected (reported) data quality can only be ascertained once the analysis is being performed.
- Impacts beyond the marketing authorisation holder.

Conclusions

Disease registries in SMA have demonstrated the opportunities that exist to address key questions, accumulate additional scientific knowledge and broaden understanding of the disease.

However, the availability and quality of registry data are crucial to their utility and any steps to support this are supported.

- Data Quality Framework, feasibility assessments and checklists.
  - The framework and tool landscape for fit for use evaluation is evolving, reinforcing the need for increasing multi-stakeholder dialogue.
- A separate inventory of all qualified registries, plus disease areas which could benefit most from qualified registries.
  - Proactive identification of registries for future use (in disease areas where products are not yet available but are active areas of clinical development) and early collaboration across all relevant stakeholders.