

Real-world data fill knowledge gap to assess treatment options for infants with spinal muscular atrophy

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Findings from a [recent study](#) in the *Journal of Neuromuscular Diseases* demonstrate the effectiveness of disease-modifying treatments (DMTs) in infants with spinal muscular atrophy (SMA). The study's results add further support for gene therapy as a treatment modality that can deliver durable transformative effects for these vulnerable patients.

SMA is a rare, debilitating neuromuscular disease characterized by loss of motor neurons, leading to progressive weakness and atrophy of skeletal and bulbar muscles. It has long been cited as the leading genetic cause of infant mortality, caused by the deletion or mutation of the survival motor neuron 1 (SMN1) gene.

However, prognoses have improved markedly in recent years, mainly owing to the advent of DMTs. Knowledge of these new treatments for SMA has been largely based on interventional trial data, which is limited by narrow eligibility criteria and limited follow-up duration. In this new study, real-world effectiveness and safety outcomes were assessed for patients following onasemnogene abeparvovec monotherapy, a [gene therapy](#) that replaces the missing SMN1 gene.

"When planning to deliver gene therapy to an infant with SMA, we need to be able to give evidence-based answers to parents' questions. They want to know what the risks are as well as the chances for a child to be able to walk, sit, or be independent of ventilation within several years," explains lead investigator Laurent Servais, MD, Ph.D., MDUK Oxford Neuromuscular Centre & NIHR Oxford Biomedical Research Centre, University of Oxford; and Neuromuscular Reference Center, Department of Paediatrics, University and University Hospital of Liège.

He adds, "Real-world data, i.e., data collected after approval in actual clinical use, has been crucial for filling knowledge gaps and

demonstrating through [clinical experience](#) that onasemnogene abeparvovec is associated with improvements in [motor function](#), bulbar function, and pulmonary function in a varied SMA patient population and over an extended period of observation."

Although almost all cases of SMA have the same underlying genetic cause—a biallelic deletion or mutation in the SMN1 gene—clinical severity is heterogeneous, with varying copy number of the SMN2 "backup" gene being strongly correlated with disease onset and severity as an important phenotypic modifier of SMA.

Using data on 168 patients from RESTORE, a prospective, multicenter, multinational, observational registry that captures data from a variety of sources, investigators identified 80 patients (47.6%) with two and 70 (41.7%) with three copies of SMN2. Ninety-eight (58.3%) identified by [newborn screening](#) (NBS) had a lower age at final assessment (mean age 11.5 months) and greater mean final score on the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND), compared with clinically diagnosed patients.

All patients maintained and/or achieved motor milestones, such as sitting without support for 10 seconds, crawling, and walking. Observed adverse events were consistent with the established safety profile of onasemnogene abeparvovec.

Because RESTORE provides data from a large SMA population, it can facilitate studying specific subgroups and providing answers to specific questions like what happens to patients with one copy of SMN2 and what is the benefit for patients on permanent ventilation.

"Another key finding from this study was the improved safety profile demonstrated for infants identified by NBS. Our data confirm other real-world and clinical study data that infants identified by NBS are

diagnosed and assessed earlier and had a tendency for better outcomes when treated. This provides evidence to demonstrate that the early treatment opportunity offered by NBS can be transformative for patients," Dr. Servais says.

More information: Laurent Servais et al, Real-World Outcomes in Patients with Spinal Muscular Atrophy Treated with Onasemnogene Apeparvovec Monotherapy: Findings from the RESTORE Registry, *Journal of Neuromuscular Diseases* (2024). [DOI: 10.3233/JND-230122](https://doi.org/10.3233/JND-230122)

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