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Clinical Improvements in a Patient with Spinal Muscular Atrophy Type 1 Receiving Nusinersen Therapy

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Introduction:

Spinal muscular atrophy (SMA) is a progressive autosomal-recessive neuromuscular disease and the most common genetic cause of death during childhood. Nusinersen (Spinraza) was the first therapy approved in 2016 by the U.S. Food and Drug Administration. Long term data regarding quality of life outcomes are still lacking. We report a case of a patient with SMA Type 1 receiving nusinersen with significant clinical improvement.

Case Presentation:

Patient is an eight-year-old male with Type 1 SMA who is gastrostomy tube, tracheostomy and ventilator dependent started on nusinersen therapy at seven years of age. Prior to therapy, he was only able to tolerate four to five hours off the ventilator during the daytime and required assistance during naps. Post therapy, he is able to tolerate being off the ventilator while awake, can speak, sing, and started swallowing. He required eight admissions for respiratory related illnesses prior to therapy, with only one since the initiation of nusinersen. Prior to therapy, he was diffusely hypotonic, could not sit independently, displayed poor fine motor skills, and was without nearly any oral motor skills. At his most recent visit, he can sit unassisted for 30 minutes, attends school full time, makes clear facial expressions, speaks clearly with his HME in place, can lift his feet against gravity, and is able to begin weans on his nighttime ventilator settings.

Discussion:

Children with SMA type 1 develop severe muscle weakness within the first 6 months of life. Mortality is primarily the result of respiratory failure due to diaphragm involvement. Nusinersen is an antisense oligonucleotide that promotes production of a full-length protein from the SMN2 gene, a major determinant of the SMA phenotype. Copy numbers of SMN2 correlate inversely with severity of disease. Phase 3 studies of nusinersen showed variable response to therapy. The only factors identified that influence response was a) the time between the first symptoms and the first dose in patients with type 1 SMA and b) the age of those with type 2 SMA. These factors are likely insufficient to explain variation in outcomes. In the phase 2 and 3 trial of nusinersen, respiratory outcomes were defined as the use (or not) of permanent ventilation and did not quantify the number of hours of utilization.

Conclusion:

Long term data regarding achievement of noteworthy milestones such as independent sitting, weaning off non-invasive ventilator support, number of hospitalizations, versus continued motor disability and dependence on ventilator support warrant continued evaluation.