Newborn Screening for Spinal Muscular Atrophy

Testimony of Cure SMA

Delivered by
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Good afternoon. Dr. Bocchini and members of the Advisory Committee, thank you for the opportunity to testify today. My name is Dr. Thomas Crawford and I am Director of the MDA clinic at Johns Hopkins. I'm testifying this afternoon as a representative of the medical professionals who care for patients with spinal muscular atrophy (SMA) regarding the committee's nomination and evaluation process for candidate conditions on the Recommended Uniform Screening Panel (RUSP).

I chose my specialty because I held an infant – perhaps the first infant I ever held – because in 1979, as a medical student on my Pediatrics clerkship, perhaps the first baby I ever held had SMA type 1. That baby died during that hospital admission, as have well over a hundred more I have care for since. But holding that infant was the first step in my career that has been directed to "all things SMA" with genetics, physiology, pathology, animal modeling, clinical care, and most recently the successful clinical trials, as concentrations along the way. It has been an incredible ride. We have participated in a spectacularly successful development project of a therapy, from an idea on a dry erase board in 2007, to cells and animals in 2009, to humans in 2011, to the amazing event on December 23, 2016, when the FDA approved SPINRAZA™ (nusinersen), the first-ever approved therapy to treat children and adults with all types of SMA. Clinical trials of SPINRAZA™ has shown effectiveness across the range of SMA severity, resulting in a broad label from the FDA for the drug. Infants live substantially longer with treatment, but more importantly they have a real improvement in function and independence from high-end costly and burdensome treatments as well. Both of the key enabling trials were concluded at interim data looks, rather than at scheduled completion, because of the magnitude of treatment effect.

One of the most remarkable features of the natural history, pathology, and now the enabling treatment trials, is the really profound effect that time has on outcome. A difference of just weeks can be the difference between independent walking and impaired mobility requiring a wheelchair. Infants who were treated before the onset of symptoms in the Biogen "NURTURE" study – recognized because of a previously affected sibling – had the most remarkable outcome. It isn't surprising that the therapy prevents the onset of pathology, but has less effect after degeneration has occurred, and our natural history data suggest pathology accumulates quickly after birth. Dr. Kathryn Swoboda of the University at Mass General Hospital has shown that type 1 infants suffer rapid and severe loss of motor units in the early perinatal period during the first 3 months of life. Important also is that no pre-symptomatic SMA infant treated with SPINRAZA™ has died or required permanent respiratory support. These early treated infant are achieving unheard of motor milestones of sitting, standing and walking, where their older affected siblings have either died or require ventilatory support to sustain life.

It is difficult to imagine a disorder for which the RUSP is better suited. In the newborn screening domain of rare diseases it is a common disorder. Early diagnosis, education, and initiation of treatment have massive effect on outcome. The time scale needed to achieve this is within the range of what can be achieved with screening. The tests are sensitive and accurate. All of these add to my very strong recommendation, and plaintive request, that we add this RUSP qualification as a milestone to the recent successful history of SMA science and therapeutics. I strongly urge the Advisory Committee to take up consideration of the forthcoming SMA nomination with a focus on the new availability of a life-saving treatment for SMA and the demonstrated benefits of early intervention. I thank the Committee for the opportunity to address you today.