Newborn Screening for Spinal Muscular Atrophy

Testimony of Cure SMA

Delivered by
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I am Thomas Prior Professor of Pathology and Neurology, and the Director of the Division of Molecular Pathology at The Ohio State University Medical Center. I joined The Ohio State University faculty as a tenure assistant professor in 1990, after completing post-doctoral training at the University of North Carolina. My primary function was to start up a new division of Molecular Pathology in the Department of Pathology. The laboratory has established itself as an academic DNA testing center for inherited disorders. I have a longstanding research interest in the genetics of neuromuscular disorders, specifically in clinical applications and mutation detection. I have been involved in the genetic disorder, spinal muscular atrophy (SMA) for more than 20 years. My laboratory developed the first SMA carrier test and I have been involved in both population carrier and newborn screening projects for SMA. I have also been active in determining the role of the SMN2 gene and other gene modifiers in effecting the disease phenotype and the identification of new types of mutations in the spinal muscular atrophy gene and their effect on the disease severity.

My testimony this morning focuses on the why its critical that you pass HB 397 which would add SMA to the state newborn screening panel.

As you are aware, SMA is an autosomal recessive neuromuscular disease that affects approximately 1 in 10,000 live births in the U.S., and an estimated 1 in 50 Americans is a genetic carrier. It is one of the most common inherited disorders. SMA is caused by a mutation in the Survival Motor Neuron 1 (*SMN1*) gene. This gene produces a protein that is critical to the function of the nerves that control muscles. Without this protein, those nerve cells cannot properly function and eventually die, leading to debilitating and often fatal muscle weakness robbing patients of their ability to walk, eat, or even breathe. The majority of the type I children (~60% of SMA) will not live to see their 2od birthday. It is a devastating disorder.

Until recently, therapies have been primarily supportive for SMA, nutritional and respiratory care. However on December 23, 2016 the FDA approved SPINRAZA™ (nusinersen), the first-ever specific therapy for SMA (a major breakthrough). Results from Biogen's open label study of pre-symptomatic infants, called NURTURE, demonstrate that infants receiving treatment pre-symptomatically have significant improvement compared with infants receiving treatment after the onset of symptoms. As of Oct. 31, 2016, not a single SMA infant treated pre-symptomatically with SPINRAZA™ has died or required permanent

respiratory support. Incredibly, many pre-symptomatically treated infants from the NURTURE trial are attaining age-appropriate motor milestones, such as standing or walking.

In fact a very exciting recent pilot study of SMA newborn screening in New York State, in its second year, enrolled newborns from three hospitals in the New York Presbyterian healthcare system. Of the 3,826 babies screened in the first year, one infant was identified type I SMA. This infant was enrolled in the NURTURE clinical study and treated with Spinraza at age 15 days. She is now age 16 months, meeting all normal developmental milestones, and free of any respiratory issues. In fact, she is now walking and running. This performance is in stark contrast to the natural history of SMA, in which type 1 infants never make any motor gains.

The question then becomes when is the most appropriate time for treatment with spinraza. Both human natural history data and model mice data suggest that early drug intervention is absolutely necessary. Natural history data indicates that there is only a limited window for optimal intervention in SMA type 1. Dr. Kathryn Swoboda, now at the Massachusetts General Hospital, showed us in 2005 that type 1 infants suffer rapid and irreversible loss of motor units early in infancy. This degenerative process is aggressive within the first 3-6 months of life. This often results in the loss of more than 90% of motor units within 6 months of age. Motor neurons cannot be restored after being lost. At birth the children are asymptomatic. The problem is that the average age of clinical diagnosis for type I babies is about 4-6 months months. This is a true medical emergency where every day counts and requires both an early diagnosis and treatment before the loss of motor neurons, which leads to the need for newborn screening.

Why newborn screen?

Devastating disorder with a very high incidence compared to many of the disorders currently screened for

Asymptomatic at birth

Treatment: FDA approved drug, greatly improve the quality of life

Narrow therapeutic window Significant Disease progression (irreversible loss of motor neurons) occurs before clinical diagnosis. A timely diagnosis is a must!!

We have a great DNA test which has a sensitivity of 95%. They all have the same DNA deletion of the SMN1 gene and it can easily be added on to the blood spot and should not increase the cost by very much. Furthermore our test is extremely accurate without false positives, which is a major issue with many newborn tests.

We have prognostic implications and can predict which children are at the highest risk of the type I disease and can identify the ones with milder disease

Family issues, allows the family a timely diagnosis and identifies the risk of second occurrences and the identification of at-risk carriers.

In conclusion, it is of the utmost importance that SMA be added to the Ohio newborn screening panel to ensure patients are treated early, before the irreversible loss of motor neurons. I strongly urge the committee on Health to approve HB 397 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.