Title: Comparing Developmental Outcomes of Children with CLN2 Disease Receiving Cerliponase Alfa to a Natural History Cohort

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Introduction: CLN2 disease is a fatal inherited rare pediatric neurodegenerative lysosomal storage disease caused by deficiency of the lysosomal enzyme tripeptidyl peptidase 1 (TPP1) encoded by the CLN2/TPP1 gene. Symptoms of CLN2 disease emerge most often by 3 years of age and include loss of motor, language, and vision functioning and seizures. Cerliponase alfa is an enzyme replacement therapy (ERT). It is the first FDA-approved treatment to slow the loss of ambulation of CLN2 disease and is a recombinant form of human TPP1. Initial research has demonstrated cerliponase alfa slows the progression of motor decline; however, little is known about how treatment influences other developmental domains. The aim of this study is to compare developmental outcomes of children receiving cerliponase alfa to untreated natural history cohort.

Method: Developmental data was collected over time from 16 patients with CLN2 disease. Patients with CLN2 disease were categorized into two groups: treatment group receiving cerliponase alfa (n =14) and untreated group (n =2) from the natural history cohort. Developmental data was compared across subjects and matched on chronological age at 6 and 9 years of age. Developmental functioning was measured using the Mullen Scales of Early Learning (MSEL), as well as Hamburg and Weill Cornell scales. Raw scores and age equivalencies were used as measures of developmental ability on the MSEL.

Results: Findings from this study indicate children with CLN2 disease receiving cerliponase alfa displayed more developmental skills (M= 18.45) and higher age equivalencies (M = 16.09 months) on measures of visual reception compared to the untreated group (M= 6 and M= 11 months respectively) at 6 years of age. Data suggests patients with CLN2 disease who are receiving treatment demonstrate a slower rate of decline of developmental skills across domains than the untreated group.

Discussion: Findings from this study indicate that the majority of patients with CLN2 disease receiving cerliponase alfa displayed more developmental skills and higher age equivalencies across developmental domains compared to the natural history cohort. It is important to continue longitudinal data collection as part of larger study to examine developmental outcomes over time. I tis also important to consider a multi-method approach to study developmental and cognitive abilities through parent report and direct testing.

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