Clinical Scoring for Disease Severity in Infantile CLN1 Disease

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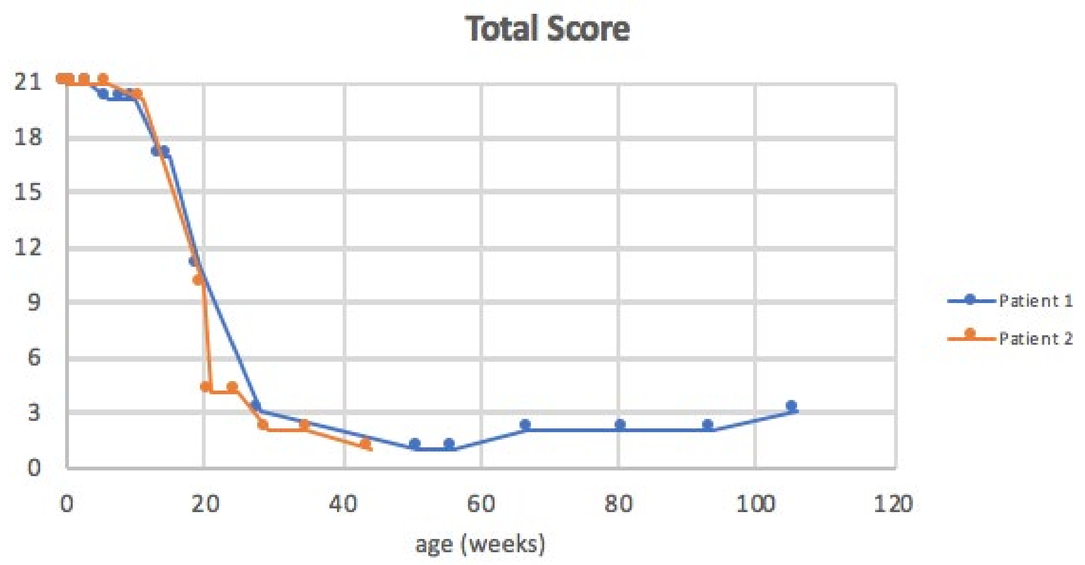
Functional Category
Mobility
Fine motor function
Expressive language
Communication and interaction

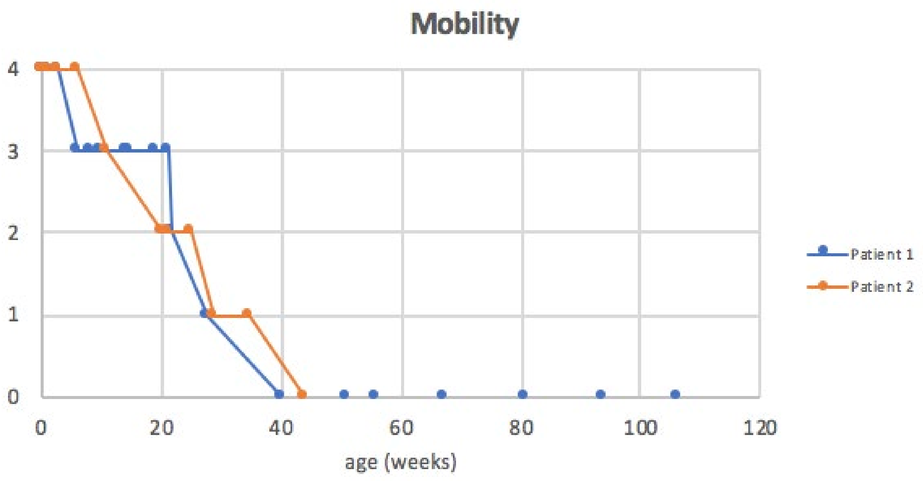
Each functional category is	scored from 4-0
Age appropriate function	= SCORE 4
Developmental delay present	= SCORE 3
First regression of function, active function without help	= SCORE 2
Active function with help	= SCORE 1
No function left	**= SCORE 0**

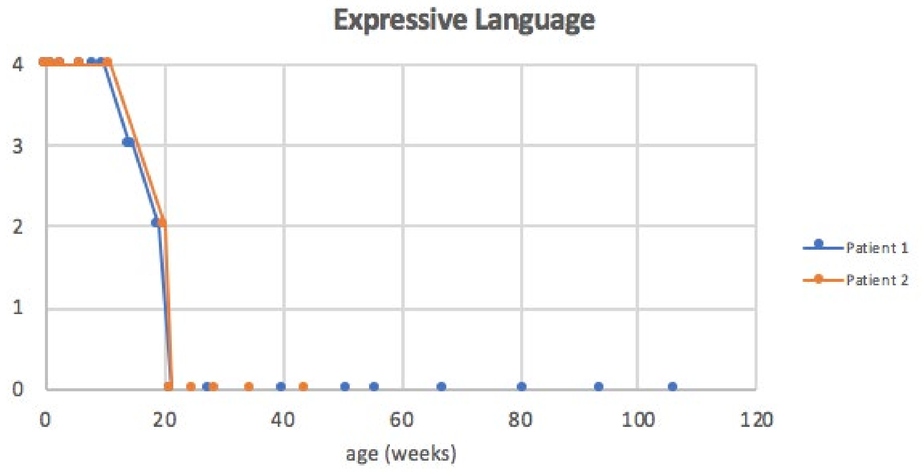
Add-on Categories		
Visual attention	Age appropriate Score=1	Pathologic Score=0
Agitation / Irritabiliy	**Age appropriate Score=1**	**Pathologic Score=0**
Seizures (any type)	Absent Score=1	Present Score=0
Feeding	**Age appropriate Score=1**	**Pathologic Score=0**
Sleep	**Age appropriate** Score=1	**Pathologic** Score=0

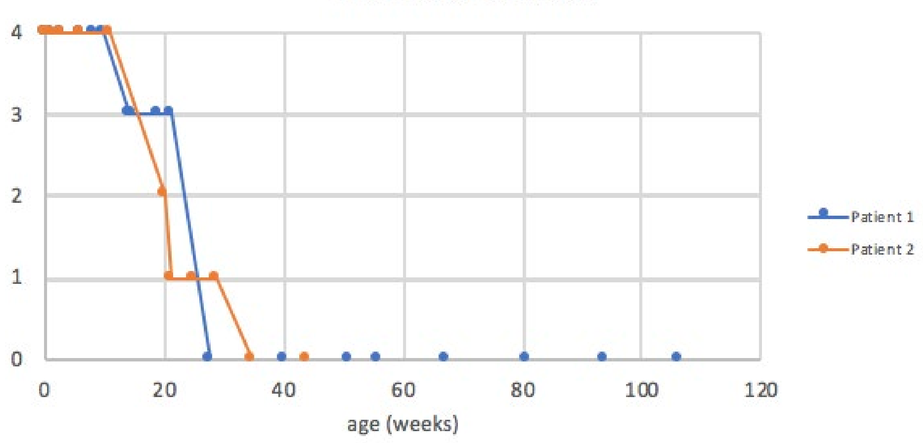
Advantages

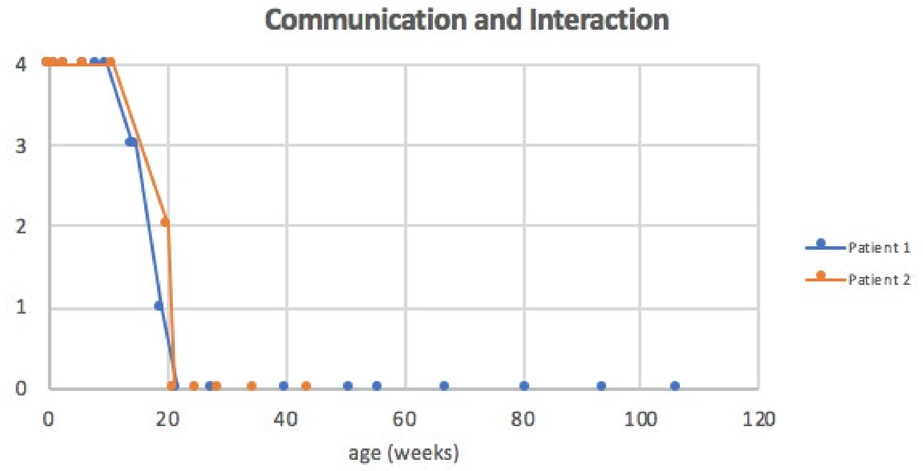
- Easy to use
- Excellent inter-rater reliability
- Retrospective and prospective use
- Focus on functional relevant outcomes











Natural History and Clinical Rating Scale

To approve a drug, a clinical trial must be run in humans to prove that the drug is both safe and effective. Proving a drug is safe often involves standard tests that assess the health of the heart, lungs, kidneys, liver, blood, and other organs and tissues.

Proving that a drug is effective, in the context of CLN1 Batten Disease, involves assessing if the drug slows or stops the progression of the disease. For most diseases, this means comparing patients who receive the drug to patients that receive a placebo (e.g. a sugar pill).

However in ultra-rare diseases, like Batten Disease, there are not enough children who have the disease to support a 'placebo' arm of the trial. For this reason, doctors throughout the world have compiled data they have collected from years of observing children with CLN1 Batten. This data includes information on how the children reach their developmental milestones (e.g. crawling, walking, talking, etc.), and regress from those milestones into the end-stages of the disease.

All of this data combined is what we call a "Natural History" of the Disease.

Haley's Heroes was instrumental in providing financial support for organizing and analyzing this CLN1 Batten Natural History. Further, through Haley's Heroes funding, clinicians at the University of Hamburg have developed a tool for assessing patients in a clinical trial, which is now called the Hamburg iNCL clinical rating scale.

This iNCL rating scale is, in essense, a questionaire that will guide clinicians to collect and score (with a value of 0-3) the results of physical exams of patients receiving a drug during a clinical trial. This rating scale is important because it standardizes the type and quality of data across all clinicians throughout the world.

When used in a clinical trial, this 'standardized' data of patients receiving the drug can then be compared to the 'standardized data' of the Natural History. In this way, if the drug is effective, the clinicians will know --- without the necessity of giving a group of children a 'sugar placebo' as a comparison group.

Building this Natural History and Clinical Rating scale was a monumental development for the CLN1 Batten community - which will enable any clinical trial for any potential treatment.

This effort was hugely successful, extremely impactful, and ultimately catalyzed by the funds raised through Haley's Heroes.

In the immediate future, this effort will help enable Circumvent's Effort for designing a clinical trial for our first drug fo CLN1 - for which we just received funding to support preclinical regulatory studies from the National Institutes of Health (NIH) through the National Institute of Neurological Diseases and Stroke (NINDS).