# LONG-TERM DATA FOR CERLIPONASE ALFA▼ (BRINEURA) IN CHILDREN WITH CLN2 DISEASE: A CLINICAL TRIAL UPDATE

The publication of this infographic was sponsored and funded by **BioMarin Pharmaceutical Inc**.
This content is intended for healthcare professionals only.

Prescribing information, details of adverse event reporting, and indications can be found at the bottom of this page.

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Graphs presented are referring to data deriving from clinical trials only and are not representative of patient population.

## Study Design: Primary Phase I/II Study and open-label extension (OLE)

**Safety profile and efficacy of cerliponase alfa in children with CLN2 disease: an OLE study with more than 5 years of follow-up[1,2]**

**Primary outcome measure: Clinical Rating Scale (CRS) Motor and Language Domains**

### Primary Phase I/II study[1]

N=24 (aged 3–16 years; CLN2 CRS motor-language score ≥3)

One patient discontinued treatment (not related to AEs)*

48-week stable-dose period (ICV 300 mg cerliponase alfa every other week)

### Open-label extension[2]

N=23 (enrolled from primary study)

Six discontinued treatment (not related to AEs)**

Up to 240 weeks

### Outcomes and control group:[1,2]

The Motor and Language Domains of the CLN2 CRS were assessed every 8 weeks during the OLE study to monitor disease progression†

Primary efficacy outcome was time to an unreversed 2-point decline,‡ or score of 0 in the combined motor-language domains of the CLN2 CRS

Historical controls with untreated CLN2 disease in the DEM-CHILD international registry were used as a comparator group

AEs were reported at every visit

*One participant withdrew from the primary study at the parents' request after receiving one dose of the study drug due to an inability to comply with study procedures, and was excluded from efficacy analyses[1]

**Four due to relocation or switch to commercial therapy; two due to meeting study stopping criteria, having a score of 0 in the combined motor and language domains assessed at consecutive study visits

‡An unreversed 2-point decline was defined as a decline that had not returned to within 1 point of baseline score by the last assessment

## Primary analysis: CLN2 motor-language domains (combined score 0-6)

| Motor | Score |
|---|---|
| Grossly normal gait, no prominent ataxia, no pathologic falls | 3 |
| Independent gait,† will have obvious instability, and may have intermittent falls | 2 |
| External assistance to walk, or can crawl only | 1 |
| Can no longer walk or crawl | 0 |

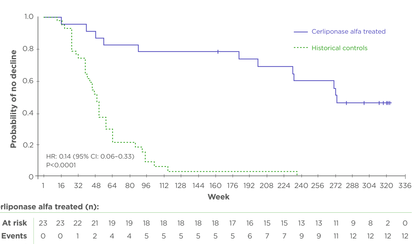
| Language | Score |
|---|---|
| Apparently normal, intelligible, and grossly age appropriate, no decline noted | 3 |
| Abnormal; some intelligible words, may form short sentences to convey concepts, requests, or needs | 2 |
| Hardly understandable, few intelligible words | 1 |
| No intelligible words or vocalisations | 0 |

†Defined by ability to walk without support for 10 steps

## Cumulative Results: Primary Phase I/II Study and OLE[3]

**Cerliponase alfa reduced the probability of decline in motor-language function**

Compared to historical untreated controls, treated patients were 86% less likely (P<0.0001) to experience a significant decline in motor-language function*




**Cerliponase alfa treated (n):**

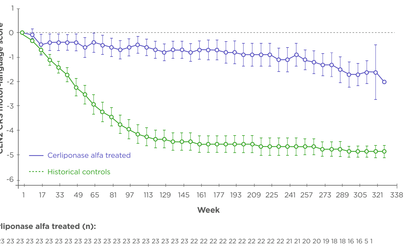
| | | | | | | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **At risk** | 23 | 23 | 22 | 21 | 19 | 19 | 18 | 18 | 18 | 18 | 18 | 17 | 16 | 15 | 15 | 13 | 13 | 11 | 9 | 8 | 2 | 0 |
| **Events** | 0 | 0 | 1 | 2 | 4 | 4 | 5 | 5 | 5 | 5 | 5 | 5 | 6 | 7 | 7 | 9 | 9 | 11 | 12 | 12 | 12 | 12 |
| **Censored** | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 2 | 3 | 9 | 11 |

**Natural history (n):**

| | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **At risk** | 42 | 41 | 32 | 21 | 11 | 7 | 3 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 0 |
| **Events** | 0 | 1 | 10 | 20 | 29 | 32 | 36 | 37 | 38 | 38 | 38 | 38 | 38 | 38 | 38 |
| **Censored** | 0 | 0 | 0 | 1 | 2 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |

*Defined as the composite of an unreversed 2-point decline or score of 0 in the combined motor-language domains of the CLN2 CRS

**Combined motor-language score declined at a slower rate in the treated group when compared with the historical controls**




**Cerliponase alfa treated (n):**

23 23 23 23 23 23 23 23 23 23 23 23 23 23 23 22 22 22 22 22 22 22 22 22 22 21 21 20 20 19 18 18 16 16 5 1

**Cerliponase alfa treated (n):**

42 42 42 42 42 41 40 39 39 38 37 37 36 35 34 34 32 32 31 30 30 29 29 26 25 25 24 23 23 22 20 20 19 19 18 17 16 15 15 14 14

**Cerliponase alfa was generally well tolerated, with an acceptable safety profile[1]**

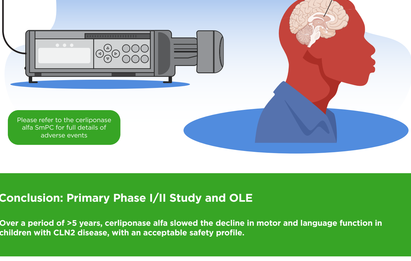
**All participants experienced at least one AE, most of which were mild-to-moderate in severity. These were the most common drug-related adverse events experienced:**

- Pyrexia
- Hypersensitivity
- Seizure
- Vomiting
- Epilepsy

**Nine participants experienced ICV device-related infections; six participants required device replacement.**

**21 participants (88%) experienced a serious AE, of whom eight (33%) experienced a serious AE considered related to study drug; these were most commonly:**

- Hypersensitivity
- Infusion-related reaction
- Pleocytosis



Please refer to the cerliponase alfa SmPC for full details of adverse events

## Conclusion: Primary Phase I/II Study and OLE

**Over a period of >5 years, cerliponase alfa slowed the decline in motor and language function in children with CLN2 disease, with an acceptable safety profile.**

**References:**

1. Schulz A et al. Study of intraventricular cerliponase alfa for CLN2 disease. N Engl J Med. 2018;378(20):1898-907.
2. Schulz A et al. Safety and efficacy of cerliponase alfa in children with neuronal ceroid lipofuscinosis type 2 (CLN2 disease): an open-label extension study. Lancet Neurol. 2024;23(1):60-70.
3. BioMarin Pharmaceutical. A safety, tolerability, and efficacy study of intracerebroventricular BMN 190 in pediatric patients < 18 years of age with CLN2 disease. NCT02678689. https://clinicaltrials.gov/study/NCT02678689

**Abbreviations**

AE: adverse event; CI: confidence interval; CLN2: neuronal ceroid lipofuscinosis Type 2; CRS: Clinical Rating Scale; HR: hazard ratio; ICV: intracerebroventricular; OLE: open-label extension.

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