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

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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.

Citation: EMJ Neurol. 2024; https://doi.org/10.33590/emjneurol/11000008.

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

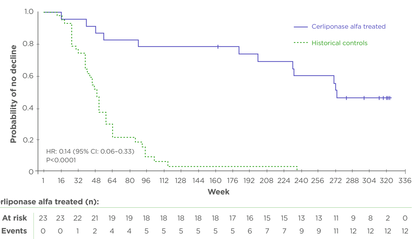
Language	Score
Apparently normal, intelligible, and grossly age appropriate, no decline noted	3
Abnormal; some intelligible words, may form short sentences to convey concepts, requests, or needs	2
Hardly understandable, few intelligible words	1
No intelligible words or vocalisations	0

†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):

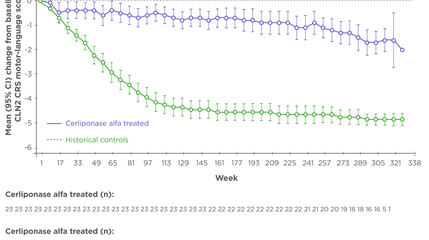
At risk	23	23	22	21	19	19	18	18	18	18	18	17	16	15	15	13	13	11	9	8	2	0
Events	0	0	1	2	4	4	5	5	5	5	5	5	6	7	7	9	9	11	12	12	12	12
Censored	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1	1	1	1	2	3	9	11

Natural history (n):

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

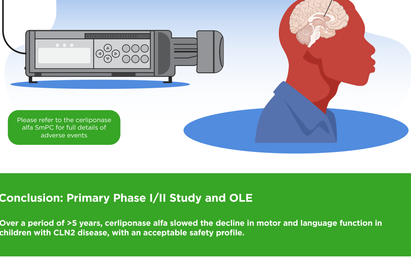
All participants experienced at least one AE, most of which were mild-to-moderate in severity. These were the most common drug-related adverse events experienced:

- 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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Please refer to full prescribing information before using BRINEURA.

Prescribing information and a full list of adverse events can be accessed here. Please access your local authorities prescribing information.

This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.

Brineura® is indicated for the treatment of neuronal ceroid lipofuscinosis type 2 (CLN2) disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency.

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V. Healthcare professionals in the UK, can report via the Yellow Card Scheme linked here or search for MHRA Yellow Card in the Google Play or Apple App Store.