

Cerliponase alfa for the treatment of CLN2 disease: Combined results from two ongoing observational studies

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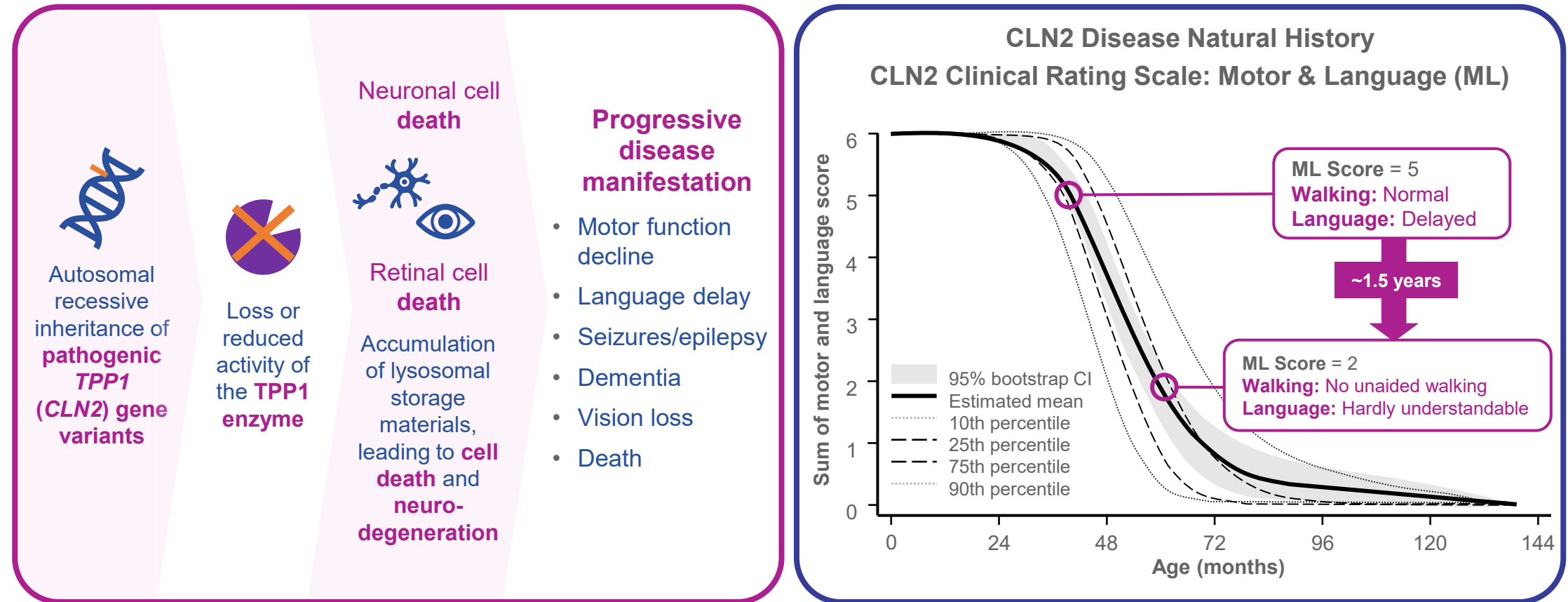
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Conflicts of interest disclosures

- **Angela Schulz** has received consulting fees from Neurogene Inc. and Regenxbio Inc. She received honoraria for speaker fees, research grants, multiple advisory boards and travel support from and was a Principal Investigator in BMN 190 clinical trials for BioMarin Pharmaceutical Inc.

CLN2 disease is a rare and rapidly progressing paediatric neurodegenerative lysosomal disorder



Intracerebroventricular **enzyme replacement therapy** with **cerliponase alfa** (recombinant human TPP1) is currently the only approved disease-modifying therapy for CLN2 disease

CLN2 Clinical Rating Scale figure adapted from Nickel M, et al. *Lancet Child Adolesc Health* 2018;2:582–90

CI, confidence interval; CLN2, neuronal ceroid lipofuscinosis type 2; ML, motor-language; TPP1, tripeptidyl peptidase 1.

1. Sleat DE et al. *Am J Hum Genet* 1999;64:1511–23. 2. Schulz A et al. *Biochim Biophys Acta* 2013;1832:1801–6. 3. Nickel M et al. *Lancet Child Adolesc Health* 2018;2:582–90. 4. Mole SE, Williams RE. Neuronal ceroid lipofuscinoses. 2001 Oct 10 [Updated 2013 Aug 1]. 5. Schulz A et al. *N Engl J Med* 2018;378:1898–907. 6. Schulz A et al. *Lancet Neurol* 2024;23:60–70.

Clinical trials have shown that treatment with cerliponase alfa reduces the rate of decline in motor and language function in CLN2 disease

Cerliponase alfa clinical program (completed)

190-201 & 190-202 pivotal phase 1/2 and extension study

n=24 (age 3 to 15 years)
240 weeks follow-up + 6-month safety period
(NCT01907087, NCT02485899)

190-203: Phase 2 study

n=14 (age <18 years, including <3 years)
144 weeks follow-up + 6-month safety period
(NCT02678689)

Cerliponase alfa real-world observational program (ongoing)

190-501: USA observational surveillance

n=45 (age 2 months to 22 years)
Enrolled participants from 16 USA sites
Initiated in 2020 (NCT04476862)

190-504: EU observational surveillance

n=66 (age 3 to 16 years)
Enrolling participants from 12 EU sites
Initiated in 2019 (EUPAS29031)

Probability of no 2-point decline or score of 0 in motor–language

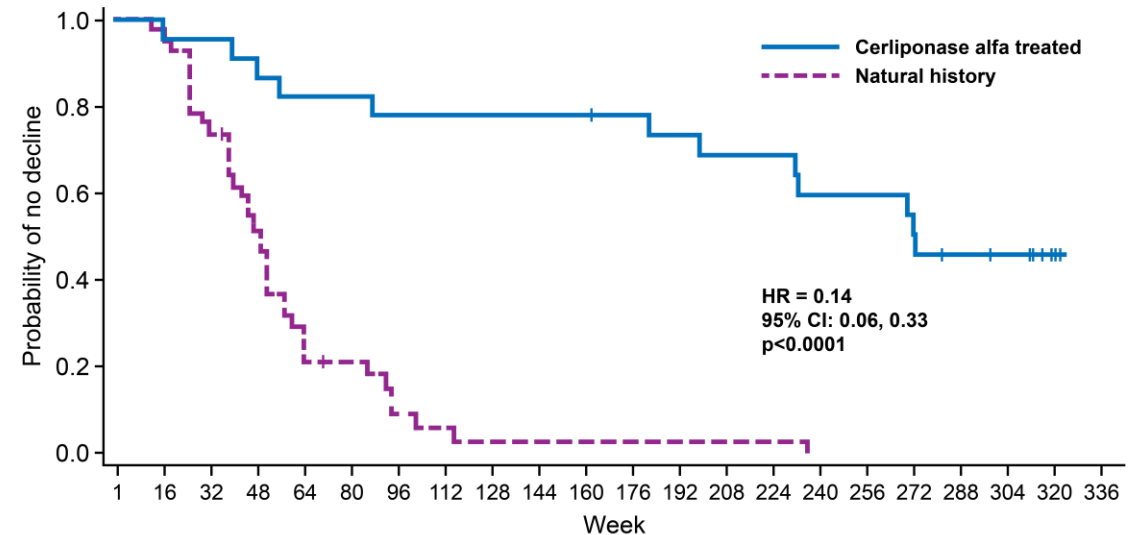


Figure adapted from Schulz A et al. *Lancet Neurol* 2024;23:60–70

CI, confidence interval; EU, Europe; HR, Hazard ratio; TPP1, tripeptidyl peptidase 1; USA, United States of America.

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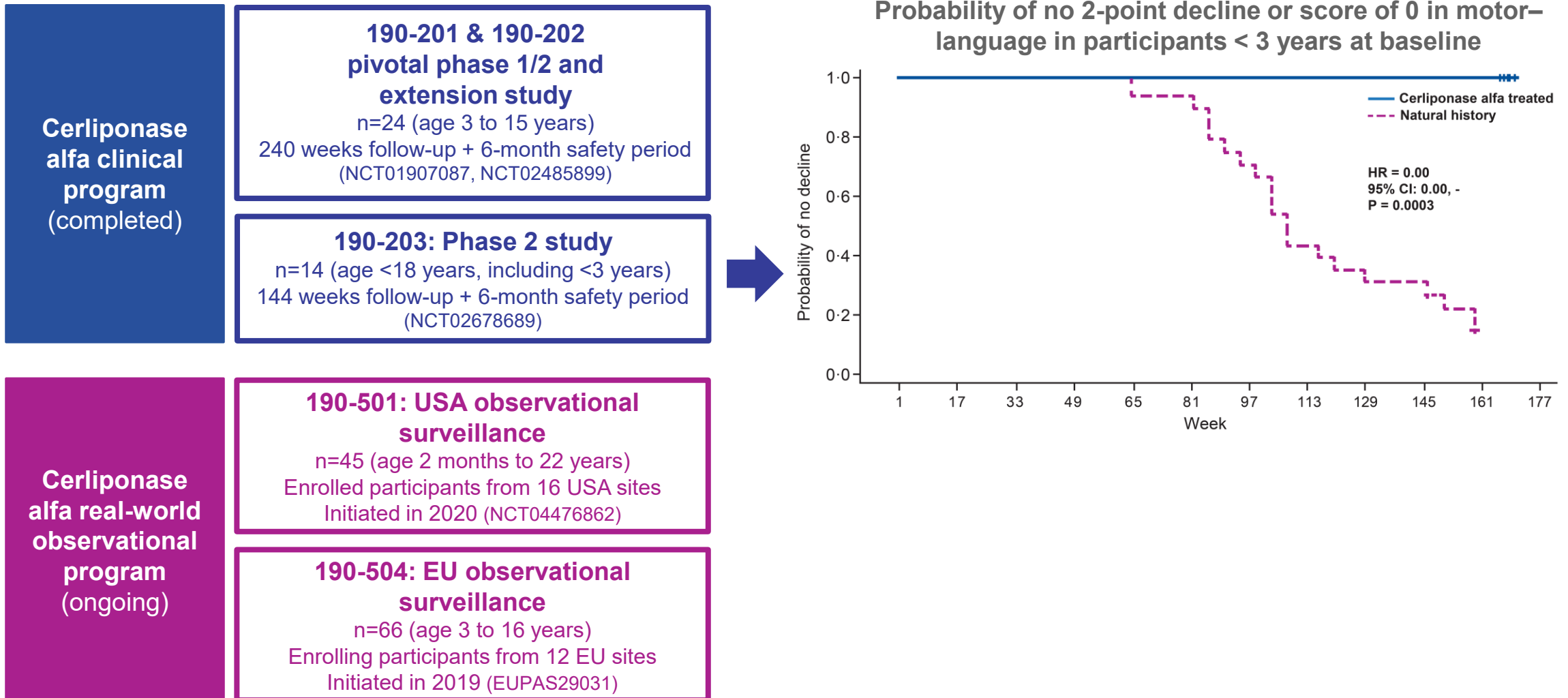


Figure adapted from Schulz A et al. WORLD Symposium 2024, Poster presentation

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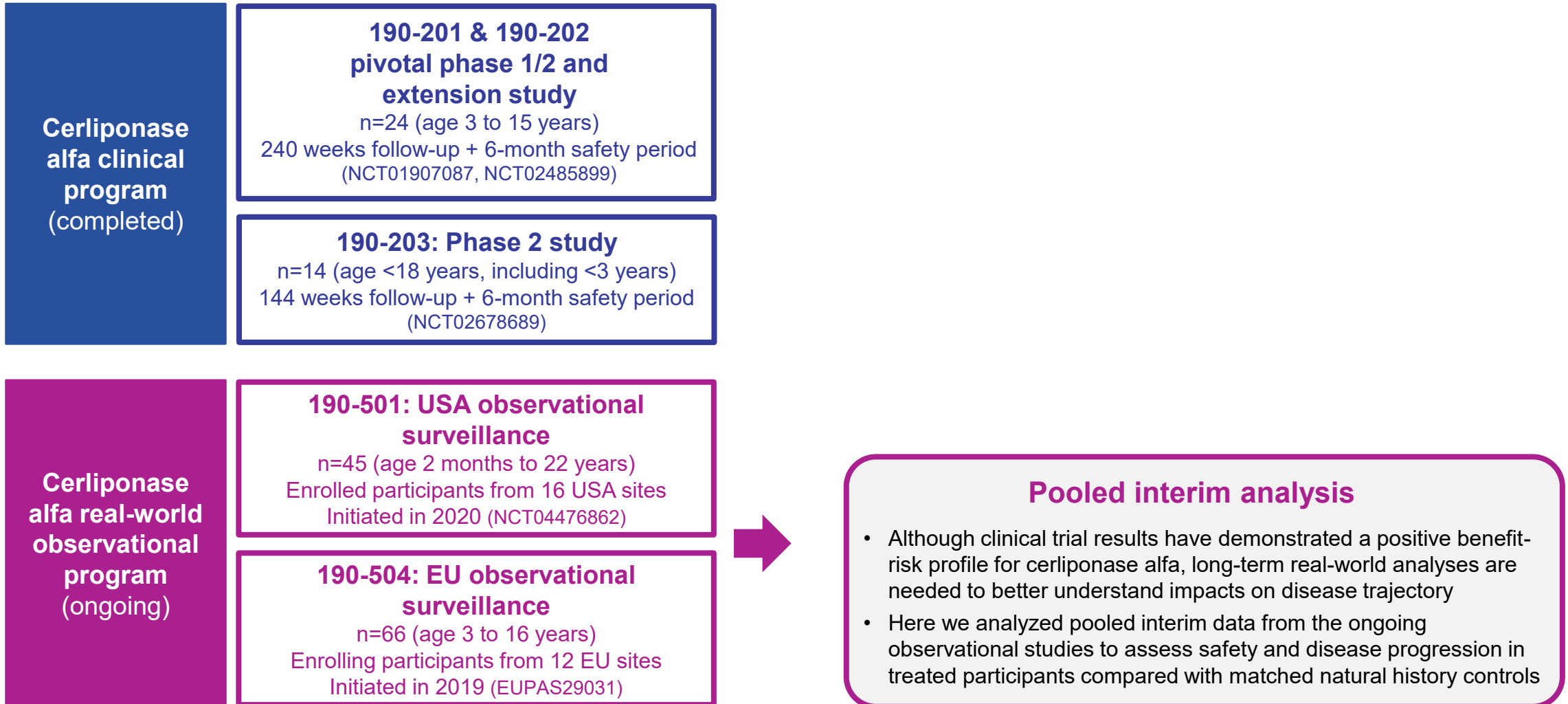
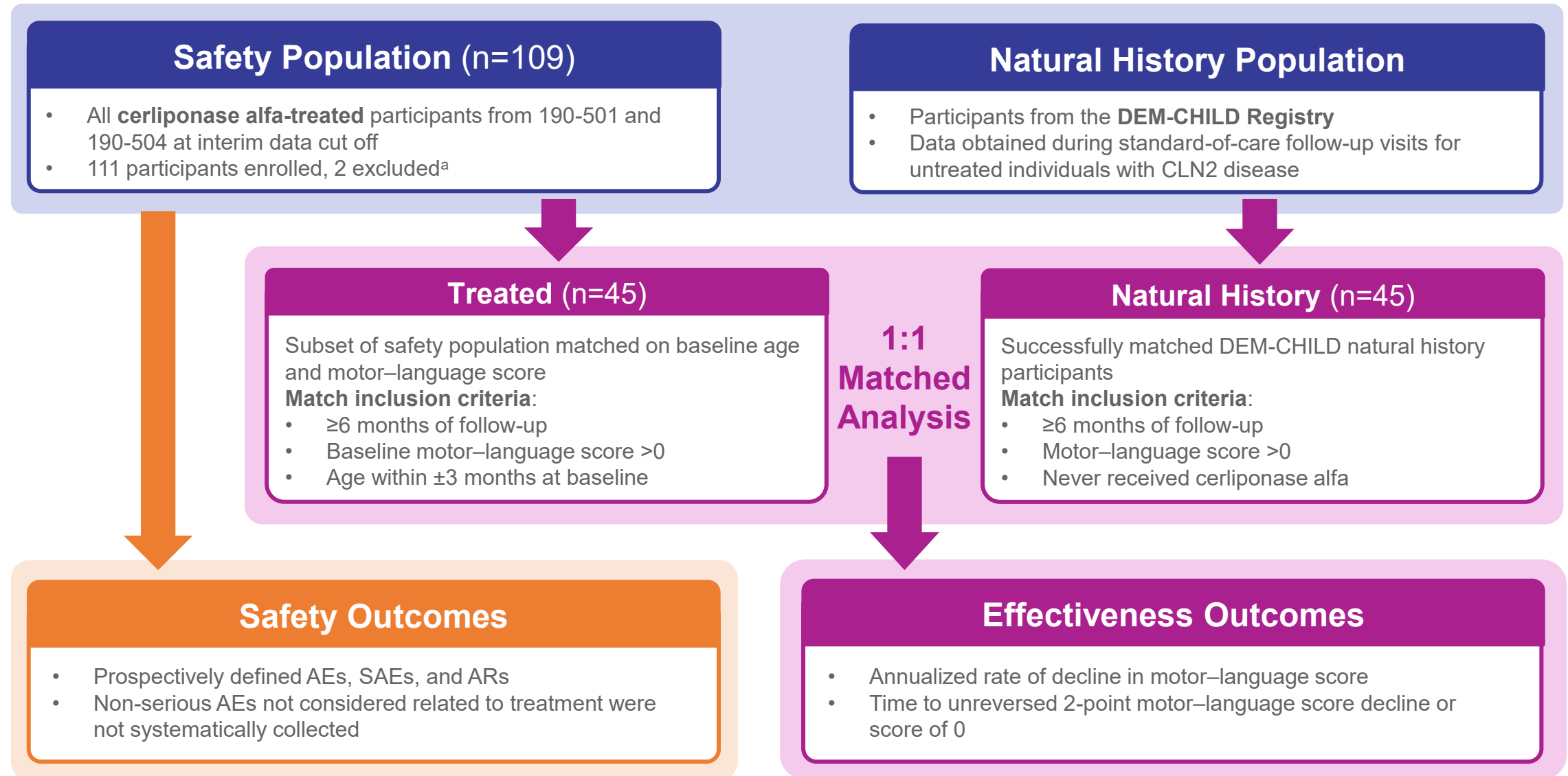


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Pooled interim analysis methods



The cut-off dates for 190-501 and 190-504 were 18th March 2025 and 8th May 2025, respectively

^a Two participants were excluded from safety analyses with no data available

AE, adverse event; AR, adverse reaction; CLN2, neuronal ceroid lipofuscinosis type 2; SAE, serious adverse event

Demographics and clinical characteristics

Baseline characteristic	Enrolled population (N=111)	Matched analysis	
		Treated (n=45)	Natural history (n=45)
Female , n (%)	54 (49)	26 (58)	20 (44)
Race , n (%) ^a			
American Indian or Alaska Native	3 (3)	2 (4)	0
Asian	4 (4)	1 (2)	0
Black or African American	1 (1)	0	0
White	82 (74)	37 (82)	0
Multiple	2 (2)	0	0
Not reported	17 (15)	5 (11)	45 (100)
Age (years), mean (SD)			
At diagnosis	4.0 (2.4)	3.8 (1.2)	4.9 (1.3)
At baseline ^b	4.6 (2.5)	4.3 (0.9)	4.3 (0.9)
Baseline motor–language score , mean (SD)	4.1 (1.3)	3.8 (1.1)	3.8 (1.1)
Genotype , n (%) ^c			
2 common alleles	23 (21)	11 (24)	26 (58)
1 common allele	36 (32)	14 (31)	12 (27)
0 common alleles	37 (33)	13 (29)	7 (16)
Not available	15 (14)	7 (16)	0

Interim data cut-offs: 190-501, March 2025; 190-504, May 2025.

^a Data for 17 participants (15%) were not provided due to participant privacy rules

^b Baseline is defined as the last assessment prior to first treatment with cerliponase alfa in treated participants; the timepoint at which the natural history participant was matched with the treated participant in the natural history cohort.

^c Common alleles were defined as c.622C>T and c.509-1G>C

CLN2, neuronal ceroid lipofuscinosis type 2; SD, standard deviation.

There were no new safety signals following long-term real-world treatment with cerliponase alfa

- The safety analyses included 109 treated individuals with a mean (SD) cerliponase alfa exposure time of 5.6 (2.5) years

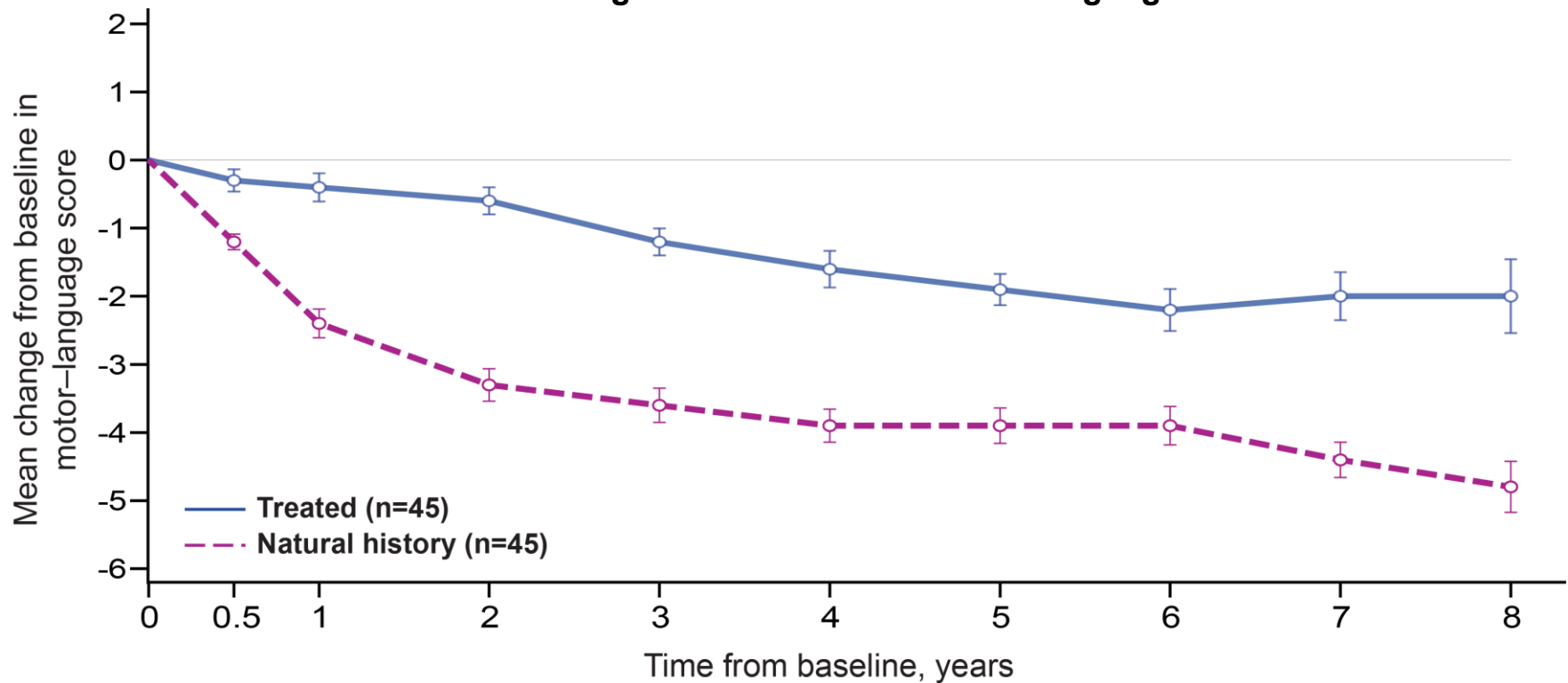
Overall summary of AEs, n (%)	Total (N=109) ^a
Any AE	67 (61.5)
Any SAE	56 (51.4)
Most common SAEs	
Seizure	15 (13.8)
Device-related infections	8 (7.3)
Device end of service	7 (6.4)
Device malfunction	7 (6.4)
Treatment related SAE	6 (5.5)
Any AE of Grade ≥3 ^b	49 (45.0)
Deaths	6 (5.5)

Participants with any AEs of interest, n (%) ^c	Total (N=109) ^a
Temporally-related adverse reactions ^d	42 (38.5)
Device-related events	37 (33.9)
Convulsions	21 (19.3)
Hypersensitivity reactions	9 (8.3)
Meningitis	5 (4.6)
Cardiovascular events	3 (2.8)
Anaphylactic reactions	0
Hydrocephalus	0

^a Two participants were excluded from safety analyses as data not available beyond consent.
^b Defined by common terminology criteria for adverse events.
^c Prospectively selected based on non-clinical findings, known treatment class effects, and literature review of AEs.
^d Occurring within 24 hours following treatment.
AE, adverse event; CLN2, neuronal ceroid lipofuscinosis type 2; SAE, serious adverse events; SD, standard deviation.

Cerliponase alfa-treated participants experienced a slower rate of decline in motor and language function compared with matched natural history controls

Mean change from baseline in motor–language score



Mean (SD) annual rate of decline in motor and language function:

Treated: 0.35 (0.43)

Natural history: 2.38 (1.40)

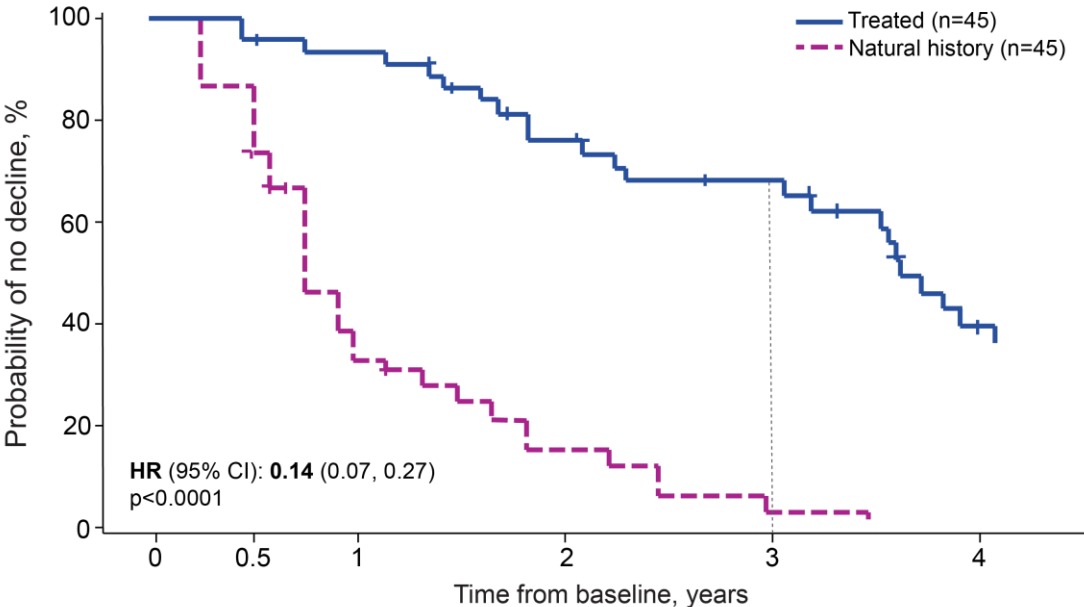
Mean difference: 2.03
(95% CI 1.59–2.47);
p<0.0001

Treated, n	45	26	32	30	32	29	25	18	11	5
Natural history, n	45	45	40	36	29	22	20	15	12	5

Mean (SD) duration of follow-up was 8.3 (4.8) in both the treated and natural history groups. Matching is 1:1 based on baseline age and motor-language score
CI, confidence interval; CLN2, neuronal ceroid lipofuscinosis type 2; SD, standard deviation.

Treated participants were significantly less likely to experience a decline motor–language score compared with matched natural history controls

Time to first unreversed 2-point decline in motor–language score or score of 0

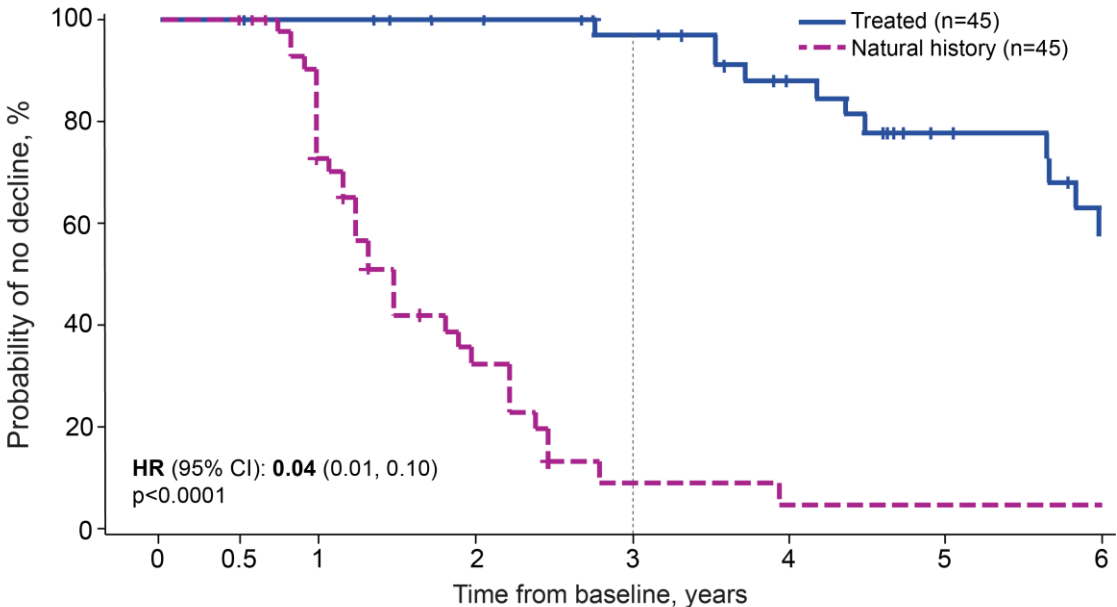


Treated, n	45	43	41	29	24	11
Natural history, n	45	32	13	5	1	0

After 3 years of follow-up, the probability of experiencing an unreversed 2-point motor–language decline or score of 0 was:

- 32% for treated participants
- 97% for natural history controls

Time to first unreversed motor–language score of 0



Treated, n	45	45	44	38	34	26	18	11
Natural history, n	45	44	28	10	2	1	1	1

After 3 years of follow-up, the probability of experiencing an unreversed motor–language score of 0 was:

- 3% for treated participants
- 91% for natural history controls

Conclusions



In real-world use, long-term cerliponase alfa slowed motor-language decline in children with CLN2 disease, with no new safety signals



These results confirm the sustained benefit seen in clinical trials, now across a broader real-world population



Longer follow-up from these ongoing studies will further define long-term outcomes

Acknowledgments

We thank the study sites, participants, and their families for contributing important data supporting this study.

Medical writing support, under the guidance of the authors, was provided by Carl Davies, MSc, an employee from the Publications and Medical Affairs Division of Omnicom Health Medical Communications and was funded by BioMarin in accordance with Good Publication Practice, GPP 2022 (*Ann Intern Med* 2022;175:1298–1304).

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