

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

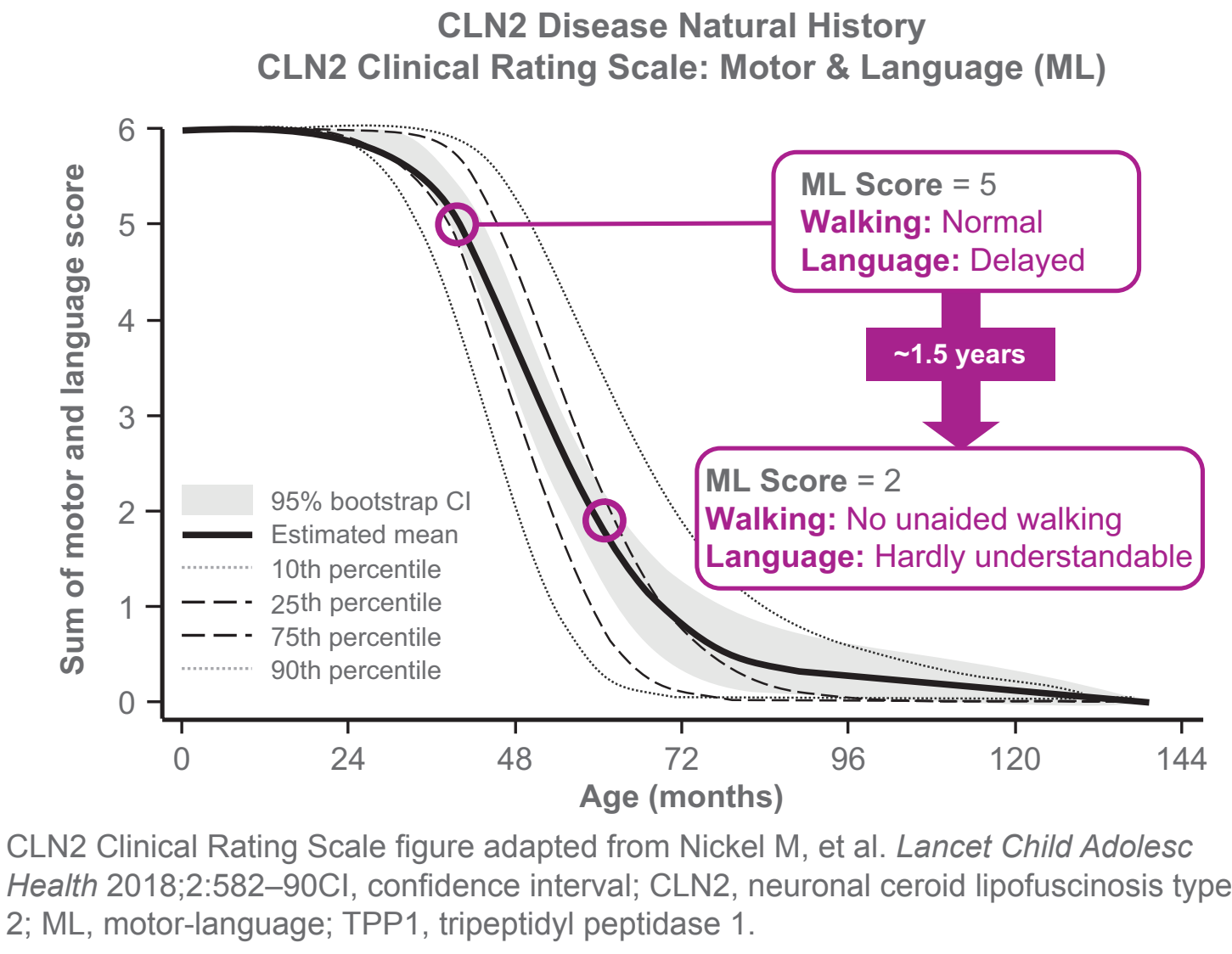
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Introduction

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

- CLN2 disease is caused by autosomal recessive inheritance of pathogenic *TPP1* gene variants, which lead to deficient activity of the TPP1 enzyme
- Resulting accumulation of lysosomal storage materials induces cell death and neuro-degeneration leading to progressive disease manifestation:
 - Motor function decline
 - Language delay
 - Seizures/epilepsy
 - Dementia
 - Vision loss
 - Death by mid adolescence
- Intracerebroventricular enzyme replacement therapy with cerliponase alfa (recombinant human TPP1) is currently the only approved disease-modifying therapy for CLN2 disease
- The efficacy and safety of cerliponase alfa has been demonstrated in children with CLN2 disease (aged 3–16 years) in the pivotal 48-week, multicenter, study (NCT01907087), an open-label extension study (NCT02485899) with up to 240 weeks of follow-up, and in a study (NCT02678689) which assessed safety and efficacy in a cohort that included children under 3 years of age
 - Intracerebroventricular administration of cerliponase alfa was shown to slow decline in motor and language function compared with natural history controls, and was generally well tolerated
- Two observational, post-marketing surveillance studies assessing long-term, real-world outcomes with cerliponase alfa are currently ongoing in the USA (study 190-501, NCT04476862) and EU (study 190-504, EUPAS29031); combined interim results from these studies are presented here

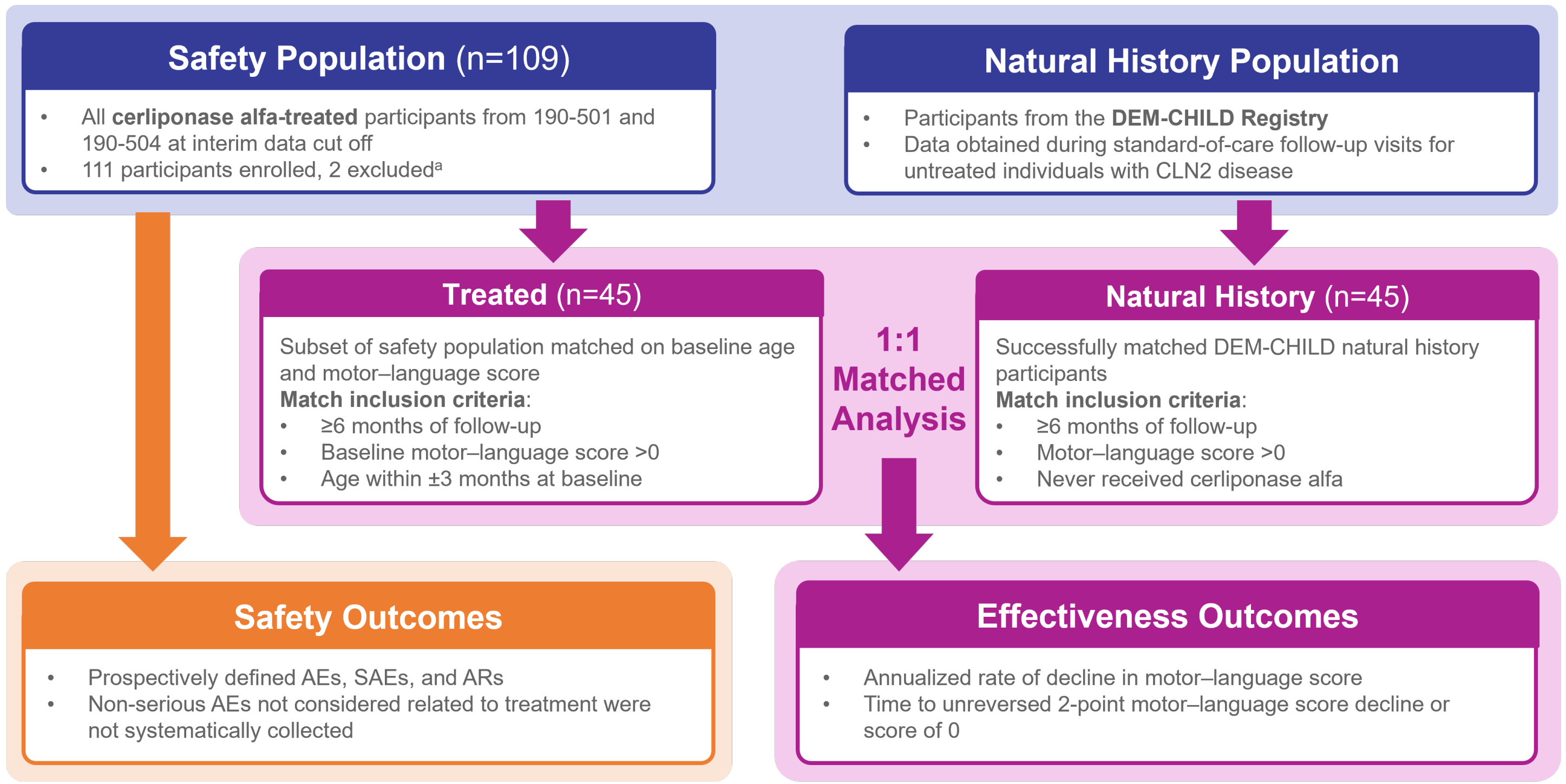


Methods

Cerliponase alfa real-world observational program

- The 190-501 and 190-504 studies are ongoing, multicenter, post-market observational studies of cerliponase alfa for the treatment of CLN2 disease
 - The 190-501 study enrolled participants at 16 sites in the United States, and was initiated in August 2020, with an interim data cut-off in March 2025
 - The 190-504 study enrolled participants at 12 sites across Europe, and was initiated in October 2019, with an interim data cut-off of May 2025
- Pooled interim data from these studies were analyzed to assess safety outcomes during longer-term treatment with cerliponase alfa and evaluate treatment effectiveness relative to matched natural hisotry controls from the DEM-CHILD database

Pooled interim analysis



The cut-off dates for 190-501 and 190-504 were 18th March 2025 and 8th May 2025, respectively
*Two participants were excluded from safety analyses as data not available beyond consent.
AE, adverse event; AR, adverse reaction; CLN2, neuronal ceroid lipofuscinosis type 2; SAE, serious adverse event

Results

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.
*Data for 17 participants (15%) were not provided due to participant privacy rules
^aBaseline 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
^bCommon alleles were defined as c.622C>T and c.509-1G>C
CLN2, neuronal ceroid lipofuscinosis type 2; SD, standard deviation.

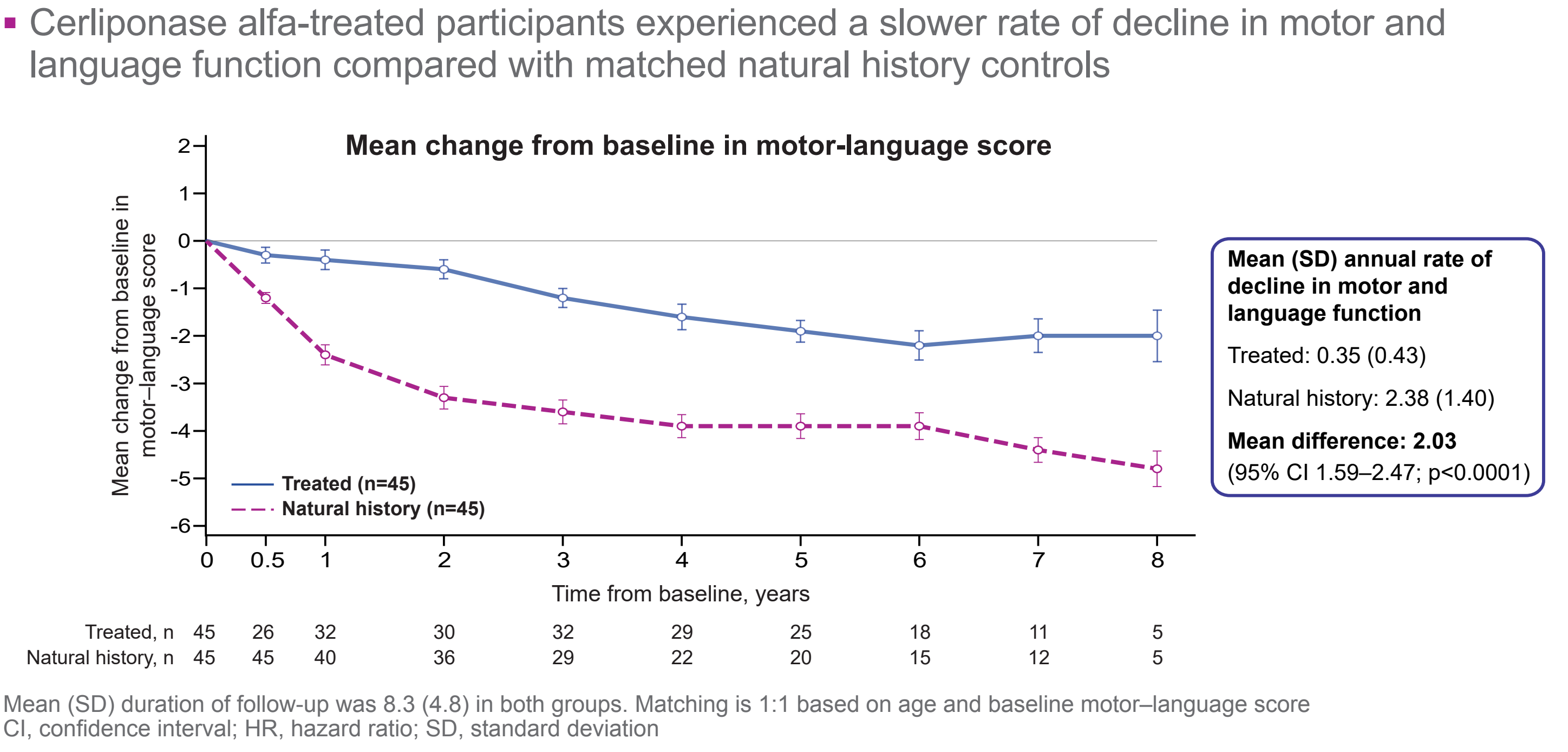
Safety

- Safety analyses included 109 treated individuals with a mean (SD) cerliponase alfa exposure time of 5.6 (2.5) years
 - 67 participants (61.5%) experienced adverse events (AEs), 49 participants (45.0%) experienced Grade ≥3 AEs; serious AEs were reported in 56 participants (51.4%) and device-related AEs in 37 participants (33.9%)

Overall summary of AEs, n (%)	Total (N=109) ^a	Participants with any AEs of interest, n (%) ^c	Total (N=109) ^a
Any AE	67 (61.5)	Temporally-related adverse reactions ^d	42 (38.5)
Any SAE	56 (51.4)	Device-related events	37 (33.9)
Most common SAEs		Convulsions	21 (19.3)
Seizure	15 (13.8)	Hypersensitivity reactions	9 (8.3)
Device-related infections	8 (7.3)	Meningitis	5 (4.6)
Device end of service	7 (6.4)	Cardiovascular events	3 (2.8)
Device malfunction	7 (6.4)	Anaphylactic reactions	0
Treatment related SAE	6 (5.5)	Hydrocephalus	0
Any AE of Grade ≥3 ^b	49 (45.0)		
Deaths	6 (5.5)		

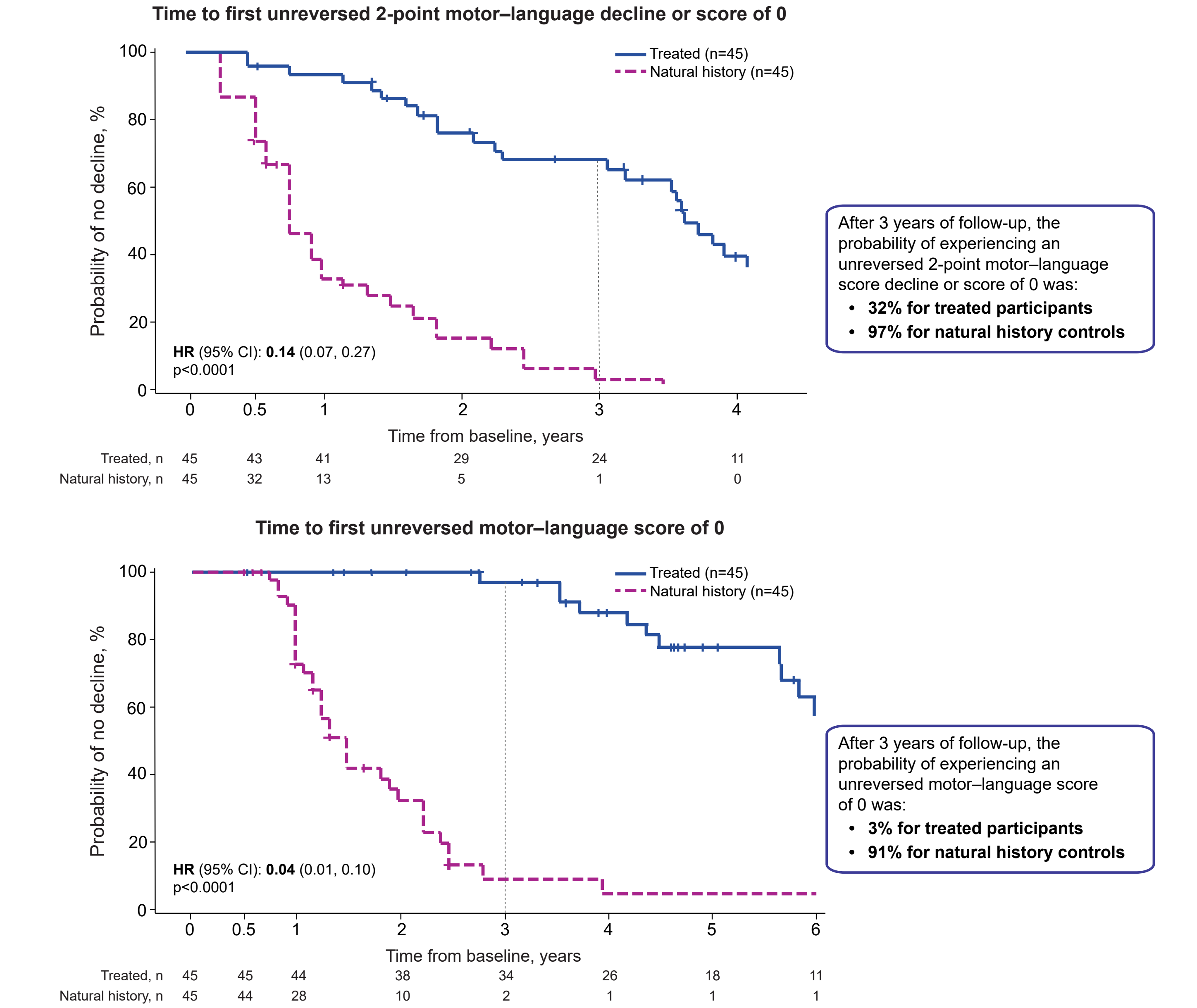
^aTwo participants were excluded from safety analyses with no data available. ^bDefined by common terminology criteria for adverse events. ^cProspectively selected based on non-clinical findings, known treatment class effects, and literature review of AEs. ^dOccurring within 24 hours following treatment.

Motor-language score: change from baseline



Motor-language score: time to unreversed 2-point decline or score of 0

- Cerliponase alfa-treated participants were significantly less likely to experience a decline in motor-language score than matched natural history controls



Mean (SD) treatment exposure was 2.7 (1.6) years.
CI, confidence interval; HR, hazard ratio

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

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Disclosures

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