Poster 193

Multi-year subgroup analyses of Niemann-Pick disease type C participants treated with arimoclomol in the US early access program (EAP)

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BACKGROUND AND OBJECTIVE

- Niemann-Pick disease type C (NPC) is an ultra-rare, debilitating, progressive neurodegenerative, heterogenous lysosomal disease. The estimated incidence is ~1:100,000 live births.[1]
- Arimoclomol is the first treatment approved, in combination with miglustat, by the United States Food and Drug Administration (US FDA) to treat neurological manifestations of NPC based on positive safety and effectiveness results of the 12-month Phase 2/3 randomized, double-blind placebo-controlled interventional trial which enrolled 50 participants (age 2-18).
- An early access program (EAP) was launched to provide arimoclomol to patients with NPC in the US who were not eligible for or able to participate in clinical trials or who stopped receiving treatment from the open-label extension (OLE) study. The EAP provides real-world insights into safety and effectiveness in a broader age range of patients, including adults.

METHODS AND STATISTICS

- Data were handled in accordance with the Regulations (US Health Insurance Portability and Accountability Act of 1996 [HIPAA] and EU General Data Protection Regulation [GDPR]) and the treating physician obtained Institutional Review Board (IRB) approval.
- Treatment decisions and therapeutic strategies for patients with NPC were made independently of participation in the study; arimoclomol was provided by the Sponsor with prescribing dose based on participant's weight and Phase 2/3 study dosing regimen.
- Physicians reported demographics, medical history, physical exam/laboratory results, adverse events (AEs), weight, concomitant medications, arimoclomol dosing, and 5-domain NPC Clinical Severity Scale (5DNPCCSS) at baseline, with ongoing clinical assessments scheduled at months 4, 7 and 12 and subsequent routine visits thereafter (however, the visit schedule was not mandatory apart from the baseline).
- Effectiveness was measured as the change from baseline in the 5DNPCCSS and rescored 4-domain NPC Clinical Severity Scale (R4DNPCCSS) score.
  - The 5DNPCCSS is an NPC disease-specific validated measure of disease progression[2,3] based on the five most clinically relevant domains (cognition, speech, swallow, fine motor skills and ambulation) of the 17-domain NPCCSS.
  - The R4DNPCCSS removes the cognition domain and rescores the swallow domain from the 5DNPCCSS.[4]
- Participants enrolled from 2020 until commercial availability of arimoclomol in 2024, providing up to 4 years of real-world experience (RWE) in 100 participants. Analyses of data comparing only participants who have data from multiple years with their baseline provides a unique opportunity to compare in-person long-term data in a real-world setting.

RESULTS

Please see Poster 273 for details on the pediatric and adult groups and Poster 041 for details about the overall group.

At the time of approval, all remaining 81 participants opted for commercially available arimoclomol; only 5 participants withdrew due to AEs.

- Of 109 exposed participants, 100 (92%) had baseline 5DNPCCSS which remained relatively stable throughout the 4-year program with mean (SD; min, max) total score of 11.0 (6.15; 0, 25) at baseline and 12.0 (7.32; 2, 25) at Year 4.
- Results of 5DNPCCSS and R4DNPCCSS remained relatively consistent with the overall population, with disease progression scores remaining relatively stable, for the participants with data from Years 1 (n=78), 2 (n=43), 3 (n=38), and 4 (n=20) to their respective baseline scores
  - Within-person 5DNPCCSS data is presented in **Table 2**. An increase in 5DNPCCSS score is reflective of an increase in disease severity. Based on natural history studies, an annualized increase of 1.5 in total 5DNPCCSS score can be expected in pediatric NPC patients.[5]
  - Results of the R4DNPCCSS (**Table 3**) were consistent with the 5DNPCCSS.

Table 1: Demographics and Treatment Characteristics of Participants in the Arimoclomol Early Access Program

Demographic Variable Detail	Overall (N=109)	Arimoclomol only (N=38)	Arimoclomol + miglustat (N=71)
Gender – n (%)			
Male / Female	57 (52.3) / 52 (47.7)	22 (57.9) / 16 (42.1)	35 (49.3) / 36 (50.7)
Age at diagnosis (years)			
n	106	36	70
Mean (SD)	16.4 (13.0)	19.2 (15.6)	15.0 (11.2)
Median (min, max)	12.0 (0.0, 62.0)	13.2 (0.0, 62.0)	12.0 (0.1, 43.0)
Year of Enrollment – n (%)*			
n	102	34	68
2020	23 (22.5)	10 (29.4)	13 (19.1)
2021	35 (34.3)	8 (23.5)	27 (39.7)
2022	10 (9.8)	3 (8.8)	7 (10.3)
2023	17 (16.7)	5 (14.7)	12 (17.6)
2024	17 (16.7)	8 (23.5)	9 (13.2)
Age at treatment initiation (years)			
n	109	38	71
Mean (SD)	19.9 (13.1)	22.1 (15.4)	18.7 (11.6)
Median (min, max)	17.3 (2.0, 64.5)	17.5 (2.0, 64.5)	17.5 (2.2, 43.0)
Duration of treatment with arimoclomol (days)**			
n	102	34	68
Mean (SD)	820 (539)	668 (566)	897 (513)
Median (min, max)	836 (15,1622)	460 (15,1622)	1038 (54,1590)

* Participants with known exposure duration.
**Duration = time on treatment from the date of treatment initiation to their final dose date of arimoclomol in the EAP.

Figure 1: Mean (+/-SE) 5DNPCCSS Total Score for Participants with a Baseline and Subsequent Year Visit

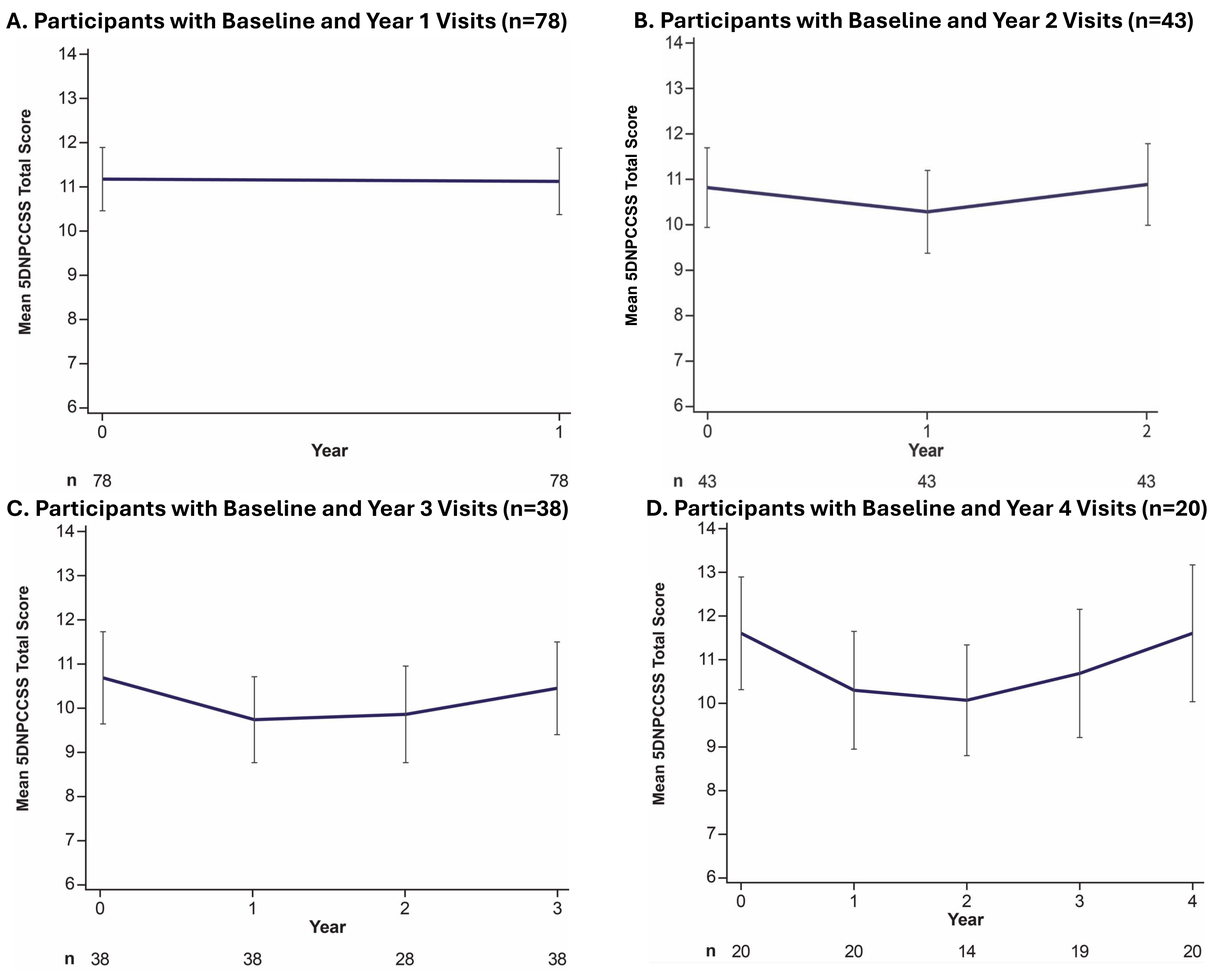

Table 2. Summary of 5DNPCCSS Total Score for Participants with Baseline and Other Year Results (Exposed Participants) N = 109

Complete data year	Year	0	1	2	3	4
Year 4	n (%)	20 (18.3)	20 (18.3)	14 (12.8)	19 (17.4)	20 (18.3)
	Mean (SE; SD)	11.6 (1.29; 5.75)	10.3 (1.34; 6.01)	10.1 (1.26; 4.73)	10.7 (1.46; 6.38)	11.6 (1.56; 6.98)
Year 3	n (%)	38 (34.9)	38 (34.9)	28 (25.7)	38 (34.9)	
	Mean (SE; SD)	10.7 (1.04; 6.44)	9.7 (0.97; 6.00)	9.9 (1.09; 5.78)	10.4 (1.05; 6.47)	
Year 2	n (%)	43 (39.4)	43 (39.4)	43 (39.4)		
	Mean (SE; SD)	10.8 (0.88; 5.76)	10.3 (0.91; 5.99)	10.9 (0.90; 5.90)		
Year 1	n (%)	78 (71.6)	78 (71.6)			
	Mean (SE; SD)	11.2 (0.72; 6.33)	11.1 (0.75; 6.63)			

Table 3. Summary of R4DNPCCSS Total Score for Participants with Baseline and Other Year Results (Exposed Participants) (N=109)

Complete data year	Year	0	1	2	3	4
Year 4	n (%)	20 (18.3)	20 (18.3)	14 (12.8)	19 (17.4)	20 (18.3)
	Mean (SE; SD)	8.7 (1.02; 4.55)	7.5 (1.10; 4.90)	7.1 (0.95; 3.57)	8.1 (1.25; 5.45)	8.6 (1.37; 6.13)
Year 3	n (%)	38 (34.9)	38 (34.9)	28 (25.7)	38 (34.9)	
	Mean (SE; SD)	7.9 (0.85; 5.27)	6.9 (0.81; 4.99)	7.0 (0.89; 4.72)	7.7 (0.87; 5.38)	
Year 2	n (%)	43 (39.4)	43 (39.4)	43 (39.4)		
	Mean (SE; SD)	7.7 (0.72; 4.72)	7.3 (0.77; 5.02)	7.8 (0.73; 4.81)		
Year 1	n (%)	78 (71.6)	78 (71.6)			
	Mean (SE; SD)	8.2 (0.59; 5.17)	8.1 (0.63; 5.52)			

DISCUSSION AND CONCLUSIONS

- Limitations of RWD collection include inconsistent reporting, quality of data collected, and potential biases. Limitations of this EAP include heterogeneity of NPC and a small number of participants with data collected over the 4-year period. While recognizing the potential for selection bias inherent to completer analyses, these results provide supportive evidence for the durability of treatment effects under conditions of sustained real-world use.
- Enrollment was done in a rolling manner, and therefore only the 23 participants who enrolled in 2020 could have completed four years of follow-up. While the 20 participants who completed Baseline and Year 4 5DNPCCSS assessments may only represent 18.3% of the overall population, they represent 87% of the participants who could have completed four years of follow-up.
- Within-person data from the EAP provides up to 4 years of RWE data consistent with clinical trials[6,7] and results from the overall EAP population.

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