Poster ID 031

Arimoclomol for the Treatment of Niemann-Pick Disease Type C in a Real-World Setting: Long-Term Outcomes From an Expanded Access Program in the United States

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BACKGROUND AND OBJECTIVE

- Niemann-Pick disease type C (NPC) is an ultra-rare, progressive neurodegenerative lysosomal storage disease with persisting unmet medical need.
- Arimoclomol, an orally available small molecule, is the first FDA-approved treatment for NPC when used in combination with miglustat.
- Rare disease data are sparse and data collection opportunities limited.
- The US arimoclomol Expanded Access Program (EAP), initiated in June 2020 (NCT04316637), provides drug access to eligible NPC patients.
- Optional real-world data (RWD) collected in an ongoing protocol-driven EAP was initiated to expand the understanding of NPC, including populations not previously studied in randomized clinical trials, for patients consenting to RWD collection.
- Here we present effectiveness and safety data from pediatric and adult NPC patients treated in the US EAP with arimoclomol over a 3-year period.

METHODS

- The protocol-driven US EAP is an ongoing, prospective real-world study designed to provide expanded access to arimoclomol for NPC patients who were not eligible for or unable to participate in clinical trials.
- The 15-site US EAP was designed to also collect RWD for those participants who consented to data collection.
- Effectiveness was measured as the change from baseline in the physician-reported 5-domain NPC Clinical Severity Scale (5DNPCCSS) and rescored 4-domain NPC Clinical Severity Scale (R4DNPCCSS) score.
- Scores were analyzed at 1-year (<13 months), 2 years (≥13 to <25 months), and 3 years (≥25 to <37 months) post-treatment initiation for patients with a minimum of 1 year of follow-up using descriptive statistics.
- All adverse events were recorded during the US EAP and were summarized.

RESULTS

Table 1: Key EAP Eligibility and Ineligibility Criteria*

Eligibility Criteria	Ineligibility Criteria
Confirmed NPC diagnosis and at least 1 neurological symptom, age ≥ 2 years, permanent US resident, if taking miglustat (Zavesca®), the patient must have been on the target dose for the past 6 weeks, if history of seizures, the condition must be adequately controlled	Severe liver disease; kidney disease; known or suspected allergy or intolerance to arimoclomol; pregnancy, planning to become pregnant or currently breastfeeding; treatment with other investigational drug during the EAP or in the 4 weeks prior to arimoclomol treatment start

*Eligibility and ineligibility criteria described are not inclusive of all criteria. Refer to WORLD Poster ID 094 or NCT04316637 for complete criteria.

Table 2: NPCCSS Assessments

5DNPCCSS				
Ambulation	**Cognition[a]**	**Fine Motor**	**Speech**	**Swallow[b]**
Domain Scoring: Individual domains: 0 (normal) – 5 (worst)			**Total Score:** 0 (normal) – 25 (worst)	

[a]R4DNPCCSS assessments exclude the cognition domain resulting in a maximal worst total score of 20.
[b]In an effort to improve the linearity of the swallow domain the scoring algorithm was simplified for the 4D NPCCSS; applying 0 to no impairment, 1 for cough while swallowing, 2 for intermittent dysphagia, 3 for dysphagia, 4 for supplemental feeding via gastric or nasogastric tube, and 5 for feeding exclusively via gastric or nasogastric tube.

Table 3: US EAP Efficacy Analysis Participant Characteristics & Demographics

Analysis Outputs	Patients Initiated to Treatment	Arimoclomol	Arimoclomol + Miglustat as Part of Routine Clinical Care
Number of Participants	56 (100%)	17 (30.4%)	39 (70%)
Age at Treatment Initiation (Years)			
Mean (SD)	20.18 (11.22)	22.88 (11.00)	19.0 (11.25)
Median (Range)	20.5 (2 – 41)	24.0 (7 – 41)	20.0 (2 – 41)
Exposure to Arimoclomol (Months)			
Mean (SD)	32.7 (8.80)	29.7 (12.19)	34.04 (6.61)
Median (Range)	34.83 (12.3 – 44.97)	30.40 (12.3 – 44.97)	35.40 (14.87 – 44.1)
NPCCSS at Baseline[a]			
5DNPCCSS Total Score	11.2 (6.2); 10.5 [1, 25]	11.7 (6.5); 11.0 [1, 25]	11.0 (6.1); 10 [1, 25]
4DNPCCSS Total Score	8.2 (5.1); 8 [0, 20]	8.5 (5.6); 9.0 [0, 20]	8.1 (4.9); 7.0 [1, 20]

[a]Data reported as Mean (SD); Median [Range]

Table 4: US EAP Patient Safety

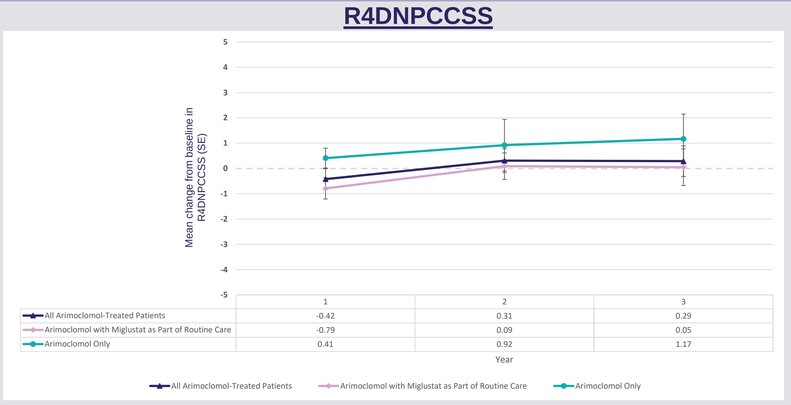
	Patients Treated With Arimoclomol (N = 56) n (%)
Adverse Events Reported	160 (75 %)
Non-Serious Adverse Events Reported	106 (39.3%)
Serious Adverse Events Reported	54 (35.7%)
Treatment Emergent Adverse Events (TEAEs) Reported	157 (73.2%)
Fatal Serious Adverse Events Reported	9 (10.7 %)

Adverse Event Summary (Serious and Non-Serious)	Patients Treated With Arimoclomol (N = 56) n (%)
Corona virus infection	12 (17.9%)
Pneumonia	11 (14.3%)
Diarrhea	6 (8.9 %)
Fall	5 (8.9 %)
Rash	4 (7.1 %)
Seizure	4 (7.1 %)
Vomiting	4 (7.1 %)

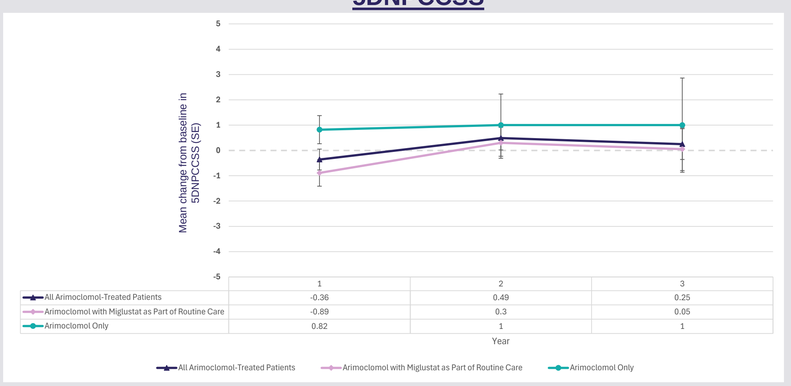
Adverse event data are reported as counts of the number of events and % of patients.
Description of Fatalities: pneumonia, 3; COVID-19, 2; acute respiratory failure, 2; disease progression, 1; sepsis, 1.
Note that 9 serious fatal adverse events occurred in a total of 6 patients, 1 patient experienced 3 events and 1 patient experienced 2 events with a fatal outcome. No fatalities were determined to have a causal relationship to arimoclomol.

Figure 1: Total Population

R4DNPCCSS



5DNPCCSS

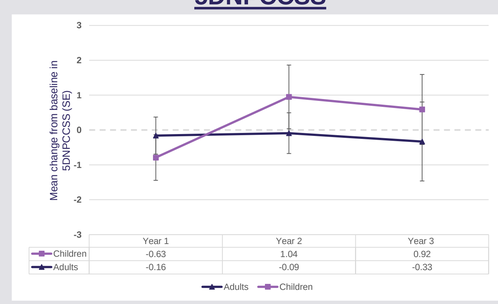


Total number of participants per year are represented: Year 1 (n) : 55, 38, and 17; Year 2: 45, 33, 12; Year 3 : 28, 22, 6 for all arimoclomol treated patients, arimoclomol with miglustat as part of routine clinical care, and arimoclomol alone respectively.

Figure 2: Adults & Children

R4DNPCCSS

5DNPCCSS



Total number of participants per year are represented: Year 1 (n) : 31 and 24; Year 2: 22 and 23; Year 3 :15 and 13 Adults and Children respectively.
5DNPCCSS- 5-Domain NPC Clinical Severity Scale; R4DNPCCSS- Rescored 4-Domain NPC Clinical Severity Scale.

RESULTS

- Results are presented with current data as of May 8, 2024.
- 56 patients (60%) had a baseline 5DNPCCSS assessment and at least one year of follow-up (**Table 3**).
- A total of 55 patients were included in the 1-year analysis, 45 in the 2-year analysis, and 28 in the 3-year analysis.
- 31 patients (55%) were ≥18 years of age and 25 patients (45%) were under 18 at the time of arimoclomol initiation in the US EAP.
- 17 patients (30.4%) were treated with arimoclomol monotherapy and 39 patients (70%) used arimoclomol and miglustat as part of routine clinical care (**Table 3**).
- Similar results were observed using the 5DNPCCSS and R4DNPCCSS. (**Figure 1 & 2**)
- Arimoclomol was well tolerated during the US EAP with no new safety signals identified.

CONCLUSIONS

- **Patients treated with arimoclomol in the US EAP, including those with and without miglustat as a component of routine clinical care, experienced relatively stable disease through the up to 3 years of follow-up reported here.**
- **Published natural history indicates that on average patients progress between ~1.0–2.0 points per year on the 5DNPCCSS.[1,2]**
- **A 1- to 2-point change in the 5DNPCCSS represents a clinically meaningful change or progression; any slowing of disease is considered meaningful.[3]**
- **Real-world outcomes from the US EAP indicate a stabilization of disease progression with arimoclomol, with or without miglustat, representing a reduction in disease progression relative to natural history data.**

Disclosures: Poster was prepared by Zevra Therapeutics
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References: 1. Mengel E, et al. Clinical disease progression and biomarkers in Niemann-Pick type C: a prospective cohort study. *Orphanet J Rare Dis.* 2020 Nov 23;15(1):328. 2. Yanjanin NM, et al. Linear clinical progression, independent of age of onset, in Niemann-Pick disease, type C. *Am J Med Genet B Neuropsychiatr Genet.* 2010 Jan 5;153B(1):132-40. 3. Patterson MC, et al. Validation of the 5-domain Niemann-Pick type C Clinical Severity Scale. *Orphanet J Rare Dis.* 2021 Feb 12;16(1):79.