Poster
P-100

Real-world use of arimoclomol in Niemann-Pick type C: Findings from a German Compassionate Use Programme

Harmeling S[1] , Arash-Kaps L[2] , Mani L[2] , Marquardt T[1] , Mengel E[2]

[1] Department of General Pediatrics, University Hospital Münster, Münster, Germany
[2] SphinCS, Institute of Clinical Science for LSD, Hochheim, Germany

Background

- Niemann-Pick disease type C (NPC) is an ultra-rare, debilitating, progressive neurodegenerative, heterogenous lysosomal disease with an estimated incidence of ~1:100,000 live births.[1]
- Arimoclomol, in combination with miglustat, is the first therapy approved by the United States Food and Drug Administration for the treatment of neurological manifestations of NPC in patients aged ≥2 years, based on a 12-month Phase 2/3 randomised, double-blind, placebo-controlled interventional trial (ClinicalTrials.gov ID NCT02612129).
- In Germany, a Compassionate Use Programme (CUP) was initiated in December 2020 to provide early access to arimoclomol.
- Here, we present real-world demographic, clinical, and treatment exposure data of participants of the CUP collected by 2 of the 6 centres currently participating in the programme.

Methods

- The German arimoclomol CUP was approved on December 23, 2020, and will continue until commercial approval of arimoclomol in the EU.
- Individuals from Germany with a confirmed diagnosis of NPC and aged ≥2 years who were not successfully treated with other therapies were eligible to participate.
- Participants were not permitted to receive treatment with other investigational treatments while participating in the CUP.
- Disease-specific assessments were conducted as part of clinical care at participating centres.
- Demographic, clinical and treatment exposure data collected by the SphinCS Institute in Hochheim and the University Hospital of Münster are presented.
- In addition, qualitative data to develop participant narratives were obtained through telephone interviews with 8 participants or their caregivers, focusing on those who discontinued treatment either permanently or temporarily.

Results

Demographics and clinical characteristics

- As of August 2025, 48 individuals with NPC had been enrolled in the arimoclomol CUP at the SphinCS Institute of Clinical Science for LSD in Hochheim (n=23) and the University Hospital of Münster (n=25).
- Participants in the CUP were clinically diverse (Tables 1 and 2):
  - Age at treatment initiation ranged from 2 to 63 years, with approximately half of the participants being adults.
  - Nine participants had neurological onset in infancy, 2 in childhood, and 7 in adulthood.
- Mean exposure to arimoclomol was 3.0 years (range 0.3–8.0 years). Most participants (95.8%) received miglustat alongside arimoclomol (Table 3).
- A total of 21 participants (43.8%) discontinued arimoclomol temporarily or permanently during the evaluation period.
  - The primary reasons were the need to meet eligibility criteria to enroll in clinical trials with investigational treatments (n=10) and death (n=5) (Figure 1). No discontinuations were due to arimoclomol-related adverse events.
  - Four participants who died had severe NPC, with neurological onset before 10 years of age; the fifth had adult-onset NPC and was 63 years old at treatment initiation. All deaths were due to multi-morbidity related to NPC (including tetraspasticity, dementia, epilepsy, weight loss).
  - Four participants resumed arimoclomol after discontinuation: 2 who initially stopped due to a perceived lack of therapeutic efficacy, 1 who discontinued because of an intercurrent illness, and 1 who withdrew to join a study with an investigational therapy but ultimately did not participate.

Table 1. Participant characteristics – Demographics

	Participants enrolled (N=48)
Age at initiation of arimoclomol, years	
Mean (SD)	20.1 (15.9)
Median (min, max)	17 (2, 63)
Age category, n (%)	
<18 years at initiation of arimoclomol	26 (54.2)
≥18 years at initiation of arimoclomol	22 (45.8)
Sex, n (%)	
Female	25 (52.1)
Male	23 (47.9)
Participated in NPC-002 clinical trial, n (%)	6 (12.5)

Max: maximum; min: minimum; n: number of participants; SD: standard deviation

Table 2. Participant characteristics – Neurological findings

	Participants enrolled (N=48)
Age at first neurological symptom, years	
Mean (SD)	10.4 (11.4)
Median (min, max)	6.0 (0, 54)
Time from first neurological symptom to treatment initiation, years	
Mean (SD)	9.5 (7.5)
Median (min, max)	8.0 (0, 32)
NPC phenotype, n (%)	
Neurological onset at ≤2 years of age	9 (18.8)
Neurological onset at >2–<18 years of age	32 (66.7)
Neurological onset at ≥18 years of age	7 (14.6)
History of epilepsy, n (%)	18 (37.5)

Max: maximum; min: minimum; n: number of participants; SD: standard deviation

Table 3. Participant characteristics – Treatment exposure

	Participants enrolled (N=48)
Time on arimoclomol, years	
Mean (SD)	3.0 (1.9)
Median (min, max)	3.0 (0.3, 8.0)
Miglustat use at enrolment, n (%)	46 (95.8)
Discontinued arimoclomol, n (%)	21 (43.8)
Permanently discontinued	17 (35.4)
Resumed arimoclomol	4 (8.3)

Max: maximum; min: minimum; n: number of participants; SD: standard deviation

Figure 1. Reasons for discontinuation of arimoclomol (n=21)

*Including hydroxypropyl beta cyclodextrin (HPβCD; n=4) and N-Acetyl-L-Leucine (NALL; n=6)
n: number of participants

Participant and caregiver interviews

- Telephone interviews were carried out to collect narrative information on 8 participants who discontinued treatment (Figure 2), including 4 who resumed therapy after discontinuation (Figure 3).

Figure 2. Summary of interview findings

8 interviews after temporary or permanent discontinuation

- 6 with caregivers
- 1 with participant and caregiver
- 1 with participant and spouse

Reasons for discontinuation

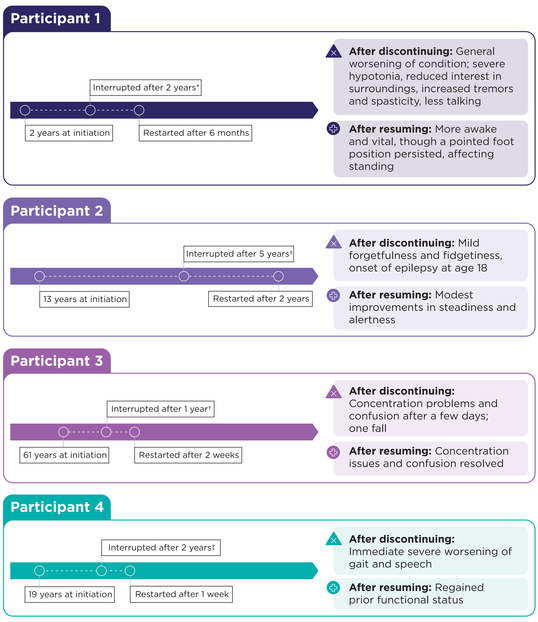
- 3 entered NALL study
- 2 entered HPβCD study
- 2 perceived lack of therapeutic effectiveness
- 1 intercurrent disease

Outcomes after discontinuation

- 3 had rapid clinically notable deterioration after discontinuation
  - Reported effects: sudden loss of controlled gait, general confusion, decreased perseverance, worsening of speech
- 4 participants resumed arimoclomol (Figure 3)

HPβCD: hydroxypropyl beta cyclodextrin; NALL: N-Acetyl-L-Leucine

Figure 3. Details of participants who discontinued and subsequently resumed arimoclomol



Reasons for stopping: *medical emergency and surgery; †Lack of perceived treatment effect; ‡Planned to participate in NALL study but ultimately did not participate due to immediate worsening condition

Conclusions

- **The German CUP data provides valuable evidence from a demographically and clinically diverse group of individuals with NPC treated with arimoclomol for up to 8 years, providing insight into long-term real-world experience with this treatment.**
- **Most treatment interruptions were driven by external factors, particularly requirements for participation in clinical trials that prohibited continuation of arimoclomol.**
- **The number of deaths during the CUP (n=5) was not unexpected given the clinical severity or advanced age of these participants and the long follow-up time.**
- **Exposure data and insights from participant and caregiver interviews indicate that adverse reactions to arimoclomol are no key driver for discontinuing arimoclomol and that treatment interruption may have immediate clinical consequences, which may resolve after resuming therapy. These findings highlight the importance of maintaining treatment continuity.**

References
1. Geberhiwot T, et al. Consensus clinical management guidelines for Niemann-Pick disease type C. Orphanet J Rare Dis. 2018;13:50

Author disclosures
SH received fees from Zevra Therapeutics, Cyclo Therapeutics, and Immedica Pharma. LAK received honoraria/travel grants from Takeda, Zevra, Amicus, and Genorph. LM and TM have no conflicts of interest. EM has received investigator fees and/or consultant honoraria from Cyclo Therapeutics, Amicus, Idorsia, Intrabio, Denali, JCR, Prevail, Freeline Therapeutics, Alexion, Zevra, Sanofi Genzyme, and Takeda

Acknowledgement and funding
Funding for the study, data analysis, writing, editing, and poster production was provided by Zevra Therapeutics Inc. Medical writing and editing assistance was provided by Ismar Healthcare