

# Safety of Arimoclomol in a Pediatric Substudy of Niemann-Pick Disease Type C Patients Aged 6 to <24 Months at Study Enrollment

Poster No.  
065

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## BACKGROUND

- Niemann-Pick disease type C (NPC) is an ultra-rare, progressive neurodegenerative lysosomal disease.
- Clinical presentation is heterogeneous with declining neurological functions.
- Onset of NPC symptoms can occur throughout life from the prenatal period to adulthood.
- Generally, the age of onset determines the speed of disease progression.
- For patients with early-infantile onset of NPC (onset of neurological symptoms <24 months of age) the median age of death is 48 months (range, 7-132 months).<sup>1</sup>
- Arimoclomol, an orally available small molecule, is the first FDA-approved treatment for NPC when used in combination with miglustat.
- To assess and evaluate safety and tolerability of arimoclomol treatment in children with NPC younger than 2 years, a pediatric substudy to the pivotal arimoclomol phase 3 trial CT-ORZY-NPC002 (NCT02612129) was implemented.

## METHODS

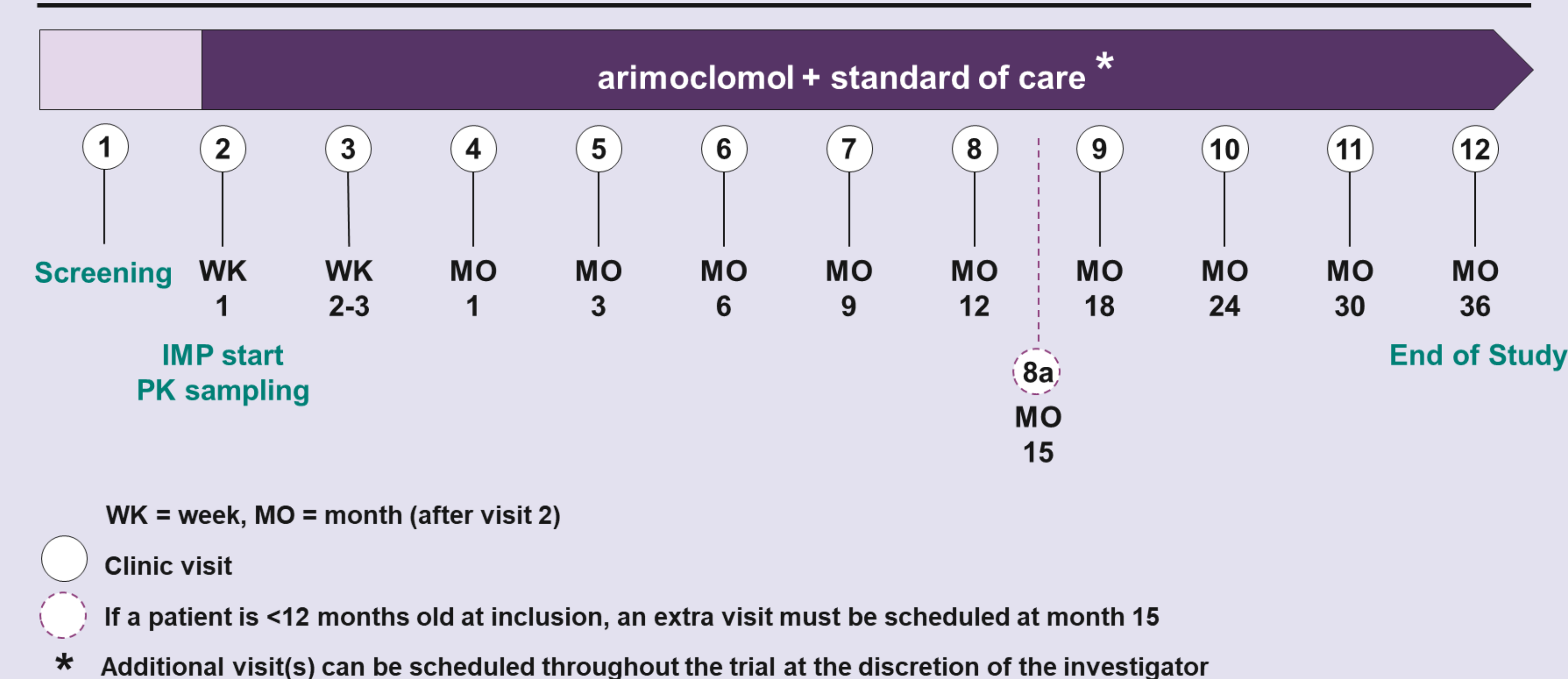
- The pediatric substudy is a multi-center, open-label, interventional study in patients with confirmed diagnosis of NPC, aged 6 to <24 months at study enrollment.
- The substudy enrolled 5 patients for a minimum of 12 months of treatment with arimoclomol on top of routine clinical care.
- Eligibility criteria included: confirmed diagnosis of NPC1 or NPC2, if patients were on background treatment with miglustat the dose should have been stable for at least 1 month prior to enrollment. Start of new treatment with miglustat was not recommended during the first 12 months of arimoclomol exposure.
- Patients were followed closely with a condensed visit schedule (**Figure 1**).
- Dosing was based on population pharmacokinetic simulation, with an arimoclomol dose of 3.2 mg/kg body weight until the age of 2 years. Arimoclomol was suspended in water and administered orally or by feeding tube.

## RESULTS

- The 5 patients were 14-23 months old at enrollment (**Table 1**). All were concomitantly treated with miglustat.
- A total of 92 AEs were reported in the substudy (**Table 2**).
- Most AEs were mild (68%) and recovered/resolved during the study.
- Most AEs and SAEs were assessed as not related to arimoclomol.
- Only 2 AEs were assessed as probably related; these were events of elevated ALT (alanine transaminase) and AST (aspartate aminotransferase), reported for the same patient (Patient 5). These 2 AEs also led to withdrawal of arimoclomol (**Table 1**).
- The most frequently reported AEs were fever, cough, common cold, and vomiting.
- None of the reported adverse events were unexpected, given the knowledge of the safety profile described in the 12-month double-blind phase and the 48-month open-label extension phase of the CT-ORZY-NPC-002 trial comprising patients aged 2 to <19 years (see also poster 229).

## Figure 1. Pediatric Substudy Design

### Open-label interventional substudy in NPC patients aged 6 to <24 months



## CONCLUSIONS

- No unexpected adverse events were reported.
- Arimoclomol appeared to be well tolerated in children aged 14-23 months in the pediatric substudy.

## Table 2. Adverse Event Overview

	n	%	e
<b>All AEs</b>	5	100	92
<b>SAEs</b>	2	40	16
<b>Severity</b>			
Mild	4	80	63
Moderate	4	80	19
Severe	1	20	9
Unassigned	1	20	1
<b>AEs possibly or probably related to arimoclomol</b>	1	20	2
<b>AEs leading to treatment discontinuation</b>	1	20	2

AE = adverse event; e = number of events; n = number of patients; SAE: serious adverse event; % = proportion of patients. Preliminary data, cutoff date: 06 February 2024.

## REFERENCE

- Yilmaz BS, Baruteau J, Rahim AA, Gissen P. Clinical and Molecular Features of Early Infantile Niemann Pick Type C Disease. *Int J Mol Sci.* 2020;21(14):5059. doi: 10.3390/ijms21145059.

**Table 1. Patient Overview**

Patient No.	Age at Enrollment (Months)	Time in Substudy <sup>a</sup> (Months)	Baseline Weight (kg)	Relevant Medical History	Serious Adverse Events and Adverse Events Leading to Treatment Discontinuation	Adverse Events Reported More Than Once
1	23	34	11.5	• Neonatal hepatitis	<ul style="list-style-type: none"> <li>Urine infection with e-coli, grade 2 (Moderate).</li> <li>Fever, grade 1 (Mild).</li> <li>CSF leakage from baklofen pump, grade 2 (Moderate).</li> <li>Fever, grade 1 (Mild).</li> <li>Common cold, grade 1 (Mild).</li> </ul>	<ul style="list-style-type: none"> <li>Common cold</li> <li>Cough</li> <li>Diarrhea</li> <li>Elevated AST</li> <li>Fever</li> <li>Vomiting</li> </ul>
2	14	31	7.8		<ul style="list-style-type: none"> <li>Flu A, grade 3 (Severe)</li> <li>Dehydration, grade 3 (Severe)</li> <li>Ketotic hypoglycaemia, grade 3 (Severe)</li> <li>Vomiting, grade 2 (Moderate)</li> <li>Lower respiratory tract infection (respiratory syncytial virus), grade 3 (Severe)</li> <li>Vomiting, grade 3 (Severe)</li> <li>Blocked NJ tube, grade 3 (Severe)</li> <li>Pyelonephritis, grade 3 (Severe)</li> <li>Left lower lobe consolidation, grade 3 (Severe)</li> <li>Diarrhoea and vomiting, grade 3 (Severe)</li> <li>Recovery post procedure, grade 1 (Mild)</li> </ul>	<ul style="list-style-type: none"> <li>Cough</li> <li>Constipation</li> <li>Fever</li> <li>Lower respiratory tract infection</li> <li>Upper respiratory tract infection</li> <li>Vomiting</li> </ul>
3	20	21	9.7	<ul style="list-style-type: none"> <li>Splenomegaly</li> <li>Episode of elevated transaminases</li> <li>Gaze palsy</li> <li>Infections</li> </ul>		<ul style="list-style-type: none"> <li>Common cold</li> <li>Ulcer on the tongue</li> <li>Upper respiratory tract infection</li> <li>Vomiting</li> </ul>
4	16	15	10.3	<ul style="list-style-type: none"> <li>Splenomegaly</li> <li>Jaundice</li> <li>Anemia</li> <li>Developmental delay</li> </ul>		
5	19	4	10.5	<ul style="list-style-type: none"> <li>Jaundice</li> <li>Hepatosplenomegaly</li> </ul>	<ul style="list-style-type: none"> <li>Elevated ALT, grade 2 (Moderate)</li> <li>Elevated AST, grade 2 (Moderate)</li> </ul>	

Preliminary data (cutoff date: 06 February 2024), terms are presented as reported – AEs have not yet been coded according to MedDRA terminology. <sup>a</sup> As of 21 February 2024, 3 patients were still ongoing.