Efficacy of Arimoclomol Combined With Miglustat at Months 3, 6, 9 and 12 of the Double-Blind, Randomized, Placebo-Controlled NPC002 Trial

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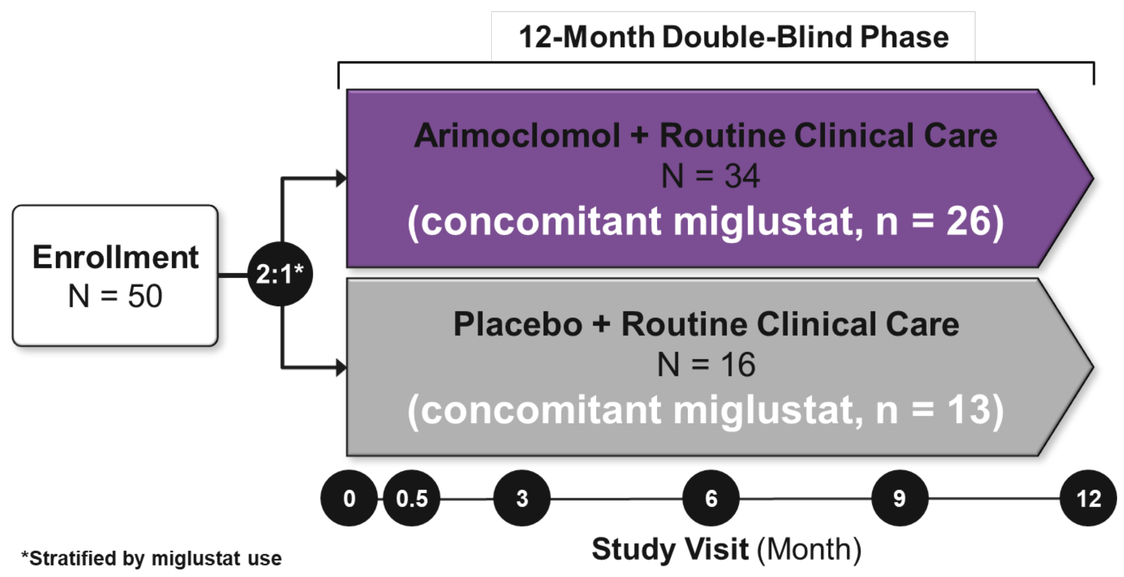
BACKGROUND

- Niemann-Pick disease type C (NPC) is an ultra-rare, progressive neurodegenerative lysosomal disease with heterogeneous clinical presentation.
- Results of a 12-month double-blind (DB), randomized, placebo-controlled trial investigating the efficacy and safety of arimoclomol showed a positive benefit-risk in patients aged 2-19 years diagnosed with NPC (NPC002, NCT02612129).[1,2]
- This effect was even more pronounced in the subset of patients concomitantly treated with miglustat.
- Arimoclomol, an orally available small molecule, is the first FDA-approved treatment for NPC when used in combination with miglustat.
- Here we present post hoc efficacy analyses for patients on concomitant miglustat treatment assessed at months 3, 6, 9 and 12 of the trial, with the rescored 4-domain NPC clinical severity scale (R4DNPCCSS: ambulation, speech, swallowing and fine motor skills).

Figure 1. NPC002 Trial Design



METHODS

- R4DNPCCSS scores[2] from the NPC002 trial were used for the post hoc analyses.
- Change from baseline to months 3, 6, 9 and 12 in R4DNPCCSS were compared using an ANCOVA (analysis of covariance) model which included treatment as fixed effect and baseline value as covariate.
  - Missing change values were imputed with 1000 imputations based on placebo participants. The change from the last non-missing visit was imputed and added to the change measured at the most recent attended visit to generate the imputed change. Values outside minimum or maximum range were set to minimum or maximum score.
  - Participants who discontinued due to death were imputed using the worst possible outcome.

Table 1: Demographic and Baseline Characteristics - Patients on Concomitant Miglustat - NPC002

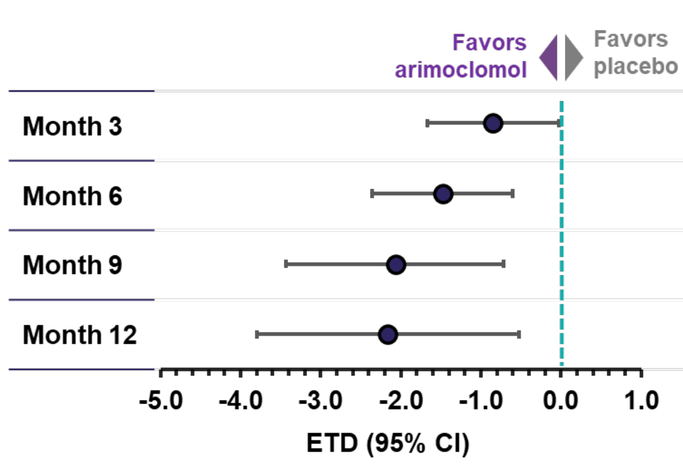
	Arimoclomol (N=26)	Placebo (N=13)
Age, mean (SD)	12.8 (4.7)	9.1 (3.6)
< 4 years, n (%)	2 (7.7%)	2 (15.4%)
4 to < 8 years, n (%)	3 (11.5%)	1 (7.7%)
8 to < 12 years, n (%)	7 (26.9%)	7 (53.8%)
≥ 12 years, n (%)	16 (61.5%)	2 (15.4%)
Female, n (%)	14 (53.8%)	8 (61.5%)
Race, n (%)		
White	24 (92.3%)	10 (76.9%)
Asian	1 (3.8%)	1 (7.7%)
Native Hawaiian or other pacific islander	0	1 (7.7%)
Unknown	1 (3.8%)	1 (7.7%)
BMI; mean (SD)	19.23 (4.57)	18.78 (3.06)
Age at first neurological symptom, mean (SD)	5.25 (3.34)	4.04 (3.20)
R4DNPCCSS score, mean (SD)	8.88 (6.07)	7.00 (5.76)

BMI = body mass index; N = number of patients; NPCCSS = Niemann-Pick Disease type C Clinical Severity Scale; R4DNPCCSS = Rescored 4-domain Niemann-Pick disease type C Clinical Severity Scale; SD = standard deviation.

RESULTS

- Out of a total of 50 patients, 26 patients on arimoclomol and 13 patients on placebo were concomitantly treated with miglustat during the NPC002 trial (**Figure 1**).
- The mean age (SD) was 12.8 (4.7) and 9.1 (3.6) years, respectively. Mean disease severity at baseline was comparable (**Table 1**).
- A statistically significant treatment effect favoring arimoclomol over placebo in R4DNPCCSS change from baseline was seen at all timepoints assessed (**Figure 2** and **Figure 3**).

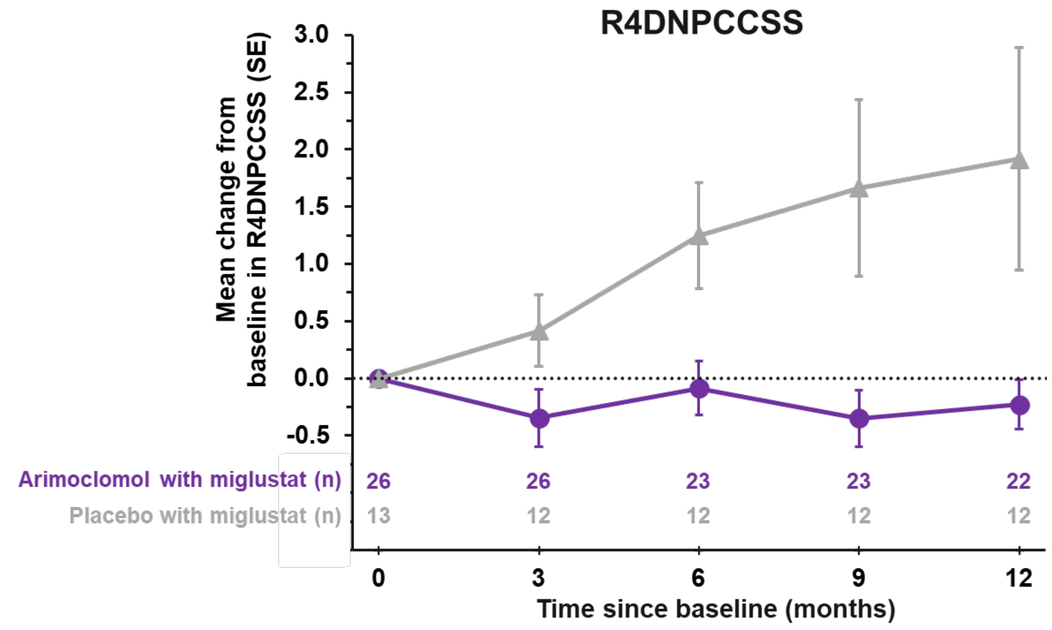
Figure 2. Change From Baseline to Month 3, 6, 9 and 12 in R4DNPCCSS - Patients on Concomitant Miglustat - NPC002



	Arimoclomol n	Placebo n	ETD (95% CI)	P-value
Month 3	26	12	-0.85 (-1.67; -0.03)	0.0415
Month 6	23	12	-1.48 (-2.36; -0.61)	0.0009
Month 9	23	12	-2.07 (-3.43; -0.72)	0.0028
Month 12	22	12	-2.17 (-3.80; -0.53)	0.0094

ANCOVA (analysis of covariance) including treatment as fixed effect and baseline value as covariate.
CI = confidence interval; ETD = estimated treatment difference.

Figure 3. Change From Baseline in R4DNPCCSS - Patients on Concomitant Miglustat - NPC002



Analysis of covariance (ANCOVA)
SE = standard error

CONCLUSIONS

- Assessments of NPC disease progression usually require observations over at least 12 months.
- Nonetheless, these results show that the statistically significant treatment difference between arimoclomol and placebo was apparent at all timepoints assessed post-base line in the NPC002 trial for patients concomitantly treated with miglustat.
- This indicates that arimoclomol combined with miglustat treatment may slow NPC disease progression from as early as 3 months after treatment initiation.

REFERENCES

1. Mengel E, Patterson MC, Da Riol RM, et al. Efficacy and safety of arimoclomol in Niemann-Pick disease type C: Results from a double-blind, randomised, placebo-controlled, multinational phase 2/3 trial of a novel treatment. *J Inherit Metab Dis*. 2021;44(6):1463-1480. doi:10.1002/jimd.12428

2. Mengel E, Patterson MC, Da Riol RM, et al. Efficacy results from a 12-month double-blind randomized trial of arimoclomol for treatment of Niemann-Pick disease type C (NPC): Presenting a rescored 4-domain NPC Clinical Severity Scale. *Mol Genet Metab Rep*. 2025 May 28;43:101233. doi: 10.1016/j.ymgmr.2025.101233

DISCLOSURES

Eugen Mengel was Principal Investigator for the NPC002 trial and has worked under consultancy agreements for Zevra Therapeutics. Christine í Dali and Adrian A. Quartel are employees at Zevra Therapeutics. This poster was prepared by Zevra Therapeutics.

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