Relaxation of Food Control Parameters Based on Improvements in the Food Safe Zone Questionnaire Occurs with Reduction of Hyperphagia in Clinical Trials of Diazoxide Choline Extended Release (DCCR) in Participants with Prader-Willi Syndrome

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INTRODUCTION

Prader-Willi syndrome (PWS) is a rare genetic neurobehavioral metabolic disorder characterized by hyperphagia, accumulation of excess fat, and behavioral/ psychological challenges.[1,2]

Diazoxide choline extended-release (DCCR) tablets have recently been approved by the FDA as VYKAT™ XR for the treatment of hyperphagia in adults and pediatric patients 4 years of age and older with Prader-Willi syndrome (PWS). DCCR is a once-daily, extended-release tablet that provides for stable plasma concentrations and absorption throughout the GI tract.[3]

Phase 3: *C601, C602-OLE, and C602-RWP*

Study C601 was a Phase 3 randomized (2:1 DCCR to Placebo), double blind, parallel arm study comparing DCCR to Placebo in participants with genetically confirmed PWS, ages 4 and older. Study C602 was a Phase 3 multicenter study that consisted of an initial open-label extension (OLE) period for approximately 2 to 4 years followed by a 16-week, double-blind, placebo-controlled randomized withdrawal period (RWP).

Study C610

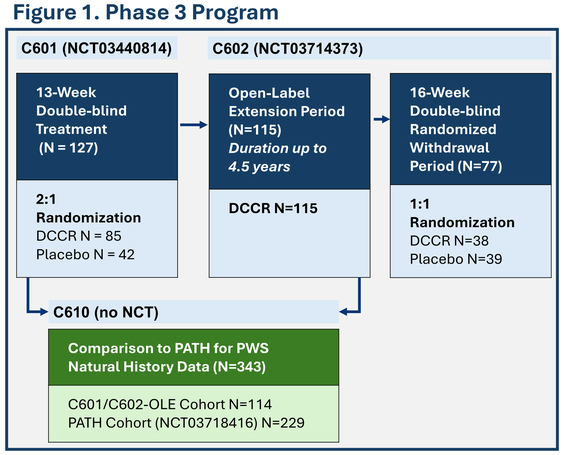
Study C610 was an externally-controlled study comparing study C602-OLE to the PATH for PWS Registry (PATH).

Objective: To analyze food controls via Food Safe Zone (FSZ) Questionnaire across several Phase 3 PWS studies in relation to changes in Hyperphagia Questionnaire for Clinical Trials (HQ-CT) Total Scores.

METHODS

- Data were included from Studies C601, C602-OLE, C602-RWP, and C610 (**Figure 1**).
- HQ-CT Total Scores and FSZ domains were analyzed across each study.
  - Decrease in FSZ represents reduction in environmental food controls.

Figure 1. Phase 3 Program



RESULTS

- 125 participants ≥ 4 years of age with genetically confirmed PWS received DCCR in the Phase 3 program (**Table 1**).
- Median duration of DCCR administration: ~3.0 years (maximum: 4.5 years)
  - 105 (84%) participants > 1 year
  - 90 (72%) participants > 2 years
  - 71 (57%) participants > 3 years

Table 1. Baseline Characteristics (Safety Population)

C601/C602-OLE Participants	N = 125
Age, years	
Mean (±SD)	13.4 (6.98)
Median (range)	12 (4-44)
Race (% White / % Black / % Multiple)	84.8 / 4.8 / 6.4
Weight (mean [±SD]), kg	62.06 (30.15)
Body mass index (mean [±SD]), kg/m²	27.56 (9.62)
Body mass index z-score (mean [±SD])	1.29 (1.12)
Growth hormone use (n [%])	103 (82%)
Geography: USA / UK (%)	80.0 / 20.0
HQ-CT total score (0-36) (mean [±SD])	21.5 (6.70)
Prader-Willi syndrome subtype	
Deletion (n [%])	77 (61.6)
Non-deletion (n [%])	47 (37.6)
Missing (n [%])	1 (0.8)

Abbreviations: BMI, body mass index; HQ-CT, Hyperphagia Questionnaire for Clinical Trials; PWS, Prader-Willi syndrome; SD, standard deviation

- Statistically significant (p<0.0001) reduction in hyperphagia occurred at all time points (**Figure 2**).
- Statistically significant decrease in HQ-CT Total Score compared to PATH at Week 52, with LS Mean change from Baseline of -9.4 and -3.4 respectively (p<0.001).
- Significant reductions (p<0.05) in 4 of 5 domains relative to Baseline were observed at all timepoints from Week 26 through Week 156 (**Figure 3**).
  - *Restrict food access*
  - *Check for food*
  - *Food supervision with others*
  - *Food supervision at home*
- Significant reductions in FSZ scores suggest caregivers reduced controls/restrictions on food access to a greater degree in DCCR-treated patients vs. non-treated patients in PATH (**Figure 4**).
- After 16 weeks of randomized withdrawal, notable increases in FSZ were observed in Placebo group, indicating greater food restrictions for Placebo group vs. DCCR group.

Figure 2. Mean (SD) HQ-CT Total Score by Week (Studies C601 + C602-OLE)

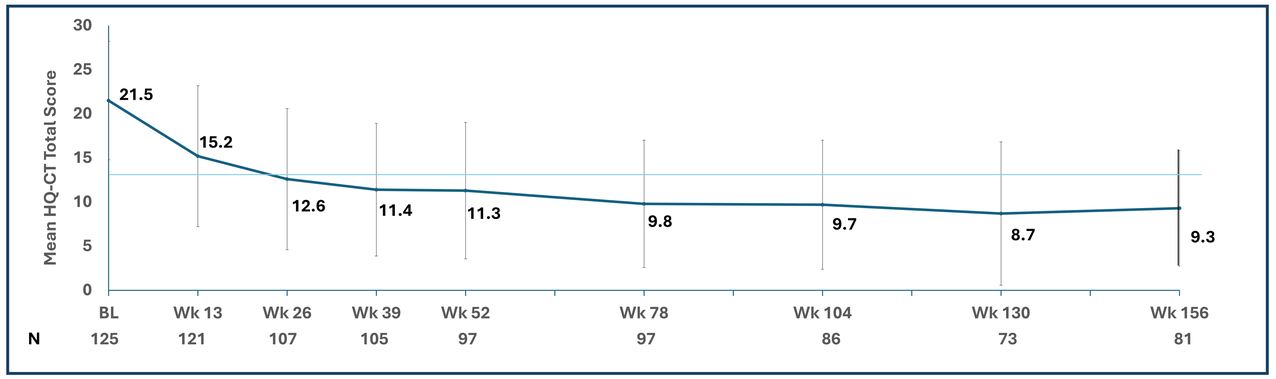


Figure 3. Changes in Food Access / Security (Studies C601 + C602-OLE)

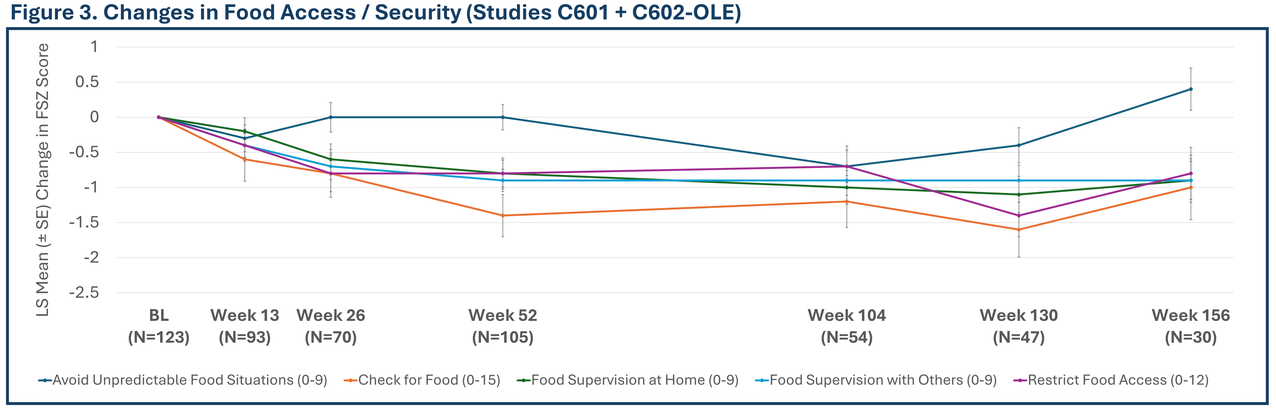
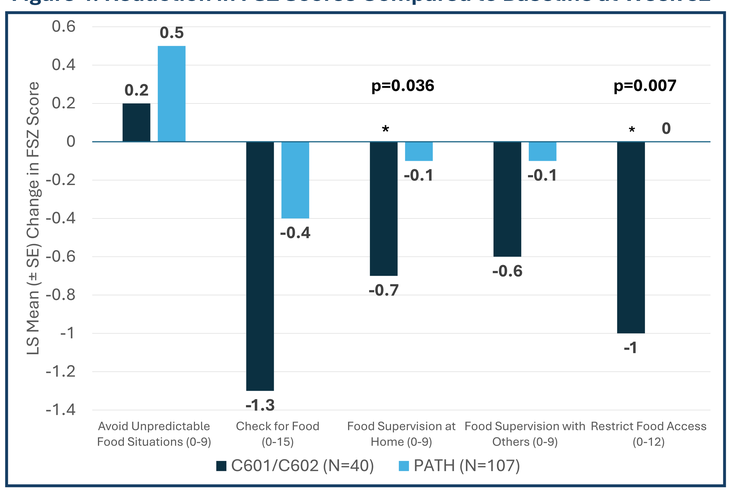


Figure 4. Reduction in FSZ Scores Compared to Baseline at Week 52



CONCLUSIONS

- Reduced hyperphagia per changes in HQ-CT Total Scores
  - Hyperphagia reduced in participants receiving DCCR across Phase 3 program
- Reduction in food controls and restrictions per improvements in the FSZ
  - Significant reductions in multiple FSZ domains in participants receiving DCCR in Studies C601 & C602-OLE and in DCCR cohort in Study C610 vs. PATH for PWS cohort
  - Worsening (increase) in FSZ domains in participants who were withdrawn from DCCR and received placebo in C602-RWP (although not statistically significant)
- **These data show that DCCR administration to participants with PWS resulted in reductions in hyperphagia and lessening of food controls.**

REFERENCES

1. Butler MG, et al. *Curr Pediatr Rev.* 2019;15(4):207-244.
2. Miller JL, et al. *Am J Med Genet A.* 2011;155A(5): 1040–1049.
3. VYKAT™ XR [package insert]. Soleno Therapeutics, Inc. 2025.

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