Diazoxide Choline Extended-Release (DCCR) Tablets Significantly Reduce Hyperphagia in Patients with PWS who are Managed with Strict Food Controls

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INTRODUCTION

Prader-Willi Syndrome

Prader-Willi syndrome (PWS) is a rare genetic neurobehavioral metabolic disorder characterized by hyperphagia, accumulation of excess fat, hypotonia, and behavioral/ psychological challenges.[1,2] Historically, management of PWS has been limited to strict dietary and environmental controls to restrict food access.

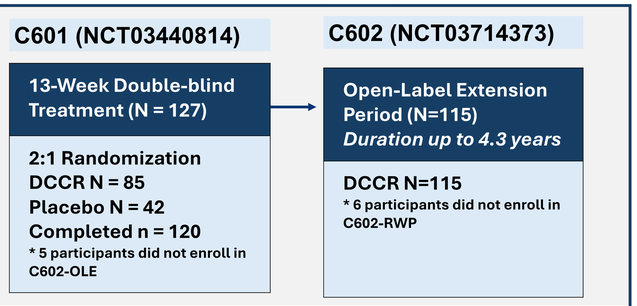
Diazoxide Choline Extended-Release (DCCR)

DCCR is a once daily, extended-release tablet, which provides for stable plasma concentrations and absorption throughout the GI tract. DCCR tablets have recently been approved by the FDA as VYKAT™ XR for the treatment of hyperphagia in individuals 4 years and over with PWS.[3]

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 **(Figure 1)** followed by a 16-week, double-blind, placebo-controlled randomized withdrawal period.

Figure 1. C601/C602-OLE Study Design



STUDY AIMS

To evaluate whether DCCR improved hyperphagia in a subset of participants who were highly food-restricted at Baseline based on the "Restrict Food Access" domain of the Food Safe Zone (FSZ) who received DCCR in two Phase 3 studies.

METHODS

- Participants were considered highly food-restricted if they scored in the highest quartile (Q4; >9 points) of the "Restrict Food Access" domain at Baseline.
- Hyperphagia was assessed by the Hyperphagia Questionnaire for Clinical Trials (HQ-CT).

RESULTS

- Of 125 participants ≥4 years old with genetically-confirmed PWS treated with DCCR in the Phase 3 studies, 25 participants scored in the highest quartile of the "Restrict Food Access" domain **(Table 1)**.
- The highly food-restricted group tended to be older than the less restricted group (15.4 vs. 12.8 years), have higher baseline HQ-CT scores (24.6 versus 20.7), and higher BMI-Z (1.8 versus 1.5) **(Table 1)**.

Table 1. Baseline Characteristics

	Less Restricted (≤Q3) (N = 98)	Highly Restricted (>Q3) (N = 25)	Overall (N = 125)
Age (mean [±SD]), years	12.8 (6.3)	15.4 (9.3)	13.4 (7.0)
Sex (% male/female)	45.9 / 54.1	44.0 / 56.0	44.8 / 55.2
Weight (mean [±SD]), kg	59.8 (29.0)	70.9 (34.1)	62.1 (30.2)
BMI (mean[±SD]), kg/m2	26.6 (8.7)	31.3 (12.0)	27.6 (9.6)
BMI z-score (mean [±SD]), kg/m^2	1.5 (1.1)	1.8 (0.9)	1.5 (1.1)
Hyperphagia (HQ-CT) Total Score	20.7 (6.8)	24.6 (5.0)	21.5 (6.7)
PWS Subtype (% Deletion / Non-deletion / NA)	63.3 / 35.7 / 1.0	60.0 / 40.0 / 0	61.6 / 37.6 / 0.8
Ongoing Growth Hormone Use (% Yes / No)	84.7 / 15.3	76.0 / 24.0	82.4 / 17.6

Abbreviations: BMI, body mass index; FSZ, Food Safe Zone; HQ-CT, Hyperphagia Questionnaire for Clinical Trials; NA, not available; PWS, Prader-Willi syndrome; SD, standard deviation.
Note: Two participants did not have Baseline FSZ Restrict Food Access Domain Scores.

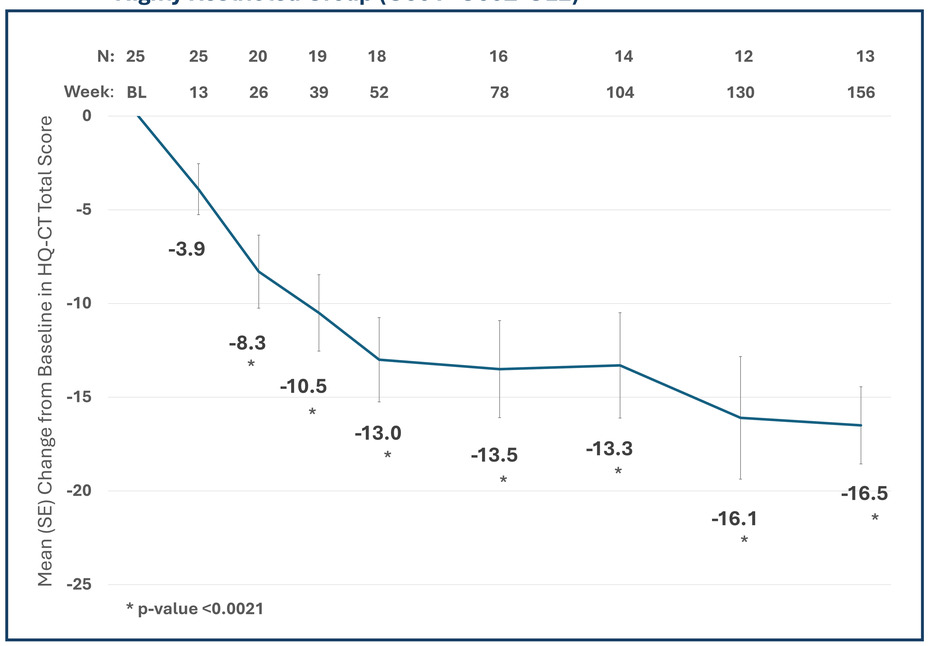
- At Baseline, greater food restriction was associated with higher HQ-CT Total Scores (Pearson correlation [95% CI]: 0.37 (0.20, 0.51); p<0.0001) **(Table 2)**.

Table 2. C602-OLE Pearson Correlation between Baseline HQ-CT Total Score (0-36) and Baseline Score of Restrict Food Access Domain (0-12)

	Less Restricted (≤Q3) (N = 98)	Highly Restricted (>Q3) (N = 25)	Overall (N = 123)
Pearson Correlation (95%CI)	0.31 (0.12, 0.48)	0.06 (-0.34, 0.45)	**0.37** (0.20, 0.51)
P-value	0.0017	0.7661	**<0.0001**

Abbreviations: CI, confidence interval; HQ-CT, Hyperphagia Questionnaire for Clinical Trials.

Figure 2. Mean (SE) HQ-CT Total Score (0-36) Change from Baseline – Highly Restricted Group (C601+C602-OLE)



- Upon treatment, statistically significant, clinically meaningful reductions (improvements) in HQ-CT Total Scores were observed in both groups at all timepoints from Week 26 (p<0.0021) through Year 3 (last assessment).
- In the highly food-restricted group, mean changes were -13.0, -13.3, and -16.5 at Weeks 52, 104, and 156, respectively (**Figure 2**). In the less-restricted group, mean changes were: -10.0, -11.2, and -11.6 at Weeks 52, 104, and 156, respectively.

CONCLUSIONS

- **Participants with stricter food controls at Baseline tended to have higher HQ-CT Total Scores compared to those with less restrictive food controls.**
- **These findings illustrate the need for new therapeutic options, since restricting food access does not lead to reduced hyperphagia symptoms.**
- **After treatment with DCCR, both groups of participants exhibited statistically significant, clinically meaningful reductions in HQ-CT Total Scores.**
- **Nonetheless, these data demonstrate that regardless of the degree of food restriction at Baseline, participants in either group appear to experience clinical benefit after treatment with DCCR.**

REFERENCES

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3. VYKAT™ XR [package insert]. Soleno Therapeutics, Inc. 2025.

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