Safety and Efficacy of DCCR in Patients with Prader-Willi Syndrome who have Pre-Diabetes or Diabetes

Jennifer L. Miller MD[1], Jack A. Yanovski MD, PhD[2], Neil M. Cowen PhD[3], Julie S. Perry MD[3], Jing Gong[3], Michael Huang MD[3], Anish Bhatnagar MD[3], Evelien Gevers MD, PhD[4,5]

1. University of Florida, Gainesville, FL, USA, 2. *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, Bethesda, MD USA 3. Soleno Therapeutics, Inc., Redwood City, CA, USA, 4. Queen Mary University of London, Barts and The London Medical School, William Harvey Research Institute, Centre for Endocrinology, London, UK, 5. Barts Health NHS Trust Royal London Hospital, London, UK.

Abstract #44
United in HOPE
2025 PWS Conference
June 25-26, 2025
Phoenix, AZ

INTRODUCTION

Prader-Willi Syndrome

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

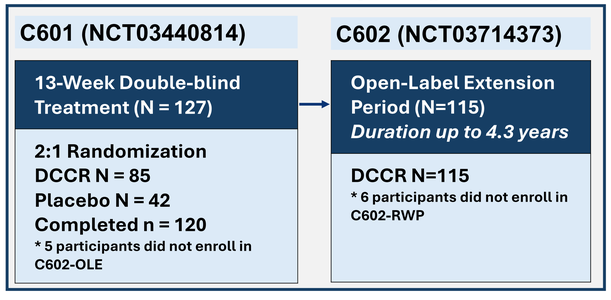
Diazoxide Choline Extended-Release (DCCR)

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, placebo-controlled, parallel arm study in participants with genetically confirmed PWS, ages 4 and older.

Study C602 was a Phase 3 multicenter study that included an open-label extension 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 AIM

To analyze data from the Phase 3 studies to assess safety and efficacy of DCCR in individuals with PWS who have evidence of pre-diabetes or diabetes at baseline

METHODS

- Participants were classified as having evidence of pre-diabetes or Type-2 diabetes at Baseline by:
  - Review of their medical history
  - Use of glucose-lowering medications
  - Clinical laboratory values (*baseline fasting plasma glucose [FPG] ≥ 100 mg/dL or HbA1c ≥5.7% [6.5 mmol/L] for pre-diabetes and ≥ 6.5% [7.8 mmol/L] for T2DM)*
- Efficacy was measured using Hyperphagia Questionnaire for Clinical Trials (HQ-CT) Total Scores
- Safety was assessed by hyperglycemia-related laboratory values and adverse events (AEs)

Table 1. Baseline Characteristics

	With Diabetes/ Prediabetes (N = 75)	With Normoglycemia (N = 50)	Overall (N = 125)
Age (mean [±SD]), years	14.4 (6.3)	12.1 (7.8)	13.4 (7.0)
Sex (% male/female)	48.0 / 52.0	40.0 / 60.0	44.8 / 55.2
Weight (mean [±SD]), kg	70.9 (29.7)	48.9 (25.9)	62.1 (30.2)
BMI (mean[±SD]), kg/m2	30.1 (9.9)	23.8 (7.9)	27.6 (9.6)
BMI z-score (mean [±SD]), kg/m^2	1.8 (1.0)	1.2 (1.1)	1.3 (1.1)
Hyperphagia (HQ-CT) Total Score	21.3 (6.8)	21.7 (6.6)	21.5 (6.7)
PWS Subtype (% Deletion / Non-deletion / NA)	65.3 / 33.3 / 1.3	56.0 / 44.0 / 0	61.6 / 37.6 / 0.8
GH Use (% Yes / No)	82.7 / 17.3	82.0 / 18.0	82.4 / 17.6
Hemoglobin A1c (mean [±SD]), %	5.7 (0.4)	5.3 (0.2)	5.6 (0.4)

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

Table 2. Adverse Events, Discontinuations, and Exposure

	With Diabetes/ Prediabetes (N = 75)	With Normoglycemia (N = 50)	Overall (N = 125)
Duration of DCCR Exposure mean (SD), days	919.5 (448.2)	921.6 (414.4)	920.4 (433.3)
Participants with any TEAE (%)	74 (98.7)	49 (98.0)	123 (98.4)
Participants with a SAE (%)	20 (26.7)	9 (18.0)	29 (23.2)
Hyperglycemia (%)	32 (42.7)	12 (24.0)	44 (35.2)
Blood glucose increased (%)	10 (13.3)	0 (0)	10 (8.0)
Diabetes mellitus (%)	0 (0)	1 (2.0)	1 (0.8)
Glucose tolerance impaired (%)	1 (1.3)	0 (0)	1 (0.8)
Glycosylated hemoglobin increased (%)	5 (5.7)	1 (2.0)	6 (4.8)
Hyperglycemia (%)	24 (32.0)	10 (20.0)	34 (27.2)
Impaired fasting glucose (%)	1 (1.3)	2 (4.0)	3 (2.4)
Type 2 diabetes mellitus (%)	4 (5.3)	0 (0)	4 (3.2)
Discontinued Study Drug early due to a TEAE (%)	3 (4.0)	3 (6.0)	6 (4.8)

Abbreviations: SAE, serious adverse event; TEAE, treatment-emergent adverse event.

Figure 2. Mean HbA1c (%) by Diabetes / Pre-diabetes Status at DCCR Baseline and Week 156

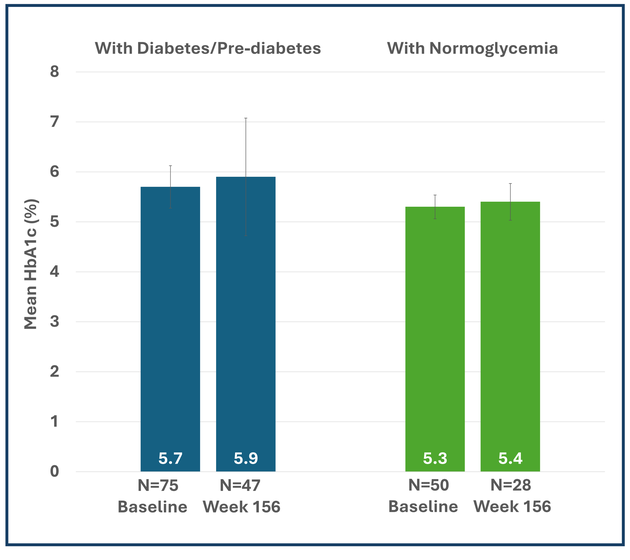
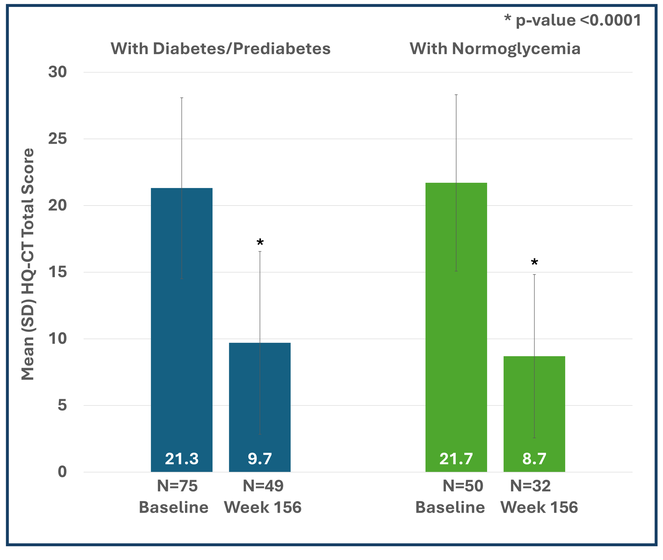


Figure 3. HQ-CT Total Score (0-36) by Diabetes / Pre-diabetes Status at DCCR Baseline and Week 156



RESULTS

- Of 125 participants ≥4 years-old with genetically confirmed PWS who received DCCR in the Phase 3 program, 75 (60.0%) participants were identified as having evidence of pre-diabetes (PD) or diabetes (DM) at baseline (group with PD/DM) **(Table 1)**.
- Mean (SD) HbA1c at Baseline and Week 156 was 5.7 (0.43) and 5.9 (1.18) vs 5.3 (0.24) and 5.4 (0.37), respectively, for participants with PD/DM and with normoglycemia **(Figure 2)**.
- Discontinuation rates due to TEAEs were low regardless of baseline status (4.0% in the PD/DM group, 6.0% in the group with normoglycemia) **(Table 2)**.
- Most TEAEs were Grade 1 or Grade 2 (75.2% overall). The number of Grade 3 TEAEs was similar between groups (26.7% in the group with PD/DM, 18.0% in the group with normoglycemia) **(Table 2)**.
- As expected, a greater proportion of hyperglycemia-related AEs were reported for participants in the group with PD/DM as compared to those in the group with normoglycemia (42.7% vs 24.0%, respectively); however, these events were generally manageable **(Table 2)**.
- Efficacy outcomes at Week 156 were similar between the 2 groups with mean (SD) reductions (improvement) in HQ-CT of 12.0 (9.4) ($p<0.0001$) and 12.9 (8.5) ($p<0.0001$) for the group with PD/DM and the group with normoglycemia, respectively **(Figure 3)**.

CONCLUSIONS

- **More than half of the participants with PWS in the DCCR Phase 3 studies had evidence of pre-diabetes or diabetes at baseline.**
- **DCCR can be administered safely and effectively to individuals with PWS who have PD/DM.**
- **Improvements in HQ-CT were comparable between participants with PD/DM and with normoglycemia.**
- **As expected, hyperglycemia-related adverse events were reported in a greater proportion of participants with a history of PD/DM. Mean HbA1c after 156 weeks of treatment remained in the prediabetic range for those with PD/DM, and below for those with normoglycemia.**
- **Importantly, participants treated with DCCR in the Phase 3 studies remained on study and had high treatment compliance, regardless of PD/DM status or occurrence of hyperglycemia-related adverse events.**

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.

ACKNOWLEDGMENTS

Phase 3 program study investigators, participants and their families. The authors acknowledge Jessica Dronen, MSc, for providing medical writing support.

CONTACT INFORMATION

For more information, contact Michael Huang at mhuang@soleno.life.

ELECTRONIC POSTER
Copies obtained through the QR code are for personal use only.