Characterization of Peripheral Edema in Individuals with Prader-Willi Syndrome During Long-term Administration of Diazoxide Choline Extended-Release Tablet (DCCR)

Abstract MON-662
ENDO 2025
July 12-15, 2025
San Francisco, CA

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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]

Diazoxide choline extended-release (DCCR)

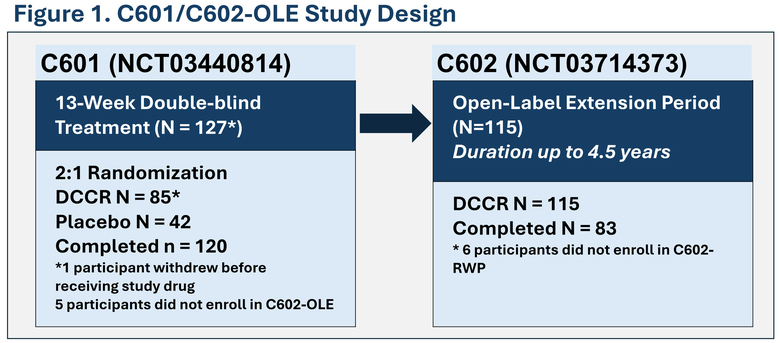
DCCR is a non-diuretic benzothiadiazine and is the choline salt of diazoxide.

DCCR is a once daily, extended-release tablet that 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 years and older.

Study C602-OLE was a Phase 3 multicenter extension of Study C601. The study included an open-label extension (OLE) period of up to 4.5 years followed by a double-blind, placebo-controlled randomized withdrawal period of 16 weeks.

Figure 1. C601/C602-OLE Study Design



AIMS

To characterize peripheral edema in clinical trial participants with PWS during administration of DCCR for up to 4.5 years across studies C601 and C602-OLE.

METHODS

- We analyzed data for 125 participants who received at least one dose of DCCR during Studies C601 or C602-OLE.
- Adverse events (AE) related to peripheral edema were analyzed and time to first onset was estimated from the product-limit (Kaplan-Meier) method.
- Additionally, lower extremity pitting examinations were performed with digital pressure and findings were reported.

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.

Table 1. Baseline Characteristics

	Overall (N = 125)
Age Mean (SD), Years	13.4 (7.0)
Sex % Male/Female	44.8 / 55.2
Weight Mean (SD), kg	62.1 (30.2)
BMI Mean (SD), kg/m^2	27.6 (9.6)
BMI z-score Mean (SD), kg/m^2	1.5 (1.1)
PWS Subtype % Deletion / Non-deletion / NA	61.6 / 37.6 / 0.8
Ongoing Growth Hormone Use % Yes / No	82.4 / 17.6
Peripheral Edema % Yes / No	15.2 / 84.8

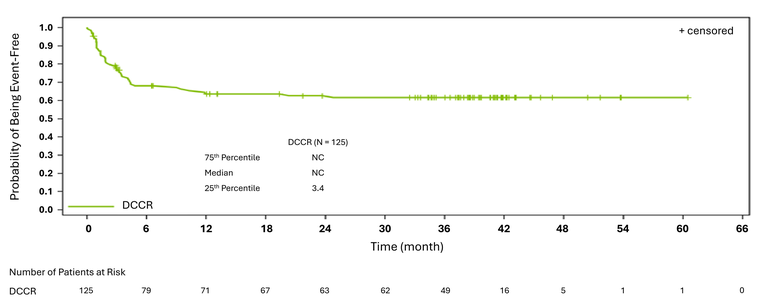
Table 2. Adverse Events

	Overall (N = 125)
Participants with any AE, n (%)	123 (98.4)
Any Peripheral Edema AE, n (%)	46 (36.8)
Edema, peripheral, n (%)	43 (34.4)
Peripheral swelling, n (%)	5 (4.0)
	With Edema (N = 46)
Severity of Peripheral Edema AE	n (%)
Grade 1 or 2	44 (95.7)
Grade 3	2 (4.3)
Grade 4 or 5	0
Study Drug Dosing Changes due to Peripheral Edema	n (%)
Any dose change	9 (19.6)
Discontinuation	3 (6.5)
Dose reduction	4 (8.7)
Dose interruption	3 (6.5)
New Diuretic Administered	2 (4.3)

Table 3. Pitting Assessment

Baseline (N1 = 125)		Week 26 (N1 = 104)		Week 104 (N1 = 85)	
Grade	**n (%)**	**Grade**	**n (%)**	**Grade**	**n (%)**
No pitting	116 (92.8)	No pitting	96 (92.3)	No pitting	79 (92.9)
1+	9 (7.2)	1+	7 (6.7)	1+	6 (7.1)
		2+	1 (1.0)		
Week 13 (N1 = 123)		**Week 52 (N1 = 96)**		**Week 156 (N1 = 80)**	
Grade	**n (%)**	**Grade**	**n (%)**	**Grade**	**n (%)**
No pitting	108 (87.8)	No pitting	88 (91.7)	No pitting	74 (92.5)
1+	10 (8.1)	1+	8 (8.3)	1+	5 (6.3)
2+	3 (2.4)			2+	1 (1.3)
3+	2 (1.6)				

Figure 2. Time to Onset of First Peripheral Edema AE



RESULTS

- Prior to starting DCCR,15.2% of participants had a history of peripheral edema (including edema peripheral and peripheral swelling).
- Across Studies C601 and C602-OLE, mean DCCR exposure was ~2.5 years (median ~3.0 years, maximum 4.5 years).
- Peripheral edema AEs occurred in 46 (36.8%) participants:
  - Most peripheral edema AEs were mild to moderate (Grade 1 or 2)
  - Severe (Grade 3) peripheral edema AEs occurred infrequently
  - Relatively few (3 [6.5%]) participants discontinued study drug due to peripheral edema AEs
  - Peripheral edema management included dose reductions, dose interruptions, and initiation of new diuretic.
  - At nearly all study visits, no pitting was observed for >90% of participants on lower extremity examination
- Time to event analysis showed:
  - First onset of peripheral edema AEs typically occurred within the first 6 months of treatment
  - 68.0% of participants remained event-free at 6 months
  - 61.6% of participants remained event-free at 3 years

CONCLUSIONS

- **Administration of DCCR in study participants with PWS was associated with peripheral edema in a minority (36.8%) of patients.**
- **When present, peripheral edema tended to occur early in treatment, was usually Grade 1 or 2, and infrequently resulted in study drug interruption or discontinuation.**
- **Overall, DCCR was well tolerated in the intended population.**

ACKNOWLEDGMENTS

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

CONTACT INFORMATION

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AUTHOR CONFLICT OF INTEREST DISCLOSURES

Potential conflicts of interest may exist. Please refer to the Meeting App for details.

ABBREVIATIONS

AE = adverse event(s); BMI = body mass index; DCCR = diazoxide choline extended-release tablets; NA = not analyzed; NC = not calculated; OLE = open-label extension; PWS = Prader-Willi syndrome; RWP = randomized withdrawal period; SD = standard deviation.

ELECTRONIC POSTER and PLAIN LANGUAGE SUMMARY

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