Long-Term Results for Diazoxide Choline Extended-Release (DCCR) Tablets in Patients with Prader-Willi Syndrome: Developmental Behaviour Checklist 2 Response and Relationship to Hyperphagia Reductions

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DISCLOSURE STATEMENT

Dr. Evelien Gevers has the following potential conflicts of interest to report:

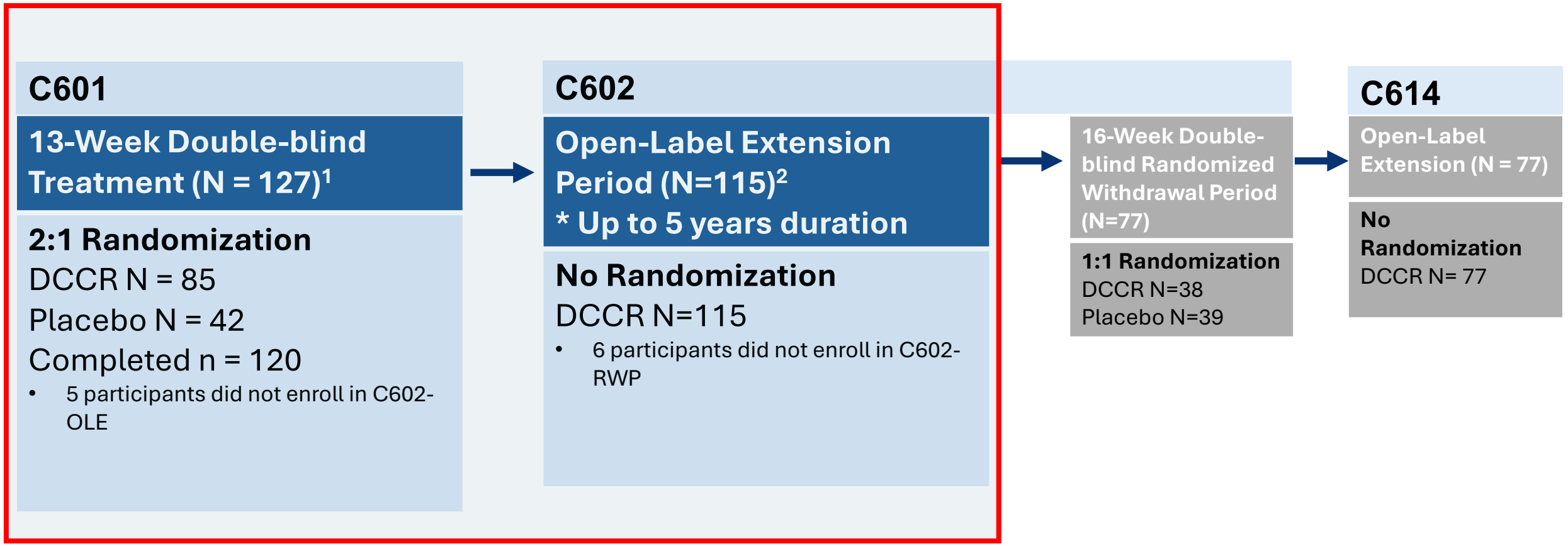
- Research Contracts: Dr. Gevers is national investigator for the UK and a principal investigator (PI) in Soleno's Prader-Willi syndrome (PWS) clinical trials

INTRODUCTION

- Prader-Willi syndrome (PWS) is a rare genetic neurobehavioural-metabolic disorder, characterized by hyperphagia, accumulation of excess fat, hypotonia, and behavioural/psychological complications.[1,2]
- There are currently no approved treatments for hyperphagia, a life-threatening hallmark of PWS, in Europe.
- Diazoxide choline extended-release tablet (DCCR) is in development for the treatment of hyperphagia in patients with PWS and was recently approved in the US by the FDA in March 2025
- DCCR is a once-daily, extended-release tablet that provides for stable plasma concentrations and absorption throughout the GI tract.

1. Butler MG, Miller JL, Forster JL. Prader-Willi syndrome – Clinical genetics, diagnosis and treatment approaches: An update. Curr Pediatr 2019; 15(4):207-244. 2. Miller Rev JL, Lynn CH, Driscoll DC, et al. Nutritional phases in Prader-Willi syndrome. Am J Med Genet Part A 2011; 155:1040–1049. Photos provided with consent of the caregiver through University of Florida, USA. Abbreviations: PWS, Prader-Willi syndrome; DCCR, diazoxide choline extended-release.

PHASE 3 DCCR PROGRAM



1. Miller et al., J Clin Endocrinol Metab 2023 Jun 16;108(7):1676-1685. 2. Miller et al., Obesity 2024 Feb;32(2):252-261.
Abbreviations: DCCR, diazoxide choline extended-release; OLE, open label extension; RWP, randomized-withdrawal period

ENDPOINTS TO BE DISCUSSED

Change in hyperphagia per Hyperphagia Questionnaire for Clinical Trials (HQ-CT) Total Score (Range: 0-36)

- Validated disease-specific scale completed by caregivers
- 9 questions focused on frequency and intensity of hyperphagia & food related-behaviours within the previous 2 weeks

Change in behaviours per Developmental Behaviour Checklist (DBC-2) Total Score (Range: 0-192)

- Validated, but non-disease-specific scale completed by parents/caregivers designed for use in people with intellectual and/or developmental disabilities
- 96-items to assess emotional and behavioural features (each item scored 0,1, or 2)
- Includes a Total Score and 6 subscales.
- Higher scores indicate worse symptoms; negative change represents improvement

Abbreviations: DBC-2, Developmental Behaviour Checklist; DCCR, diazoxide choline extended-release; HQ-CT, Hyperphagia Questionnaire for Clinical Trials; Prader-Willi syndrome

DEMOGRAPHICS AND BASELINE CHARACTERISTICS (STUDIES C601+C602)

At Baseline:

- Mean (SD) HQ-CT Total Score was 21.5 (6.7)
- Mean (SD) DBC-2 Total Score was 53.8 (24.51)*

Median duration of DCCR administration: ~3.0 years (maximum: 4.5 years)

*n=116

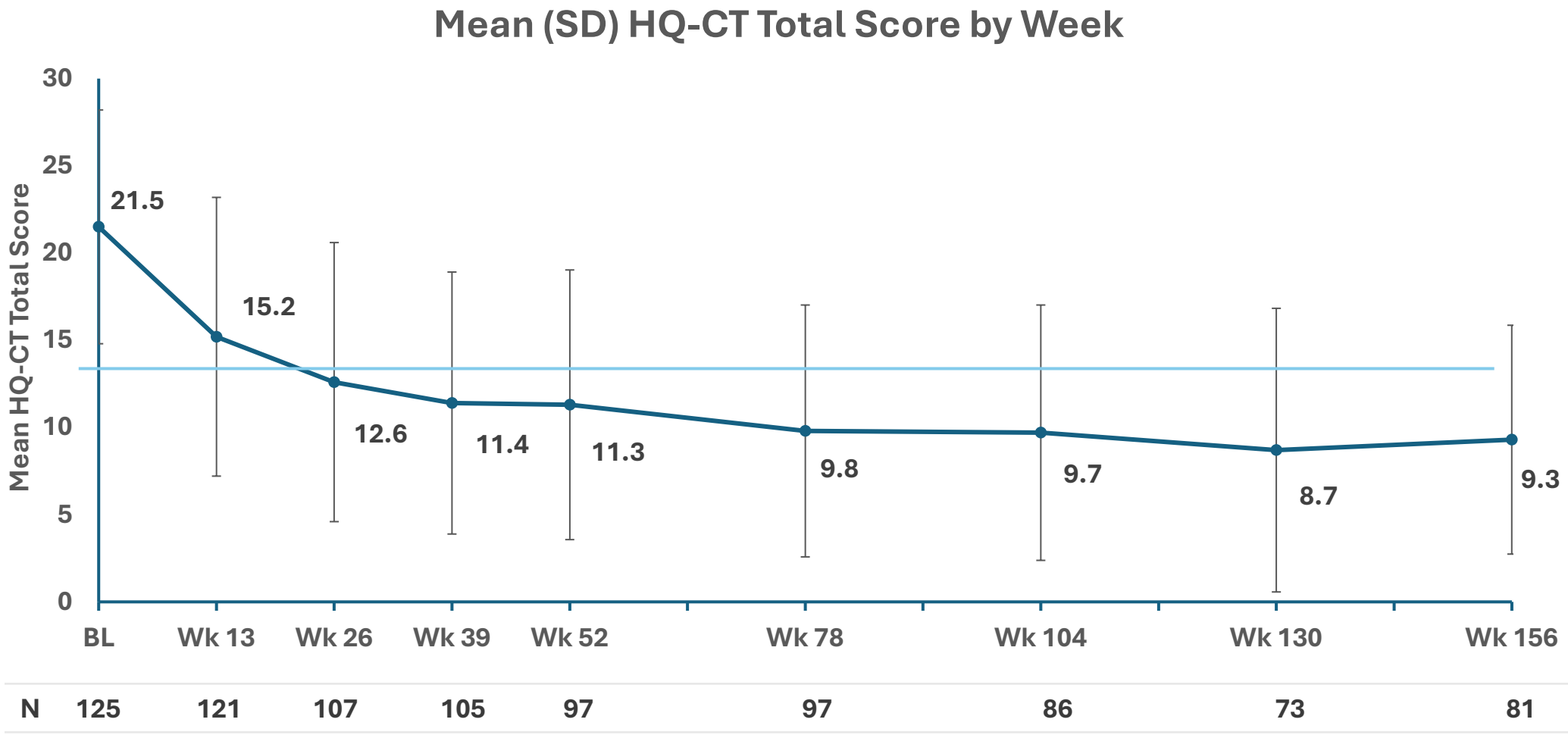
Baseline Characteristics	DCCR-Treated Participants N = 125
Age, years	
Mean (SD)	13.4 (6.98)
Median (range)	12 (4-44)
% Male / % Female	44.8 / 55.2
Race (% White / % Black / % Multiple)	84.8 / 4.8 / 6.4
Weight, mean (SD), kg	62.06 (30.15)
BMI, mean (SD), kg/m^2	27.56 (9.62)
BMI z-score, mean (SD)	1.53 (1.07)
Growth hormone, n (%)	103 (82%)
USA / UK (%)	80.0 / 20.0
HQ-CT total score (0-36), mean (SD)	21.5 (6.70)
PWS subtype	
Deletion, n (%)	77 (61.6)
Non-deletion, n (%)	47 (37.6)
Missing, n (%)	1 (0.8)

Abbreviations: BMI, body mass index; DBC-2, Developmental Behaviour Checklist; DCCR, diazoxide choline extended-release; HQ-CT, Hyperphagia Questionnaire for Clinical Trials; Prader-Willi syndrome; SD, standard deviation

REDUCTIONS IN HYPERPHAGIA OBSERVED AT ALL POST-BASELINE TIMEPOINTS (STUDIES C601+C602)

Statistically significant reduction in HQ-CT Total Scores at all time points through 3 years ($p<0.0001$)

HQ-CT Total Score Range 0-36

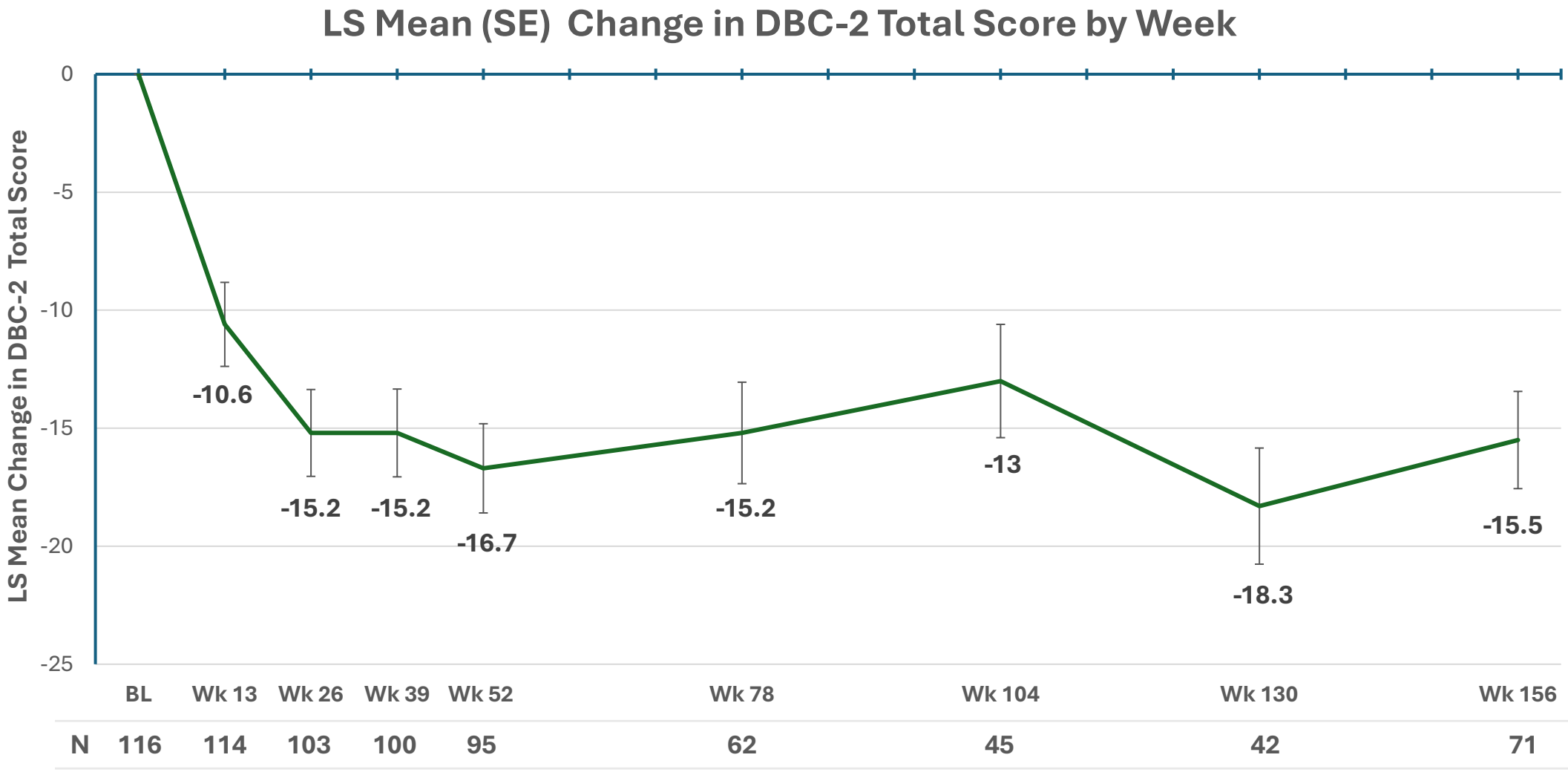


Abbreviations: BL, baseline; HQ-CT, Hyperphagia Questionnaire for Clinical Trials; SD, standard deviation; Wk, week

REDUCTION IN DBC2 SCORES OBSERVED AT ALL POST-BASELINE TIMEPOINTS (STUDIES C601+C602)

Statistically significant reduction in DBC-2 Total Scores at all time points through 3 years ($p<0.0001$)

DBC-2 Total Score Range 0-192

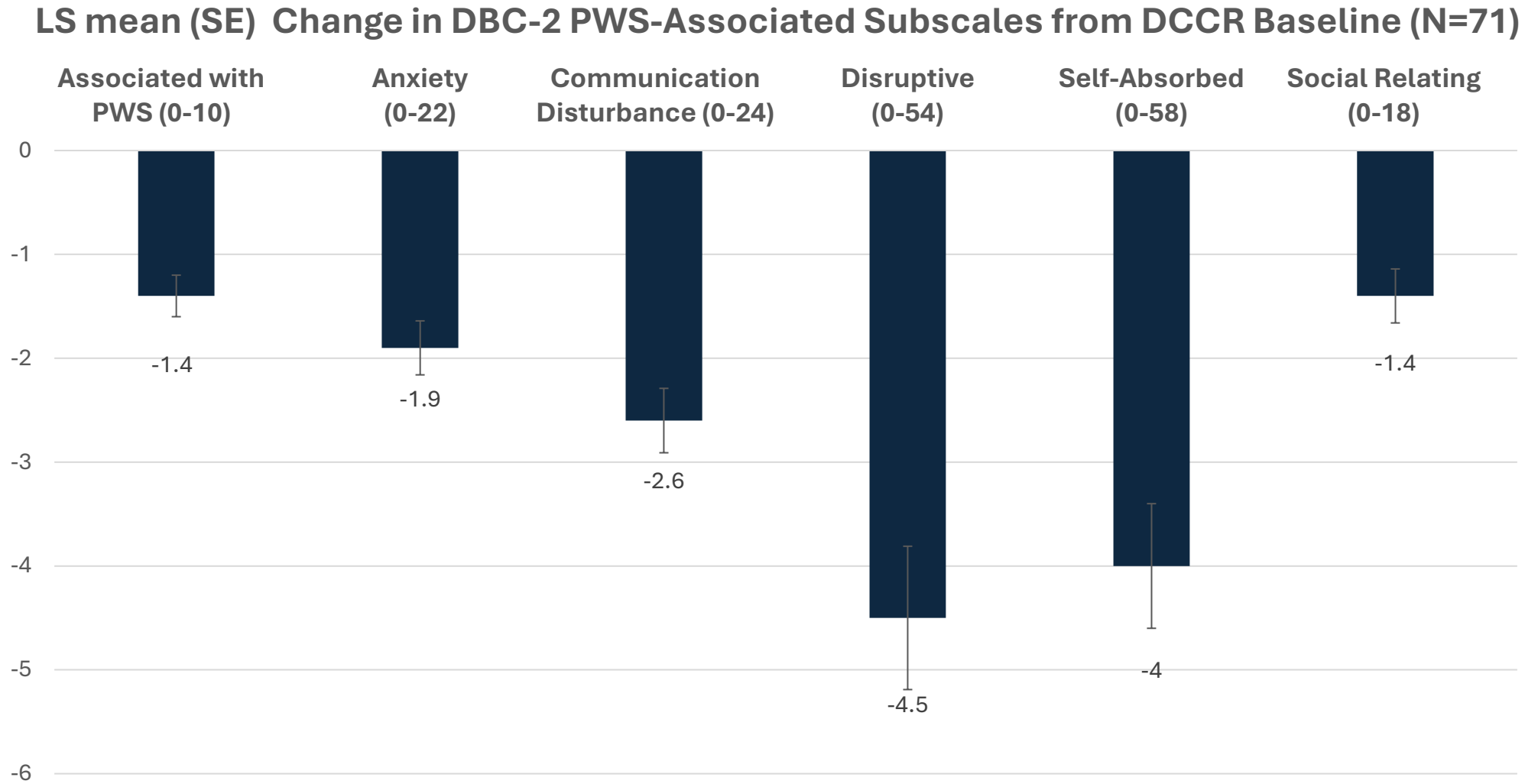


Abbreviations: DBC-2, Developmental Behaviour Checklist; DCCR, diazoxide choline extended-release; LS, least squares; SE, standard error; Wk, week

REDUCTIONS IN DBC2 SUBSCALES AT THREE YEARS POST DCCR-BASELINE (STUDIES C601+C602)

Significant reduction in all DBC-2 subscales at 3 years ($p<0.001$)

Improvements in DBC-2 subscale scores ranged from 29% to 39%



Abbreviations: DBC-2, Developmental Behaviour Checklist; DCCR, diazoxide choline extended-release; LS, least squares; PWS, Prader-Willi syndrome; SE, standard error

CORRELATION BETWEEN HYPERPHAGIA CHANGES AND BEHAVIOURAL CHANGES

Changes in hyperphagia (per changes in HQ-CT Total Score) and behaviours (per changes in DBC-2) appear to show some degree of independence.

DBC-2 Total Score & majority of subscales show moderate degree of correlation to HQ-CT Total Score (correlation coefficient 0.4-0.6)

Anxiety & Social Relating subscales show low degree of correlation to HQ-CT Total Score (correlation coefficient <0.4)

Correlation between changes in HQ-CT Total Score and DBC-2 Total Score/subscales at 52 weeks

Domain	Correlation
DBC-2 Total Score (N=91)	0.53
Anxiety (n=91)	0.25
Communication Disturbance (n=91)	0.46
Disruptive (n=91)	0.51
Associated with PWS (n=90)	0.41
Self-Absorbed (n=91)	0.56
Social Relating (n=91)	0.38

Abbreviations: DBC-2, Developmental Behaviour Checklist; DCCR, diazoxide choline extended-release; HQ-CT, Hyperphagia Questionnaire for Clinical Trials; PWS, Prader-Willi syndrome

CONCLUSIONS

Long-term administration of DCCR (for up to 3 years) was associated with clinically significant changes in key outcome measures in people with PWS.

- Improvements in hyperphagia per HQ-CT Total Score from Baseline
- Improvements in behaviours per DBC-2 Total Score from Baseline
- Changes in DBC-2 Total Scores (and most subscales) were moderately correlated to changes in HQ-CT Total Scores

Findings support the efficacy of DCCR in improving PWS-related behaviours. Notably, behavioural improvements were not solely the result or consequence of reductions in hyperphagia, suggesting a broader therapeutic effect.

Abbreviations: DBC-2, Developmental Behaviour Checklist; DCCR, diazoxide choline extended-release; HQ-CT, Hyperphagia Questionnaire for Clinical Trials; PWS, Prader-Willi syndrome

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Abbreviations: FPWR, Foundation for Prader-Willi Research; PWS, Prader-Willi syndrome; PWSA, Prader-Willi Syndrome Association; UK, United Kingdom; USA, United States of America