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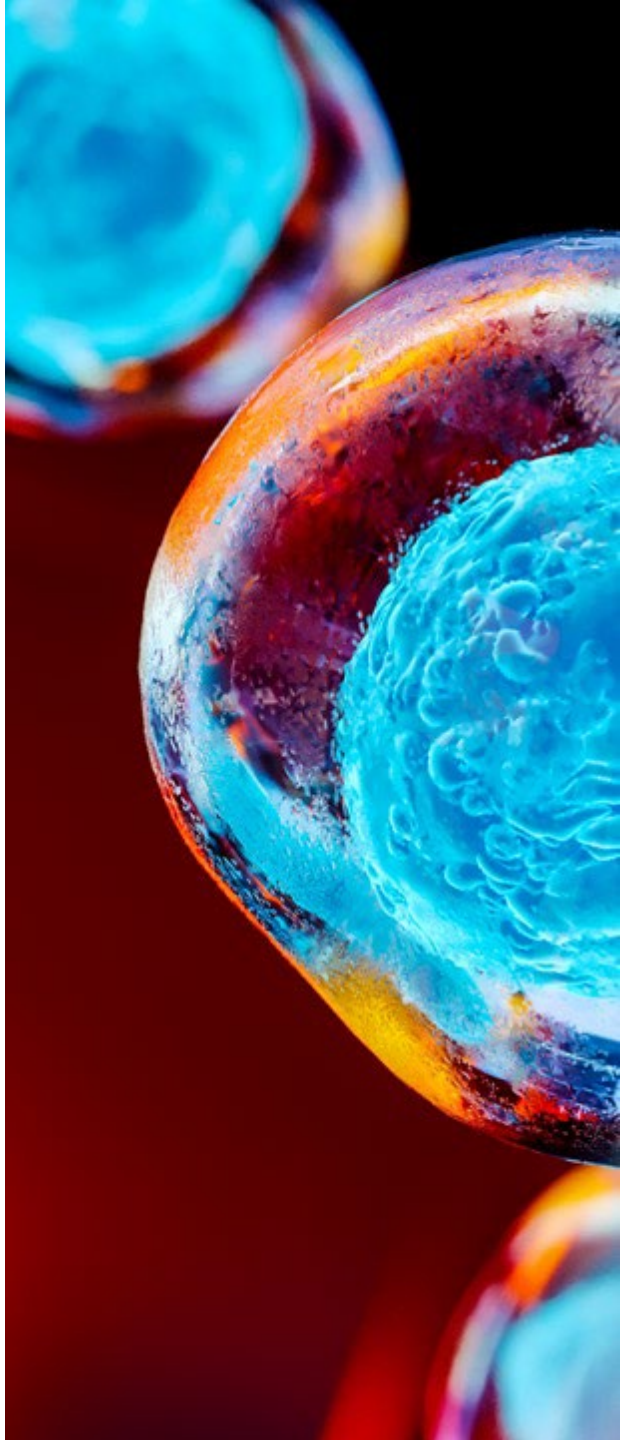

GLYCEMIC OUTCOMES OF DIAZOXIDE CHOLINE EXTENDED-RELEASE (DCCR) TABLETS ADMINISTERED FOR HYPERPHAGIA IN INDIVIDUALS WITH PRADER-WILLI SYNDROME OVER 4 YEARS

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ELECTRONIC PRESENTATION AND PLAIN LANGUAGE SUMMARY

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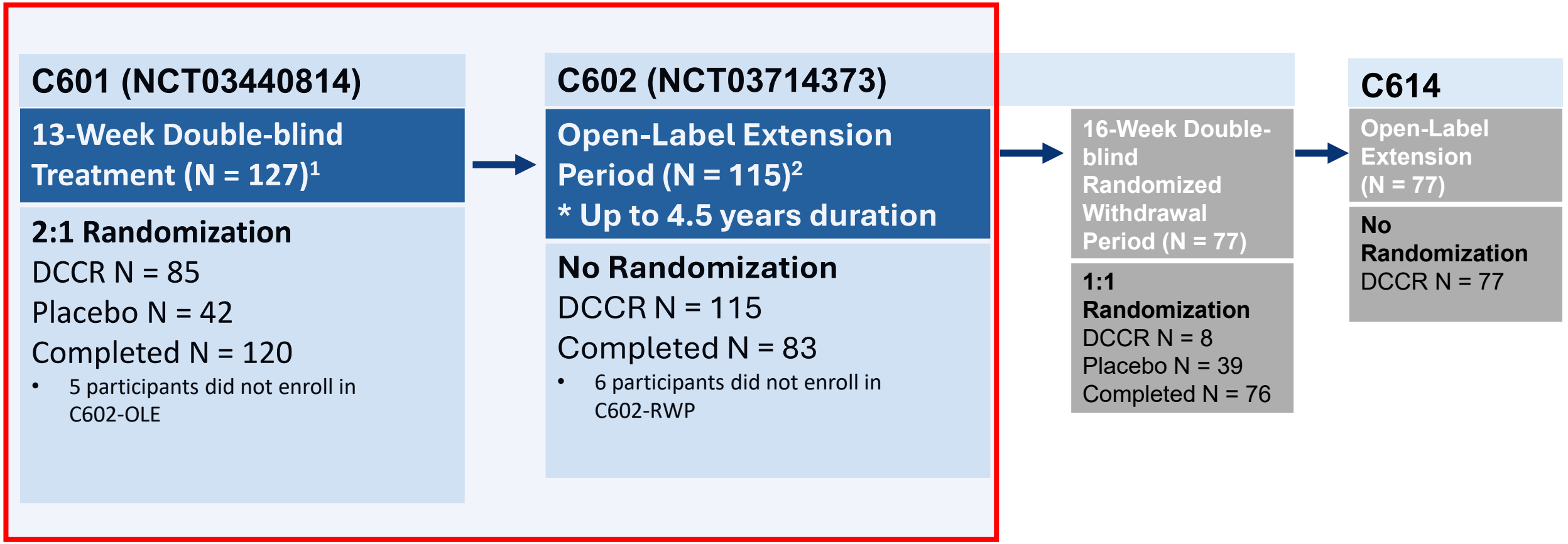
INTRODUCTION

- Prader-Willi syndrome (PWS) is a rare genetic neurobehavioral metabolic disorder, characterized by hyperphagia, accumulation of excess fat, hypotonia, and behavioral / psychological complications.[1,2]
- People living with PWS are at high risk of developing impaired glycemic control and diabetes.
- DCCR is a once-daily, extended-release tablet that provides for stable plasma concentrations and absorption throughout the GI tract.
- DCCR is approved under the brand name VYKAT™ XR. It is the first product approved by the FDA for the treatment of hyperphagia in individuals 4 years and over with PWS.
- We will review glycemic outcomes in clinical trial participants with PWS after long-term DCCR treatment.

1. Butler MG, Miller JL, Forster JL. Curr Pediatr 2019; 15(4):207-244. 2. Miller Rev JL, Lynn CH, Driscoll DC, et al. 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



The combined population from C601+C602-OLE includes 125 participants who received DCCR

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.

DEMOGRAPHICS AND BASELINE CHARACTERISTICS (STUDIES C601+C602-OLE)

At Baseline:

- 8.8% took glucose-lowering medications
- Mean (SD) HbA1c% was 5.55 (0.41)
- Mean (SD) fasting glucose (mg/dL) was 90 (11.45)
- 60% had a history of diabetes or prediabetes

DCCR exposure:

- Mean: ~2.5 years
- Median: ~3.0 years
- Maximum: 4.5 years
- 52% exceeded 3 years

DCCR 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, (%)	61.6
Non-deletion, (%)	37.6
Not available, (%)	0.8

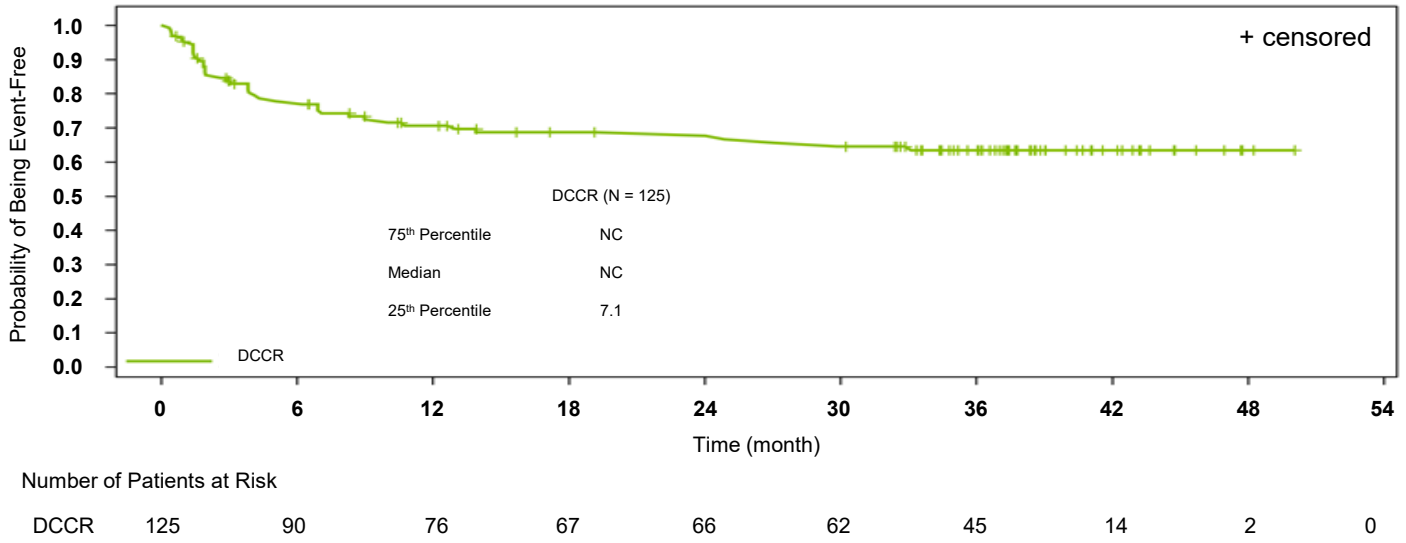
Abbreviations: BMI, body mass index; DCCR, diazoxide choline extended-release; HQ-CT, Hyperphagia Questionnaire for Clinical Trials; PWS, Prader-Willi syndrome; SD, standard deviation.

GYLCEMIC-RELATED ADVERSE EVENTS

Analysis Population (N = 125)	
Participants with any TEAE (%)	123 (98.4)
Hyperglycemia-related AE (%)	42 (33.6)
Blood glucose increased (%)	10 (8.0)
Diabetes mellitus (%)	1 (0.8)
Glucose tolerance impaired (%)	1 (0.8)
Hyperglycemia (%)	34 (27.2)
Insulin resistance (%)	2 (1.6)
Type 2 diabetes mellitus (%)	4 (3.2)
Dose changes due to hyperglycemia-related events	n (%)
Any study drug action	19 (15.2)
Discontinuation	2 (1.6)
Dose reduction	10 (8.0)
Dose interruption	8 (6.4)
Concomitant blood glucose-lowering medication initiated (%)	22 (17.6)

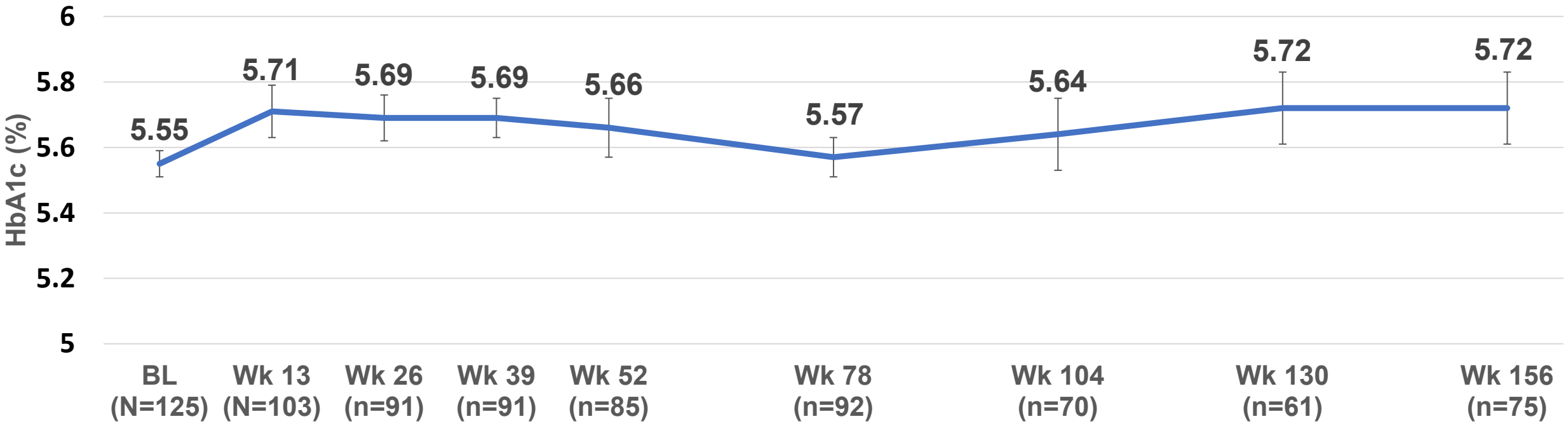
- Adverse events of hyperglycemia were reported by Investigators using a variety of preferred terms.
- Overall, hyperglycemia-related AEs were reported for 33.6% of participants in the analysis population.
- 77.7% of participants remained event-free at 6 months, 63.4% were event-free at 3 years

Time to Onset of First Hyperglycemia-related AE



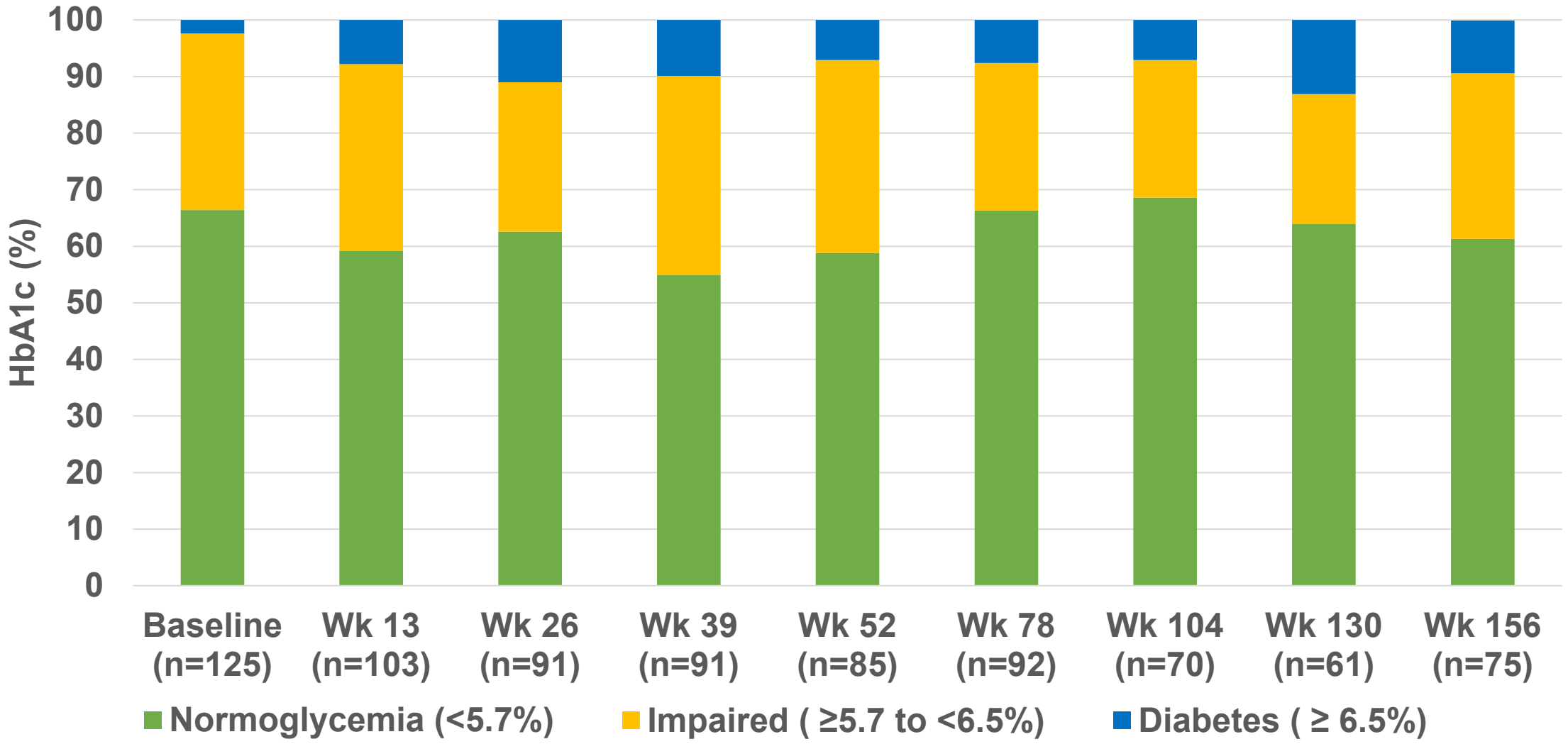
Abbreviations: AE, adverse event; DCCR, diazoxide choline extended-release; NC, not calculated; TEAE, treatment-emergent adverse event.

MEAN (SE) HBA1C OVER TIME



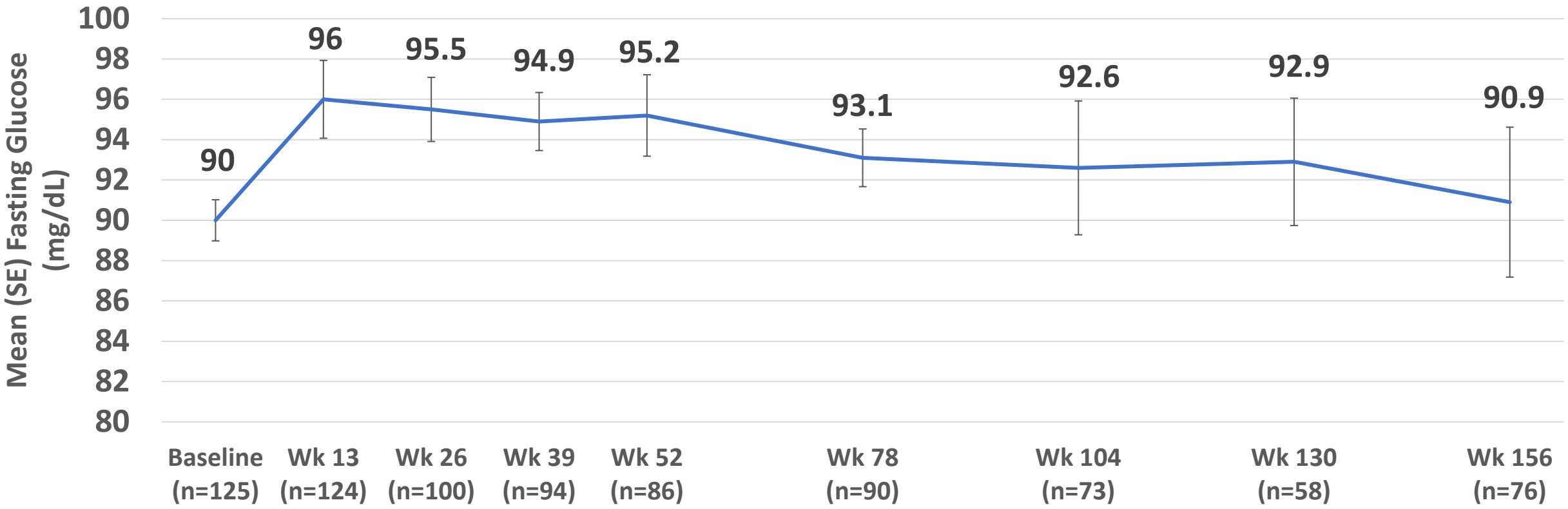
Abbreviations: BL, baseline; SE, standard error; Wk, week.

HBA1C (%) OVER TIME- CATEGORICAL



Abbreviation: Wk, week.

MEAN (SE) FASTING GLUCOSE OVER TIME



Abbreviations: SE, standard error; Wk, week.

CONCLUSIONS

- **Long-term (~3 years) administration of DCCR for the treatment of hyperphagia in individuals with PWS was generally well tolerated.**
  - Small mean increases observed in HbA1c after DCCR administration. Infrequently associated with clinically significant events.
  - Blood glucose increases typically occurred early, most commonly during titration.
- **Hyperglycemic adverse events were monitorable and generally manageable with standard of care concomitant medications, allowing for continuation of DCCR therapy.**

These findings support a favorable safety profile of DCCR, including consideration of hyperglycemia-related events, in the treatment of hyperphagia in patients with PWS.

Abbreviations: DCCR, diazoxide choline extended-release; 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.