

MARKED IMPROVEMENT IN METABOLIC PARAMETERS IN A PATIENT WITH ACTH-INDEPENDENT HYPERCORTISOLISM WHILE ON MIFEPRISTONE

Rebecca Ray, CRNP¹; Rachel Bunta, MBA¹; Pascal Dauphin, MD²

¹Corcept Therapeutics, Menlo Park, CA, United States; ²The Metabolic Group, Hendersonville, TN, United States



INTRODUCTION

Hypercortisolism is associated with metabolic disorders, including diabetes, hypertension, and obesity. If left untreated, hypercortisolism can lead to significant morbidity and mortality. The competitive glucocorticoid receptor antagonist mifepristone (Korlym[®], Corcept Therapeutics) is approved to control hyperglycemia secondary to hypercortisolism in adult patients with endogenous Cushing syndrome (CS) who have type 2 diabetes mellitus (T2DM) or glucose intolerance and have failed surgery or are not candidates for surgery.¹

We describe a case of a patient with a cortisol-secreting left adrenal adenoma (2.9 cm x 2.8 cm, HU=8) with high insulin requirements, obesity, and elevated blood pressure, treated with 5 antihypertensive agents. To the best of our knowledge, this is the first case report of a patient with only 1 adrenal gland and 1 kidney to be treated with mifepristone.

CLINICAL PRESENTATION

- A 75-year-old woman presented with a 22-year history of poorly controlled T2DM, polyneuropathy, and nephropathy (**Table 1**)

Table 1. Baseline Characteristics	
Age	75 y/o
Sex	Female
Weight	215 pounds
BMI	39.3 kg/m ²
Fasting blood glucose	198 mg/dL
HbA1c	7.7%
Daily insulin requirement	115 units
DST	4.64 µg/dL
ACTH	12 pg/mL
DHEAS	88 µg/dL
Adrenal imaging	Left adrenal adenoma 2.9 cm x 2.8 cm, HU=8
Potassium	4.4 mmol/L
GFR	37 mL/min/1.73 m ²
Creatinine	1.44 mg/dL

ACTH = adrenocorticotrophic hormone; BMI = body mass index; DHEAS = dehydroepiandrosterone sulfate; DST = dexamethasone suppression test; GFR = glomerular filtration rate; HbA1c = glycated hemoglobin; HU = Hounsfield units.

- She previously had a right nephrectomy and adrenalectomy secondary to renal carcinoma
- The patient was taking 5 antihypertensive medications, which controlled hypertension (**Table 2**)
- Biochemical workup and imaging confirmed hypercortisolism

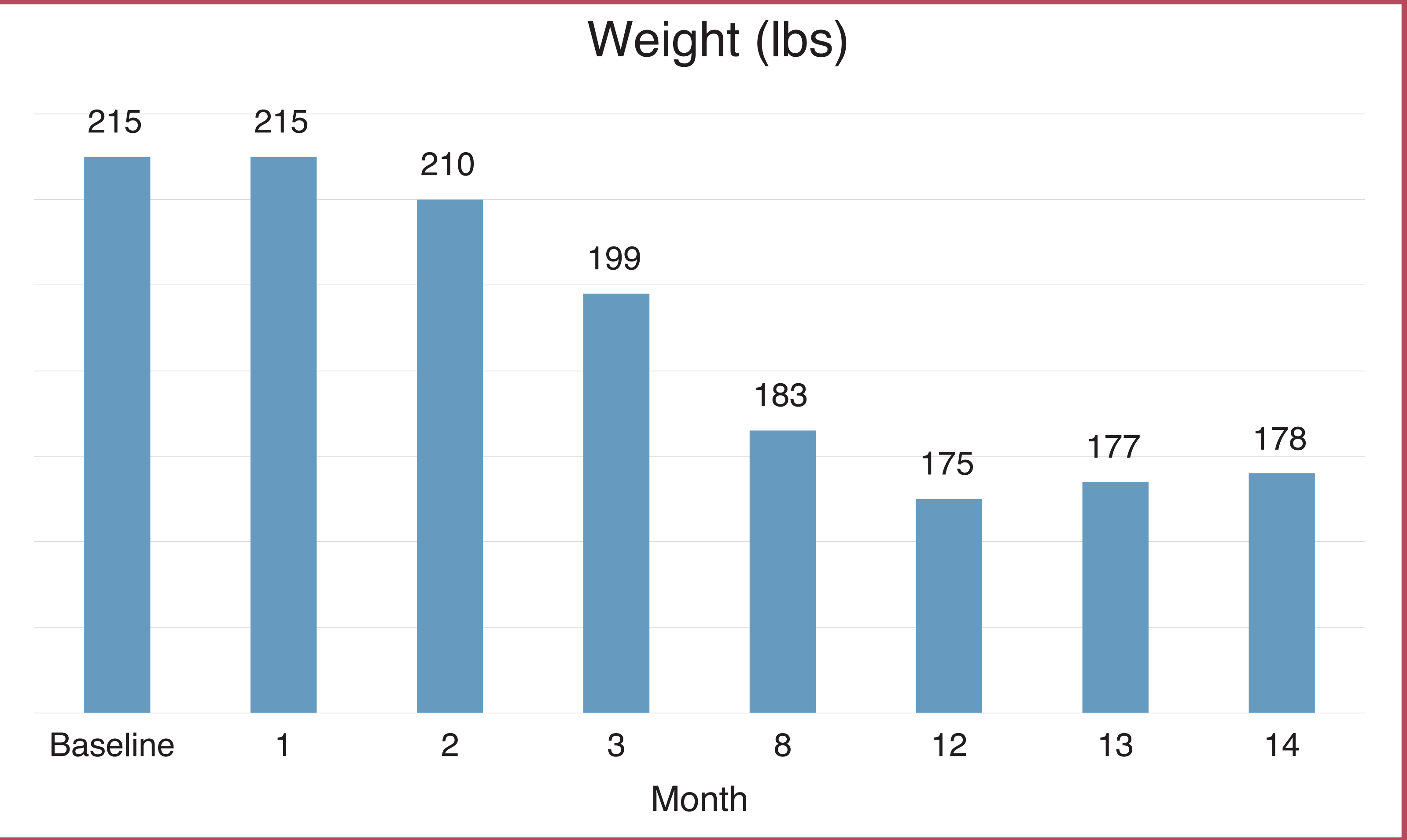
Table 2. Antihypertensive Medications	
Medication	Baseline Dosage
Spironolactone	50 mg QD
Metoprolol tartrate	50 mg BID
Hydrochlorothiazide	50 mg QD
Hydralazine	75 mg TID
Losartan	50 mg QD

BID = twice daily; QD = every day; TID = three times daily.

TREATMENT SELECTION AND RESULTS

- A second adrenalectomy was considered but rejected because the patient would require lifelong corticosteroid and mineralocorticoid replacement
- Mifepristone was initiated at 300 mg and titrated to 600 mg 2 weeks later
- Clinical response with improvement in blood sugars and blood pressure was observed by month 2: the patient was discontinued from losartan and hydrochlorothiazide in the second month while maintaining blood pressure control of 125/65 mmHg
- The patient experienced cortisol withdrawal symptoms, including nausea and fatigue, so she was switched to doses of 300 mg and 600 mg of mifepristone on alternate days
- After the first month of mifepristone initiation, the patient experienced hypokalemia with a potassium level of 2.9 mmol/L. Spironolactone was increased to 50 mg BID; her potassium increased to 3.2 mmol/L. Potassium chloride 20 mEq was then started, and potassium increased to 3.7 mmol/L
- The patient lost a total of 37 pounds (**Figure 1**), and body mass index decreased from 39.3 kg/m² to 32.6 kg/m² after 14 months

Figure 1. Change in Weight Over 14 Months



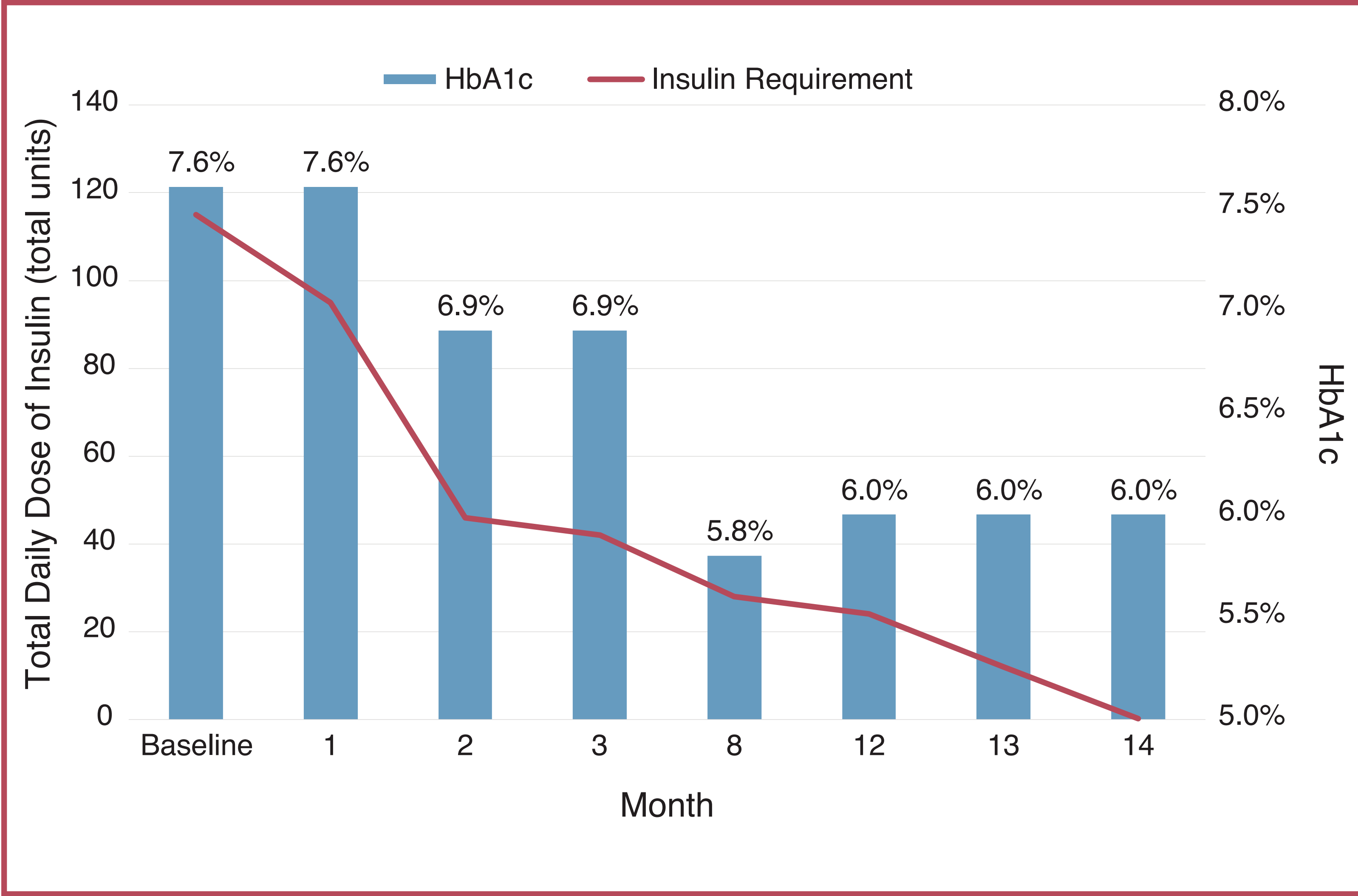
- Blood pressure remained controlled through 14 months

- The patient’s HbA1c improved from 7.6% to 6% while consistently lowering the insulin requirements (**Figure 2**). However, the patient experienced an observed in-office episode of hypoglycemia unawareness that prompted a professional continuous glucose monitor to be placed. Results of continuous glucose monitoring (CGM) revealed prolonged episodes of nocturnal hypoglycemia unawareness, leading to the eventual discontinuation of insulin and initiation of a glucagon-like peptide 1 (GLP-1) (**Figure 3**)

- ACTH level increased from 12 pg/mL to 52 pg/mL after 8 months

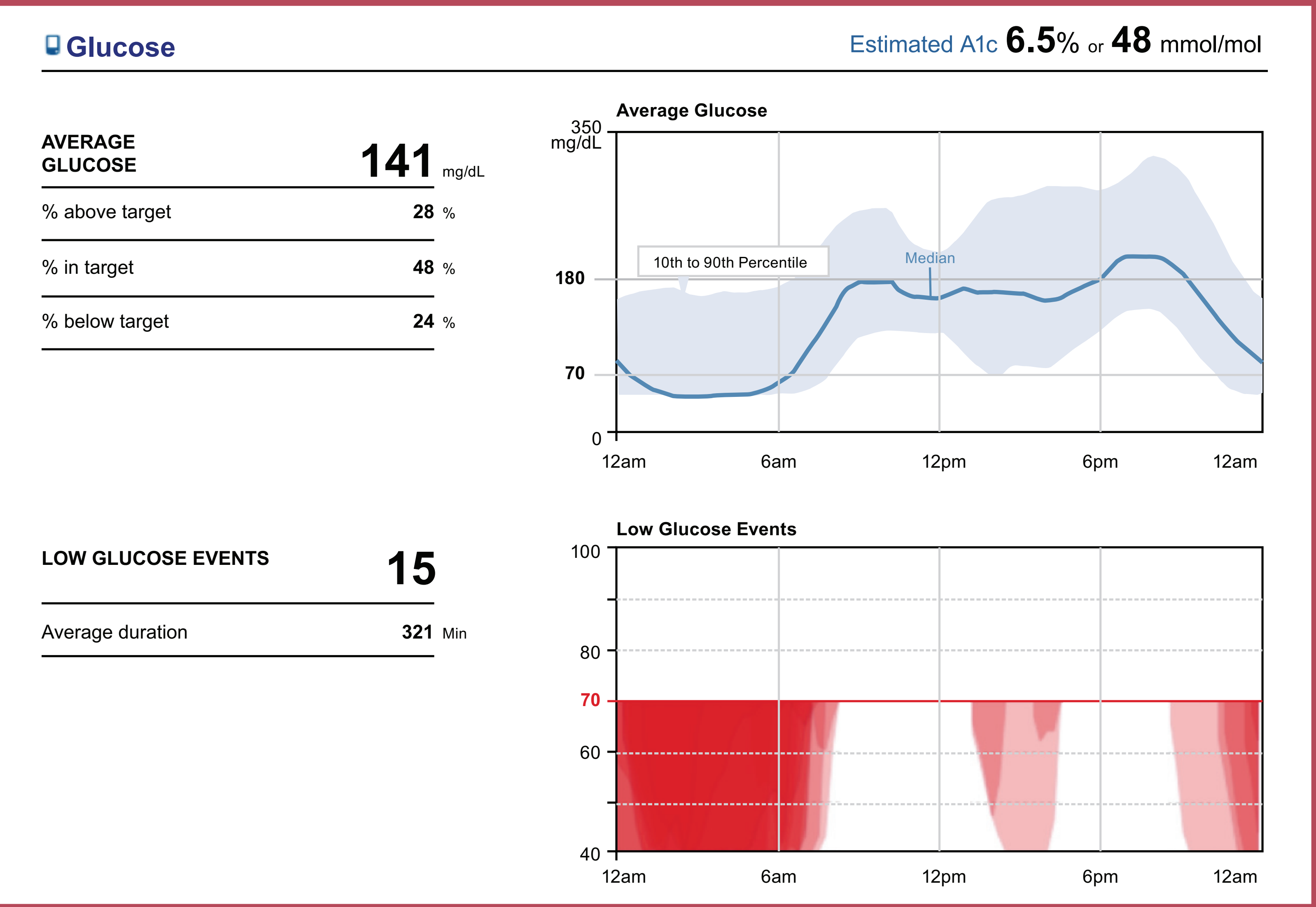
- GFR was maintained throughout therapy

Figure 2. Change in HbA1c and Insulin Requirements Over 14 Months



HbA1c = glycated hemoglobin.

Figure 3. CGM Data



CGM = continuous glucose monitoring.

DISCUSSION

- Per the AACE/ACE 2016 Consensus Statement, “CGM can be used to identify hypoglycemia in elderly patients and those with hypoglycemia unawareness”²
- Mifepristone is an insulin sensitizer and works quickly within the cells’ DNA; therefore, close monitoring of glycemic control is paramount to prevent hypoglycemia
- This report details a patient with CS who was treated with mifepristone for 14 months and had improved metabolic parameters such as weight loss, discontinuation of insulin, and discontinuation of 2 blood pressure medications

REFERENCES

- Korlym [package insert]. Menlo Park, CA: Corcept Therapeutics; 2017.
- Fonseca VA, et al. *Endocr Pract.* 2016;22 (8):1008-21.

DISCLOSURES

RR: Employee, Corcept Therapeutics.
RB: Employee, Corcept Therapeutics.
PD: Speaker, Takeda, BI, Astra Zeneca, Merck, Janssen, AbbVie, Lilly, Sanofi-Aventis, Novo Nordisk, Orexigen.

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