Characterization of Patients With Difficult-to-Control Type 2 Diabetes and a Post–Dexamethasone Suppression Test Cortisol of 1.2–1.8 µg/dL: Findings From a Large Prospective Study

Robert S. Busch,[1] Richard J. Auchus,[2] Timothy Bailey,[3] Lawrence Blonde,[4] John B. Buse,[5] Elena A. Christofides,[6] Ralph A. DeFronzo,[7] Bradley Eilerman,[8] Vivian Fonseca,[9] Yehuda Handelsman,[10] Michael H. Shanik,[11] Lance Sloan,[12] Guillermo Umpierrez,[13] Iulia Cristina Tudor,[14] Daniel Einhorn[14] for the CATALYST Investigators

[1]Albany Medical College, Community Endocrine Group, Albany, NY; [2]Departments of Pharmacology & Internal Medicine, Division of Metabolism, Endocrinology, & Diabetes, University of Michigan, Ann Arbor, MI; [3]Headlands Research AMCR Institute, Escondido, CA; [4]Ochsner Diabetes Clinical Research Unit, Frank Riddick Diabetes Institute, Endocrinology Department, Ochsner Health, New Orleans, LA; [5]University of North Carolina School of Medicine, Chapel Hill, NC; [6]Endocrinology Associates, Columbus, OH; [7]University of Texas Health Science Center, San Antonio, TX; [8]St. Elizabeth Physicians, Covington, KY; [9]Tulane University, New Orleans, LA; [10]Metabolic Institute of America, Tarzana, CA; [11]Endocrine Associates of Long Island, Smithtown, NY; [12]Texas Institute for Kidney and Endocrine Disorders, Lufkin, TX; [13]Emory University School of Medicine, Atlanta, GA; [14]Corcept Therapeutics Incorporated, Redwood City, CA

Contact: Daniel Einhorn (deinhorn@corcept.com)

INTRODUCTION

- Part 1 of the CATALYST study (NCT05772169), the largest prospective study to date to assess the prevalence of endogenous hypercortisolism in participants with difficult-to-control type 2 diabetes (T2D), found a hypercortisolism prevalence of 23.8% in this population[1,2]
- In the CATALYST study, hypercortisolism was defined as post–1-mg dexamethasone suppression test (DST) cortisol >1.8 µg/dL with appropriate dexamethasone level (≥140 ng/dL) and common causes for false-positive DST results excluded.[2] However, any level of hypercortisolism has been associated with increased cardiometabolic risk and morbidity[3]
- Although the DST threshold for hypercortisolism diagnosis is >1.8 µg/dL,[4] data suggest that the 95th percentile value for post-DST cortisol in normal control individuals is 1.2 µg/dL[5]
- CATALYST Part 1 collected data on participants with post-DST cortisol <1.2 µg/dL, 1.2–1.8 µg/dL, and >1.8 µg/dL, which allowed an assessment of whether there are any commonalities or differences among these groups

AIM

- To compare characteristics of participants in the CATALYST study with post-DST cortisol levels <1.2 µg/dL, 1.2–1.8 µg/dL, and >1.8 µg/dL

METHODS

- CATALYST enrolled adults aged 18 to 80 years with difficult-to-control T2D and hemoglobin A1c 7.5% to 11.5% despite taking:
  - ≥3 glucose-lowering medications
  - Insulin and any other glucose-lowering medication(s)
  - ≥2 glucose-lowering medications and having ≥1 microvascular or macrovascular complication(s) and/or
  - ≥2 glucose-lowering and ≥2 blood pressure–lowering medications
- Participants were screened for hypercortisolism, defined as above
- Participants with common causes of false-positive DST results (eg, use of oral contraceptive pills; excessive alcohol consumption; severe untreated sleep apnea; severe psychiatric, medical, or surgical illness; night-shift work; or hemodialysis/end-stage renal disease) were excluded
- Baseline characteristics were assessed and summarized using descriptive statistics
- Univariate and multivariate logistic regressions were performed

RESULTS

- Post-DST cortisol levels were <1.2 µg/dL in 51%, 1.2–1.8 µg/dL in 25%, and >1.8 µg/dL in 24% of participants (**Table 1**)
  - Post-DST cortisol values appeared to follow a normal distribution in both the <1.2 µg/dL and 1.2–1.8 µg/dL groups, with similar within-group mean and median post-DST cortisol values

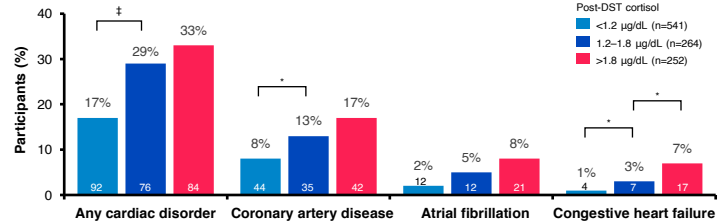
Table 1. Baseline Demographics and Characteristics Across Post-DST Cortisol Groups

	Post-DST cortisol <1.2 µg/dL (n=541)	Post-DST cortisol 1.2–1.8 µg/dL (n=264)	Post-DST cortisol >1.8 µg/dL (hypercortisolism) (n=252)
Age, y, mean (SD)	58.3 (10.7)	62.8 (9.5)	63.8 (9.6)
Female, n (%)	250 (46.2)	120 (45.5)	109 (43.3)
Race, n (%) Asian Black or African American White Other	 30 (5.5) 93 (17.2) 378 (69.9) 40 (7.4)	 12 (4.5) 53 (20.1) 183 (69.3) 16 (6.1)	 5 (2.0) 55 (21.8) 187 (74.2) 5 (2.0)
Ethnicity not Hispanic/Latino,[a] n (%)	347 (64.1)	200 (75.8)	218 (86.5)
BMI, kg/m^2, mean (SD)	33.9 (7.1)	33.0 (7.0)	33.1 (7.7)
Waist circumference, cm, mean (SD) [n]	113.1 (16.6) [534]	111.3 (17.1) [262]	113.5 (17.7) [249]
Post-DST cortisol, µg/dL Mean (SD) Median (range)	 0.9 (0.2) 0.9 (0.1–1.2)	 1.4 (0.2) 1.4 (1.2–1.8)	 3.5 (2.8) 2.6 (1.8–24.8)
SBP, mm Hg, mean (SD) [n]	127.6 (15.7) [541]	127.7 (16.9) [263]	127.4 (16.4) [252]
DBP, mm Hg, mean (SD) [n]	75.5 (9.6) [541]	75.4 (10.6) [263]	74.8 (9.5) [252]
HbA1c, %, mean (SD)	8.8 (1.1)	8.7 (1.0)	8.8 (1.1)

[a]Ethnicity group missing for 14 participants for the <1.2 µg/dL group, 10 participants for the 1.2–1.8 µg/dL group, and 13 participants for the >1.8 µg/dL group.
BMI, body mass index; DBP, diastolic blood pressure; DST, dexamethasone suppression test; HbA1c, hemoglobin A1c; SBP, systolic blood pressure; SD, standard deviation.

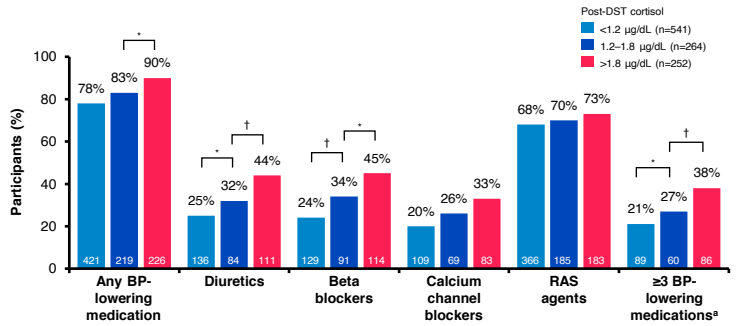
- An increasing post-DST cortisol level was associated with a greater prevalence of cardiac comorbidities (**Figure 1**) and use of a higher number of blood pressure medications (**Figure 2**)

Figure 1. Prevalence of Cardiac Comorbidities Across Post-DST Cortisol Subgroups



*P<0.05. †P=0.0001.
DST, dexamethasone suppression test.

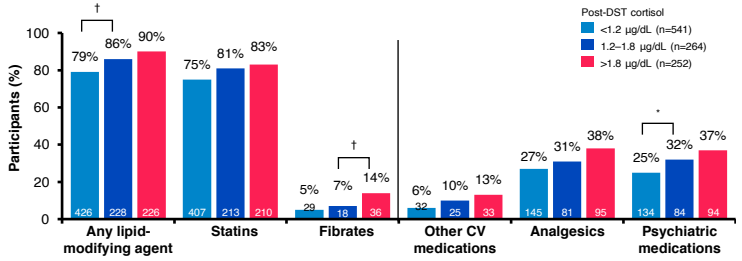
Figure 2. Blood Pressure–Lowering Medication Use Across Post-DST Cortisol Subgroups



*P<0.05. †P<0.01.
[a]Total population numbers by post-DST cortisol level: <1.2 µg/dL, n=421; 1.2–1.8 µg/dL, n=219; >1.8 µg/dL, n=226.
BP, blood pressure; DST, dexamethasone suppression test; RAS, renin-angiotensin system.

- The use of lipid-modifying agents, including statins and fibrates, as well as other cardiovascular medications, analgesics, and psychiatric medications was more prevalent with increasing post-DST cortisol levels (**Figure 3**)

Figure 3. Use of Lipid-Lowering Agents, Analgesics, and Psychiatric Medications Across Post-DST Cortisol Subgroups



*P<0.05. †P<0.01.
CV, cardiovascular; DST, dexamethasone suppression test.

- Factors independently associated with post-DST cortisol >1.8 µg/dL versus 1.2–1.8 µg/dL included ethnicity, fibrate use, and number of blood pressure medication classes used (all $P<0.01$)
- Factors independently associated with post-DST cortisol 1.2–1.8 µg/dL versus <1.2 µg/dL included age ($P<0.0001$), ethnicity ($P<0.05$), and taking ≥4 antihyperglycemic classes of medications ($P<0.001$)

CONCLUSIONS

- Data collected in CATALYST allowed us to explore characteristics associated with different post-DST cortisol values and to better understand the impact of different post-DST cortisol levels on comorbidities
- The results of this analysis suggest that there is a continuum of cardiometabolic risk as a function of nonsuppressible cortisol[3]
- As this analysis showed, individuals with post-DST cortisol 1.2–1.8 µg/dL share similarities in clinical characteristics with those who have DST results above the current hypercortisolism diagnostic cutoff, suggesting that further investigation of this group may be warranted

ACKNOWLEDGEMENTS

- The authors want to thank all those who are participating in this study: The study participants and their families, the investigators, and the sponsor team
- This study is sponsored by Corcept Therapeutics Incorporated. Medical writing assistance was provided by Tina Schlafly, PhD, CMPP of Corcept and R&R Healthcare Communications

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