The Design of MOMENTUM: A Prospective Study of the Prevalence of Endogenous Hypercortisolism in Individuals With Resistant Hypertension

Jorge Plutzky,[1] Richard J. Auchus,[2] Jan N. Basile,[3] Deepak L. Bhatt,[4] Michael J. Bloch,[5] Matthew A. Cavender,[6] James W. Findling,[7] Yehuda Handelsman,[8] Silvio E. Inzucchi,[9] Norman E. Lepor,[10] Neha J. Pagidipati,[11] Raymond R. Townsend,[12] Matthew R. Weir,[13] Iulia Cristina Tudor,[14] Daniel Einhorn[14]

[1]Cardiovascular Medicine Division, Brigham and Women's Hospital, Boston, MA; [2]University of Michigan, Ann Arbor, MI; [3]Division of Cardiology, Medical University of South Carolina, Charleston, SC; [4]Mount Sinai Fuster Heart Hospital, New York, NY; [5]Renown Institute for Heart and Vascular Health, Reno, NV; [6]University of North Carolina at Chapel Hill, Chapel Hill, NC; [7]Medical College of Wisconsin, Milwaukee, WI; [8]The Metabolic Institute of America, Tarzana, CA; [9]Yale School of Medicine, New Haven, CT; [10]Cedars Sinai Hospital, Beverly Hills, CA; [11]Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC; [12]University of Pennsylvania School of Medicine, Philadelphia, PA; [13]University of Maryland School of Medicine, Baltimore, MD; [14]Corcept Therapeutics Incorporated, Redwood City, CA

Abstract 0096

Scan QR code to access poster

SUMMARY AND CONCLUSIONS

- **Previously, the prospective CATALYST study (N=1,057) found endogenous hypercortisolism in 24% of individuals with difficult-to-control type 2 diabetes and in 40% of the subgroup who also had systolic blood pressure ≥135 mm Hg despite taking ≥3 blood pressure-lowering medications[1,2]**
  - **These findings demonstrated a need to investigate the prevalence of endogenous hypercortisolism in a wider population with resistant hypertension**
- **The currently enrolling MOMENTUM study is designed to provide an estimate of endogenous hypercortisolism prevalence and its associated clinical characteristics in a US population of individuals with resistant hypertension**
- **It is anticipated that the data from MOMENTUM will expand our understanding of the association between endogenous hypercortisolism and resistant hypertension**

ABSTRACT

Hypertension affects up to 50% of US adults and resistant hypertension (rHTN) occurs in 10-20% of cases. Endogenous hypercortisolism (eHC) may contribute to rHTN in some individuals, but the prevalence of eHC in individuals with rHTN is currently unknown. The CATALYST study assessing eHC prevalence in individuals with difficult-to-control type 2 diabetes, reported a 40% prevalence of eHC in participants with systolic blood pressure (BP) ≥135 mm Hg despite taking ≥3 BP medications.[2] MOMENTUM is the first large, prospective study to examine the prevalence of eHC in people with rHTN in the US.

MOMENTUM is an observational study of ~1,000 adults with rHTN using American Heart Association criteria. Key exclusion criteria are investigator-determined white coat hypertension, nonadherence to BP medications, and individuals in whom the dexamethasone suppression test is difficult to interpret. The primary endpoint is to assess the eHC prevalence in this population. Key secondary endpoints are to assess clinical and laboratory features associated with increased eHC risk. Hyperaldosteronism will also be screened for. Descriptive statistics will be used to characterize participants with and without eHC.

In conclusion, the MOMENTUM study, as designed and currently enrolling, will provide an estimate of eHC prevalence and its associated clinical characteristics in people with rHTN. (ClinicalTrials.gov Identifier: NCT06829537)

BACKGROUND

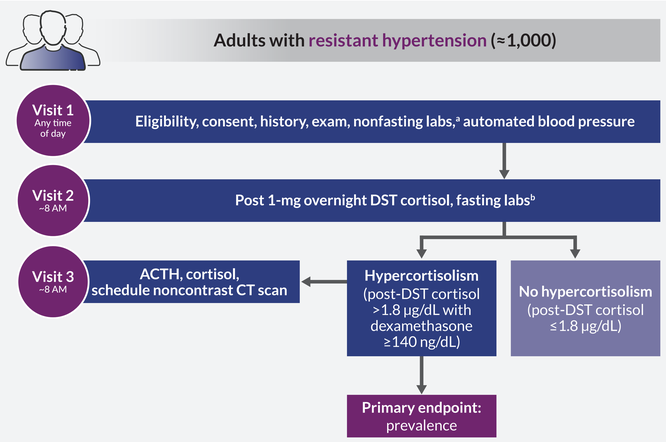
- Affecting nearly 50% of adults, hypertension (HTN) is one of the most common disorders in the United States[3]
- Despite the availability of multiple medications, resistant hypertension (rHTN) occurs in ~10% to 20% of individuals treated for HTN[4]
- Endogenous hypercortisolism (eHC) may contribute to rHTN through multiple, well-understood physiologic mechanisms, including metabolic, vascular, and cardiac alterations[5]
- However, screening for eHC is low due to its perceived rarity and challenges in screening[6,7]
- The prevalence of eHC in individuals with rHTN in the United States is currently unknown
  - Findings from the recent CATALYST study, the largest prospective study assessing eHC prevalence in >1,000 individuals with difficult-to-control type 2 diabetes,[1] demonstrated that 40% of the participant subgroup who also had systolic blood pressure [BP] ≥135 mm Hg despite taking ≥3 BP-lowering medications had eHC[2]
- This finding also showed a need to investigate eHC prevalence in individuals with rHTN with and without diabetes
  - CATALYST also demonstrated that in a population that excluded common causes of false-positive results, eHC screening could consist of a 1-mg overnight dexamethasone suppression test (DST), which is readily performed in clinical practice[1]
- The ongoing MOMENTUM study (NCT06829537) is the first large, prospective US study to examine the prevalence of eHC in individuals with rHTN

OBJECTIVES

- The MOMENTUM study's primary objective is to assess the prevalence of eHC in individuals with rHTN
- Secondary objectives include evaluating:
  - Clinical and laboratory characteristics that increase the likelihood of eHC
  - The proportion of individuals with markers of hyperaldosteronism and other causes of HTN
  - The percentage of individuals with eHC and rHTN who have abnormal adrenal imaging
  - Clinical and laboratory characteristics of individuals with and without abnormal adrenal imaging
- Exploratory objectives include:
  - Percentage and clinical and laboratory characteristics of individuals with post-DST cortisol 1.2 to 1.8 µg/dL and <1.2 µg/dL
  - Performance of a complete blood count to predict the results of DST based on subsets of white blood cells
  - Whether the degree of cortisol elevation post-DST has predictive value for comorbidity severity and/or presence and size of adrenal nodules

METHODS

Figure 1. Flow of Participants in the MOMENTUM Study



[a]Plasma renin activity, aldosterone, dehydroepiandrosterone sulfate, N-terminal-pro-brain natriuretic peptide, hemoglobin A1c, Fibrosis-4, aspartate aminotransferase-to-platelet-ratio index, uric acid, high-sensitivity C-reactive protein, complete blood count, comprehensive metabolic panel, estimated glomerular filtration rate, creatinine kystatin C, and urine albumin-to-creatinine ratio.
[b]ACTH, fasting glucose, and fasting lipids.
ACTH, adrenocorticotropic hormone; CT, computed tomography; DST, dexamethasone suppression test.

Study Design and Procedures

- MOMENTUM is a multicenter, prospective, noninterventional, observational study with a target enrollment of approximately 1,000 participants with rHTN defined per the American Heart Association criteria:
  - Systolic BP above target (≥130 mm Hg) despite concurrent use of ≥3 antihypertensive medications from different classes at maximally tolerated doses (ie, clinically appropriate doses in the judgment of the Investigator), with 1 medication being a diuretic **or**
  - Systolic BP at any level requiring concurrent use of ≥4 antihypertensive medications from different classes
- BP will be assessed at the initial clinic visit (**Figure 1**)
  - 3 automated BP measurements will be taken at intervals of 1 minute between readings, and the mean BP will be recorded
- Eligible participants will be assessed for eHC at the second visit using the 1-mg overnight DST
  - eHC is defined as post-DST cortisol >1.8 µg/dL with dexamethasone ≥140 ng/dL in individuals for whom causes of false-positive DSTs have been excluded
- Participants with eHC will undergo noncontrast adrenal computed tomography scans and a nonfasting 8 AM blood draw for evaluation of adrenocorticotropic hormone and cortisol
- Descriptive statistics will be used to characterize participants with and without eHC in the enrolled population

Inclusion and Exclusion Criteria

- MOMENTUM is enrolling male and female individuals aged ≥18 years with rHTN (**Table 1**)
- Major exclusion criteria include investigator-determined white coat HTN, nonadherence to BP medications, and individuals in whom DST results may be difficult to interpret

Table 1. MOMENTUM Study Inclusion and Exclusion Criteria

Inclusion criteria	▪ Aged ≥18 years ▪ Resistant hypertension defined according to American Heart Association criteria

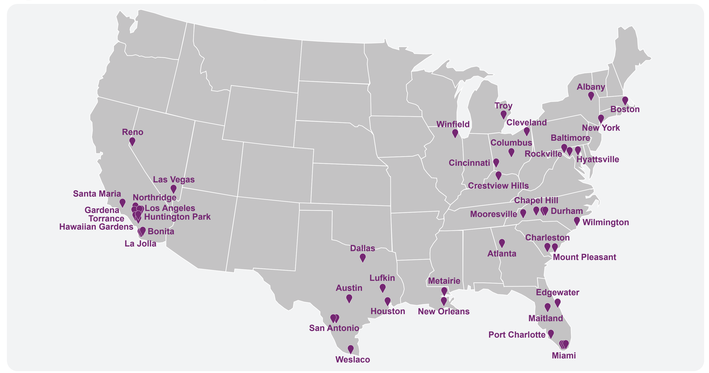
Exclusion criteria	▪ Investigator-determined white coat hypertension (ie, elevated blood pressure in the office only)
	▪ Investigator-determined nonadherence to blood pressure medications
	▪ Systemic glucocorticoid medications exposure (excluding inhalers or topical) ≤3 months of screening
	▪ Historical eGFR <30 mL/min/1.73 m^2
	▪ Investigator-determined:
	  ○ Severe untreated sleep apnea
	  ○ Excessive alcohol consumption (eg, >14 units/week for male, >7 units/week for female)
	  ○ Severe acute psychiatric, medical, or surgical illness
	▪ Pregnant or lactating
	▪ History of congenital adrenal hyperplasia
	▪ Diagnosed with endogenous hypercortisolism and/or has used or plans to use endogenous hypercortisolism medications[a]
	▪ History of hypersensitivity or severe reaction to dexamethasone
	▪ Patients on OCPs who are unable to stop for ≥6 weeks prior to screening

[a]Mifepristone, metyrapone, osilodrostat, ketoconazole, fluconazole, aminoglutethimide, etomidate, octreotide, lanreotide, pasireotide, long-acting octreotide, or pasireotide.
DST, dexamethasone suppression test; eGFR, estimated glomerular filtration rate; OCP, oral contraceptive pills.

Study Sites

- The study is being conducted at 48 geographically diverse US sites (**Figure 2**) chosen to reflect different clinical practice settings and specialties and to facilitate enrollment of participants of diverse race and ethnicity

Figure 2. MOMENTUM Study Sites



References

1. Buse JB, et al. *Diabetes Care*. 2025:dc242841. **2.** Handelsman Y, et al. Presented at: 22nd World Congress on Insulin Resistance, Diabetes & Cardiovascular Disease; December 12–14, 2024; Universal City, CA. Poster 0050. **3.** Centers for Disease Control and Prevention. May 12, 2023. Accessed April 23, 2025. https://millionhearts.hhs.gov/data-reports/hypertension-prevalence.html **4.** Carey RM, et al. *Hypertension*. 2018;72(5):e53–e90. **5.** De Leo M, et al. *Neuroendocrinology*. 2010;92(suppl 1):50–54. **6.** Rubinstein G, et al. *J Clin Endocrinol Metab*. 2020;105(3):dgz136. **7.** Valassi E. *J Neuroendocrinol*. 2022;34(8):e13114.

Acknowledgments

- 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 Farida Khan, PhD, CMPP, of Corcept and R&R Healthcare Communications

Presenter Disclosures

Jorge Plutzky reports: Consultant to Altimmune, Amgen, Boehringer Ingelheim, Corcept Therapeutics Incorporated, New Amsterdam, Novo Nordisk, Toku Eyes; Clinical trial steering committee membership at Esperion, Novo Nordisk; research grant support from Boehringer Ingelheim, Novartis

Presented at: Heart in Diabetes; June 6–8, 2025