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

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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 36.6% of the subgroup who also had systolic blood pressure ≥135 mmHg despite taking ≥3 blood pressure-lowering medications[1]
  - 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

BACKGROUND

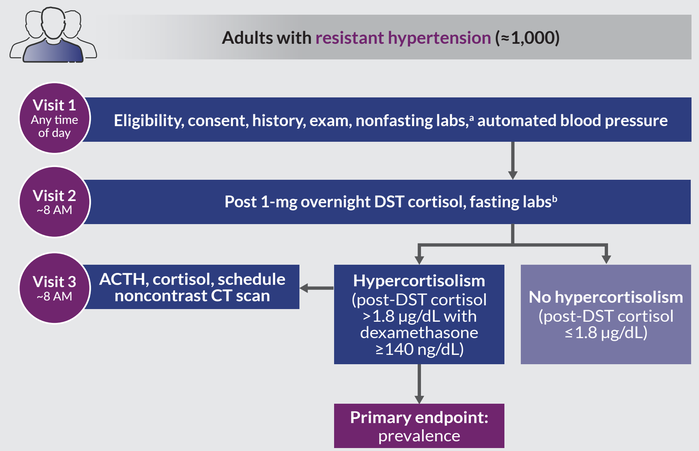
- Affecting nearly 50% of adults, hypertension (HTN) is one of the most common disorders in the United States[2]
- Despite the availability of multiple medications, resistant hypertension (rHTN) occurs in ~10–20% of individuals treated for HTN[3]
- Endogenous hypercortisolism (eHC) may contribute to rHTN through multiple, well-understood physiologic mechanisms, including metabolic, vascular, and cardiac alterations[4]
- However, screening for eHC is low due to its perceived rarity and the perception that screening is challenging[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 36.6% of the participant subgroup who also had systolic blood pressure (BP) ≥135 mmHg despite taking ≥3 BP-lowering medications had eHC
- 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 1.2–1.8 µg/dL and <1.2 µg/dL
  - Performance of a complete blood count to predict the results of the 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, eGFR, and urine albumin-to-creatinine ratio.
[b]ACTH, fasting glucose, and fasting lipids.
ACTH, adrenocorticotropic hormone; CT, computed tomography; DST, dexamethasone suppression test; eGFR, estimated glomerular filtration rate.

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 (AHA) criteria:
  - Systolic BP above target (≥130 mmHg) 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**)
  - Systolic BP will be measured by an Omron device, which automatically takes 3 BP measurements separated by 1 minute and provides the mean result. The clinical conditions for measuring BP will follow the recommendations of the AHA and Centers for Disease Control and Prevention
- 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

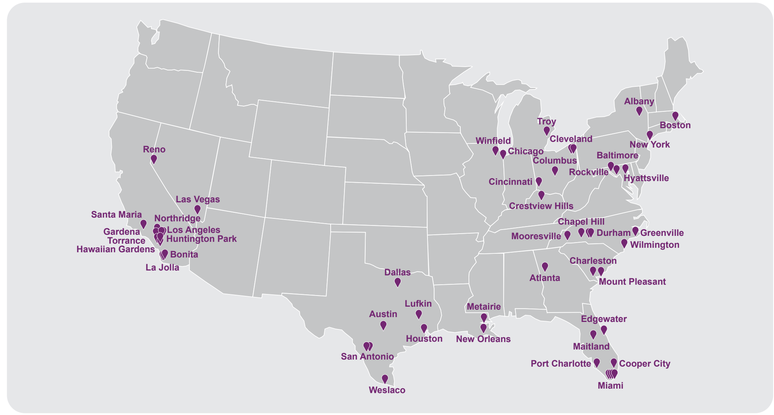
Exclusion criteria	▪ Investigator-determined white coat hypertension (ie, elevated blood pressure in the office only)
	▪ Investigator-determined nonadherence to blood pressure medications
	▪ Systemic glucocorticoid medications exposure (excluding inhalers or topical) ≤3 months of screening
	▪ Historical 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 sites in the United States (**Figure 2**), and enrollment is currently ongoing

Figure 2. MOMENTUM Study Sites



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Disclosures

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Previous presentation

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