

Blood Pressure Responder Analysis in the Global Launch-HTN Trial of Lorundrostat in Uncontrolled and Resistant Hypertension

Manish Saxena, MBBS¹; Keith C. Ferdinand, MD²; Branko Kopjar, MD, PhD³; Matthew Novin, DO⁴; Debbie L. Cohen, MD⁵

¹Barts Health NHS Trust and Queen Mary University, London, England; ²Tulane University School of Medicine, New Orleans, LA, USA; ³University of Washington, Seattle, WA, USA; ⁴Mineralys Therapeutics, Radnor, PA, USA; ⁵University of Pennsylvania, Philadelphia, PA, USA

INTRODUCTION

- Hypertension is the most important modifiable risk factor for cardiovascular diseases (CVD), but less than 25% of patients achieve the guideline recommended blood pressure (BP) target¹
- The 2025 AHA/ACC Guidelines recommend a systolic BP (SBP) target of <130 mmHg to reduce the risk of CVD morbidity and mortality²
- Blood pressure is a well-established and powerful surrogate for cardiovascular events, and every 10-mmHg reduction in office SBP reduces risk of CV events by 20%³
- In the phase 3 global, randomized, double-blind, placebo-controlled Launch-HTN trial, the selective aldosterone synthase inhibitor lorundrostat demonstrated statistically significant and clinically meaningful reduction in automated office SBP (AOSBP) at Week 6 that was sustained at Week 12 in participants with uncontrolled hypertension, including resistant hypertension⁴
- The objective of this analysis was to evaluate the responder rate achieving guideline-based targets and clinically meaningful reductions in BP in the Launch-HTN trial

METHODS

- Participants eligible for the Launch-HTN trial were on a stable regimen of 2-5 prescribed background antihypertensive medications (AHTs), including a diuretic, with systolic or isolated diastolic uncontrolled hypertension
- For this analysis, only participants with baseline SBP ≥130 mmHg were included
- Analysis of proportion of participants achieving 2025 AHA/ACC Guideline recommended SBP target of <130 mmHg at Week 12 was a pre-specified endpoint
- Odds ratio of SBP <130 mmHg at Week 12 between placebo and lorundrostat arms was calculated in imputed data set
- In addition, the proportions of participants achieving AOSBP reductions of 10 mmHg and 20 mmHg from baseline were calculated

RESULTS

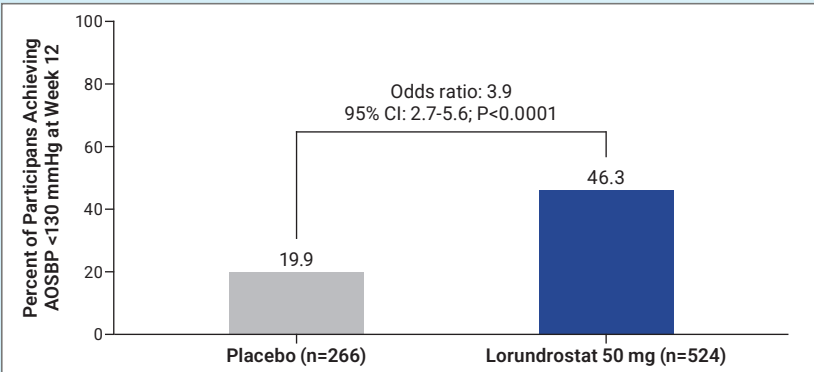
Table 1: Baseline Demographics and Participant Characteristics

Measure	Placebo (n=266)	Lorundrostat 50 mg (n=524)
Age, mean (SD), y	61.8 (10.17)	61.9 (10.56)
Female sex, n (%)	131 (49.2)	241 (46.0)
AOBP		
SBP, mean (SD), mmHg	149.0 (11.9)	149.7 (11.8)
DBP, mean (SD), mmHg	87.1 (9.09)	87.8 (9.00)
Race, n (%)		
White	171 (64.3)	355 (67.7)
Black or African American	87 (32.7)	147 (28.1)
Asian	6 (2.3)	14 (2.7)
Ethnicity, n (%)		
Hispanic	99 (38.2)	184 (35.5)
Not Hispanic	160 (61.8)	335 (64.5)
BMI, mean (SD), kg/m²	32.6 (7.47)	33.03 (6.91)
eGFR (creatinine), mean (SD), mL/min/1.73 m²	91.0 (16.3)	91.1 (17.7)
AHT regimen, n (%)		
≤2 AHT medications	110 (41.4)	205 (39.1)
≥3 AHT medications	156 (58.6)	319 (60.9)
AHT drug class		
Thiazide/Like Diuretics, n (%)	247 (92.9)	492 (93.9)
ACE/ARB, n (%)	220 (82.7)	453 (86.5)
Calcium Channel Blockers, n (%)	124 (46.6)	256 (48.9)
Beta blockers, n (%)	81 (30.5)	175 (33.4)
Diabetes, n (%)	99 (37.2)	207 (39.5)

ACE, angiotensin-converting enzyme; AHT, antihypertensive therapy; AOBP, automated office blood pressure, ARB, angiotensin receptor blockers; BMI, body mass index; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; SBP, systolic blood pressure, SD, standard deviation.

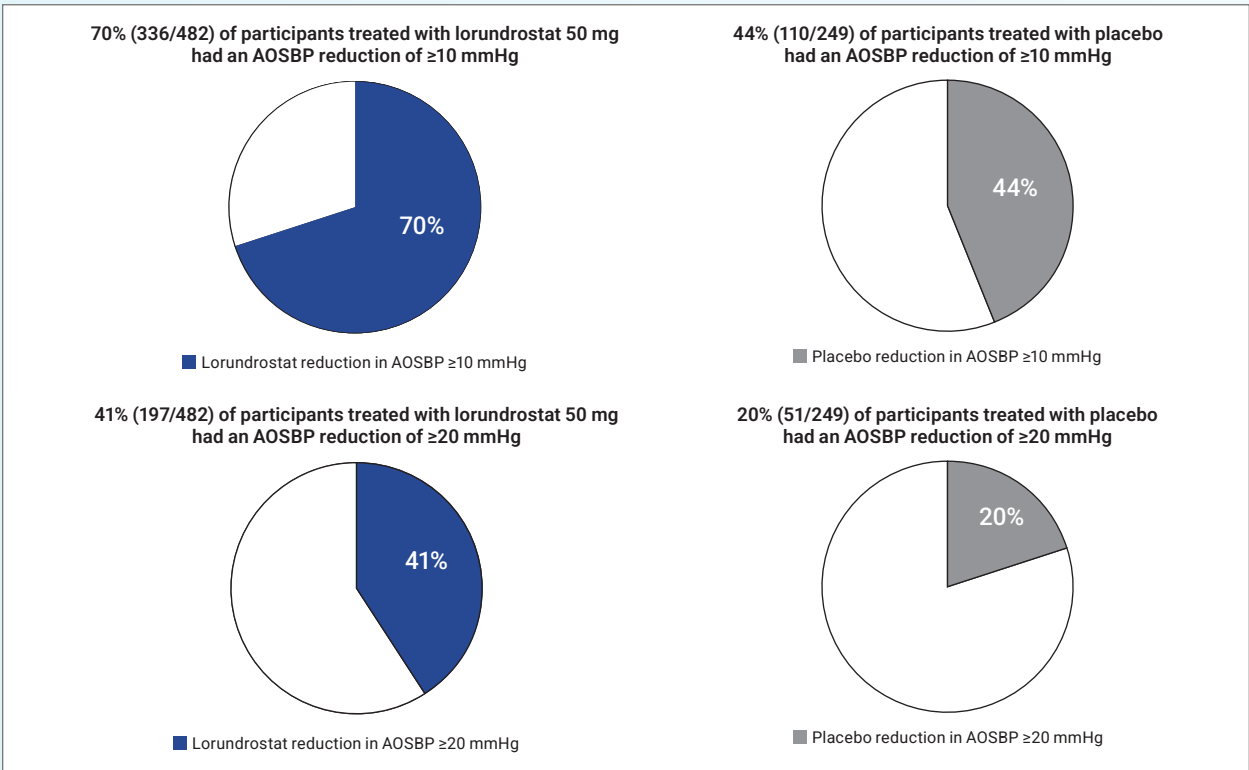
- AOSBP <130 mmHg at Week 12 was achieved by 46.3% of participants receiving lorundrostat 50 mg and 19.9% of participants receiving placebo (Figure 1)

Figure 1: Percentage of Participants Achieving the Target AOSBP (<130 mmHg) at Week 12



AOSBP, automated office systolic blood pressure.

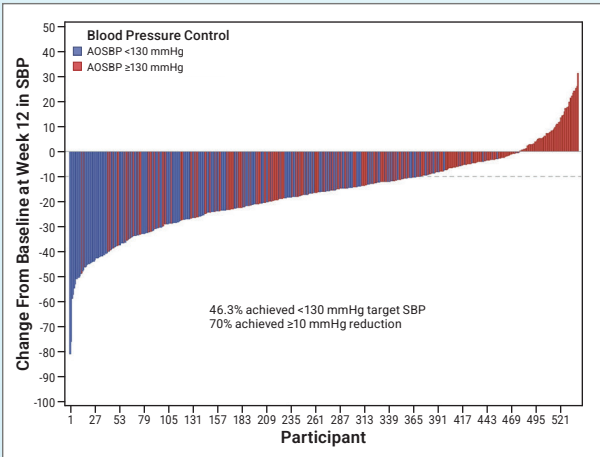
Figure 2: Percentage of Participants Receiving Lorundrostat 50 mg Who Achieved AOSBP Reduction Thresholds of ≥10 mmHg and ≥20 mmHg at Week 12



AOSBP, automated office systolic blood pressure.

Figure 3: More Patients Achieve <130 mmHg Target SBP and ≥10 mmHg Reduction with Lorundrostat Waterfall Plot of Change in AOSBP at Week 12 with Lorundrostat 50 mg (A) and Placebo (B)

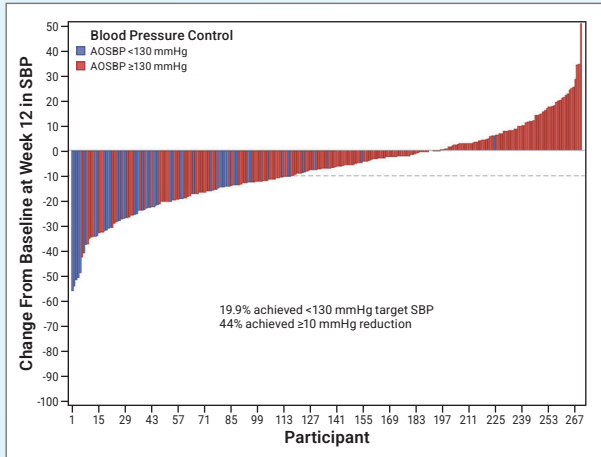
A. Lorundrostat 50 mg daily



Dotted line represents SBP reduction of 10 mmHg.

AOSBP, automated office systolic blood pressure.

B. Placebo



Safety

- Symptomatic hypotension was reported in 11 (2.1%) participants in the lorundrostat 50 mg group and 1 (0.4%) in the placebo group
- Confirmed serum potassium >6 mmol/L was observed in 3 (0.6%) participants treated with lorundrostat and 1 (0.4%) participant treated with placebo
- The most common AEs associated with lorundrostat treatment were modification of dose due to hyponatremia and modification of dose due to reduction in kidney function

Table 2: Summary of Adverse Events of Special Interest by Achievement of Target AOSBP (<130 mmHg) at Week 12

	Placebo (n=249)		Lorundrostat 50 mg (n=482)	
	≥130 mmHg (n=198)	<130 mmHg (n=51)	≥130 mmHg (n=259)	<130 mmHg (n=223)
Modification of study drug dose due to hyperkalemia ^a	1 (0.5)	0 (0.0)	7 (2.7)	4 (1.8)
Modification of study drug dose due to hyponatremia ^a	6 (3.0)	2 (3.9)	18 (6.9)	18 (8.1)
Modification of study drug dose due to reduction in kidney function ^a	2 (1.0)	0 (0.0)	4 (1.5)	12 (5.4)
Hypotension with symptoms ^b	1 (0.5)	0 (0.0)	4 (1.5)	6 (2.7)
Severely elevated blood pressure ^c	9 (4.5)	1 (2.0)	10 (3.9)	0 (0.0)
Discontinuation of study drug due to hypocortisolism ^d	3 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)

^aDose modification is dose reduction, dose hold, or permanent study drug discontinuation.

^bE.g. Light-headedness, dizziness, presyncope, or syncope.

^cAOSBP SBP >180 mmHg or AOBP DBP >110 mmHg.

^dConfirmed by ACTH (cosyntropin or regional equivalent) stimulation test.

17 participants in the placebo group and 42 participants in the lorundrostat group could not be classified due to missing Week 12 AOSBP.

AOBP, automated office blood pressure, DBP, diastolic blood pressure; SBP, systolic blood pressure.

CONCLUSIONS

- Lorundrostat was associated with clinically meaningful BP improvements, with nearly half of participants achieving the guideline-recommended BP target of <130 mmHg and more than two-thirds achieving an SBP reduction of at least 10 mmHg
- Lorundrostat exhibited a favorable safety and tolerability profile, with infrequent occurrences of clinically relevant hyperkalemia and symptomatic hypotension
- The reduction in CVD event risk with these levels of SBP reductions is well established, and these findings support the potential for improved CV outcomes in participants receiving lorundrostat 50 mg



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Disclosures

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