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Efficacy and Safety of Lorundrostat in Hypertension Patients With High Unmet Medical Need: Subgroup Analyses of the Launch-HTN Trial in Uncontrolled and Treatment-Resistant Hypertension

Manish Saxena, MBBS[1]; Luke Laffin, MD[2]; James M. Luther, MD[3]; Matthew R. Weir, MD[4]; Branko Kopjar, MD, PhD[5]; and David Rodman, MD[6]

[1]Barts Health NHS Trust and Queen Mary University London, London, United Kingdom; [2]Cleveland Clinic Foundation, Cleveland, OH, USA; [3]Vanderbilt University Medical Center, Nashville, TN, USA; [4]University of Maryland School of Medicine, Baltimore, MD, USA; [5]University of Washington, Seattle, WA, USA; [6]Mineralys Therapeutics, Radnor, PA, USA

INTRODUCTION

- Certain patient subgroups, including adults ≥65 years, women, Black/African American (AA), adults with comorbid obesity, and ≥3 antihypertensive medications, have high unmet clinical need due to difficult to control blood pressure (BP) and high cardiovascular risk[1-6]
- Aldosterone dysregulation plays an important role in uncontrolled hypertension (HTN), including treatment-resistant HTN[7]
- Treatment with lorundrostat, a novel, highly selective aldosterone synthase inhibitor (ASI), targets aldosterone biosynthesis to reduce aldosterone production[8]
- Launch-HTN evaluated the BP-lowering efficacy and safety of lorundrostat in diverse participants, including these difficult to treat and high-risk patient subgroups[9]
- The objective of this analysis was to describe subgroups of patients with high unmet clinical need in Launch-HTN and to evaluate the reduction in automated office systolic BP (AOSBP) in these patients receiving lorundrostat 50 mg/day compared with placebo while receiving 2 to 5 prescribed antihypertensive medications

METHODS

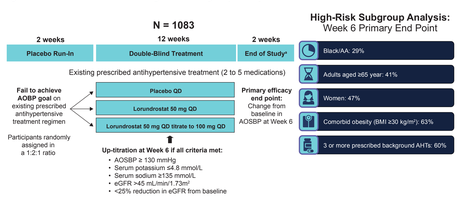
- Launch-HTN was a global, double-blind, placebo-controlled, randomized, phase 3 trial in adults with uncontrolled HTN, including treatment-resistant HTN (**Figure 1**)

Figure 1. Launch-HTN Global Phase 3 Trial

Global Trial With 159 Sites
Australia
Bulgaria
Canada
France
Germany
Italy
The Netherlands
Poland
Puerto Rico
Romania
Spain
United Kingdom
United States

- Participants taking 2 to 5 prescribed antihypertensive therapies (AHTs) including a diuretic and with AOSBP of 135-180 mmHg and diastolic BP of 65-110 mmHg were randomized to receive once daily placebo, lorundrostat 50 mg, or lorundrostat 50 mg and then possibly 100 mg (**Figure 2**)

Figure 2. Launch-HTN Trial Design and Subgroup Analysis



[a]Participants who do not enter the OLE attend a 2-week end-of-study safety follow-up visit.
AA, African American; AHT, antihypertensive therapy; AOSBP, automated office systolic blood pressure; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate; OLE, open-label extension; QD, once daily.

- The primary end point of Launch-HTN was change in AOSBP with lorundrostat compared with placebo after 6 weeks of treatment
- All participants randomized to lorundrostat treatment received 50 mg/day through Week 6 (pooled n=808)
- This analysis of prespecified participant subgroups examined baseline demographics and clinical characteristics and assessed the BP-lowering efficacy of once daily lorundrostat 50 mg at Week 6 (**Figure 2**)
- Safety was assessed as the incidence and severity of adverse events (AEs)

RESULTS

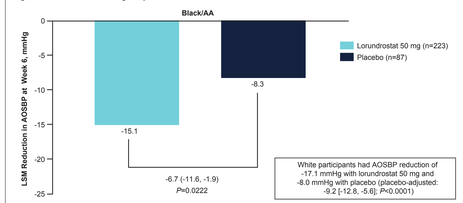
- Baseline characteristics of each participant subgroup are shown in **Table 1**

Table 1. Subgroup Baseline Demographics

	Black/AA (n=310)		Women (n=506)		Comorbid obesity (n=682)		≥3 AHTs (n=648)		65-74 y (n=345)		≥75 y (n=101)	
Baseline Demographics	Lorundrostat 50 mg/day	Placebo	Lorundrostat 50 mg/day	Placebo	Lorundrostat 50 mg/day	Placebo	Lorundrostat 50 mg/day	Placebo	Lorundrostat 50 mg/day	Placebo	Lorundrostat 50 mg/day	Placebo
Mean age, years	60.4	59.9	62.1	61.7	60.2	60.4	62.4	61.8	69.1	69.4	78.9	77.3
Women, %	57	54	100	100	49	48	41	45	45	48	56	48
AA/Black, %	100	100	34	36	29	30	29	33	26	25	14	17
BMI <30 kg/m², %	33	43	33	39	100	100	33	35	40	41	60	62
BMI ≥30 kg/m², %	67	57	67	61	0	0	67	65	60	59	40	38
Mean SBP, mmHg	149.0	148.5	149.1	148.7	148.5	149.2	148.6	149.0	149.3	148.8	149.3	152.2
Mean DBP, mmHg	89.2	88.3	86.0	85.4	87.6	87.7	87.0	87.4	83.9	83.5	79.5	80.3
Heart rate, BPM	74.1	71.7	74.5	74.0	73.9	73.5	72.2	72.7	71.3	70.7	66.9	67.2
Mean eGFR, mL/min/1.73 m²	87.1	87.2	91.7	92.2	92.2	93.1	89.9	90.9	86.0	87.4	73.5	78.7
Diabetes, %	32	26	31	34	33	37	33	38	38	39	36	52
2 antihypertensives, %	37	40	46	46	37	38	0	0	38	35	25	55
≥3 antihypertensives, %	63	60	54	54	63	62	100	100	62	65	75	45
Thiazide or thiazide-like diuretic, %	99	95	98	98	97	95	96	96	95	96	93	93
ACEi or ARB, %	76	70	85	83	89	87	92	91	88	86	93	90
CCB, %	64	62	44	39	50	49	73	69	50	46	63	45
GLP-1 RA, %	7	6	6	5	7	4	6	4	6	0	6	7
SGLT2i, %	2	5	3	2	4	5	6	8	5	5	6	14

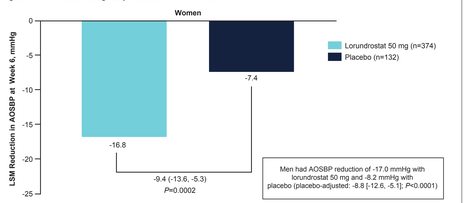
- Reductions in AOSBP for each participant subgroup are shown in **Figures 3-7**

Figure 3. Black/AA Subgroup Reduction in AOSBP



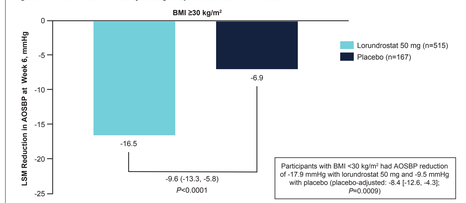
AA, African American; AOSBP, automated office systolic blood pressure; LSM, least squares mean.

Figure 4. Women Subgroup Reduction in AOSBP



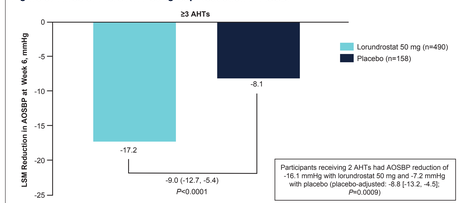
AOSBP, automated office systolic blood pressure; LSM, least squares mean.

Figure 5. Comorbid Obesity Subgroup Reduction in AOSBP



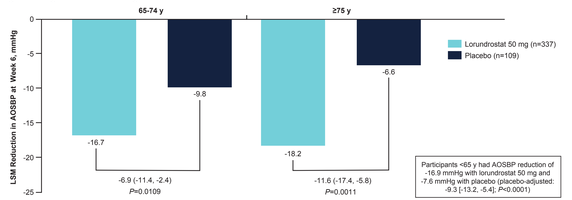
AOSBP, automated office systolic blood pressure; BMI, body mass index; BP, blood pressure; LSM, least squares mean.

Figure 6. Three or More AHT Subgroup Reduction in AOSBP



AHT, antihypertensive therapy; AOSBP, automated office systolic blood pressure; LSM, least squares mean.

Figure 7. Age ≥65 Years Subgroup Reduction in AOSBP



Lorundrostat 50 mg n=337 (265 participants 65-74 y + 72 participants ≥75 y); Placebo n=109 (80 participants 65-74 y + 29 participants ≥75 y)
AOSBP, automated office systolic blood pressure; LSM, least squares mean.

- Black/AA participants had AOSBP reductions of -15.1 mmHg with lorundrostat 50 mg and -8.3 mmHg with placebo (placebo-adjusted: -6.7 [-11.6, -1.9]; P=0.022; **Figure 3**)
- Women participants had AOSBP reductions of -16.8 mmHg with lorundrostat 50 mg and -7.4 mmHg with placebo (placebo-adjusted: -9.4 [-13.6, -5.3]; P=0.0002; **Figure 4**)
- Participants with obesity had AOSBP reductions of -16.5 mmHg with lorundrostat 50 mg and -6.9 mmHg with placebo (placebo-adjusted: -9.6 [-13.3, -5.8]; P<0.0001; **Figure 5**)
- Participants receiving ≥3 AHTs had AOSBP reductions of -17.2 mmHg with lorundrostat 50 mg and -8.1 mmHg with placebo (placebo-adjusted: -9.0 [-12.7, -5.4]; P<0.0001; **Figure 6**)
- Participants 65-74 y had AOSBP reductions of −16.7 mmHg with lorundrostat 50 mg and −9.8 mmHg with placebo (placebo-adjusted: -6.9 [-11.4, -2.4]; P=0.0109; **Figure 7**)
- Participants ≥75 y had AOSBP reductions of -18.2 mmHg with lorundrostat 50 mg and -6.6 mmHg with placebo (placebo-adjusted: -11.6 [-17.4, -5.8]; P=0.011; **Figure 7**)
- Safety results for participant subgroups were consistent with the overall population (**Tables 2** and **3**)
- In the Launch-HTN trial, TEAEs were experienced by 54% of participants receiving once daily lorundrostat 50 mg, and most were mild or moderate in severity (**Table 2**)

Table 2. Overall Adverse Events

Adverse Events, %	Placebo	Lorundrostat 50 mg	Lorundrostat 50 to 100 mg
Any TEAE	36	54	56
Mild	22	34	43
Moderate	12	19	11
Severe	3	2	2
Any serious AE	3	2	1
Serum potassium >6.0 mmol/L[a]	0.4	0.6	1.1
Death[b]	0.4	0	0

[a]Confirmed per protocol repeat testing. [b]One death occurred and was not related to treatment.
AE, adverse event; TEAE, treatment-emergent adverse event.

- No participants treated with lorundrostat experienced glucocorticoid deficiency confirmed by stimulation testing (**Table 3**)

Table 3. Overall AESIs

AESIs, %[a]	Placebo	Lorundrostat 50 mg	Lorundrostat 50 to 100 mg
Severely elevated BP	4.1	1.9	0.7
Symptomatic hypotension	0.4	2.0	1.9
Hyperkalemia[b]	0.4	2.0	2.6
Hyponatremia[b]	3.3	6.9	10.4
Glucocorticoid deficiency[c]	1.1	0	0
eGFR reduction[b]	0.7	3.0	3.3

[a]AESI reporting required modification or discontinuation of trial drug. [b]Required modification of trial drug. [c]Confirmed by ACTH stimulation test and required discontinuation of trial drug.
ACTH, adrenocorticotropic hormone; AESI, adverse events of special interest; BP, blood pressure; eGFR, estimated glomerular filtration rate.

CONCLUSIONS

- **Launch-HTN demonstrated consistent efficacy and safety of the novel, highly selective ASI lorundrostat in a large cohort of diverse participants[9]**
- **These participant subgroups with difficult to treat HTN have high cardiovascular risk with poor outcomes[1-6]**
- **Lorundrostat led to clinically meaningful and significant BP reduction in these high-risk participant subgroups with high unmet clinical need**
- **Lorundrostat had a good safety and tolerability profile, consistent with the overall Launch-HTN trial, in these high-risk participants with uncontrolled HTN, including treatment-resistant HTN**

REFERENCES

1. Muntner P, et al. *JAMA*. 2020;324(12):1190-200.
2. U.S. Department of Health and Human Services. 2016. https://www.cdc.gov/nchs/data/hus/hus15.pdf.
3. Tajeu GS, et al. *PLoS One*. 2022;17(8):e0270675.
4. Henry A, et al. *Hypertension*. 2024;81(4):851-60.
5. Million Hearts®. 2023. https://millionhearts.hhs.gov/data-reports/hypertension-prevalence.html.
6. Jaeger BC, et al. *Hypertension*. 2023;80(6):1311-20.
7. Verma S, et al. *Am J Physiol Heart Circ Physiol*. 2024;326(3):H670-H88.
8. Shimizu H, et al. *Clin Transl Sci*. 2024;17(8):e70000.
9. Saxena M, et al. *JAMA*. 2025;334(5):409-18.

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