Phase 3 Efficacy and Safety of Lorundrostat, a Novel Aldosterone Synthase Inhibitor, in Patients With Uncontrolled and Treatment-Resistant Hypertension: Launch-HTN Study

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Late Breakers 1
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Disclosures

- Dr. Saxena reports personal consulting fees from Alnylam, Arrowhead, Astra Zeneca, Boehringer Ingelheim, C4 Research, Daiichi Sankyo, IQVIA, Mineralys Therapeutics, Menarini Group, Novartis, PPD, Recor Medical, and Vifor Pharma; Institutional grants from Ablative Solutions, MSD, Recor Medical, and Applied Therapeutics; Honoraria for presentations from Sanofi; Participation in advisory boards with Alnylam, AZ, BI, DSI, and Menarini Group

- Honorary Executive Committee member of the British & Irish Hypertension Society

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Background

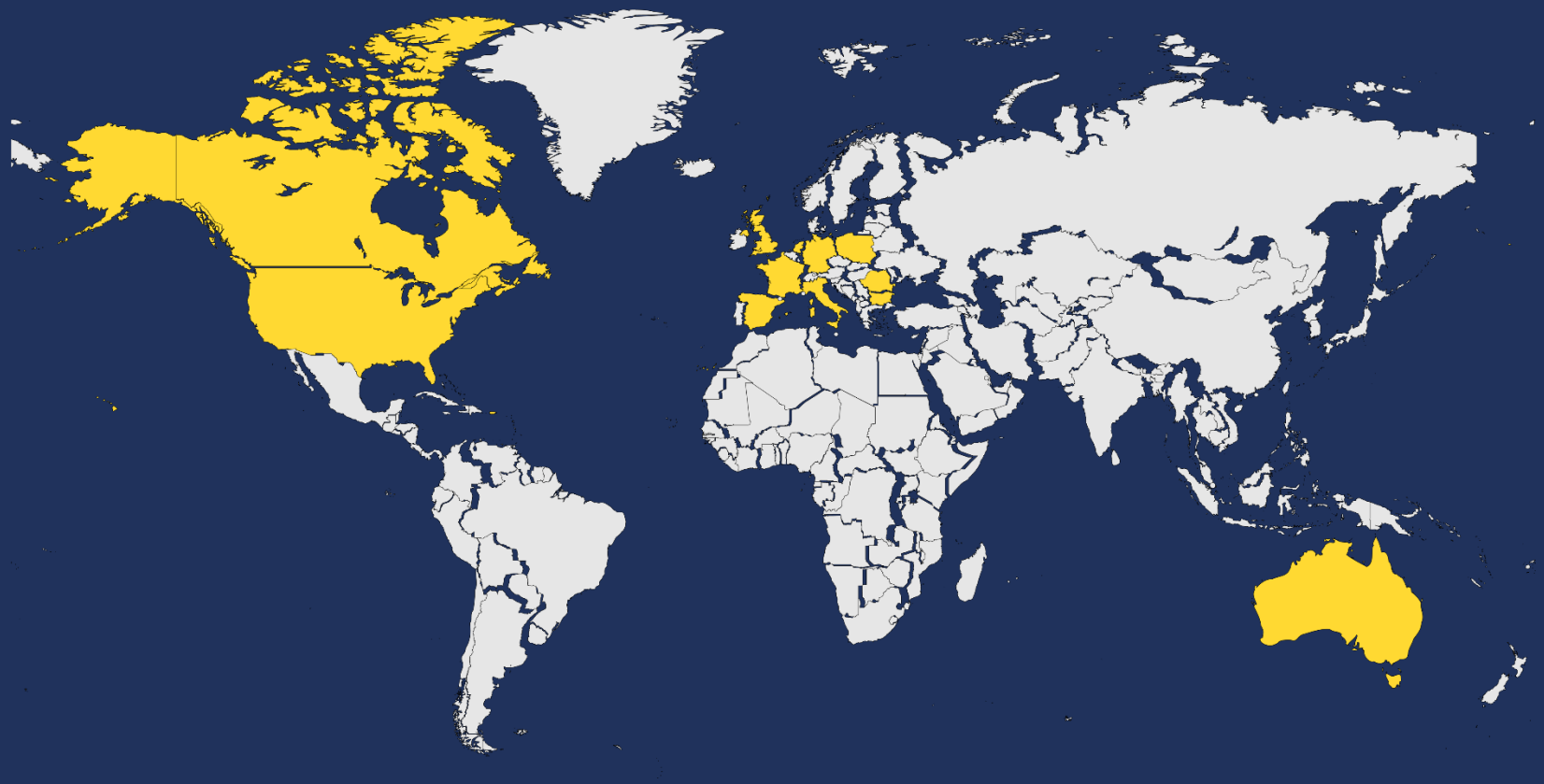
- Hypertension (HTN) affects 1 in 3 adults worldwide[1]
- Despite available treatment options, >40% of adults with HTN worldwide are not at blood pressure (BP) target[2]
- ~30% of patients with HTN have dysregulated aldosterone secretion[3]
- Spironolactone (MRAs) is 4th line add-on treatment option for patients with treatment-resistant HTN[4,5]; however, it is underutilized in clinical practice[6]

1. World Health Organization. Global report on hypertension: the race against a silent killer. 2023. Available at: https://www.who.int/teams/noncommunicable-diseases/hypertension-report (Accessed May 2024). 2. Global Cardiovascular Risk Consortium, et al. *NEJM* 2023; 389(14):1273-85. 3. Brown JM, et al. *Ann Intern Med* 2020;173(1):10-20. 4. McEvoy JW, et al. *Eur Heart J* 2024;45(38):3912-4018. 5. Whelton PK, et al. *Hypertension* 2018;71(6):e13-e115. 6. Lachaine J, Beauchemin C, Ramos E. *BMC Clin Pharmacol* 2011;11:4.

Launch-HTN: Objective

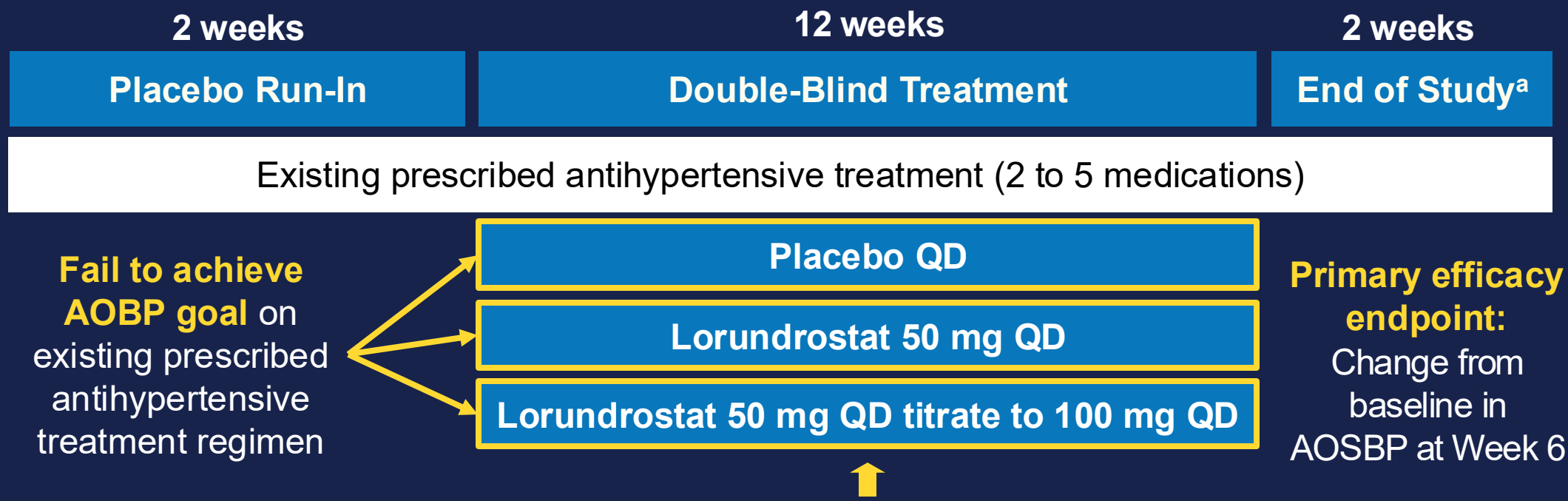
To assess the blood pressure lowering efficacy and safety of lorundrostat, an aldosterone synthase inhibitor, in patients with uncontrolled hypertension, including treatment-resistant hypertension, who were taking 2 to 5 prescribed antihypertensive medications

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

Launch-HTN: Trial Design



Up-titration at Week 6 if all criteria met:

- AOSBP ≥ 130 mmHg
- Serum potassium ≤4.8 mmol/L
- Serum sodium ≥135 mmol/L
- eGFR >45 mL/min/1.73m^2
- <25% reduction in eGFR from baseline

[a]Participants who do not enter the OLE attend a 2-week End of Study safety follow-up visit.

Key Inclusion & Exclusion Criteria

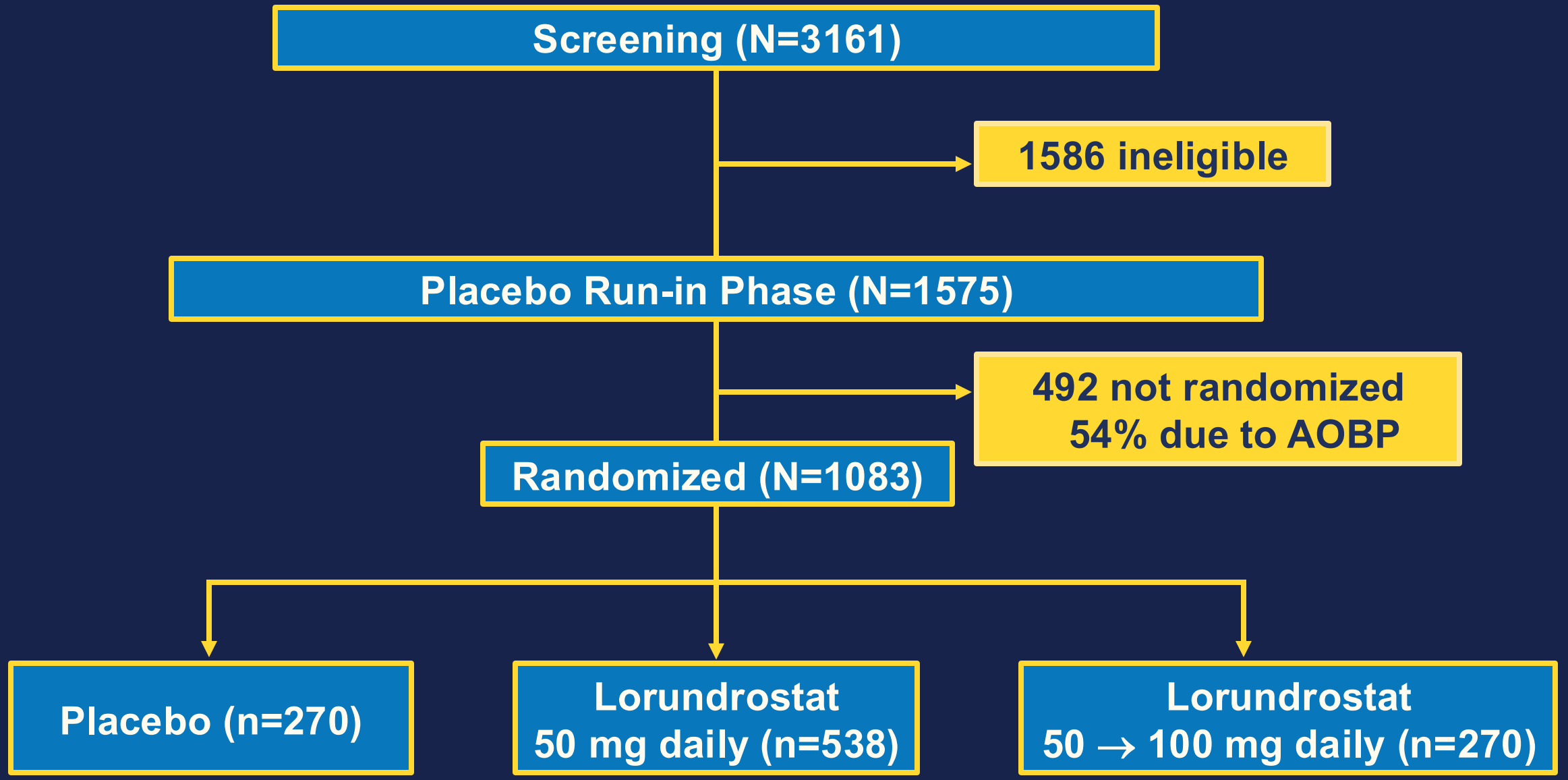
Inclusion Criteria

- Males or females aged ≥18 years
- AOSBP of 135-180 mmHg and diastolic BP of 65-110 mmHg at screening and randomization
- On stable doses of 2 to 5 prescribed antihypertensive treatments, including a thiazide or thiazide-like diuretic

Exclusion Criteria

- eGFR <45 ml/min/1.73m^2
- Serum potassium >5.0 mmol/L at screening or >4.8 mmol/L at randomization
- Serum sodium <135 mmol/L at screening
- Use of epithelial sodium channel inhibitors or MRAs/potassium sparing diuretics

Launch-HTN: Participant Flow



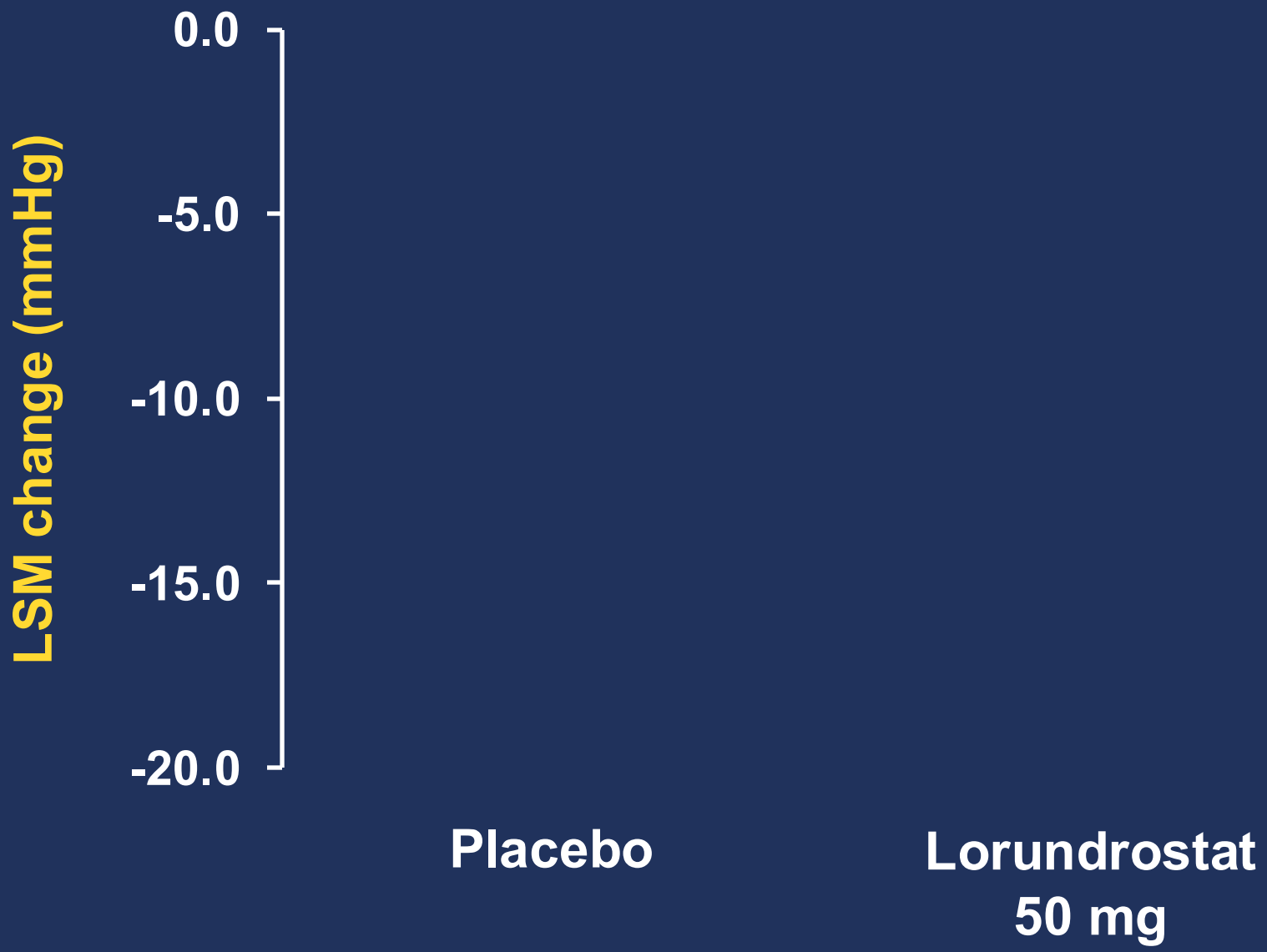
Baseline Demographics & Clinical Characteristics

	Placebo (n=272)	Lorundrostat 50 mg (n=541)	Lorundrostat 50 mg to 100 mg (n=270)
Mean age, years	61.8	61.7	61.4
Female, %	48.9	45.7	47.4
African American/Black, %	32.0	28.1	26.7
BMI ≥30 kg/m^2, %	61.8	64.9	61.5
Mean eGFR, mL/min/1.73 m^2	91.2	90.1	92.8
Diabetes, %	33.0	32.2	28.2
GLP-1 receptor antagonist, %	3.3	5.6	4.8
SGLT2i, %	4.8	3.9	5.2
Mean AOBP at randomization, mmHg	149 / 87	149 / 88	147 / 86

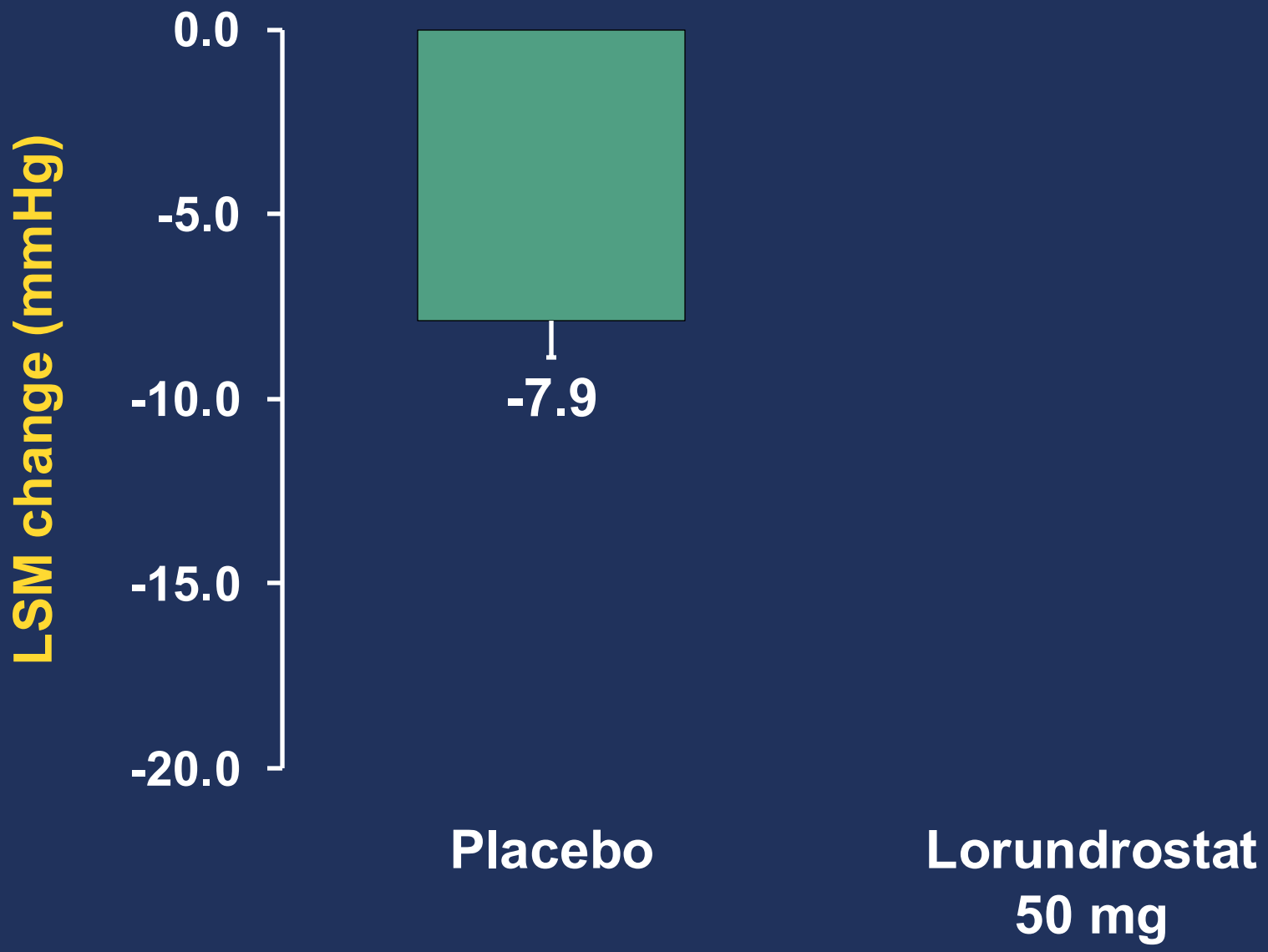
Antihypertensive Medications at Baseline

	Placebo (n=272)	Lorundrostat 50 mg (n=541)	Lorundrostat 50 mg to 100 mg (n=270)
2 prescribed antihypertensives, %	41.5	39.4	39.3
≥3 prescribed antihypertensives, %	58.5	60.6	60.7
Antihypertensive drug class			
Thiazide/thiazide-like diuretics, %	95.2	96.1	95.9
ACE inhibitor or ARB, %	82.7	86.3	87.8
Calcium channel blocker, %	49.6	51.4	51.9

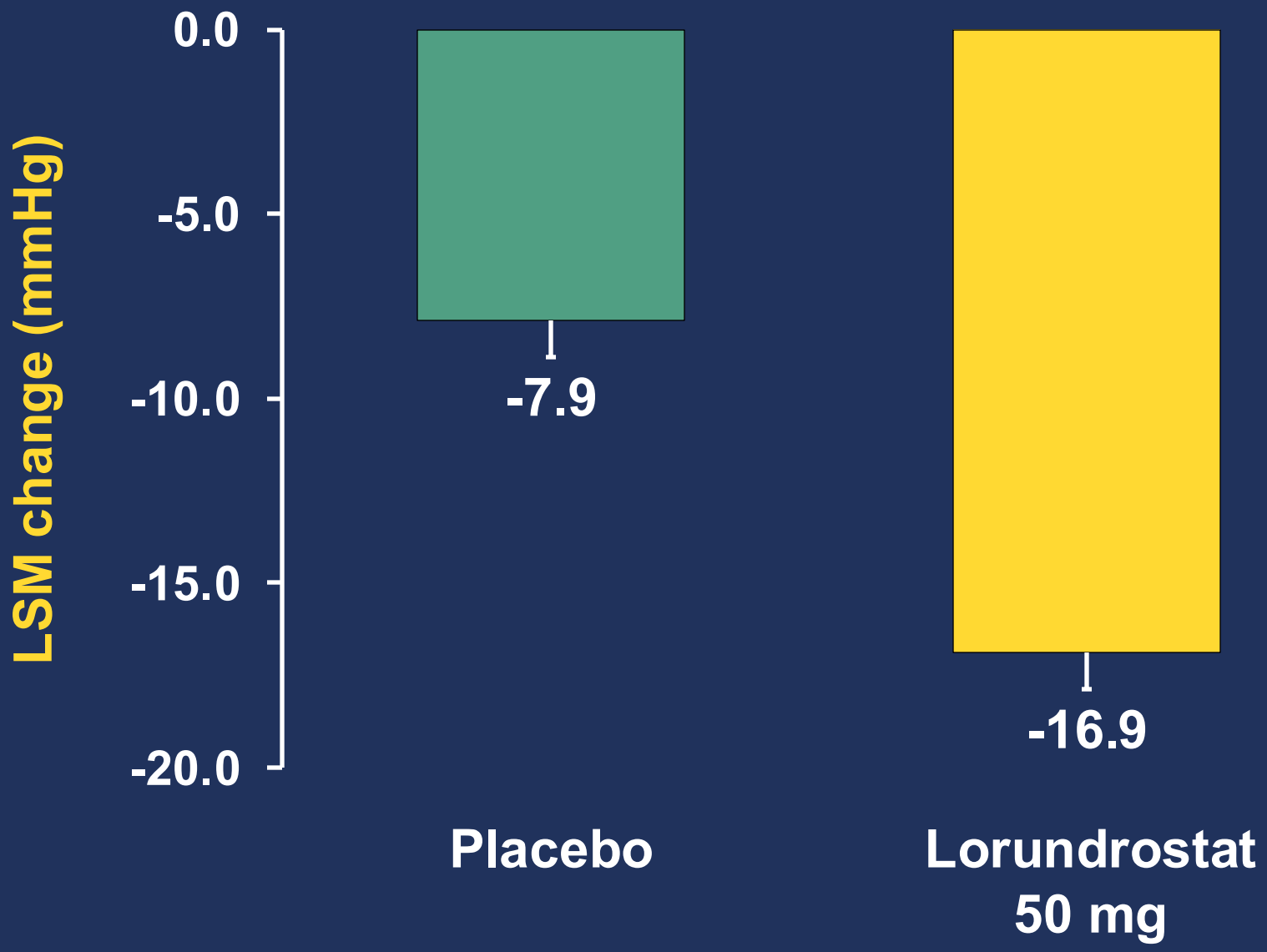
Primary End Point: AOSBP Change at Week 6



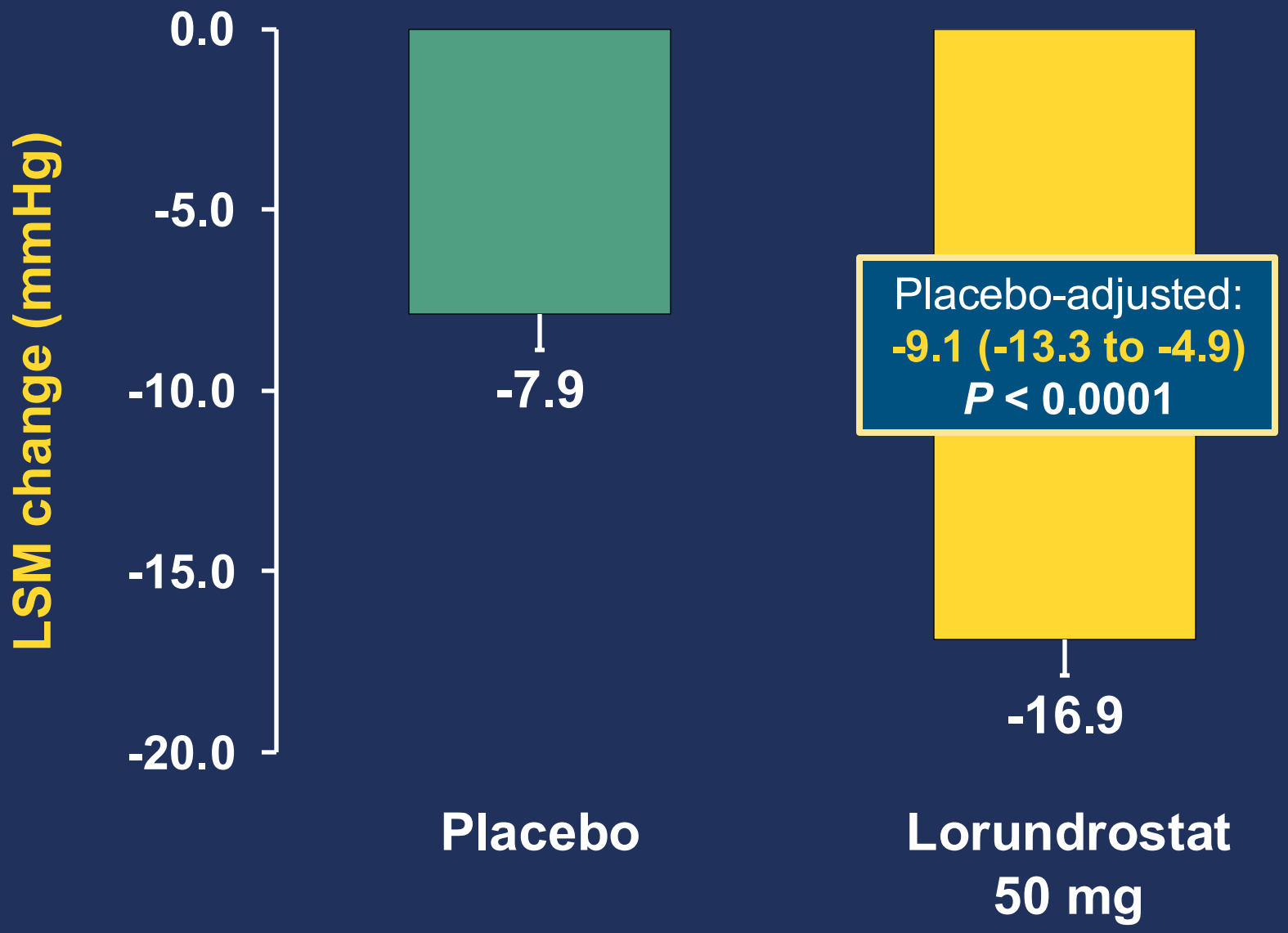
Primary End Point: AOSBP Change at Week 6



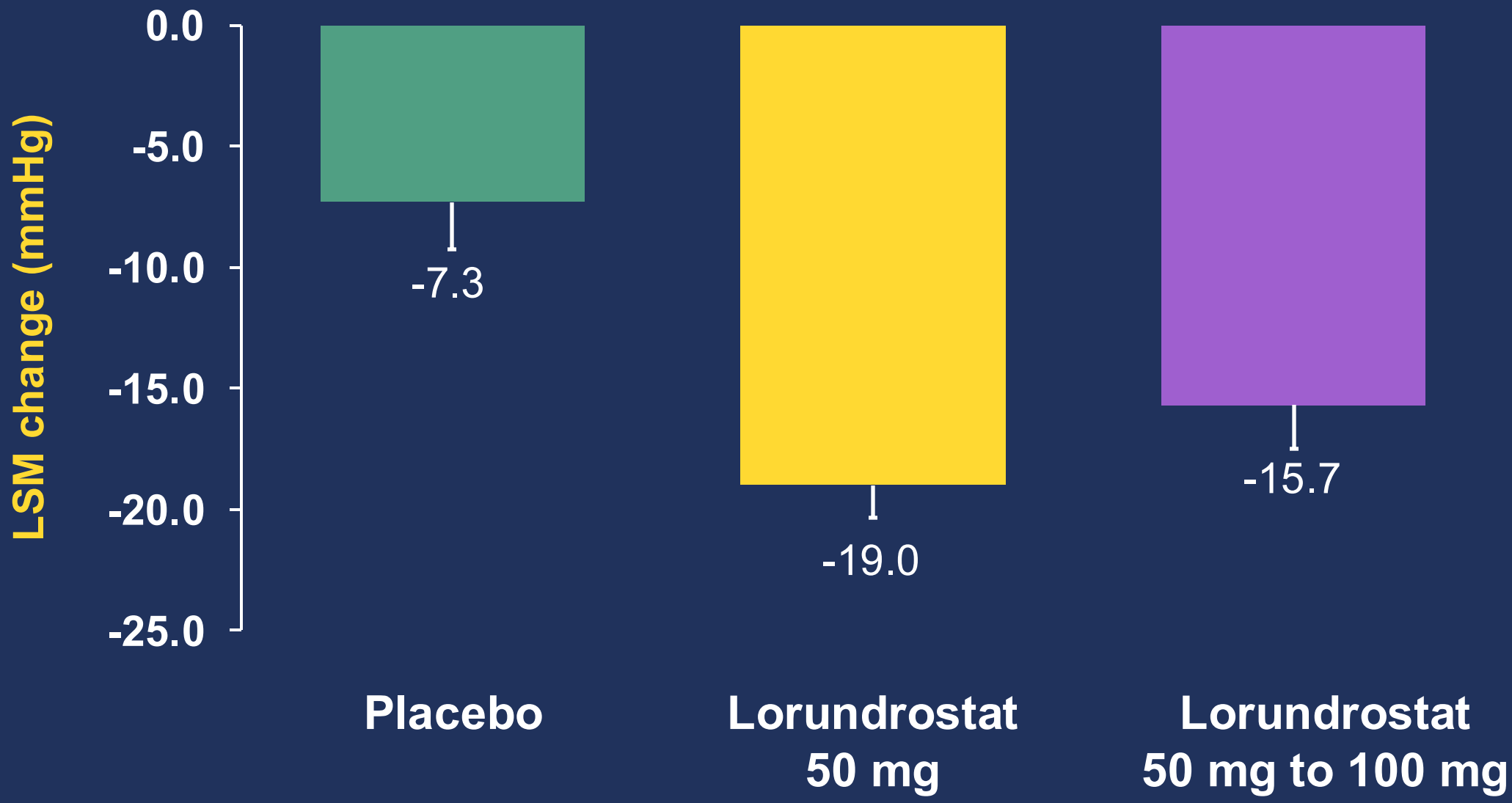
Primary End Point: AOSBP Change at Week 6



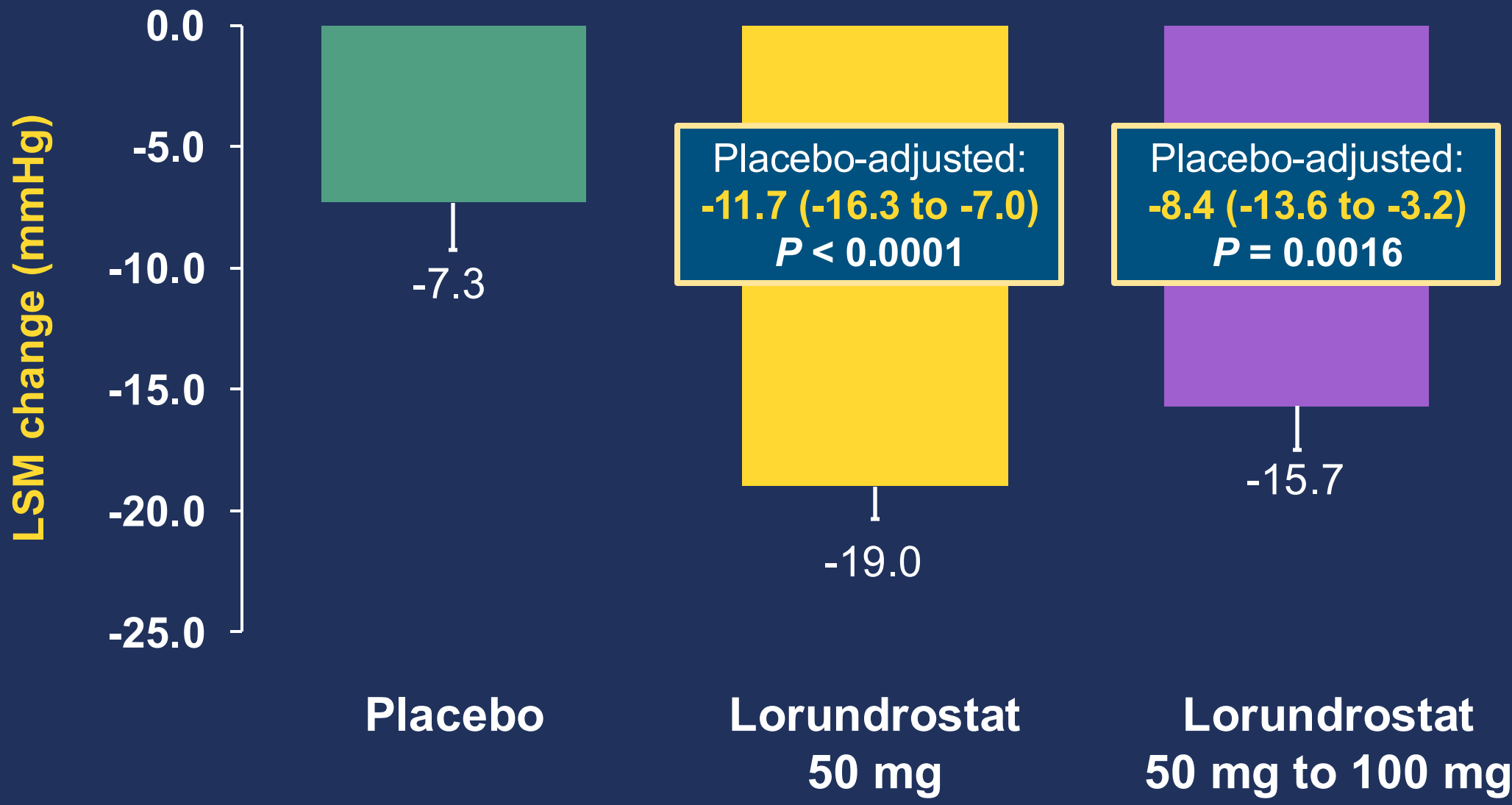
Primary End Point: AOSBP Change at Week 6



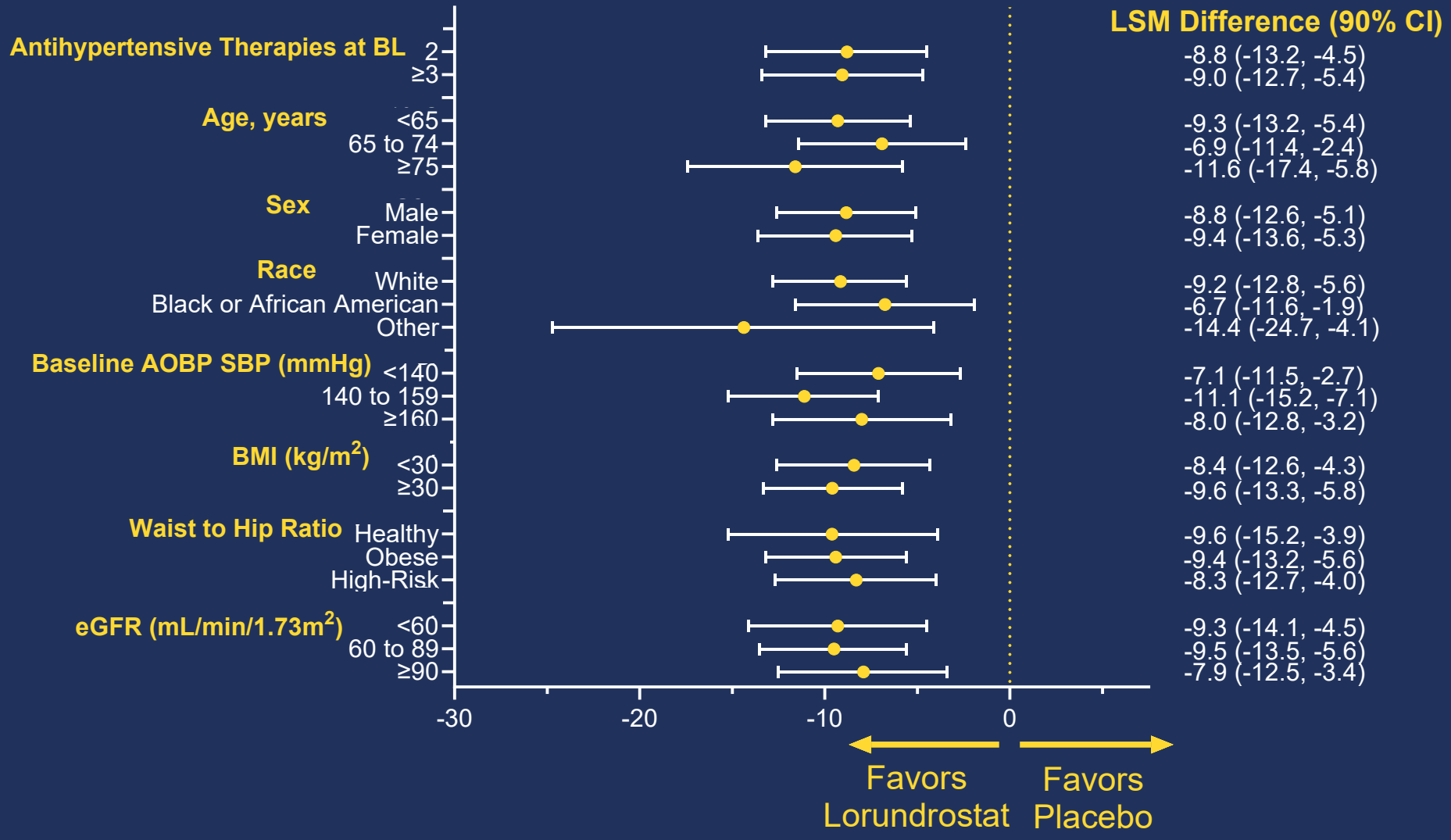
Predefined End Point: AOSBP Change at Week 12



Predefined End Point: AOSBP Change at Week 12



Lorundrostat 50mg at Week 6 (Pooled): Efficacy was Consistent Across Subgroups



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 -Single value	0.7%	1.1%	1.5%
Serum Potassium >6.0 mmol / L -Confirmed per protocol repeat testing	0.4%	0.6%	1.1%
Death*	0.4%	0	0

*One death occurred and was not related to treatment

Adverse Events of Special Interest[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%	2.6%
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.

Conclusions

- Launch-HTN demonstrated efficacy, safety, and tolerability of lorundrostat in a large cohort of diverse participants sustained through week 12
- Consistent efficacy and safety across all subgroups in Launch-HTN supports broad patient selection for lorundrostat treatment
- Lorundrostat was well tolerated with modest increase in serum potassium
- Reduction in AOSBP was clinically meaningful and sustained reduction with long-term treatment would confer cardiovascular-renal protection
- Lorundrostat has demonstrated consistent results across 3 clinical trials
  - The results of Launch-HTN (AOBP) and Advance-HTN (ABPM)[1] complement each other

1. Laffin LJ, et al. *NEJM* 2025[epub ahead of print].

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