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Scientific Sessions

TRANSFORM-HTN: LONG-TERM EFFICACY AND SAFETY OF NOVEL ALDOSTERONE SYNTHASE INHIBITOR LORUNDROSTAT IN UNCONTROLLED HYPERTENSION

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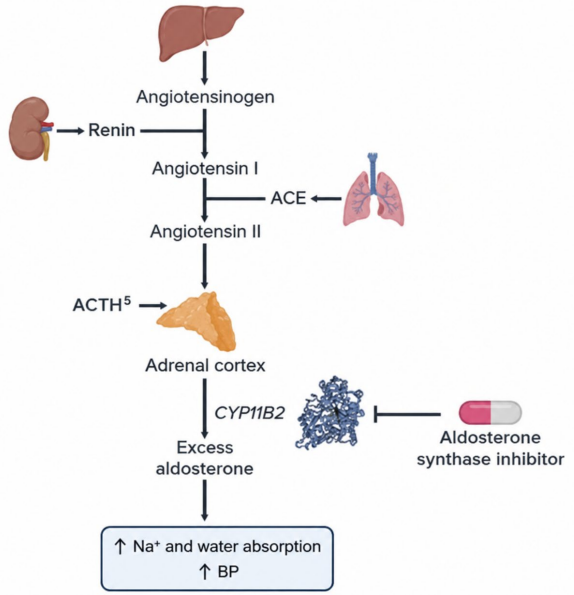
DISCLOSURES

- Consulting fees from Alnylam, Arrowhead, AstraZeneca, Boehringer Ingelheim, C4 Research, Daiichi Sankyo, Sanofi, IQVIA, Mineralys Therapeutics, Menarini Group, Novartis, PPD, Recor Medical, Vifor Pharma
- Institutional grant from Ablative Solutions, MSD, Recor Medical, and Applied Therapeutics
- Advisory boards for Alnylam, Arrowhead, AstraZeneca, BMS, Boehringer Ingelheim, Daiichi Sankyo, Menarini Group, Sobi, MSD
- Executive Committee member British & Irish Hypertension Society

BACKGROUND

- Dysregulated aldosterone contributes to uncontrolled and resistant HTN, and increases the risk for adverse cardiorenal outcomes[1,2]
- Lorundrostat demonstrated BP-lowering efficacy and safety in the randomized, 12-week, double-blind, placebo-controlled phase 3 Launch-HTN trial[3]
- Transform-HTN is an open-label extension trial of lorundrostat for participants enrolled in 1 of 3 parent studies, including Launch-HTN

Lorundrostat is a highly selective ASI[4]



This presentation focuses on long-term efficacy and safety of lorundrostat for participants in the lorundrostat arms of the Launch-HTN trial who enrolled in the Transform-HTN OLE trial

ACE, angiotensin converting enzyme; ACTH, adrenocorticotropic hormone; ASI, aldosterone synthase inhibitor; BP, blood pressure; HTN, hypertension; OLE, open-label extension.

Figure adapted from: Patel SK, et al. *Card Fail Rev*. 2025:11:e20. **1**. Monticone S, et al. *Lancet Diabetes Endocrinol*. 2018;6(1):41-50. **2**. Verma A, et al. *Eur Heart J*. 2022;43:3781-3791. **3**. Saxena M, et al. *JAMA*. 2025;334(5):409-418. **4**. Patel SK, et al. *Card Fail Rev*. 2025:11:e20. **5**. Papadopoulou-Marketou N, et al. Hyperaldosteronism. In: Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc. Accessed October 2026

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STUDY POPULATION KEY ELIGIBILITY CRITERIA

Launch-HTN Double-Blind Phase 3 Trial (NCT06153693)

Inclusion Criteria

- Male or female aged ≥18 years
- Office SBP 135-180 mmHg and diastolic BP 65-110 mmHg or isolated office diastolic BP 90-110 mmHg at screening and randomization
- 2-5 AHTs, including thiazide/thiazide-like diuretic, for ≥1 month pre-screening

Exclusion Criteria

- eGFR <45 ml/min/1.73 m^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

Transform-HTN Open-Label Extension Trial (NCT05968430)

Inclusion Criteria

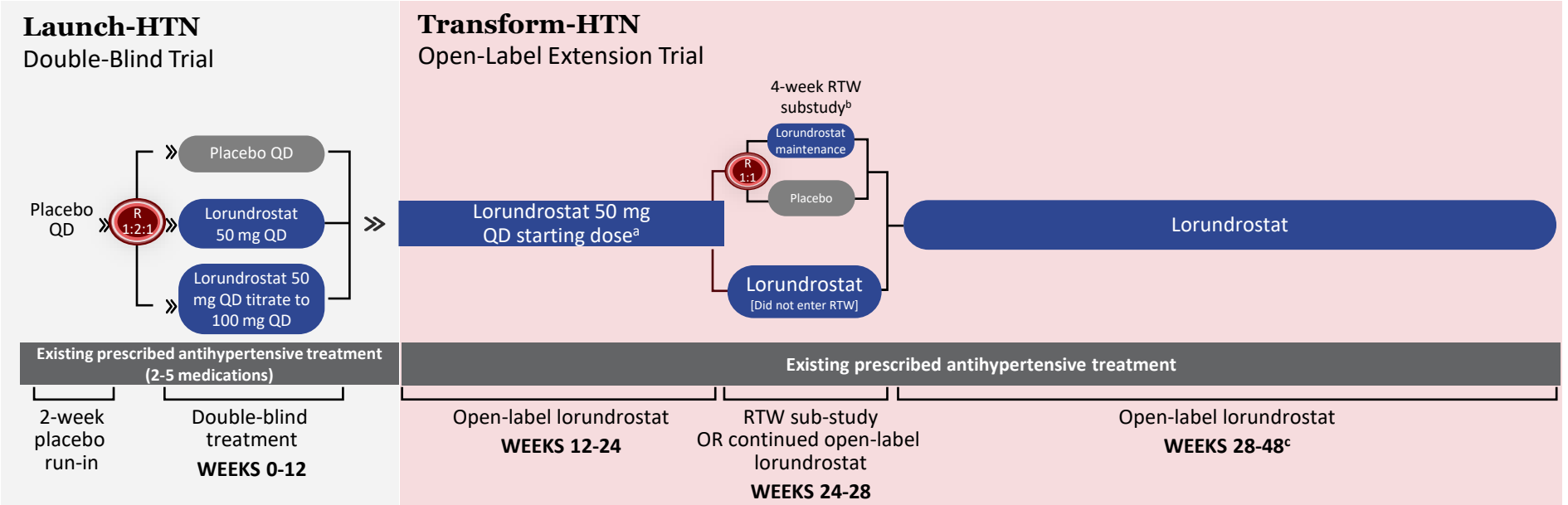
- Completed the End of Treatment Visit in Launch-HTN, Advance-HTN, or Explore-CKD

Exclusion Criteria

- Use, or anticipated use during the course of the study, of a prohibited medication
- In the opinion of the investigator, any condition that will preclude participation in the study

AHT, antihypertensive treatment; BP, blood pressure; eGFR, estimated glomerular filtration rate; MRA, mineralocorticoid receptor antagonist; SBP, systolic blood pressure.

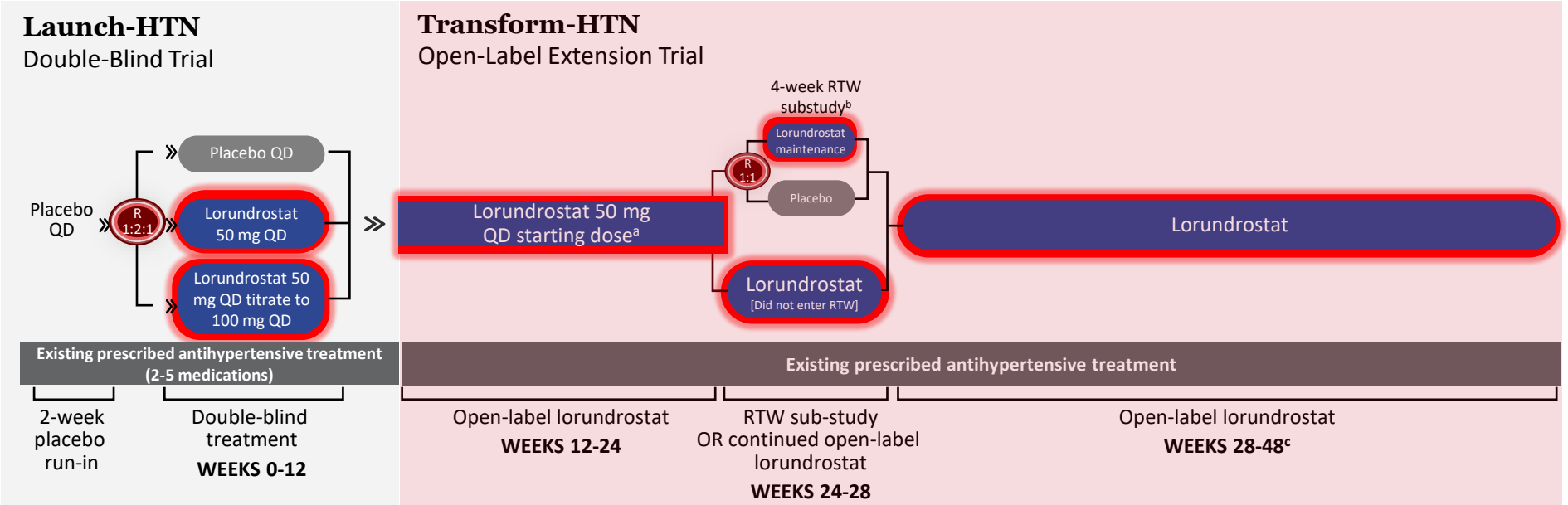
LAUNCH-HTN PHASE 3 TRIAL AND TRANSFORM-HTN OLE TRIAL DESIGN



[a]Participants who had a permanent dose reduction in Launch-HTN started the OLE at a lorundrostat dose of 25 mg QD.

[b]Participants eligible for the RTW sub-study had to have a reduction of ≥5 mmHg in office SBP from Launch-HTN baseline at Week 24. [c]Analysis conducted at Week 48. Transform-HTN comprises a 52-week treatment period following the 12-week double-blind period in Launch-HTN (overall treatment duration 64 weeks). OLE, open-label extension; QD, once-daily; R, randomized; RTW, randomized treatment withdrawal; SBP, systolic blood pressure.

EFFICACY EVALUATION

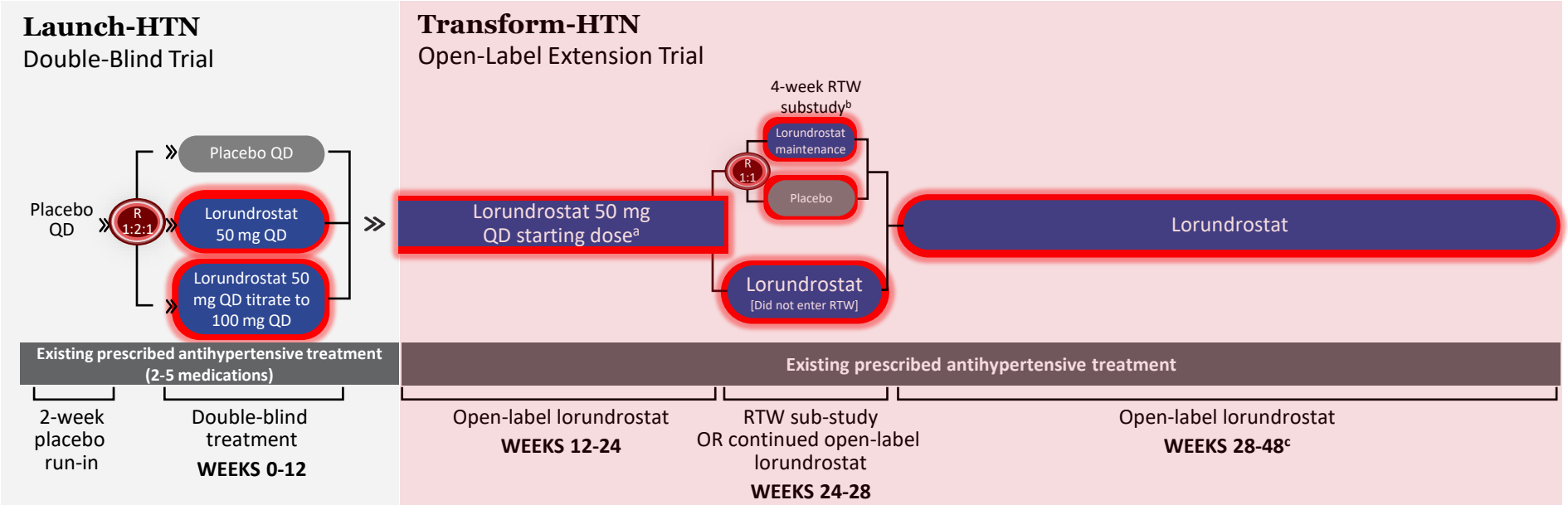


Efficacy analyses include participants assigned to lorundrostat arms in Launch-HTN who received ≥1 dose of lorundrostat in the OLE and were not assigned to placebo in the RTW (n=504)

[a]Participants who had a permanent dose reduction in Launch-HTN started the OLE at a lorundrostat dose of 25 mg QD.

[b]Participants eligible for the RTW sub-study had to have a reduction of ≥5 mmHg in office SBP from Launch-HTN baseline at Week 24. [c]Analysis conducted at Week 48. Transform-HTN comprises a 52-week treatment period following the 12-week double-blind period in Launch-HTN (overall treatment duration 64 weeks). OLE, open-label extension; QD, once-daily; R, randomized; RTW, randomized treatment withdrawal; SBP, systolic blood pressure.

SAFETY EVALUATION



Safety analyses include participants assigned to lorundrostat arms in Launch-HTN who received ≥1 dose of lorundrostat in the OLE (n=632)

[a]Participants who had a permanent dose reduction in Launch-HTN started the OLE at a lorundrostat dose of 25 mg QD.

[b]Participants eligible for the RTW sub-study had to have a reduction of ≥5 mmHg in office SBP from Launch-HTN baseline at Week 24. [c]Analysis conducted at Week 48. Transform-HTN comprises a 52-week treatment period following the 12-week double-blind period in Launch-HTN (overall treatment duration 64 weeks). OLE, open-label extension; QD, once-daily; R, randomized; RTW, randomized treatment withdrawal; SBP, systolic blood pressure.

LONG-TERM EFFICACY AND SAFETY OUTCOMES

Efficacy Endpoints*

- **Primary**: Change in office SBP from baseline of Launch-HTN to Week 48*
- Proportion achieving office SBP <130 mmHg at Week 48*
- RAAS biomarker changes

Safety

- TEAEs, AESIs, and confirmed serum potassium elevation
  - Assessed in the OLE period (Weeks 12-48)
- Change in eGFR and serum potassium and sodium
  - Assessed during the double-blind period in Launch-HTN (Weeks 0-12) and the OLE period in Transform-HTN (Weeks 12-48)

Asterisk denotes prespecified efficacy endpoints; other efficacy endpoints were not prespecified. AESI, adverse event of special interest; eGFR, estimated glomerular filtration rate; OLE, open-label extension; RAAS, renin-angiotensin-aldosterone system; SBP, systolic blood pressure; TEAE, treatment-emergent adverse event.

DISPOSITION AND BASELINE CHARACTERISTICS

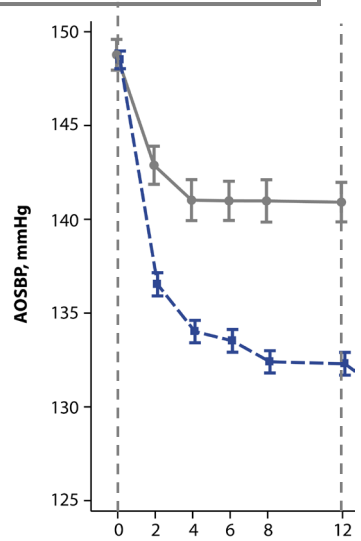
- Of 808 patients who received ≥1 dose of lorundrostat in Launch-HTN, 632 (78%) enrolled in the OLE
- 549/632 (87%) completed treatment at Week 48
- 583/632 (92%) completed 48 weeks of follow-up
- The median (IQR) duration of treatment was 47.9 weeks (46.7, 48.4)[a]

	Lorundrostat (N=632)
Age, mean ±SD, years	61.2 ± 10.5
Female, n (%)	292 (46.2)
Black or African American, n (%)	155 (24.5)
Hispanic or Latino, n (%)	248 (39.2)
BMI ≥30 kg/m^2	395 (62.5)
Mean ±SD eGFR[b], mL/min/1.73 m^2	92.7 ± 17.4
Office SBP, mean ±SD, mmHg	148.5 ± 11.9
Concomitant AHT medications, n (%)	
2 AHTs	262 (41.5)
≥3 AHTs	370 (58.5)
AHT drug class, n (%)	
Thiazide or thiazide-like diuretic	601 (95.1)
ACE inhibitor or ARB	546 (86.4)
Calcium channel blocker	295 (46.7)
Beta blockers	209 (33.1)

[a]Analysis includes participants assigned to double-blind treatment in the 4-week RTW. [b]eGFR based on CKD-EPI 2021 equation. ACE, angiotensin-converting enzyme; AHT, antihypertensive; ARB, angiotensin receptor blockers; BMI, body mass index; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; IQR, interquartile range; OLE, open-label extension; SBP, systolic blood pressure; SD, standard deviation.

OFFICE SBP REDUCTIONS WITH LORUNDROSTAT MAINTAINED THROUGH 48 WEEKS

Baseline mean office SBP: 147.9 mmHg



Placebo

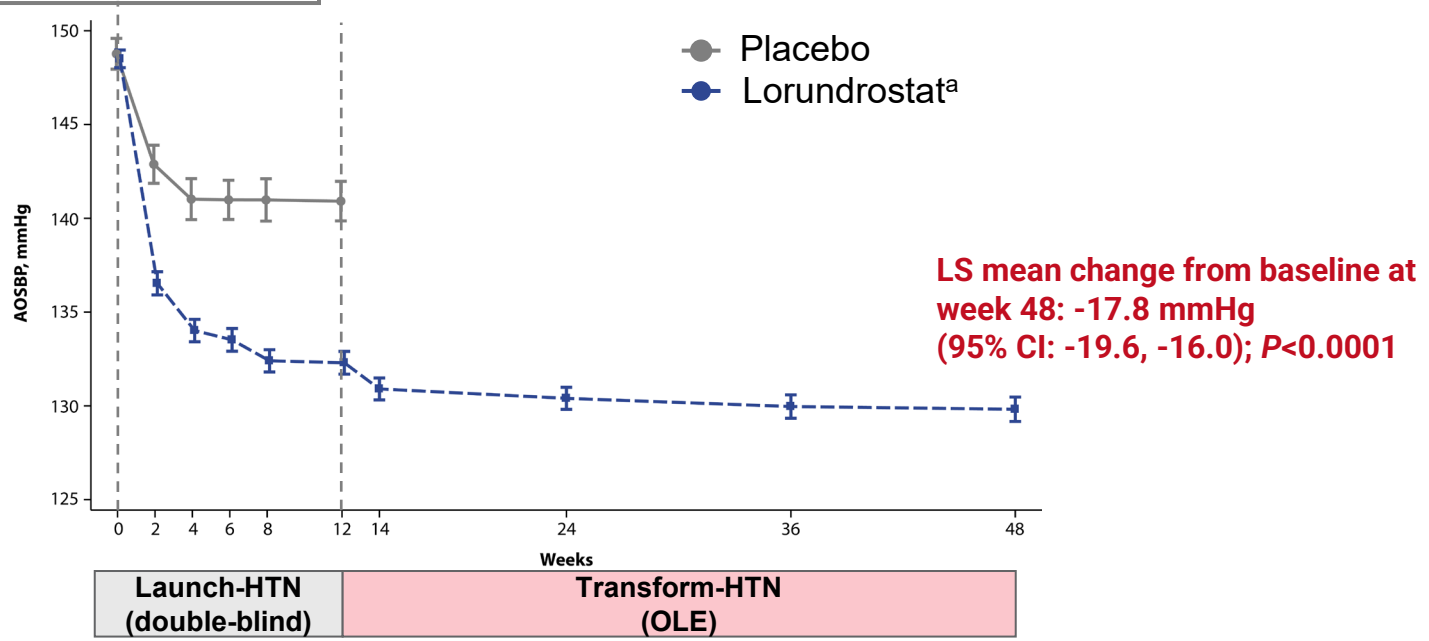
Lorundrostat[a]

Launch-HTN (double-blind)

[a]Baseline to Week 12 data for lorundrostat include participants in the 50 mg and 50-100 mg lorundrostat groups of Launch-HTN who entered the OLE.
Data in the figure are observed SBP. Error bars represent SE. The LS mean estimate is based on 1,000 imputed datasets using a treatment policy approach. Data for missing observations at Week 48 were imputed using a shift factor based on change in SBP at Week 12 in the subjects who were randomized to placebo during the double-blind phase. LS, least-squares; OLE, open-label extension; SBP, systolic blood pressure; SE, standard error.

OFFICE SBP REDUCTIONS WITH LORUNDROSTAT MAINTAINED THROUGH 48 WEEKS

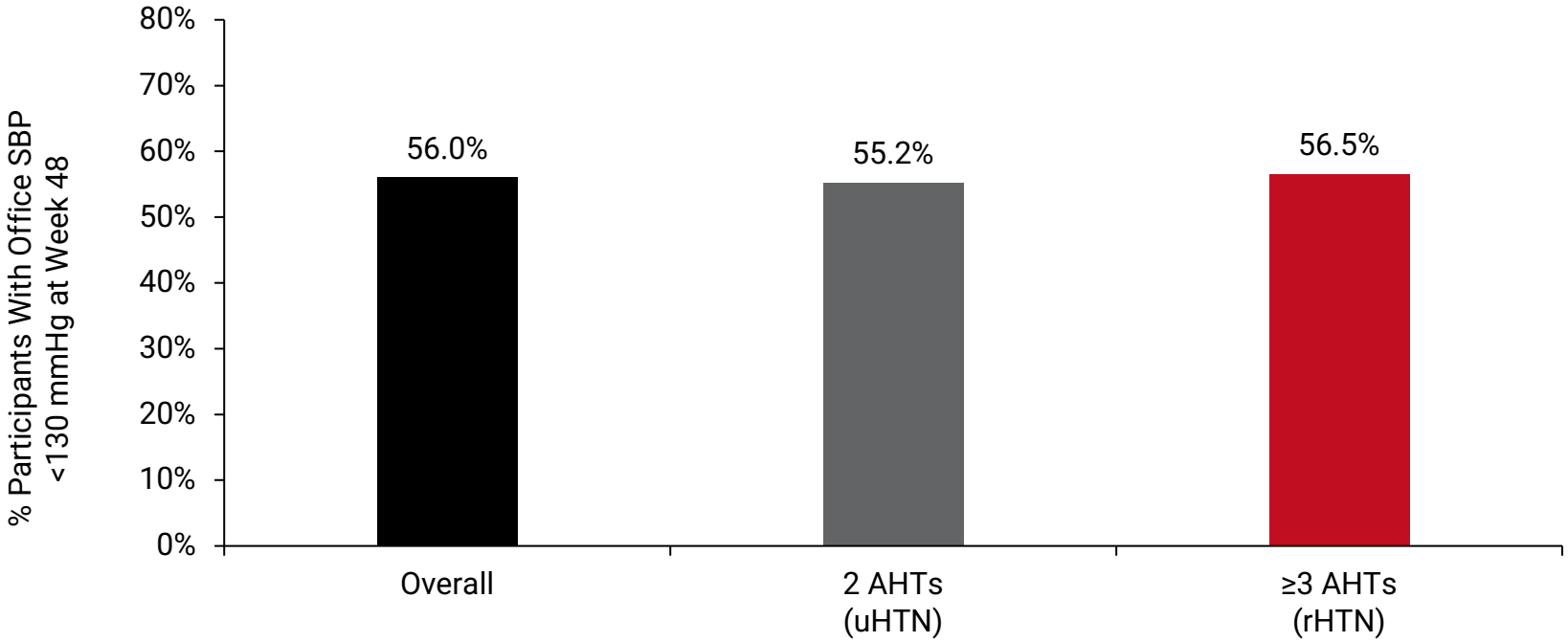
Baseline mean office SBP: 147.9 mmHg



LS mean change from baseline at week 48: -17.8 mmHg (95% CI: -19.6, -16.0); *P*<0.0001

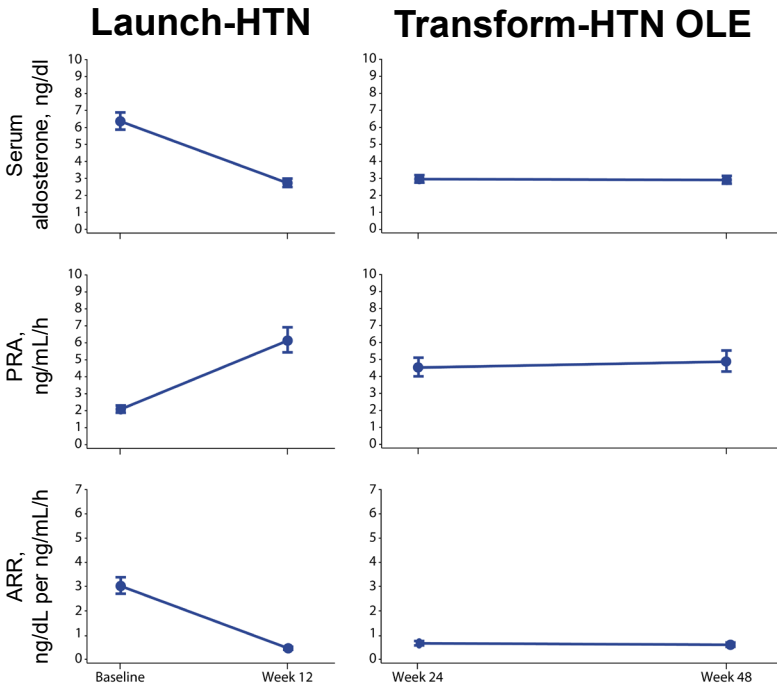
[a]Baseline to Week 12 data for lorundrostat include participants in the 50 mg and 50-100 mg lorundrostat groups of Launch-HTN who entered the OLE.
Data in the figure are observed SBP. Error bars represent SE. The LS mean estimate is based on 1,000 imputed datasets using a treatment policy approach. Data for missing observations at Week 48 were imputed using a shift factor based on change in SBP at Week 12 in the subjects who were randomized to placebo during the double-blind phase. LS, least-squares; OLE, open-label extension; SBP, systolic blood pressure; SE, standard error.

PROPORTION ACHIEVING OFFICE SBP TARGET OF <130 mmHg WITH LORUNDROSTAT AT 48 WEEKS



AHT, antihypertensive; rHTN, resistant hypertension; SBP, systolic blood pressure; uHTN, uncontrolled hypertension.

REDUCTIONS IN ALDOSTERONE MAINTAINED THROUGH 48 WEEKS



Percent change in geometric mean from baseline at Week 48: -54.8%

Percent change in geometric mean from baseline at Week 48: +123.9%

Percent change in geometric mean from baseline at Week 48: -79.8%

Figures show geometric mean, with error bars for 95% CI.
ARR, aldosterone-renin ratio; OLE, open-label extension.

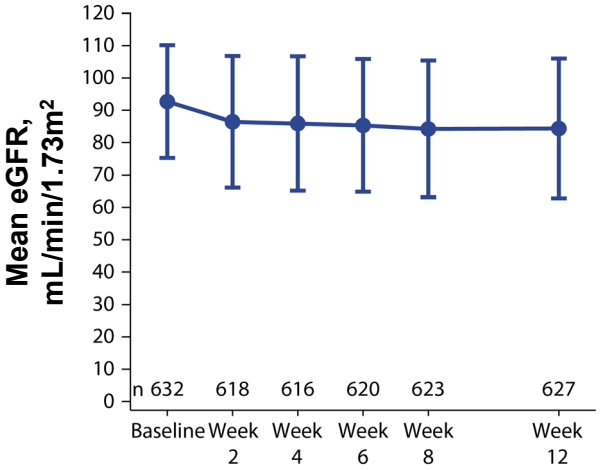
SAFETY DURING THE 36-WEEK OPEN-LABEL PERIOD

Participant, n (%)	Lorundrostat (N=632)
Any TEAE	413 (65.3)
Moderate intensity	141 (22.3)
Severe intensity	20 (3.2)
TEAE leading to study drug withdrawal	37 (5.9)
Hyperkalemia leading to study drug withdrawal	10 (1.6)
Any serious AE	27 (4.3)
Death	0
Treatment-related serious TEAE[a]	2 (0.3)
AESIs	
Hyperkalemia[b]	32 (5.1)
Hyponatremia[b]	28 (4.4)
Hypotension with symptoms	13 (2.1)
Serum Potassium >6.0 mmol/L (confirmed per protocol repeat testing)	**16 (2.5)**

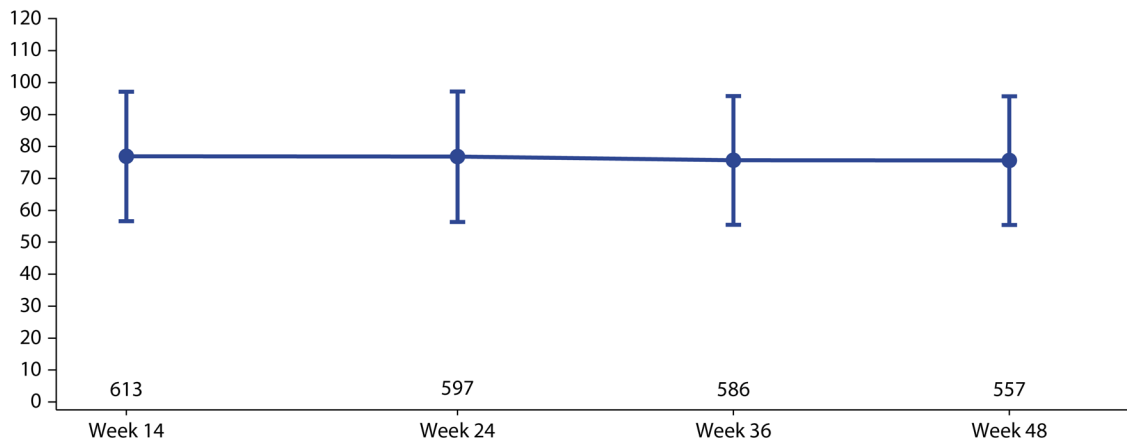
[a]Investigator determined. [b]Trial drug had to be modified due to the adverse event (dose reduction, interruption, or discontinuation).
AE, adverse event; AESI, adverse event of special interest; TEAE, treatment-emergent adverse event. .

eGFR OVER TIME WITH LORUNDROSTAT

Launch-HTN (Weeks 0-12)
Creatinine: enzymatic assay



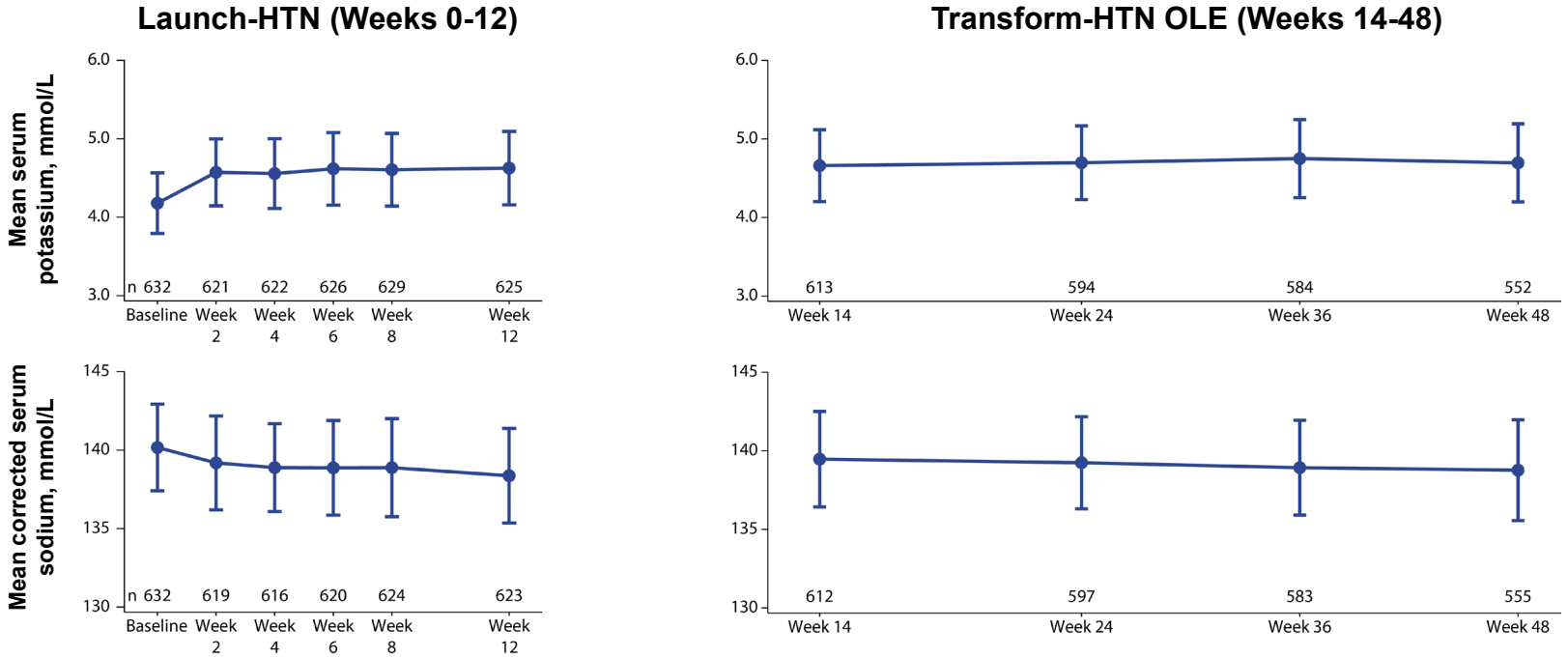
Transform-HTN OLE (Weeks 14-48)
Creatinine: Jaffe assay



- An early drop in eGFR was observed, as expected, after which eGFR remained stable within each study

Error bars show SD.
eGFR, estimated glomerular filtration rate; OLE, open-label extension; SD, standard deviation.

SERUM POTASSIUM AND SODIUM OVER TIME WITH LORUNDROSTAT



Error bars show SD.
OLE, open-label extension; SD, standard deviation.

SUMMARY

The Launch cohort of Transform-HTN is the largest long-term study of an ASI for the treatment of hypertension reported to date

Lorundrostat demonstrated consistent efficacy and safety with stable biomarker changes

Sustained BP control in adults with uncontrolled and resistant hypertension with up to 48 weeks of lorundrostat

- LS mean change from baseline at Week 48: -17.8 mmHg
- Office SBP <130 mmHg at Week 48 achieved by 56% of participants

Treatment with long-term lorundrostat was well tolerated, with no new clinically relevant safety findings

ASI, aldosterone synthase inhibitor; BP, blood pressure; LS, least squares; SBP, systolic blood pressure.

ACKNOWLEDGEMENTS

Participants

Investigators and Site Staff

Mineralys Therapeutics

THANK YOU

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