HIGHLY EFFECTIVE BLOOD PRESSURE LOWERING WITH LORUNDROSTAT, A NEW ALDOSTERONE SYNTHASE INHIBITOR, IN INDIVIDUALS WITH OBESITY AND RAAS DYSREGULATION

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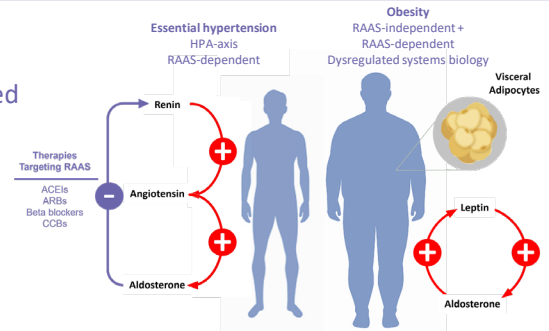
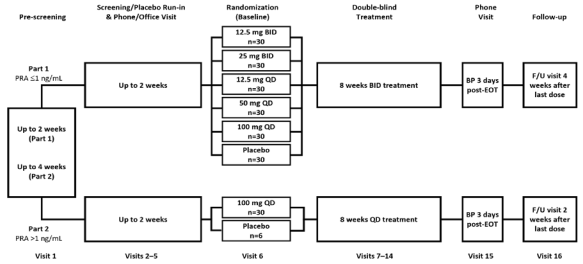
Lorundrostat is a novel aldosterone synthase inhibitor (ASI) with 374-fold selectivity for aldosterone vs. cortisol synthesis.

HYPOTHESIS: The endotype characterized by obesity-associated excess aldosterone production can be used to define a targeted approach for the development of lorundrostat.



ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CCB, calcium channel blocker; HPA, hypothalamic-pituitary-adrenal; RAAS, renin-angiotensin-aldosterone system.

TARGET-HTN TRIAL DESIGN



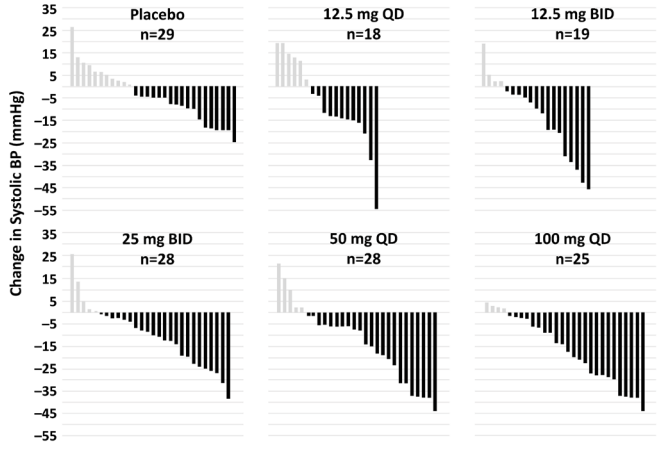
BID, twice daily; BP, blood pressure; EOT, end of treatment; FU, follow-up; PRA, plasma renin activity; QD, once daily.

BASELINE CHARACTERISTICS

CHARACTERISTIC	Part 1 (N=163)	Part 2 (N=37)
Mean ±SEM of baseline characteristic		
Age (years)	65.6±0.79	66.0±1.78
BMI (kg/m²)	31.2±0.41	30.7±0.70
Systolic BP (mmHg)	142.2±0.98	139.1±1.43
Diastolic BP (mmHg)	81.5±0.76	79.1±1.59
Baseline eGFR (mL/min)	78.9±1.3	79.6±2.4
Percentage (%) with baseline characteristic		
Male	41.7	32.4
Black	39.3	21.6
Hispanic or Latino	46.6	51.4
Diabetes	37.4	48.6
Heart failure	3.1	0
Previous myocardial infarction	5.5	5.4
Background anti-hypertensive medications ≤2	52.8	56.8
Background anti-hypertensive medications ≥3	47.2	35.1
Use of thiazide or thiazide-like diuretic	56.4	62.2
Use of ACEI or ARB	77.9	94.6

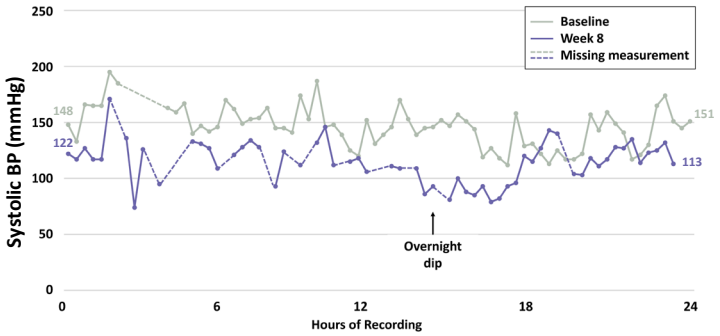
ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BMI, body mass index; BP, blood pressure; eGFR, estimated glomerular filtration rate.

CHANGE IN AOBP-MEASURED SYSTOLIC BP AT WEEK 8



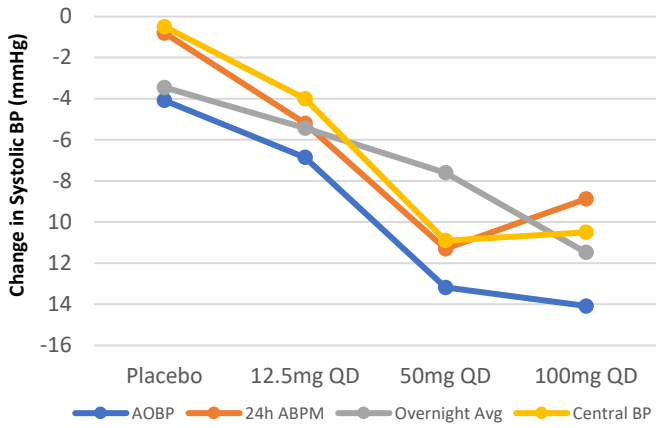
AOBP, automated office blood pressure; BID, twice daily; BP, blood pressure; QD, once daily.

EXAMPLE OF 24-H AMBULATORY SYSTOLIC BP 100 MG QD



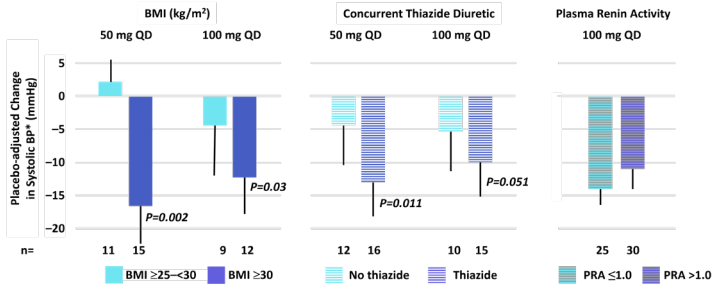
BP, blood pressure; H, hour; QD, once daily.

AOBP AND ABPM DOSE-RESPONSE CHANGE IN SYSTOLIC BP



AOBP, automated office blood pressure; ABPM, ambulatory blood pressure monitoring; BP, blood pressure; h, hour; QD, once daily.

BOTH BMI AND CONCURRENT USE OF A THIAZIDE, BUT NOT BASELINE RENIN, PREDICT RESPONSE TO LORUNDROSTAT



*Mean ± SEM

BMI, body mass index; BP, blood pressure; PRA, plasma renin activity; QD, once daily; SEM, standard error of the mean.

CONCLUSIONS: This phase 2 trial supports the continued development of once-daily lorundrostat for the treatment of hypertension. The efficacy results suggest that lorundrostat may be especially effective in obese individuals who have not responded to current standard-of-care anti-hypertensive therapy. Not shown were safety data demonstrating infrequent episodes of hyperkalemia and hyponatremia consistent with the mechanism of action.

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Disclosures: DR is an employee of Mineralys Therapeutics, LLC.
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