

Identification of a Hypertensive Endotype with a Median Treatment Effect of -32 mmHg in Response to the Novel Aldosterone Synthase Inhibitor Lorundrostat

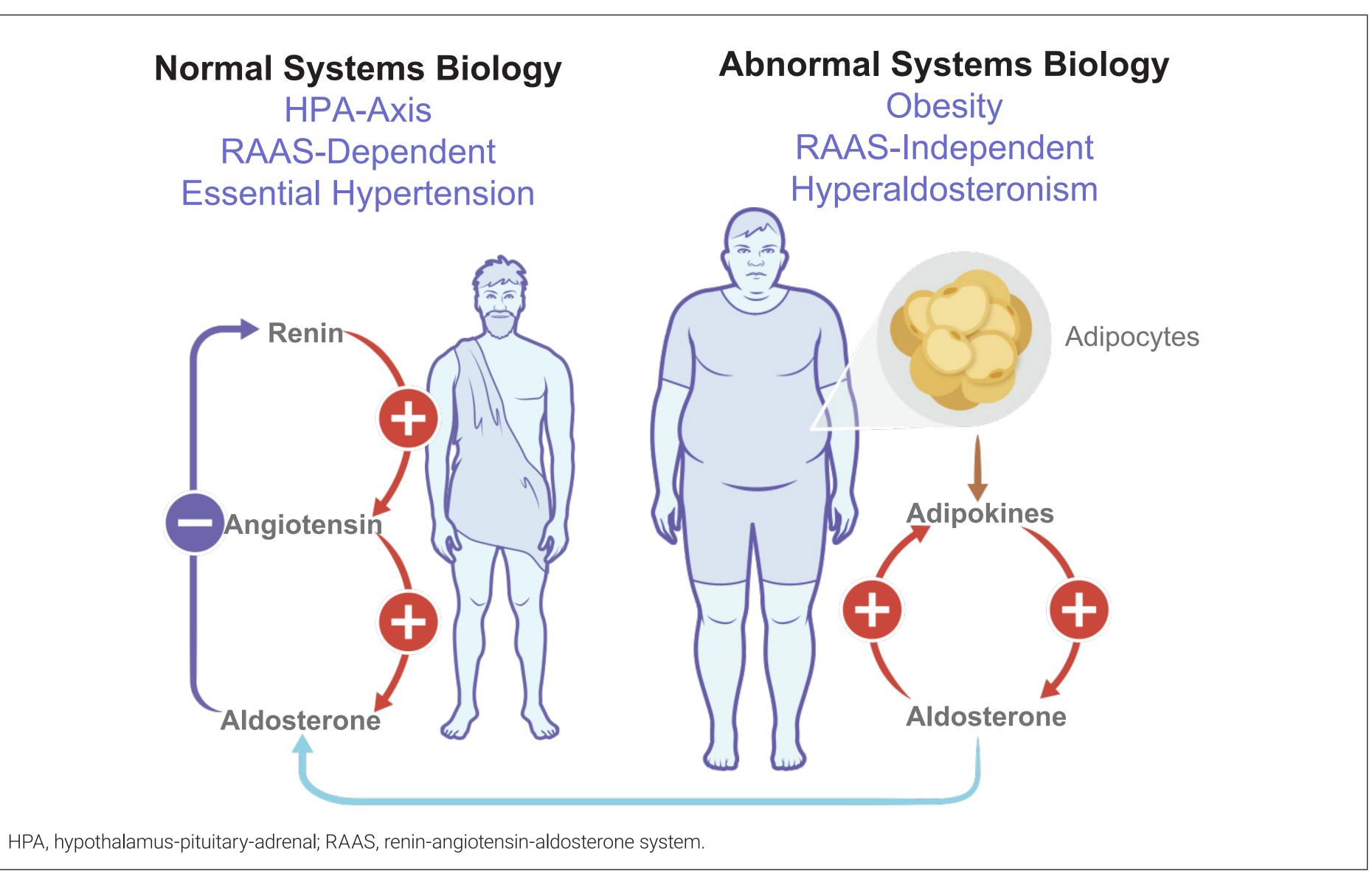
Borut Cizman¹, Luke Laffin², Natasa Rajicic³, and David M. Rodman¹

¹Mineralys Therapeutics, Radnor, PA; ²Cleveland Clinic Center for Clinical Research, Cleveland, OH; ³Cytel Inc, Waltham, MA

INTRODUCTION

- Effective, precision directed treatment of patients with uncontrolled and treatment-resistant hypertension who do not respond to current standard-of-care antihypertensive therapy is an urgent unmet need
- Dysregulated aldosterone is growing in prevalence, contributes to uncontrolled hypertension (uHTN), and may be particularly important in individuals with obesity¹
- Lorundrostat, a novel, highly selective aldosterone synthase inhibitor (ASI), led to substantial blood pressure (BP) reduction in adults with uHTN and an enhanced response in the subset of individuals with obesity in the TARGET-HTN trial²

Figure 1. Hypertensive endotype



OBJECTIVES

- To identify the adults with uHTN despite taking ≥2 antihypertensives who had an enhanced systolic BP reduction with lorundrostat treatment in TARGET-HTN
- To characterize the hypertensive endotype that supports an aldosterone targeted, precision directed treatment in uHTN

METHODS

Figure 2. TARGET-HTN study design

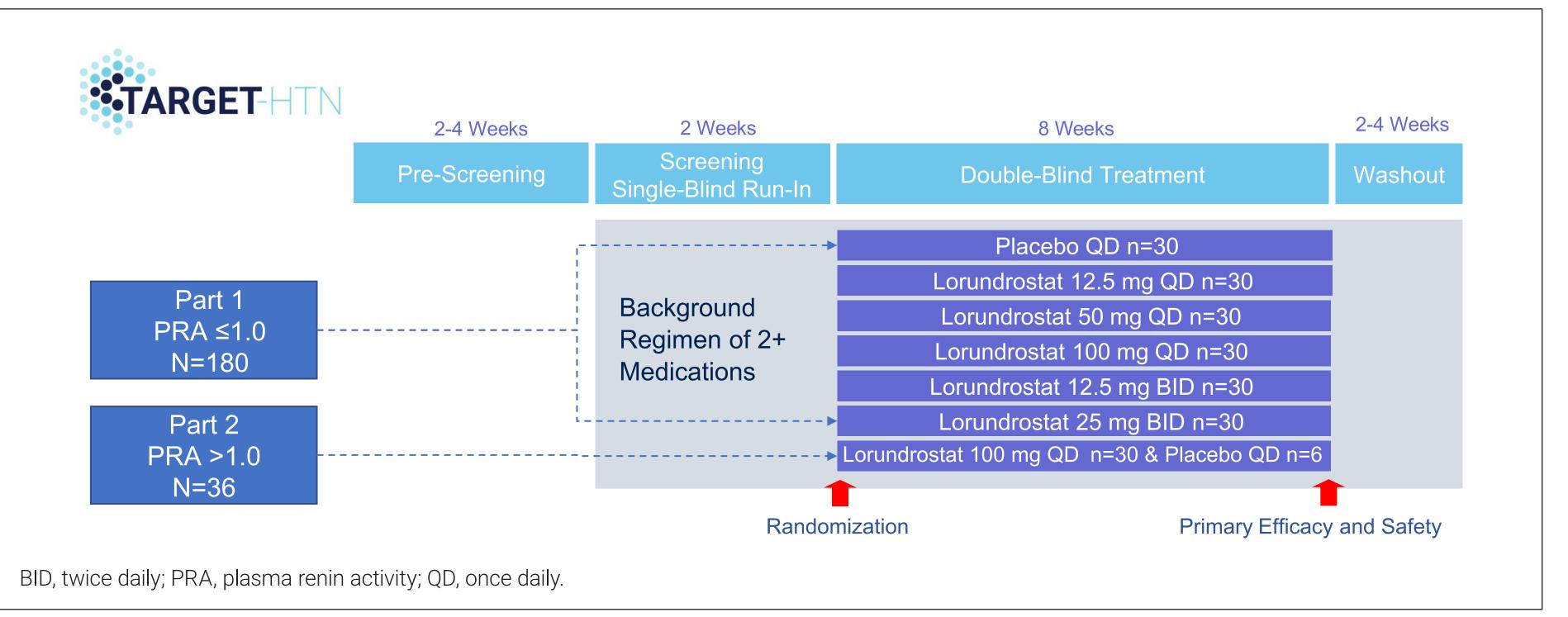


Table 1. Baseline demographics of non-obese and obese subjects in TARGET-HTN

Full Analysis Set (N=200), n (%)	BMI 25 to 29.9 (n=71)	BMI ≥30 (n=107)
Using 2 baseline HT meds	43 (60.6)	56 (52.3)
Using 3+ baseline HT meds	28 (39.4)	51 (47.7)
Using thiazide at baseline	37 (52.1)	66 (61.7)
Baseline systolic BP by AOBP <140 mmHg	35 (49.3)	52 (48.6)
Baseline systolic BP by AOBP ≥140 mmHg	36 (50.7)	55 (51.4)
African American	23 (32.4)	46 (43.0)
Male	30 (42.3)	43 (40.2)
AOBP systolic BP (mean, SD)	141.5 (9.6)	143 (10.9)
ABPM 24h systolic BP (mean, SD)	135.0 (13.2)	140.1 (14.0)
ABPM, ambulatory blood pressure monitoring; AOBP, automated offic	ce blood pressure; BMI, body mass index; BP, blo	od pressure; HT, hypertension; SD, standard

Figure 3. Percent change in serum aldosterone at week 4

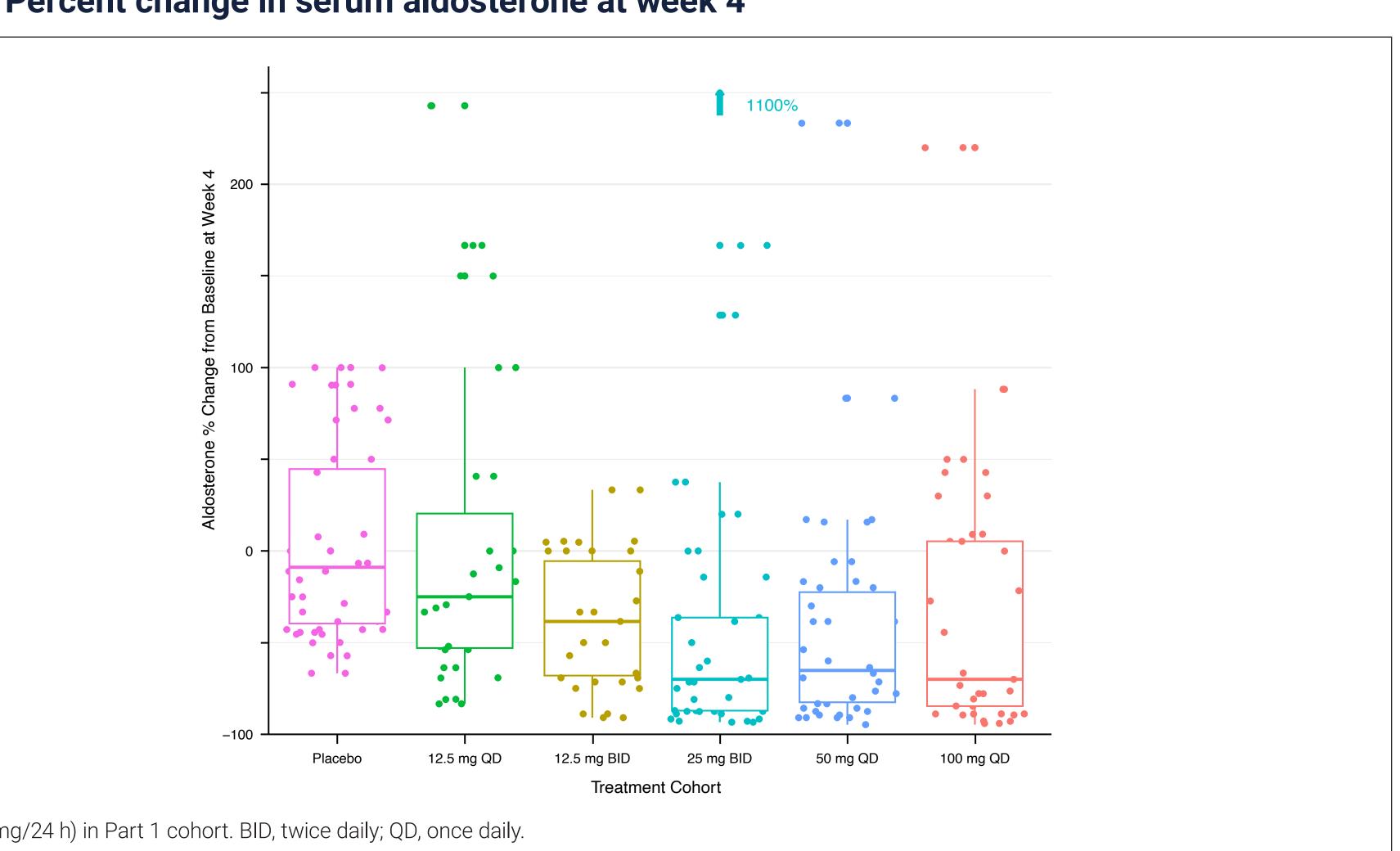


Figure 4. Change in systolic BP at week 8

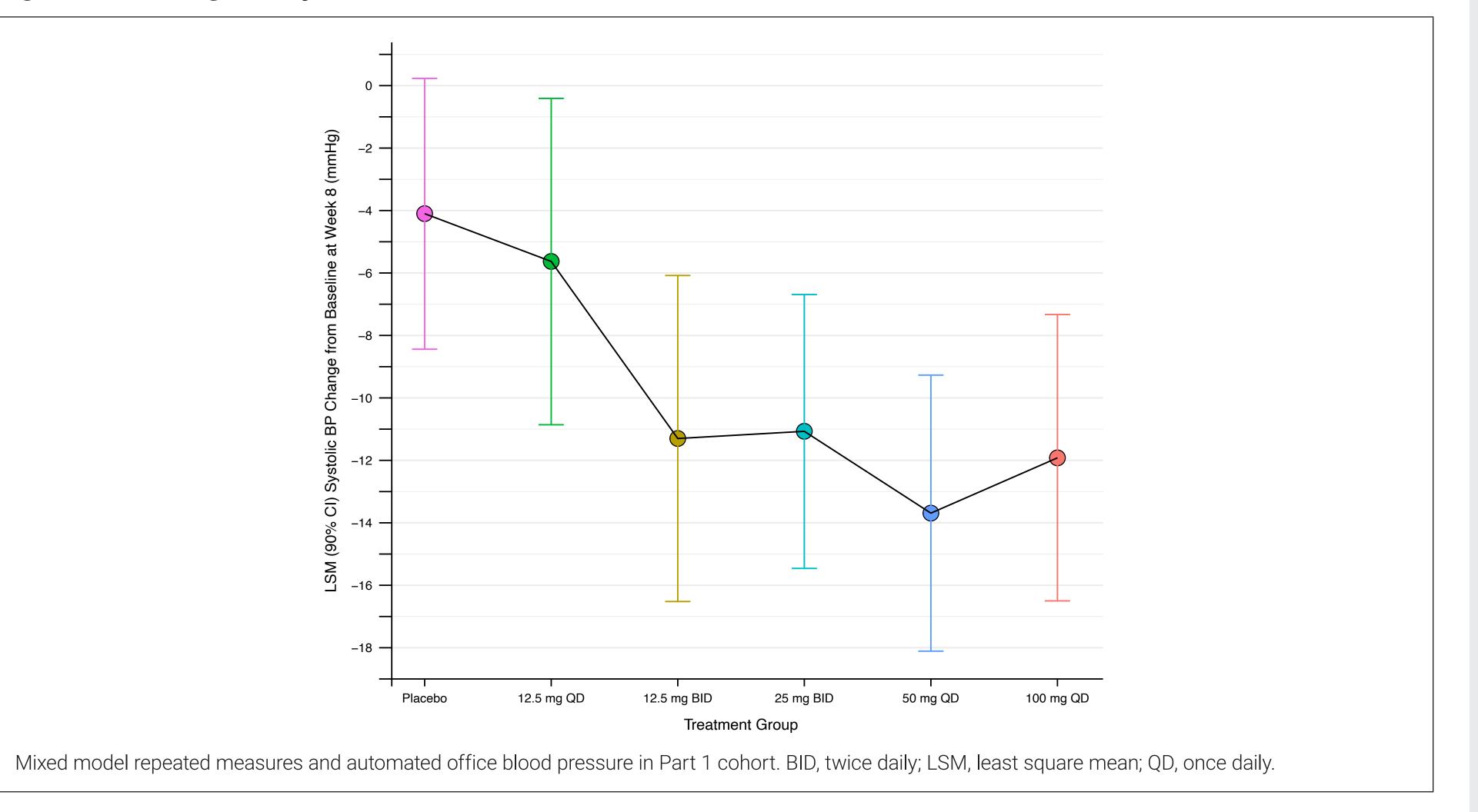


Figure 5. Change in systolic BP at week 8 pooled across lorundrostat doses 25 mg BID, 50 mg QD,

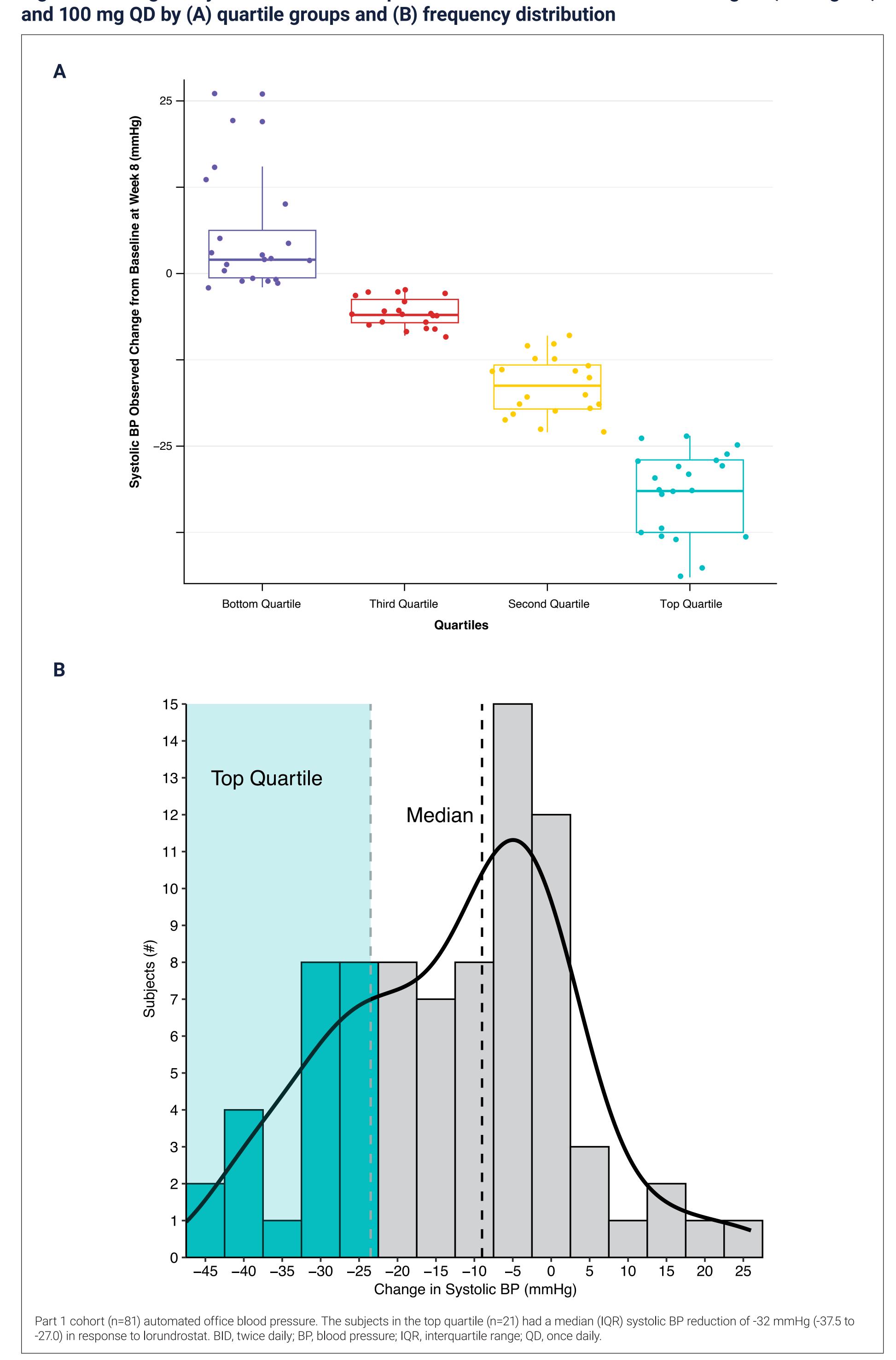
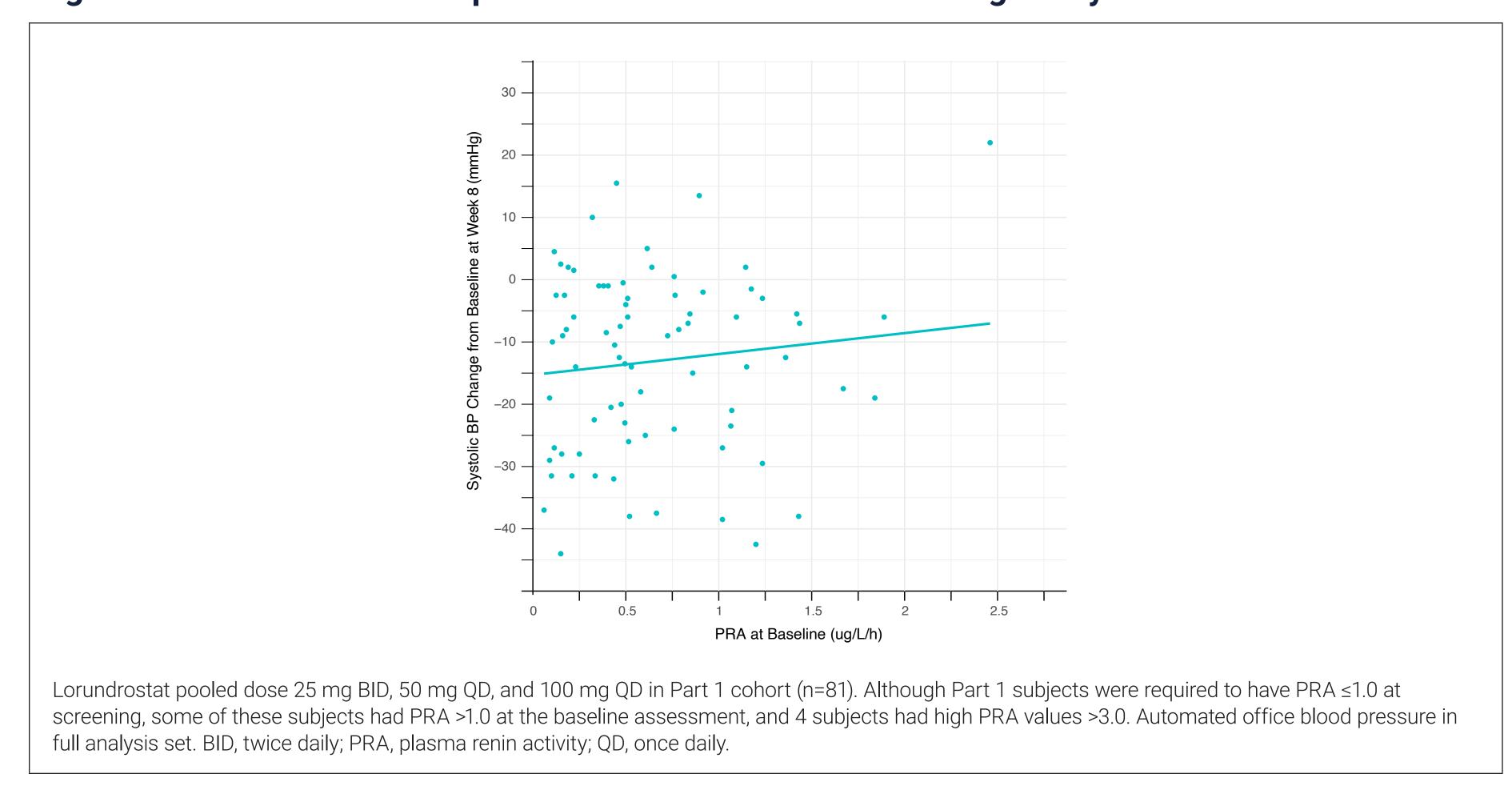
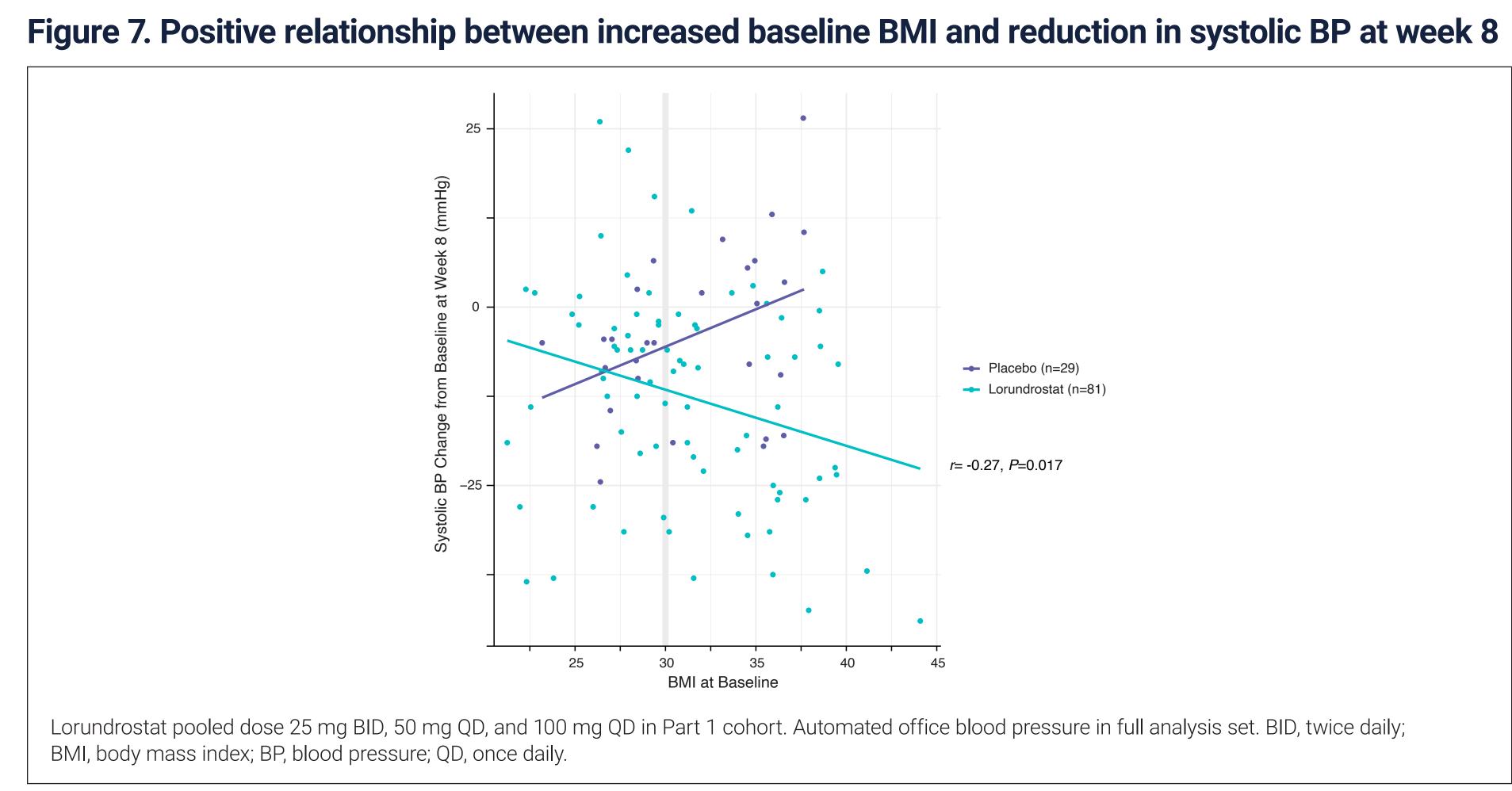


Figure 6. Minimal relationship between baseline PRA and change in systolic BP at week 8





CONCLUSIONS

- A population of adults with enhanced response to lorundrostat was identified. The enhanced response was associated with increasing BMI.
- An obesity-related, aldosterone-dependent hypertensive endotype indicates a need for a paradigm shift toward aldosterone targeted, precision therapy for hypertension management in these patients

REFERENCES

1. Kawarazaki W, Fujita, T. Am J Hypertens. 2016;29(4):415-42

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DISCLOSURES

BC and DMR: Employee of Mineralys Therapeutics, LLC. LL: Cleveland Clinic, his employer, was a study site for the TARGET-HTN trial; C5Research, the academic research organization of the Cleveland Clinic, receives payment for services related to other Mineralys Therapeutics clinical trials; consultant to Medtronic, Lilly, and Crispr Therapeutics; received grants from AstraZeneca and stock options for LucidAct Health and Gordy Health. NR: Payment for contract research organization services provided by Cytel from Mineralys Therapeutics, LLC.