

Paradise Ultrasound Renal Denervation (uRDN) System Reduces Blood Pressure in Patients with Uncontrolled Hypertension

August 22, 2023

Circulatory Systems Devices Panel

ReCor Medical



Introduction

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Hypertension is a Major Public Health Burden

- Lifestyle modifications and antihypertensive (anti-HTN) medications recommended based upon the severity of hypertension
- Reducing blood pressure lowers risk of CV morbidity and mortality^{1,2}
- Some patients are unable to control their blood pressure despite standard-of-care anti-HTN medications and remain at increased risk
 - Inadequately responsive or intolerant to standard-of-care
 - Unable to comply with prescribed treatment regimen

Unmet need for a safe and effective treatment alternative that reduces blood pressure with potential to improve outcomes

Paradise uRDN System is a Novel, Minimally Invasive, Catheter-Based Procedure

- Delivers circumferential ultrasound energy to thermally ablate and disrupt overactive sympathetic nerves along renal arteries
 - Simultaneously protects arterial wall from thermal injury
- Paradise System has two key components
 - Portable generator
 - Balloon catheter

Paradise System Components – Paradise Generator

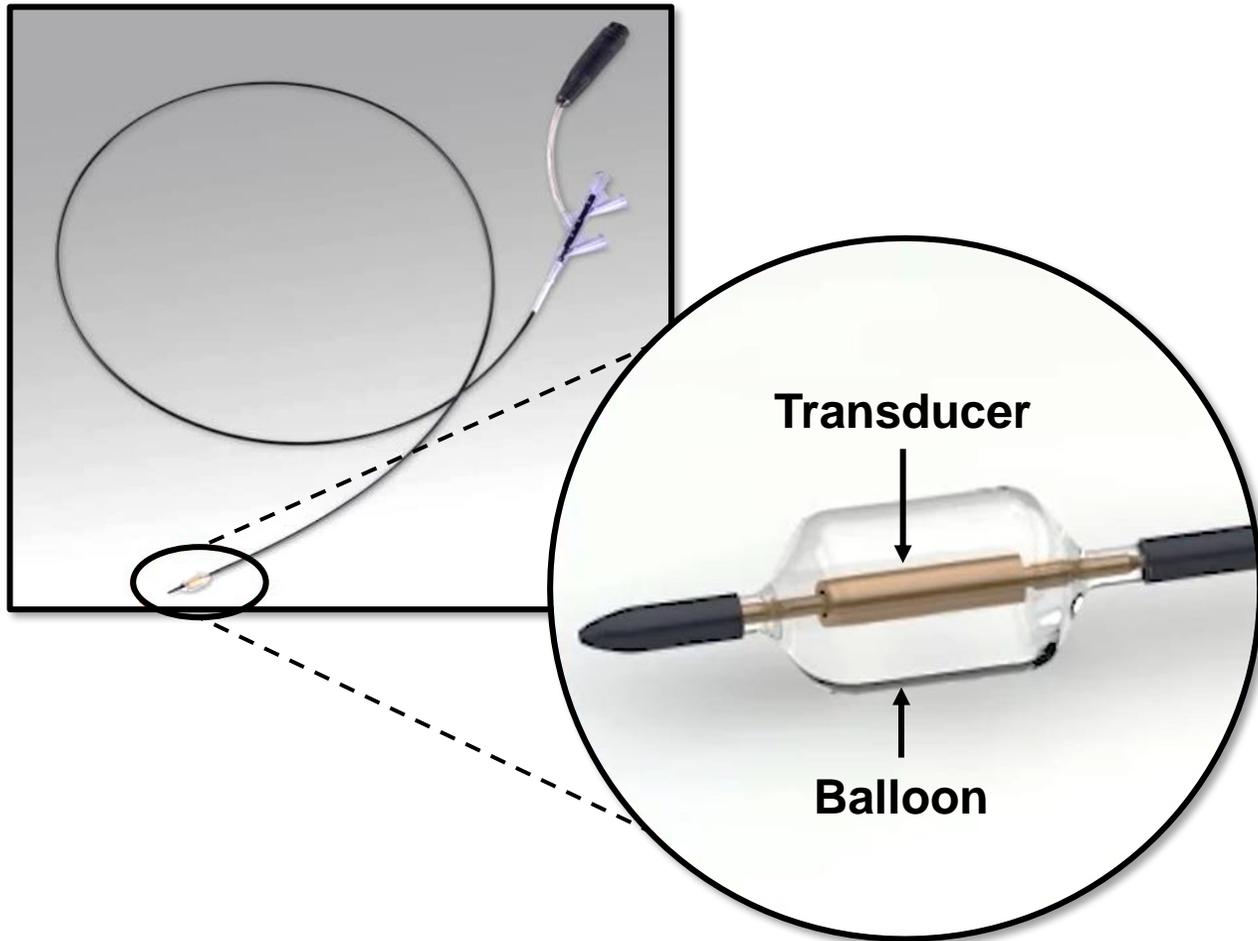
Paradise Generator



- Facilitates each step of procedure
- Controls ultrasound energy delivery parameters through automated process
- Adjusts acoustic power based on catheter size to achieve a consistent target depth of 1 – 6 mm ablation from arterial wall
 - All artery diameters ranging from 3 – 8 mm

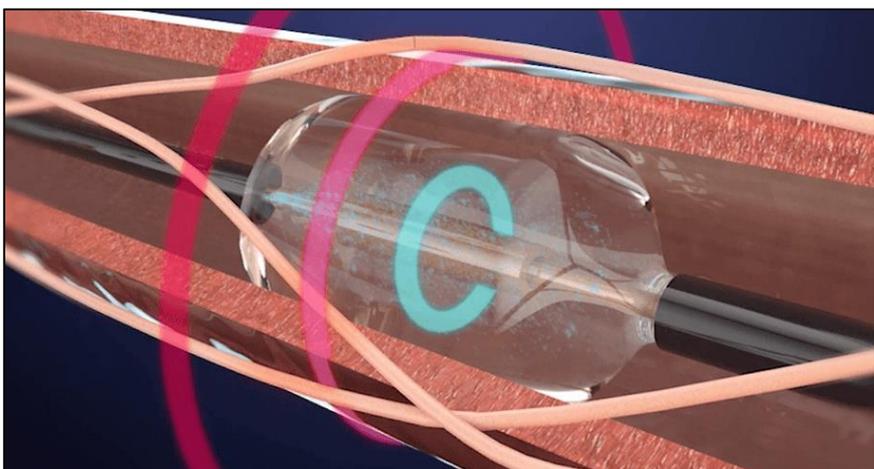
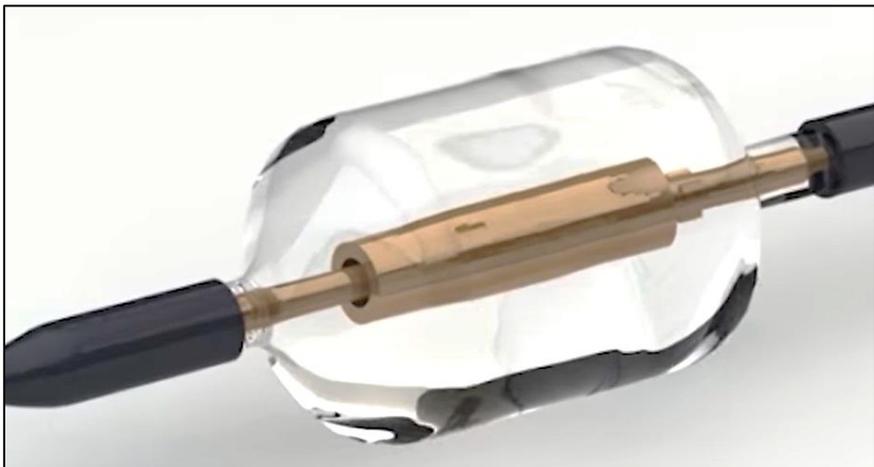
Paradise System Components – Paradise uRDN Balloon Catheter

Paradise Catheter



- Ultrasound transducer centered inside inflatable balloon
- Transducer converts electrical energy from generator to ultrasound energy
- Circulating sterile water within balloon cools artery wall
 - Protects arterial wall from thermal damage during energy delivery process

Paradise uRDN Delivers 360° Ultrasound Energy for Effective Nerve Ablation



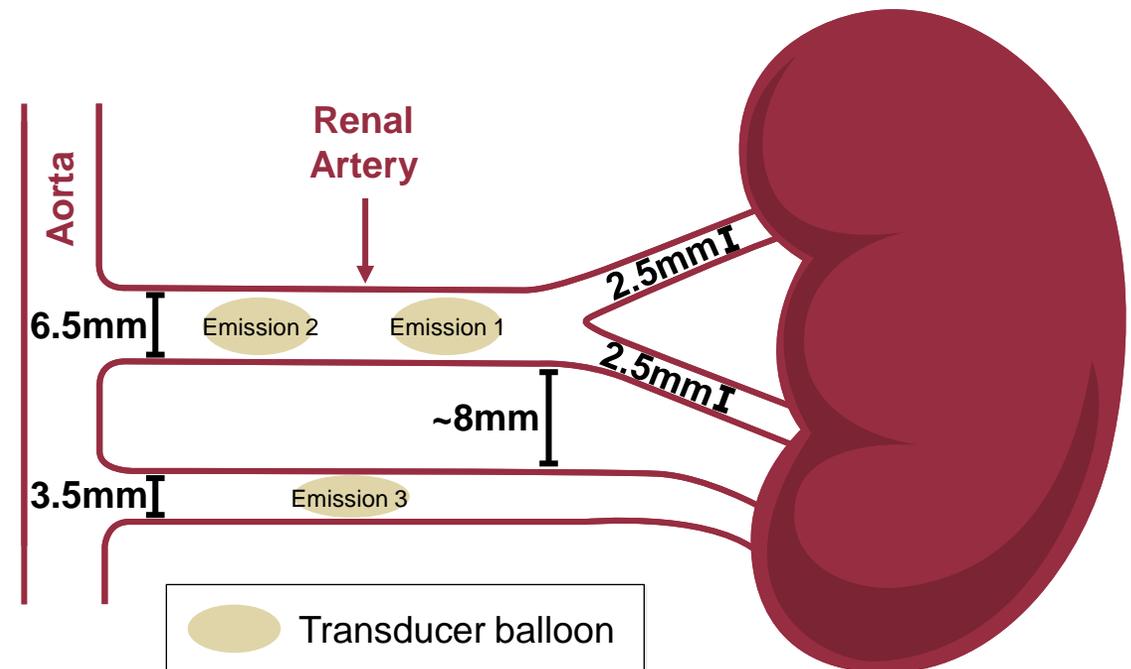
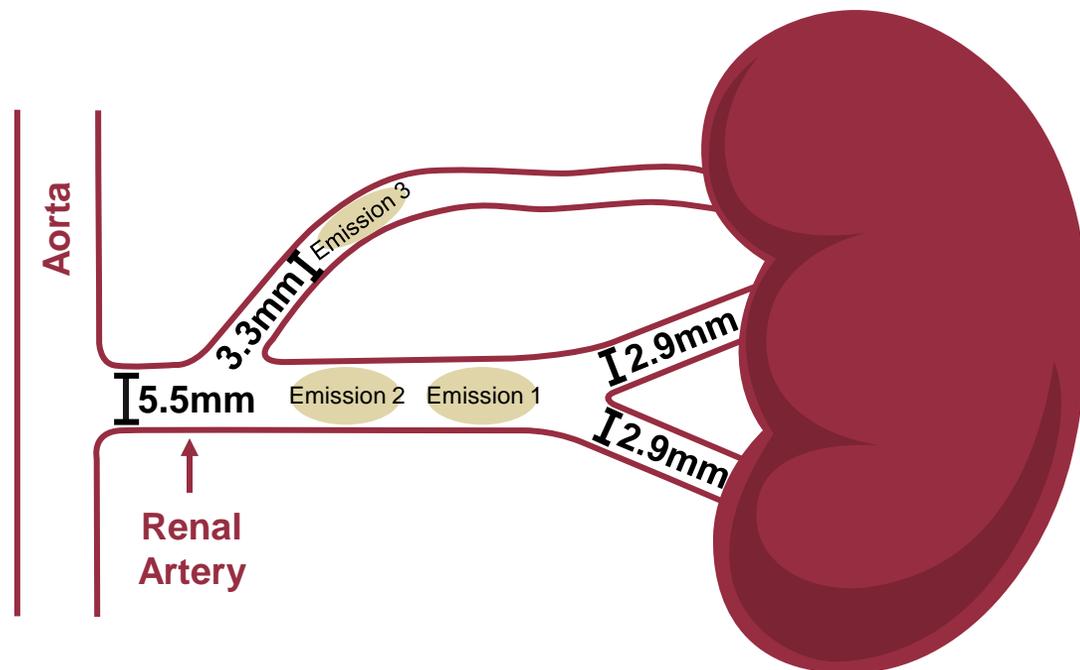
- Ablation profile confirmed by preclinical animal studies
 - Effectively ablates majority of renal sympathetic nerves at target depth of between 1 – 6 mm
 - Unique thermal profile and cooling system actively protects arterial wall, and non-target tissues eliminating potential for thermal damage

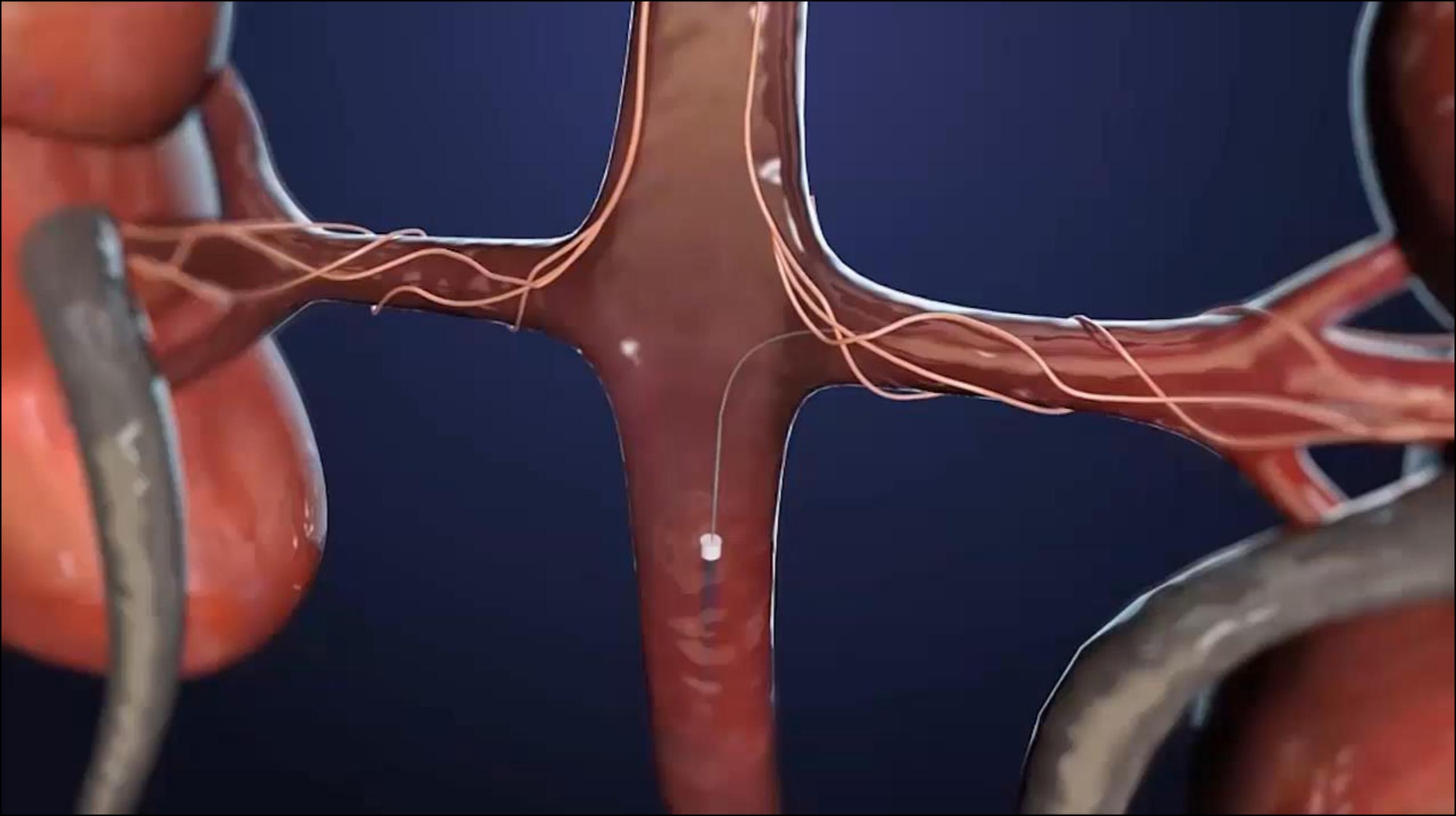
Treatment Strategy Developed Based on Preclinical Learnings and Confirmed in Clinical Studies

Treatment Strategy (3 – 8 mm diameter)

- **Main renal artery: 2 – 3 emissions**
- **Accessory/proximal side branch: 1 emission**
- **Renal parenchyma: No emissions**

- Preclinical studies demonstrated 90% reduction in kidney norepinephrine levels





Clinical Development Program Provides Robust Assessment of Paradise uRDN Safety and Efficacy

RADIANCE II

Mild-Moderate HTN

Uncontrolled 0–2 Anti-HTN Meds

N = 224

Randomized, Double-Blind
Sham-Controlled

US and Europe

6-Month Data Available
(Follow-Up Ongoing)

RADIANCE-HTN SOLO

Mild-Moderate HTN

Uncontrolled 0–2 Anti-HTN Meds
Controlled 1–2 Anti-HTN Meds

N = 146

Randomized, Double-Blind
Sham-Controlled

US and Europe

36-Month Data Available
(Follow-Up Ongoing)

RADIANCE-HTN TRIO

Resistant HTN

Uncontrolled 3+ Anti-HTN Meds

N = 136

Randomized, Double-Blind
Sham-Controlled

US and Europe

24-Month Data Available
(Follow-Up Ongoing)

Patients OFF Anti-HTN Meds
2-Month Primary Endpoint

**Patients ON Standardized
Single 3-Drug Combo Pill**
2-Month Primary Endpoint

Totality of Evidence Supports a Positive Benefit-Risk for Paradise uRDN System

Unmet Need

- Many patients unable to achieve blood pressure control with standard of care treatment
- High blood pressure linked to increased risk of significant CV morbidity

Efficacy

- Met prespecified primary endpoint in all 3 studies
- Significant and meaningful reductions across multiple measures of blood pressure
- Benefits sustained long-term

Safety

- Favorable safety profile
- No significant safety risks identified acutely or through long-term follow-up
- RADIANCE II: Primary safety composite endpoint met

Proposed Indication

Reduce blood pressure in patients with uncontrolled hypertension, who may be inadequately responsive to, or who are intolerant to, antihypertensive medications

Unmet Need

Michael A. Weber, MD

Professor of Medicine
SUNY Downstate College of Medicine

Efficacy

Ajay Kirtane, MD, SM

Professor of Medicine at Columbia University Medical Center
Director, Columbia Interventional Cardiovascular Care
Chief Academic Officer, Division of Cardiology

Safety

Glenn Chertow, MD, MPH

Norman S. Coplon Professor of Medicine
Stanford University

Post-Approval Study

Helen Reeve-Stoffer, PhD

Chief Clinical Officer
ReCor Medical

Clinical Perspective

Naomi Fisher, MD

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Brigham and Women's Hospital
Associate Professor, Harvard Medical School

Additional Experts

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Chris Mullin, MS

Director, Product Strategy
NAMSA

Kevin Marsh, PhD

Vice President, Patient-centered Research
Evidera

Albert Hsiao, MD, PhD

Associate Professor of Radiology
University of California, San Diego
San Diego, CA



Hypertension: Unmet Clinical Need

Michael A. Weber, MD

Professor of Medicine

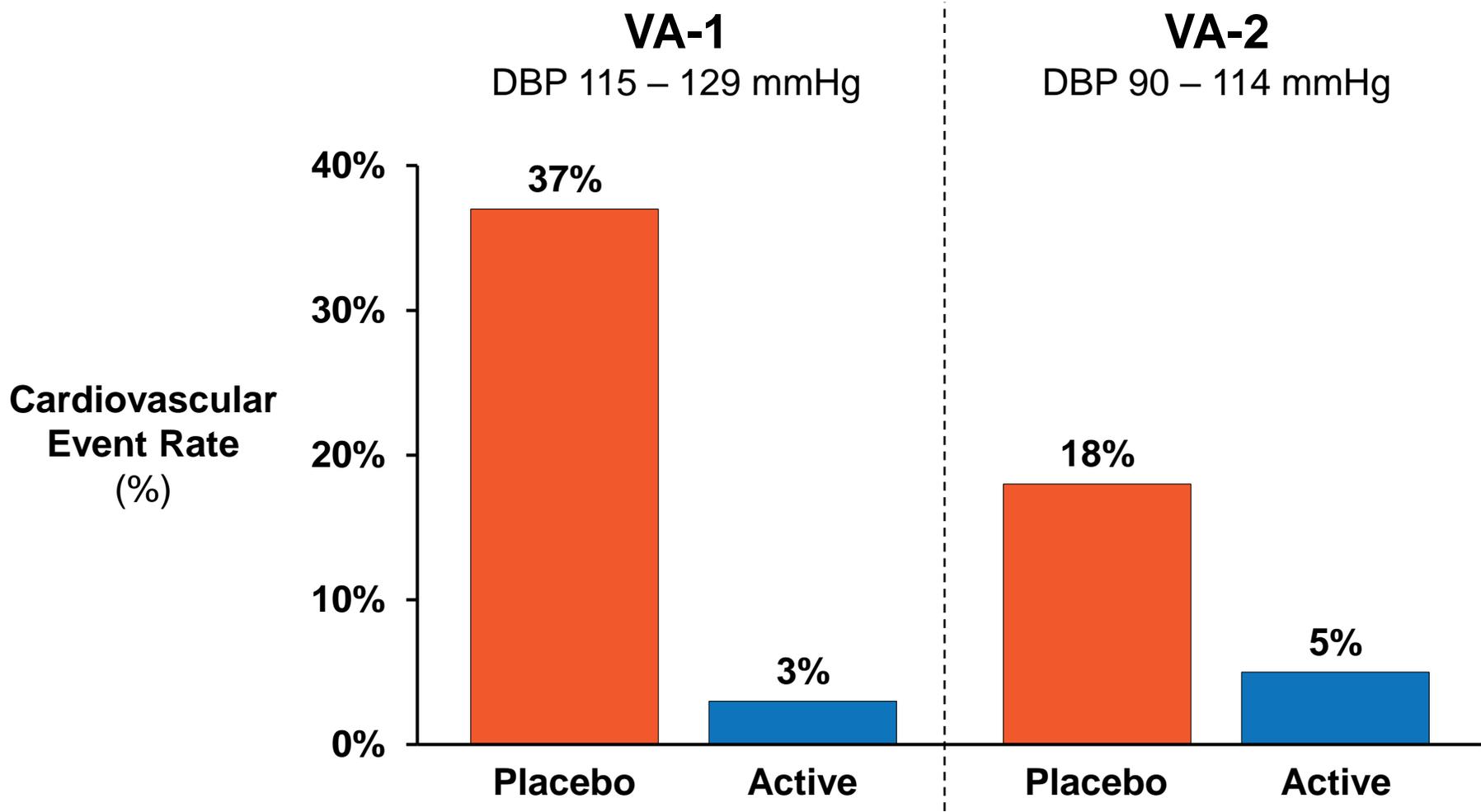
SUNY Downstate College of Medicine

Brooklyn, NY

Hypertension is #1 Cause of Global Disease Burden

- > 100 million people with hypertension in US
- 670,000 deaths estimated per year due to hypertension in US
- World Health Organization has identified hypertension as the world's leading cause of premature death and disability

What Made Antihypertensive Therapy Finally Accepted? The Initial Placebo-Controlled VA Cooperative Studies



Active Treatment:

- HCTZ 50 – 100 mg
- Reserpine 0.1 – 0.2 mg
- Hydralazine 100 – 200 mg

On assigned medications at end of study:

- VA-1: 92%
- VA-2: 85%

New US Classification for Blood Pressure Led to Lower Threshold for Starting Therapy (130/80 mmHg)

	Blood Pressure Reading (mmHg)	
	Systolic	Diastolic
Normal	< 120	< 80
Elevated	120 – 129	< 80
Stage 1 hypertension	130 – 139	80 – 89
Stage 2 hypertension	≥ 140	≥ 90
Hypertensive crisis	> 180	> 120

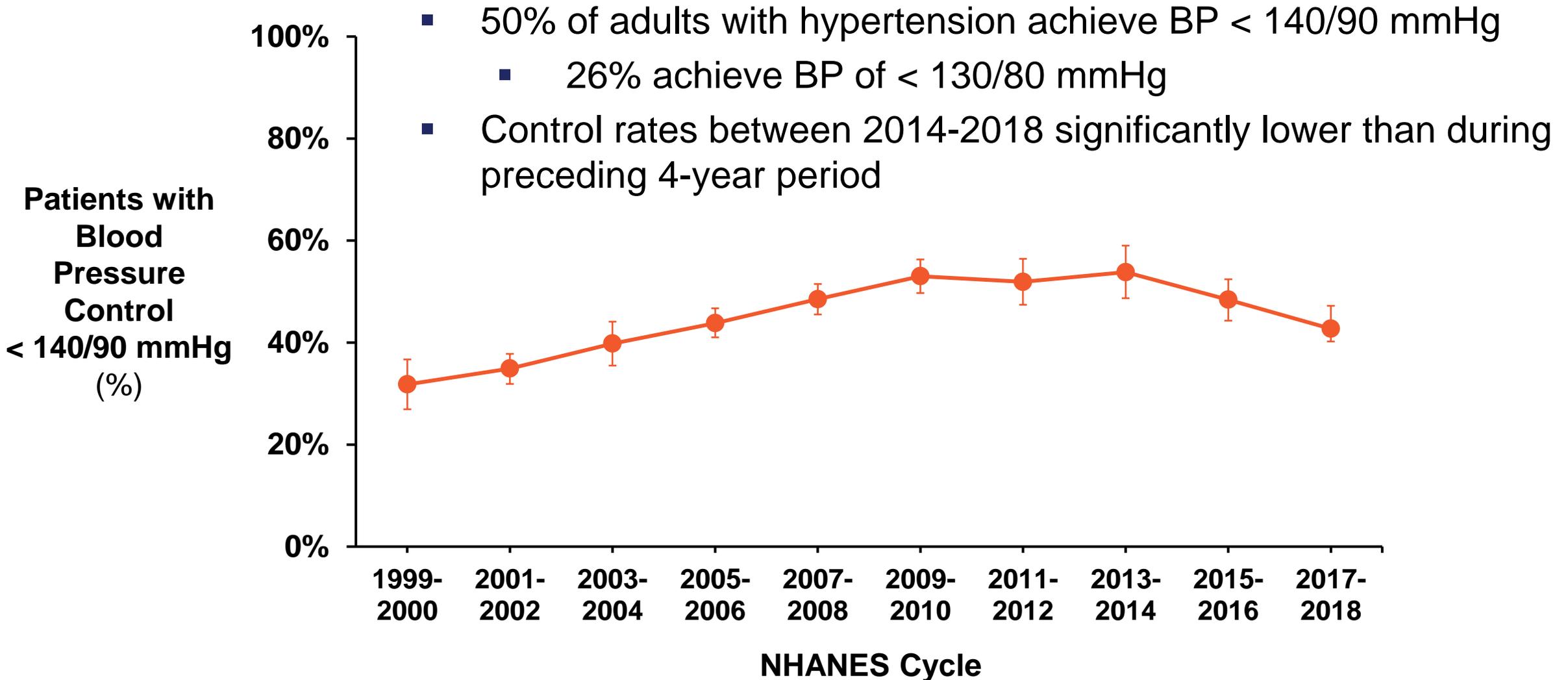
Blood Pressure Measurements in RADIANCE Studies

- Ambulatory blood pressure monitoring
- Office blood pressure measurements by automated device
- Home blood pressures measured by patients at home

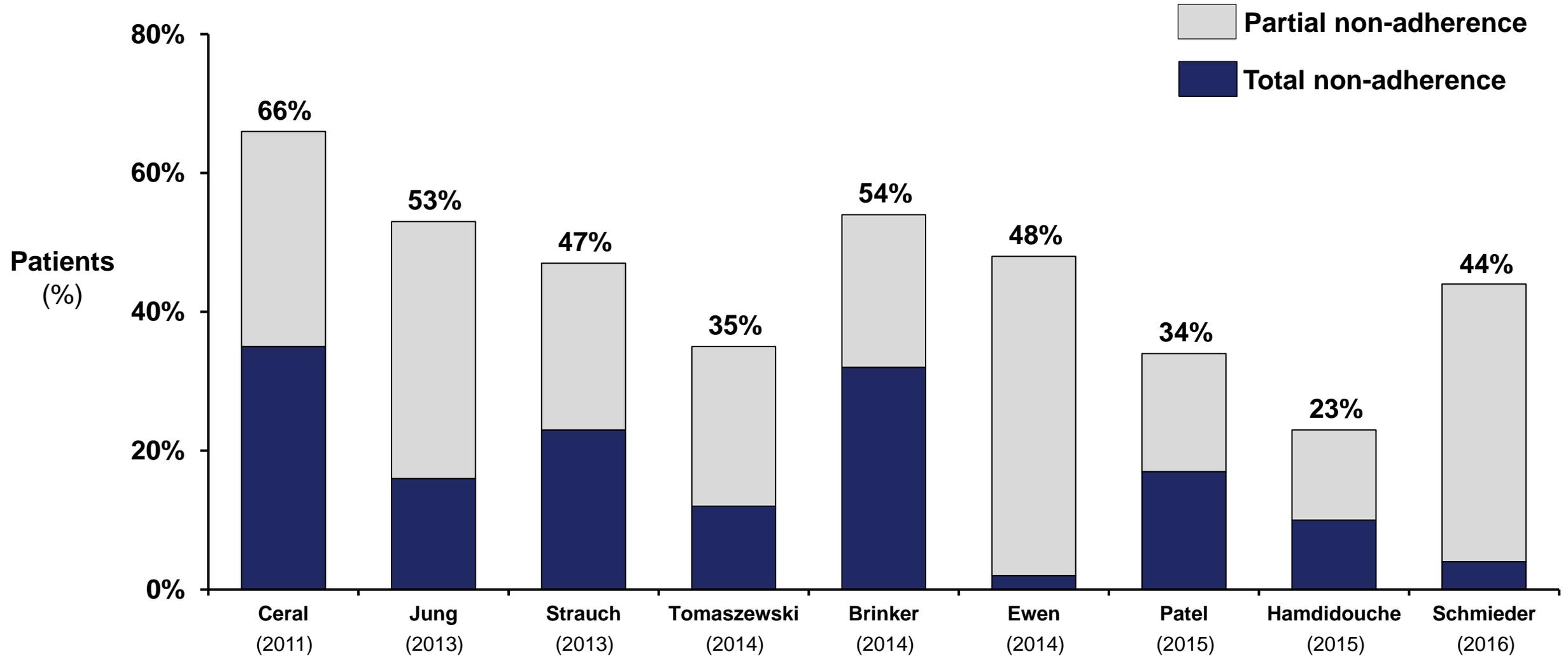
Standard of Care Anti-HTN Medication

- Typically includes daily administration of 1, 2 or 3 drugs from 3 classes:
 - Calcium channel blockers
 - ACE inhibitors or ARBs
 - Thiazide diuretics
- And, if needed, clinician can add:
 - Aldosterone antagonists / beta blockers / alpha blockers / alpha-2 agonists / direct vasodilators
- Adherence worsens with additional drugs
- Hypertension patients typically require multiple drugs for other conditions

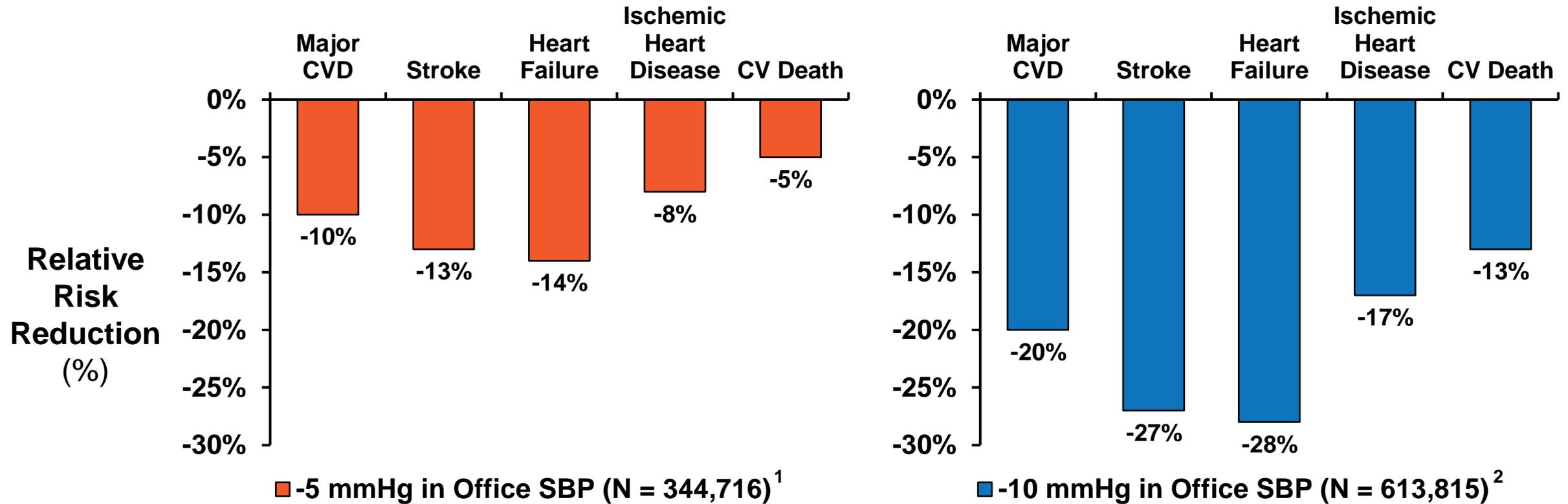
Control of Hypertension in US is Poor and Deteriorating



Non-Adherence to Anti-HTN Medications is Widespread



Benefits on Risk of Major Cardiovascular Disease at Different Levels of Achieved Office Systolic BP (SBP)

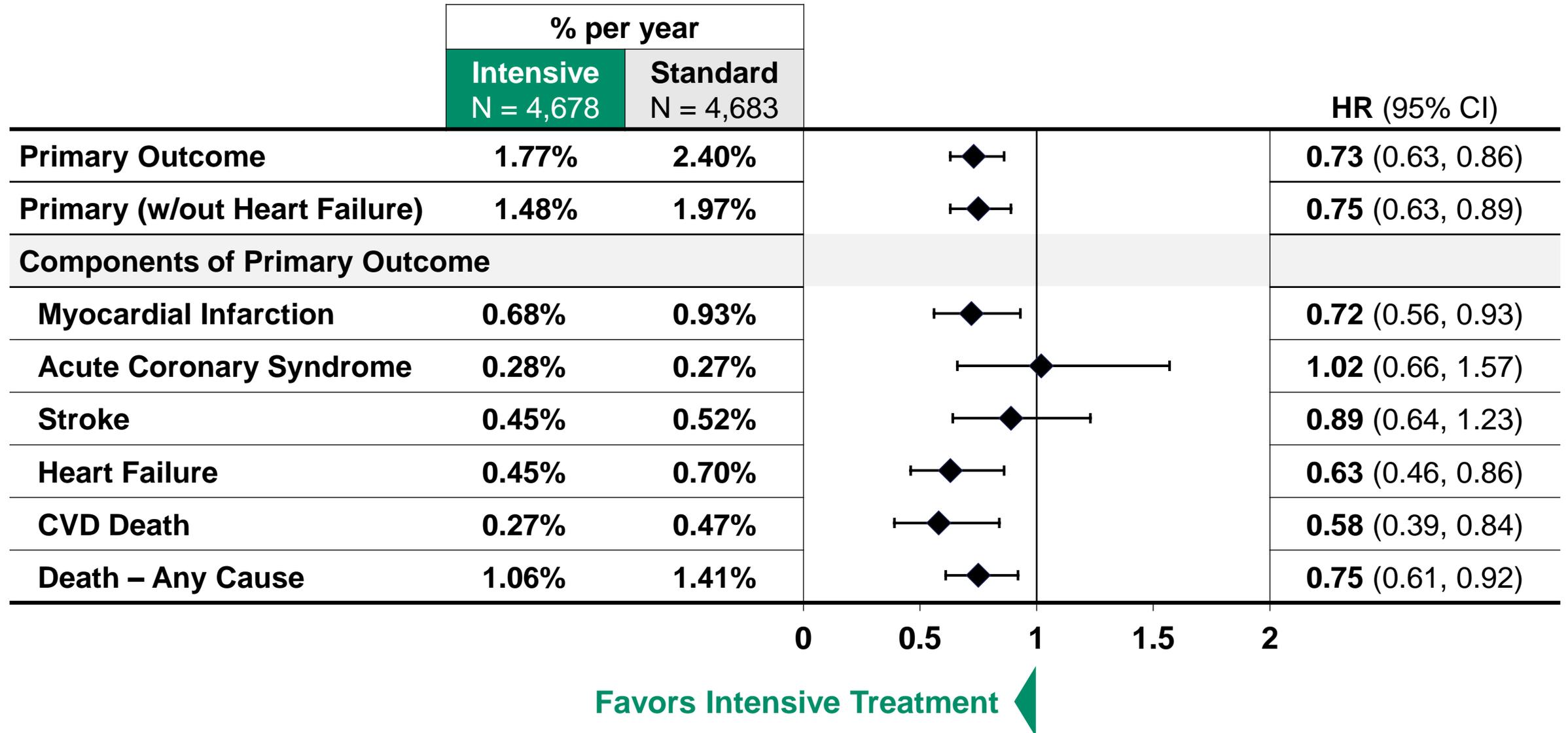


Data are office SBP measures and regardless of BP and CVD history

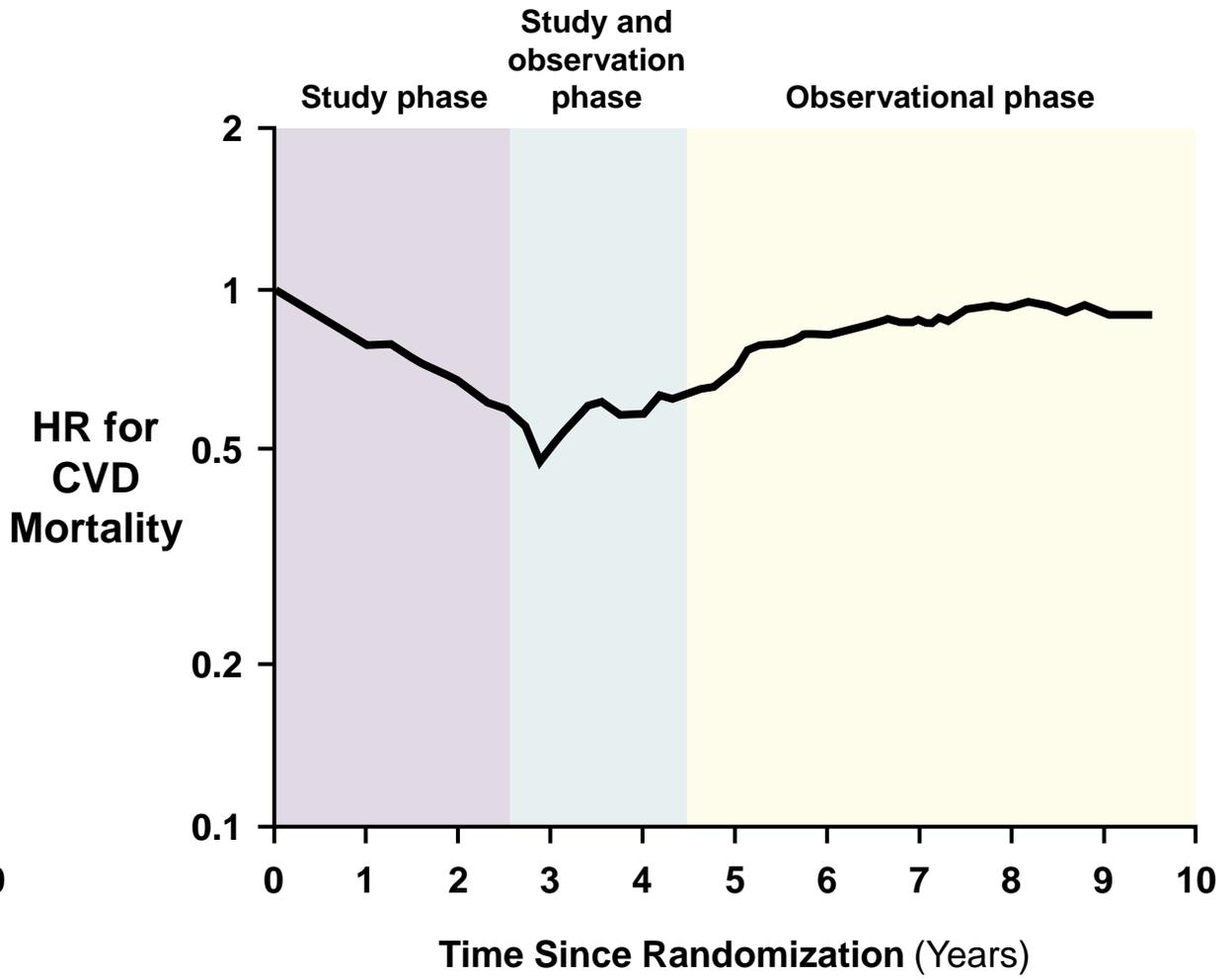
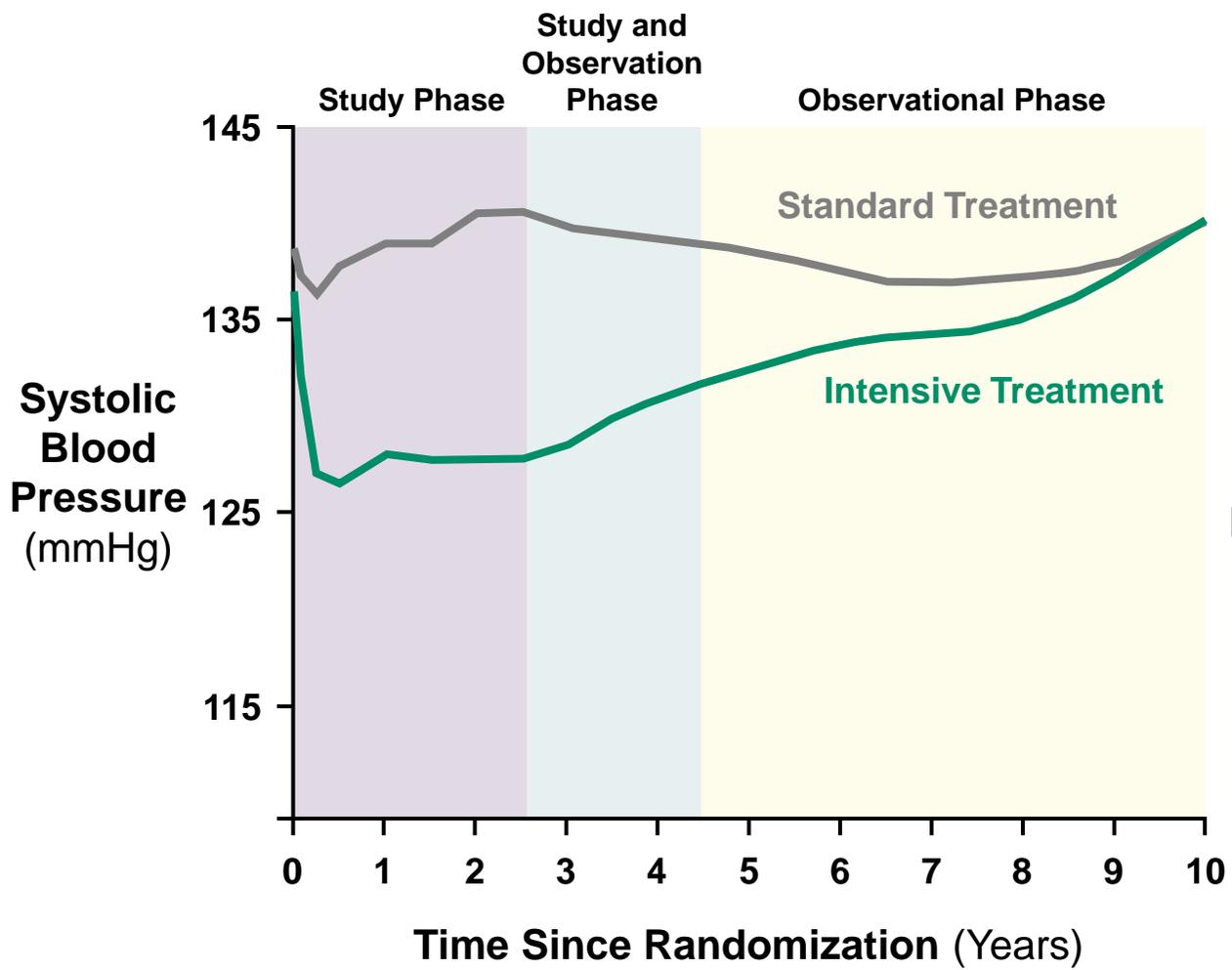
1. Blood Pressure Lowering Treatment Trialists' Collaboration, 2021

2. Ettehad D et al., 2016

SPRINT Major CVD Outcomes (Event First Occurrence During Study Follow-up)



SPRINT: Long-Term Follow-Up Shows Increase in Systolic BP of 7 mmHg Resulted in Loss of Mortality Benefit



Patients with Uncontrolled Hypertension Remain at Increased Risk of Significant Cardiovascular Events

- Patients who continue to experience high blood pressure should benefit from additional treatment options that:
 - Provide meaningful blood pressure reductions
 - Provide durable effects that don't depend on obtaining and adhering to anti-HTN medications

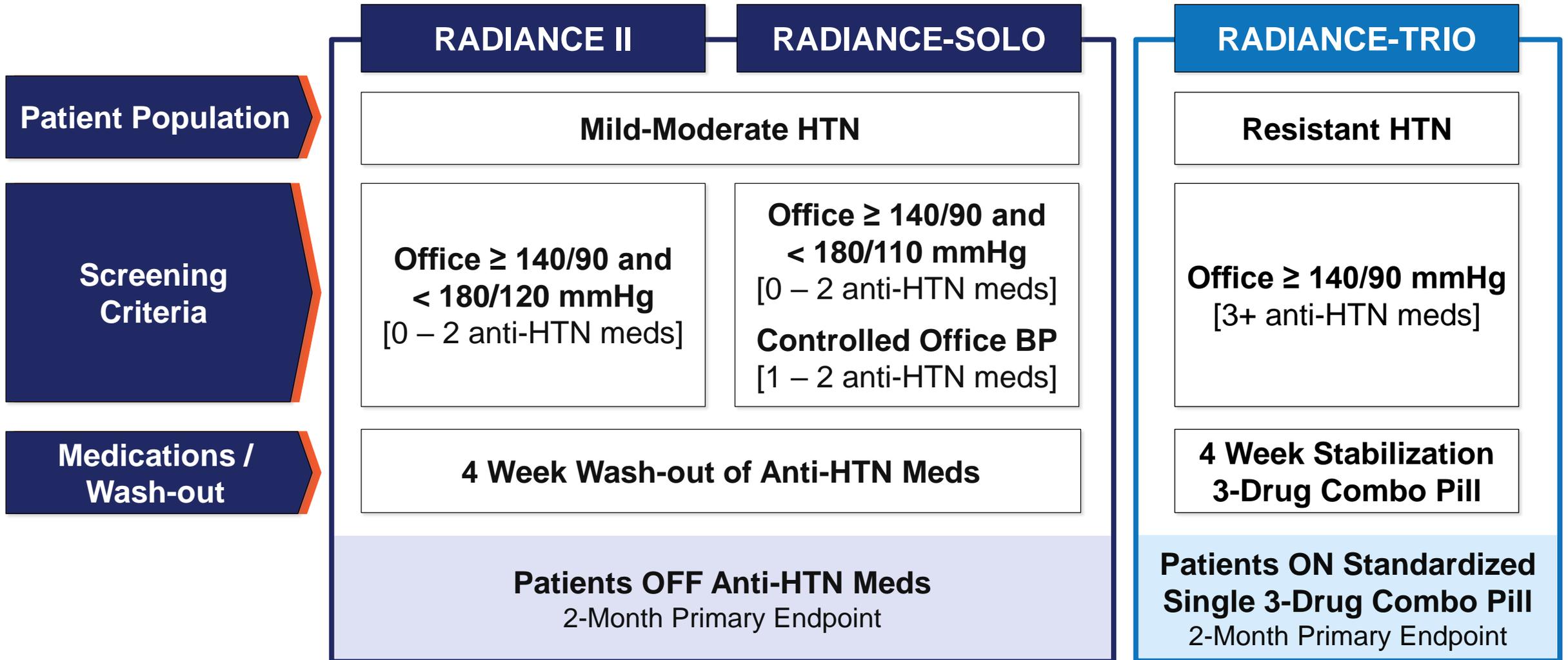


RADIANCE Studies Design and Efficacy Results

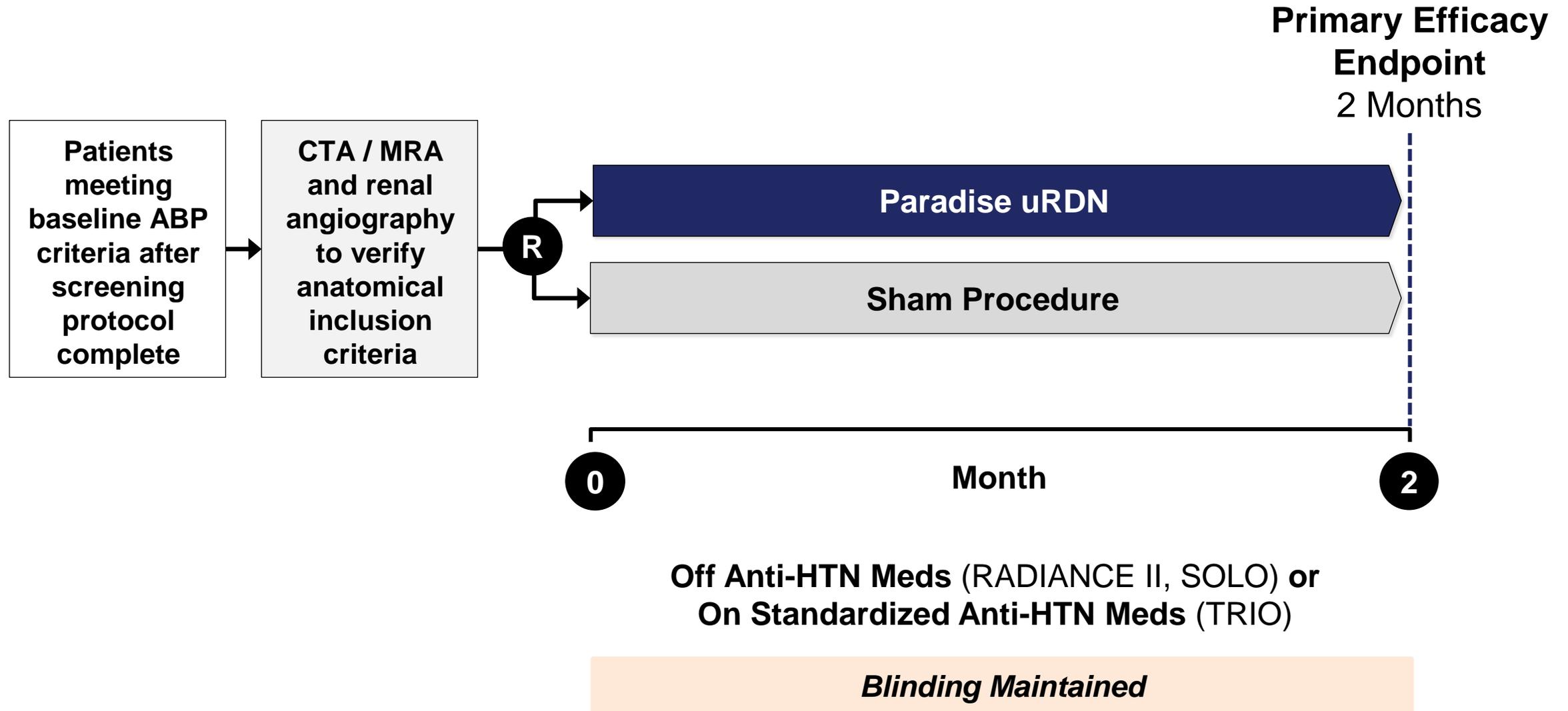
Ajay Kirtane, MD, SM

Professor of Medicine at Columbia University Medical Center
Director, Columbia Interventional Cardiovascular Care
Chief Academic Officer, Division of Cardiology

Paradise uRDN Clinical Program Includes 3 Randomized, Double-Blind, Sham Controlled Studies



Primary Efficacy Endpoint of Daytime Ambulatory Blood Pressure (ABP) Ascertained at 2 Months



Three Independently Powered Randomized Studies

- Frequentist, fixed sample size study design with primary analysis by intent-to-treat
- Each study independently powered for efficacy at 2 months
 - Assumed mean \pm SD difference of 6 ± 12 mmHg
 - Two-sided 0.05 alpha, 80% power
- Primary safety endpoint for RADIANCE II
 - Assumed event rate of 3%, performance goal of 9.8%
 - One-sided 0.05 alpha, 95% power

RADIANCE Studies Randomized > 500 Patients; 293 Received Paradise Ultrasound Renal Denervation (uRDN)

	RADIANCE II	RADIANCE-SOLO	RADIANCE-TRIO						
Enrollment Dates	2019 – 2022	2016 – 2017	2016 – 2020						
Enrolling Centers	37 US / 24 OUS	21 US / 18 OUS	28 US / 25 OUS						
Randomization	2:1	1:1	1:1						
Treatment	<table border="1"> <tr> <td>uRDN N = 150</td> <td>Sham N = 74</td> </tr> </table>	uRDN N = 150	Sham N = 74	<table border="1"> <tr> <td>uRDN N = 74</td> <td>Sham N = 72</td> </tr> </table>	uRDN N = 74	Sham N = 72	<table border="1"> <tr> <td>uRDN N = 69</td> <td>Sham N = 67</td> </tr> </table>	uRDN N = 69	Sham N = 67
uRDN N = 150	Sham N = 74								
uRDN N = 74	Sham N = 72								
uRDN N = 69	Sham N = 67								

- Sham procedure consisted of renal angiogram
- Long-term follow-up ongoing for up to 5 years

Efficacy Endpoints Characterize Benefits of Paradise uRDN

Primary (2 Months)

- Reduction in daytime ambulatory systolic BP

Secondary (2 Months)

Systolic BP (SBP)

- 24-hr ambulatory
- Home
- Office

Diastolic BP (DBP)

- Daytime ambulatory
- 24-hr ambulatory
- Home
- Office

Observational (2 – 36M)

- Long-term ambulatory home and office SBP and DBP
- Ambulatory SBP reductions by thresholds
- Medication burden (BP control and changes in anti-HTN meds)

Baseline Demographics

Measure (Baseline)	RADIANCE II		SOLO		TRIO	
	uRDN N = 150	Sham N = 74	uRDN N = 74	Sham N = 72	uRDN N = 69	Sham N = 67
Male	69%	77%	62%	54%	81%	79%
Age						
Mean, years (SD)	55 (9.9)	55 (7.9)	54 (10.2)	54 (10.0)	52 (7.5)	53 (9.1)
≥ 65 years	17%	12%	14%	11%	4%	10%
Race						
White	76%	76%	81%	72%	65%	76%
Black or African American	14%	20%	16%	18%	20%	19%
BMI (kg/m²)	30.1	30.6	29.9	29.0	32.8	32.6

Antihypertension Medications at Screening

Measure (Screening)	RADIANCE II		SOLO		TRIO	
	uRDN N = 150	Sham N = 74	uRDN N = 74	Sham N = 72	uRDN N = 69	Sham N = 67
0	36%	31%	16%	22%		
1	35%	34%	45%	39%		
2	29%	34%	38%	38%		
3			1%*	1%*	39%	42%
4		1%*			29%	36%
5					23%	15%
6+					9%	7%

Anti-HTN
Meds

*3 Patients (2 in RADIANCE II and 1 in SOLO) were on > 2 medications at screening, violating study inclusion criteria. Deviations created for each patient.

Baseline Blood Pressure Measurements

Measure (Baseline), Mean Systolic / Diastolic (mmHg)	RADIANCE II		SOLO		TRIO	
	uRDN N = 150	Sham N = 74	uRDN N = 74	Sham N = 72	uRDN N = 69	Sham N = 67
Daytime Ambulatory	150 / 94	151 / 93	150 / 93	150 / 94	150 / 94	151 / 92
24-Hour Ambulatory	143 / 88	145 / 88	143 / 87	144 / 89	144 / 89	145 / 90
Nighttime Ambulatory	132 / 80	134 / 81	130 / 78	133 / 80	134 / 81	136 / 81
Home	153 / 98	150 / 96	148 / 95	148 / 95	154 / 97	153 / 97
Office	157 / 102	156 / 101	155 / 100	154 / 99	155 / 101	155 / 100

- Baseline blood pressures similar across studies and balanced between groups

Successful Treatment Delivery Achieved in > 95% of uRDN-Treated Patients

Measure	RADIANCE II	SOLO	TRIO
	uRDN N = 150	uRDN N = 74	uRDN N = 69
Treatment Delivery Success*	99%	95%	97%
Procedure Time, mean (min)	77	72	83
Number of Emissions, mean (IQR)	5.6 (5 – 6)	5.3 (5 – 6)	5.8 (5 – 6)
Total Emission Time, mean (seconds)	38.9	37.4	40.7

*Success defined as minimum of 2 emissions bilaterally

2-Month Primary and Secondary Efficacy

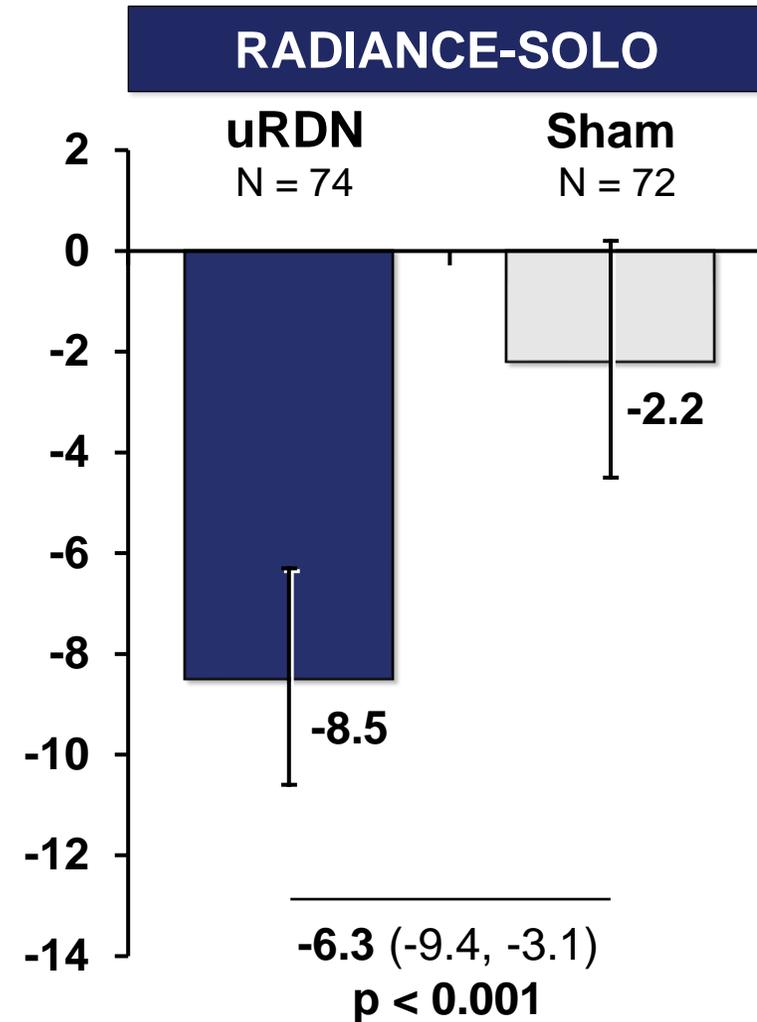
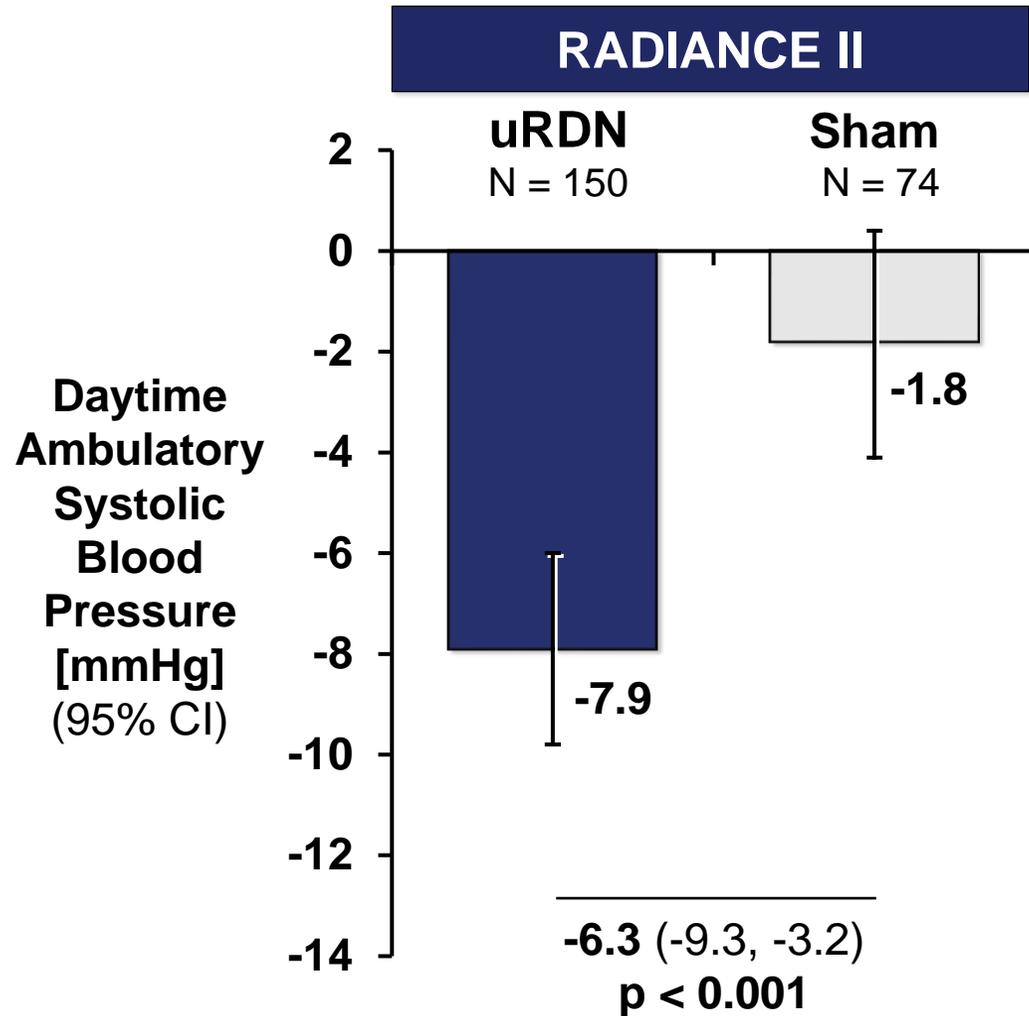
RADIANCE II, RADIANCE-HTN SOLO

Patients with Mild-Moderate Hypertension

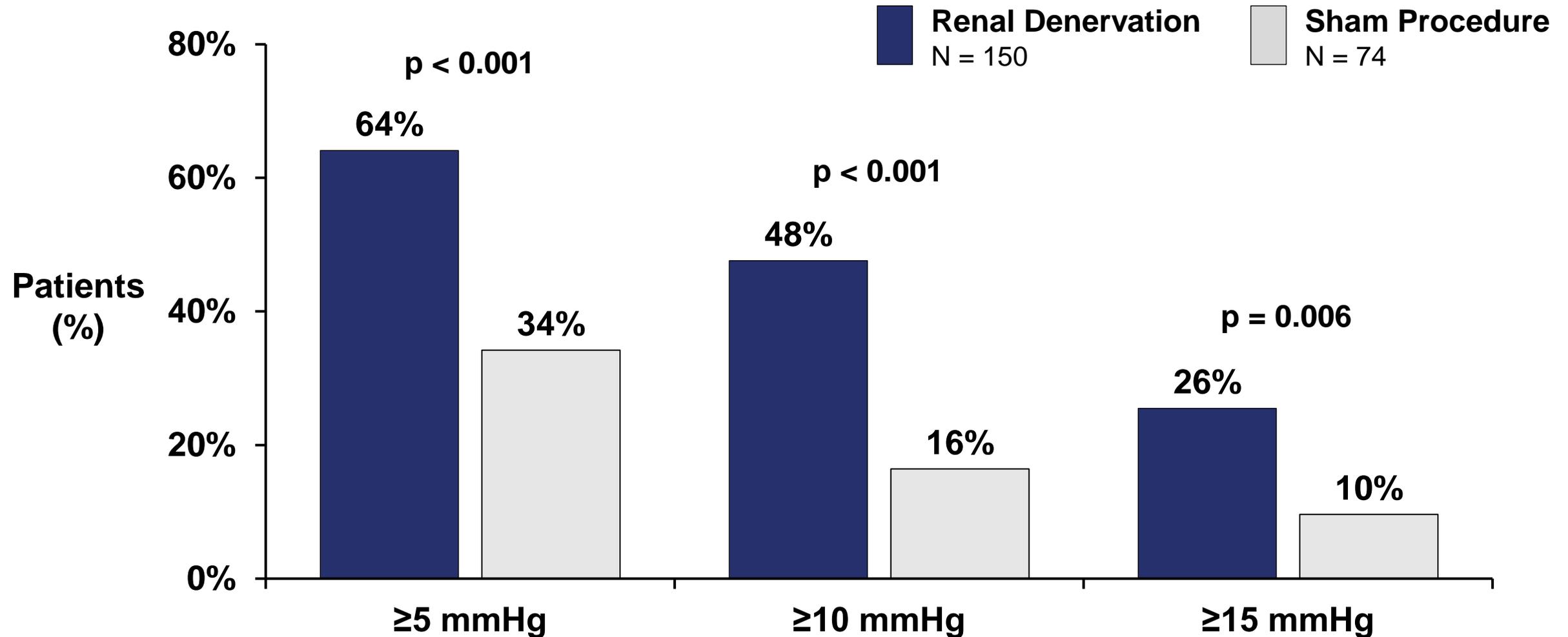
RADIANCE-HTN TRIO

Patients with Resistant Hypertension

RADIANCE II and RADIANCE-SOLO Met Primary Endpoint: uRDN Provides Statistically Significant BP Reductions



RADIANCE II: Observational Efficacy Assessment: Blood Pressure Reduction Magnitude

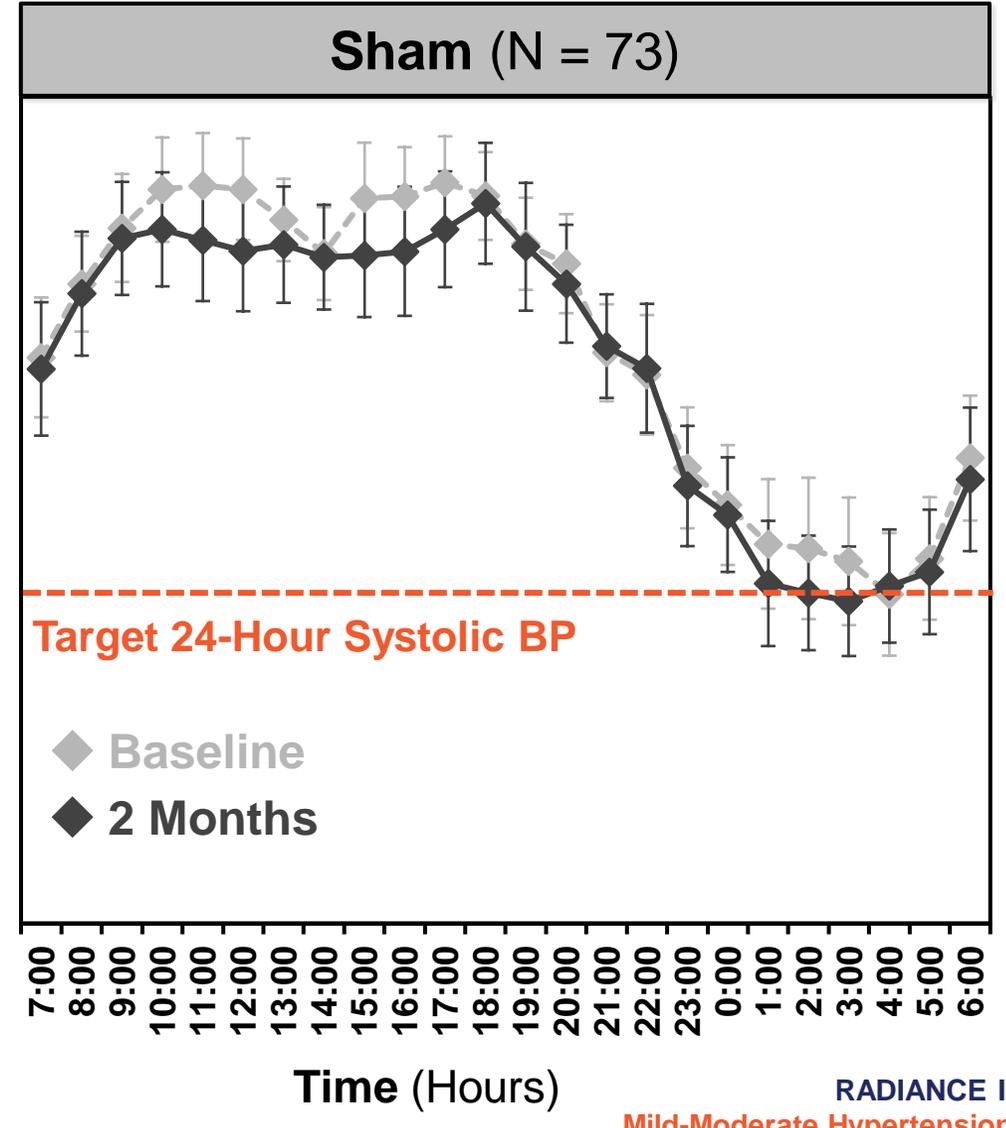
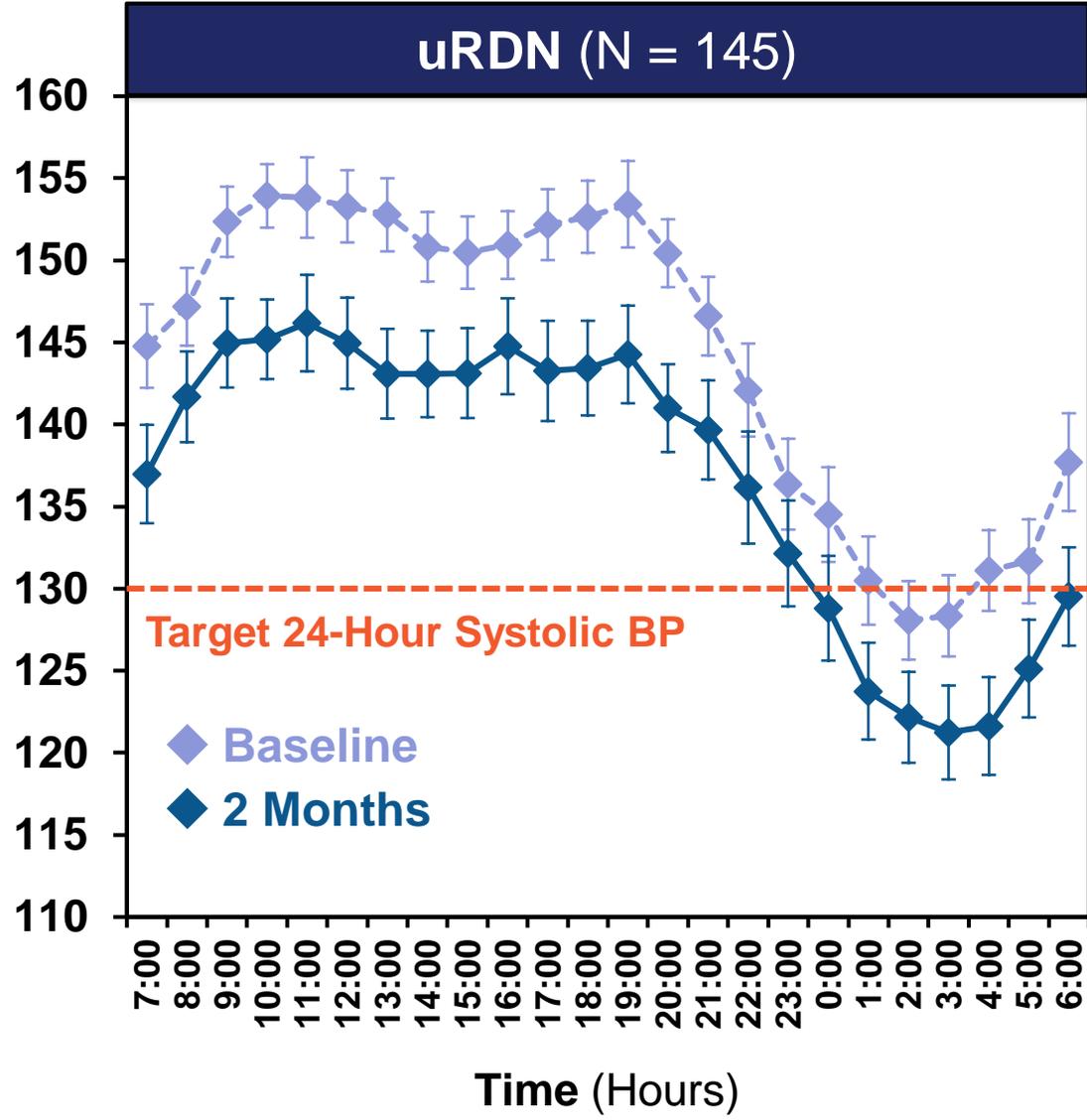


Daytime Ambulatory Systolic Blood Pressure Reduction

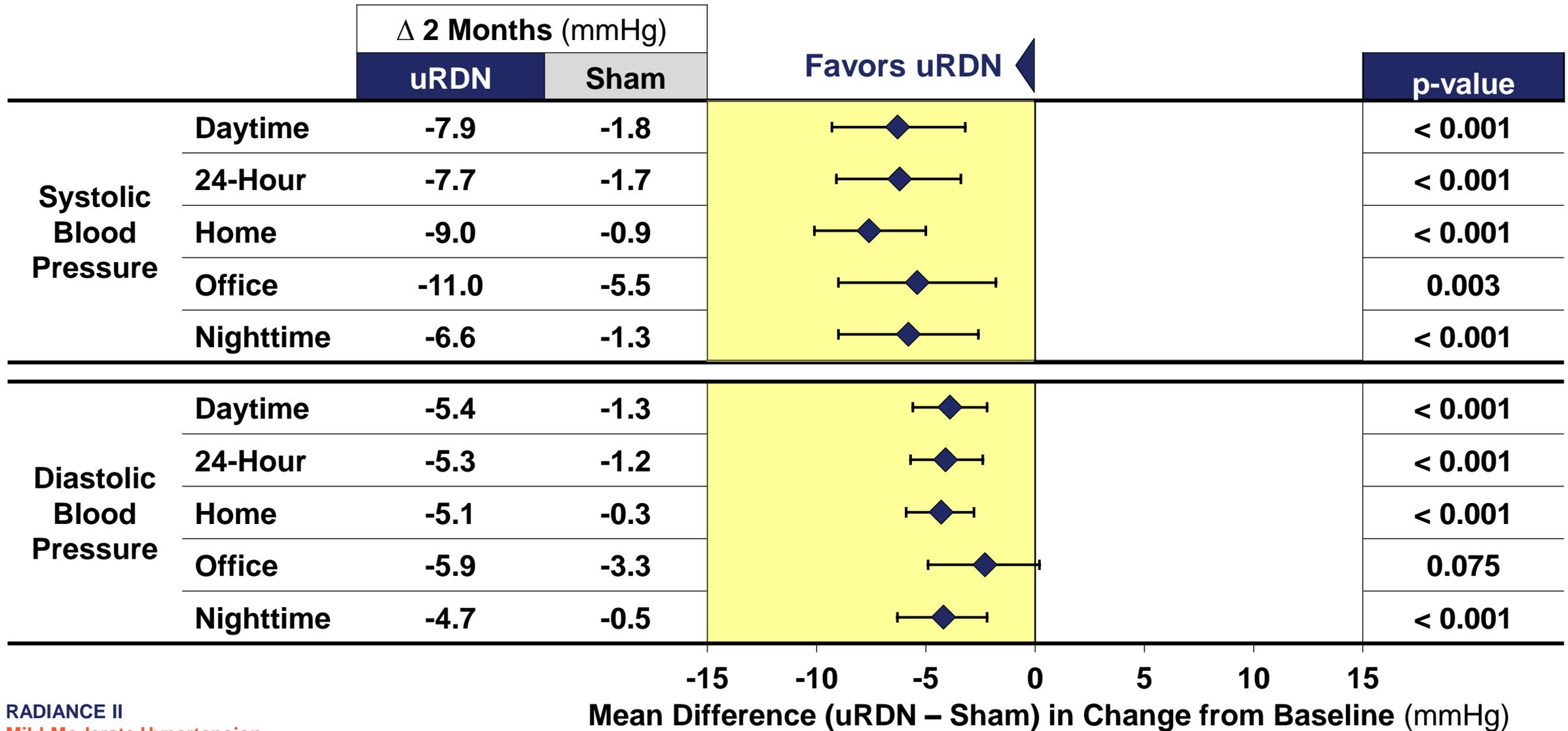


RADIANCE II: Paradise uRDN Provides Continuous Benefit Throughout 24-Hour Circadian Cycle

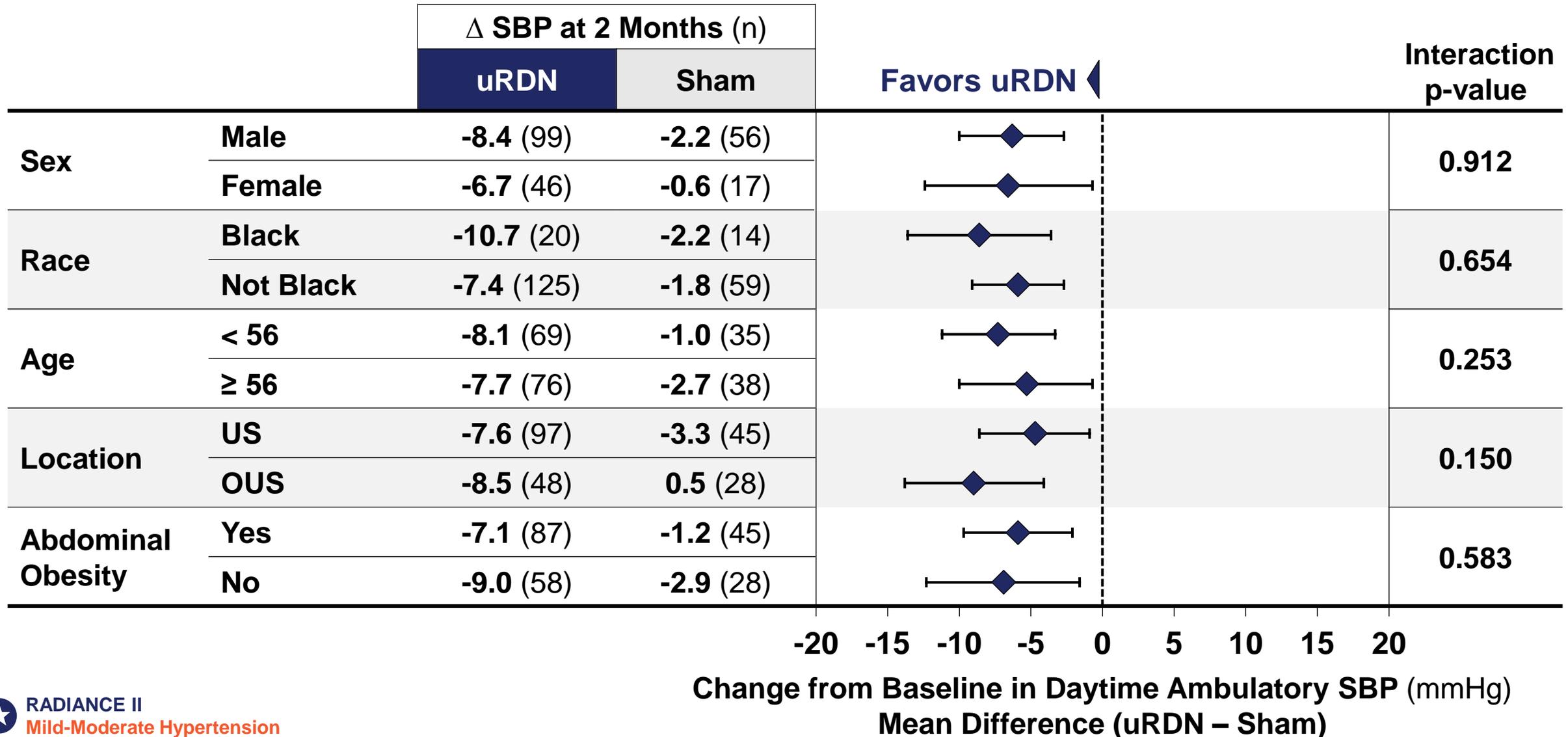
24-Hour Ambulatory Systolic BP [mmHg] (95% CI)



RADIANCE II: Consistent Benefit with uRDN Across Systolic and Diastolic BP Endpoints at 2-Months



RADIANCE II: Benefits of uRDN on Daytime Ambulatory Systolic BP Consistent by Patient Characteristics



2-Month Primary and Secondary Efficacy

RADIANCE II, RADIANCE-HTN SOLO

Patients with Mild-Moderate Hypertension

RADIANCE-HTN TRIO

Patients with Resistant Hypertension

RADIANCE-TRIO: Average of 4 Meds at Screening and Still Hypertensive on Fixed-Dose 3-Drug Combo Pill

Patient Population

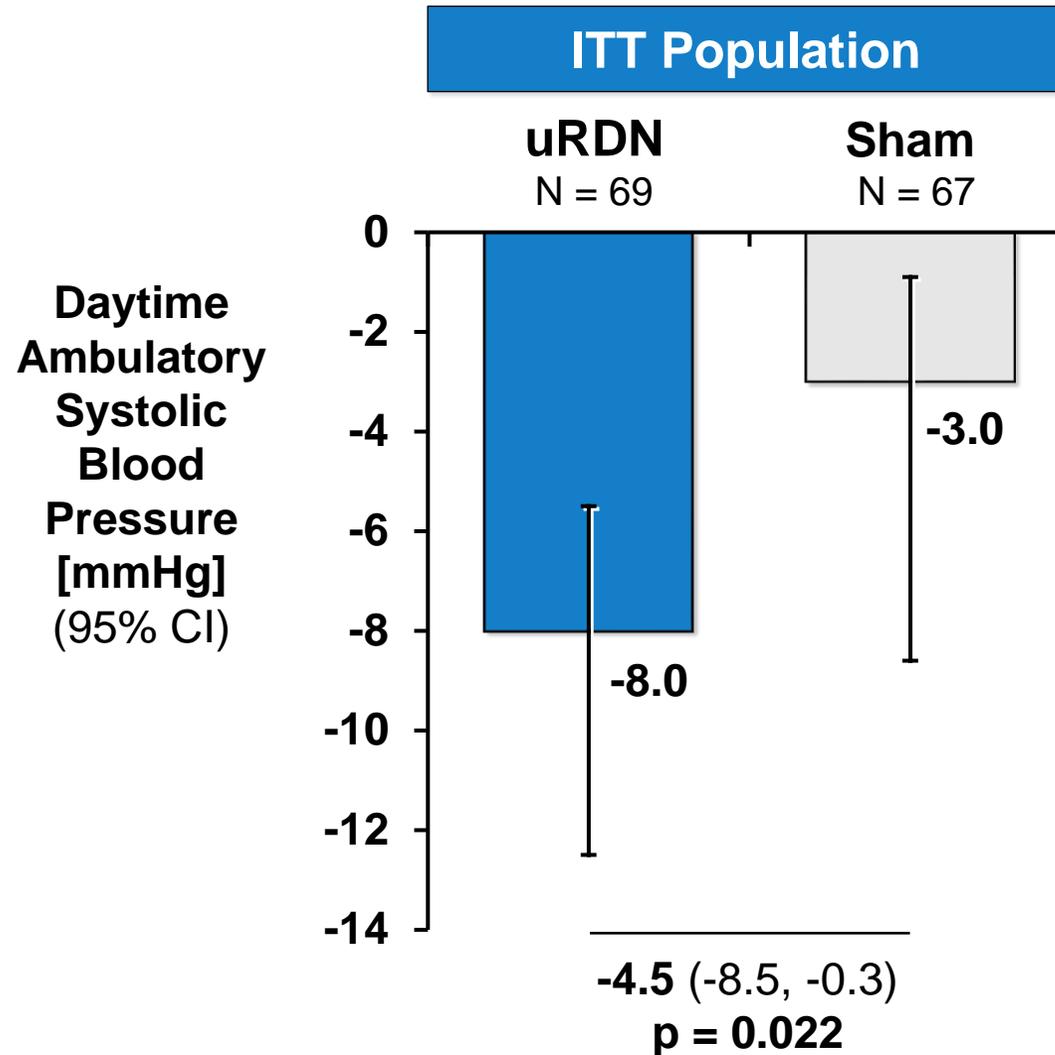
Screening Criteria

Medications / Wash-out

RADIANCE II	RADIANCE-SOLO
Mild-Moderate HTN	
Office \geq 140/90 and $<$ 180/120 mmHg [0 – 2 anti-HTN meds]	Office \geq 140/90 and $<$ 180/110 mmHg [0 – 2 anti-HTN meds] Controlled Office BP [1 – 2 anti-HTN meds]
4 Week Wash-out of Anti-HTN Meds	
Patients OFF Anti-HTN Meds 2-Month Primary Endpoint	

RADIANCE-TRIO
Resistant HTN
Office \geq 140/90 mmHg [3+ anti-HTN meds]
4 Week Stabilization 3-Drug Combo Pill
Patients ON Standardized Single 3-Drug Combo Pill 2-Month Primary Endpoint

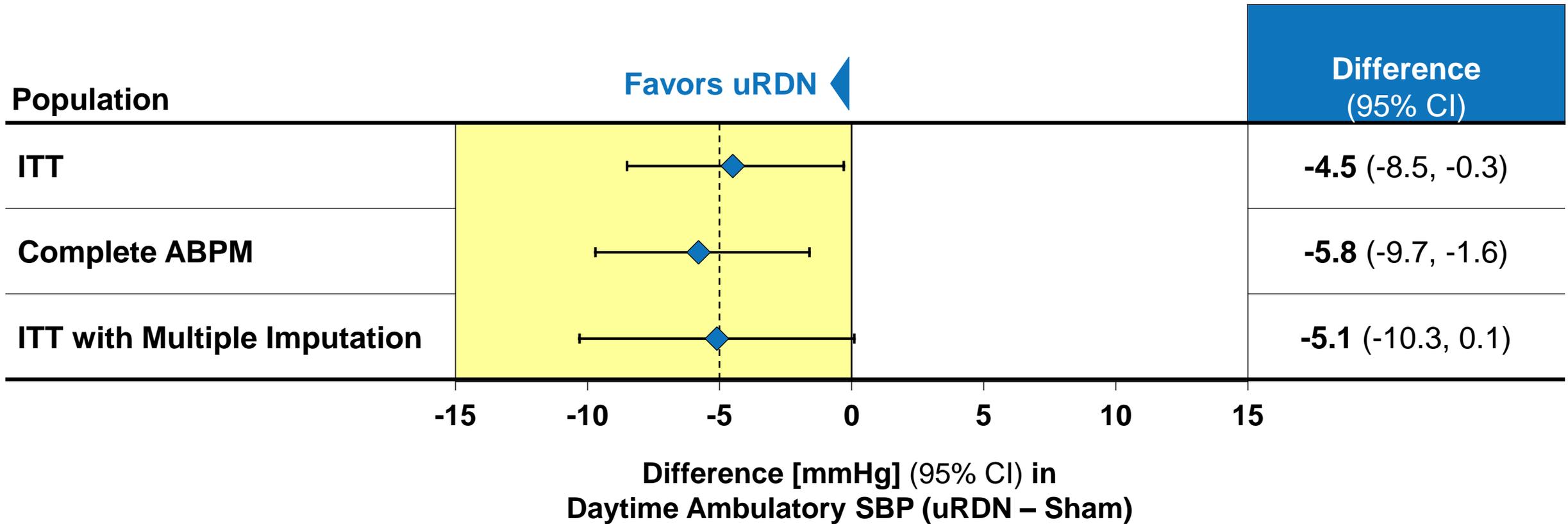
RADIANCE-TRIO: uRDN-Treated Patients Achieved Significantly Greater BP Reductions vs Sham



RADIANCE-TRIO: Complete ABPM Population Provides Meaningful Assessment of uRDN Effects on BP Reductions

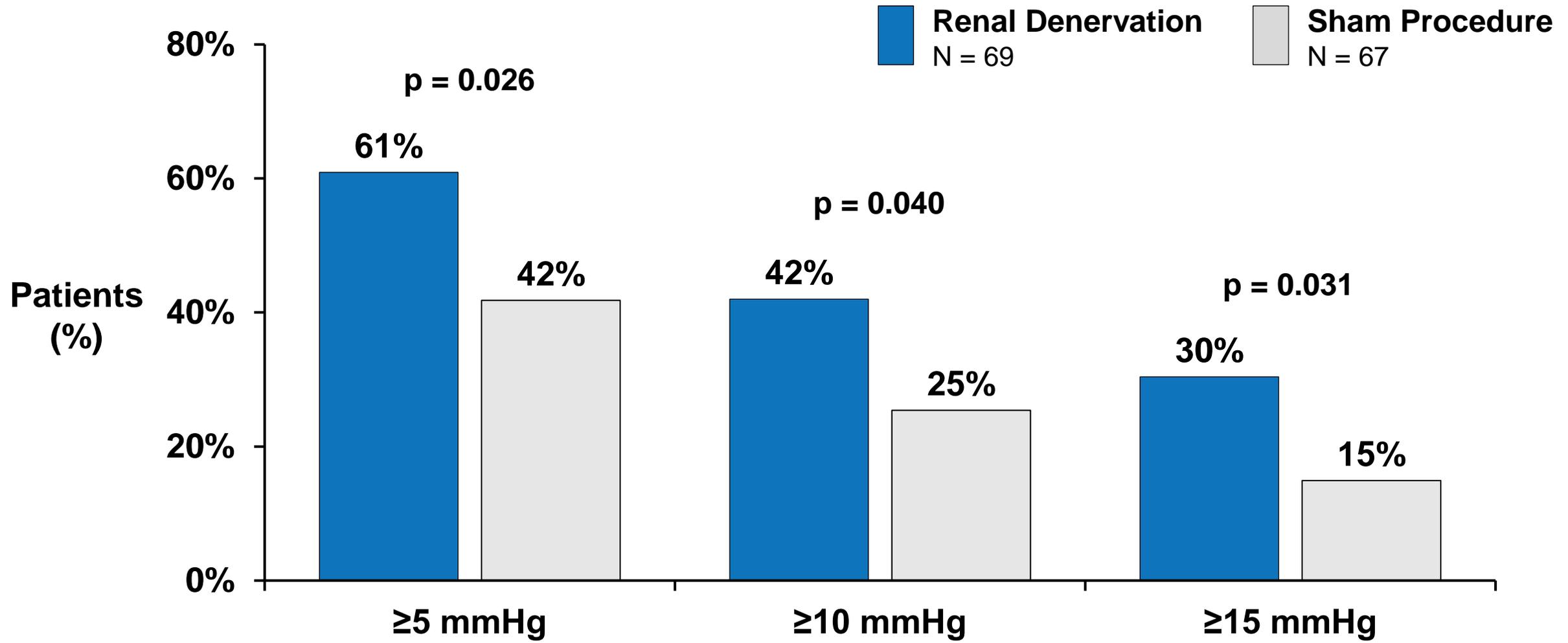
	Patients (N)	
	uRDN	Sham
ITT Population [Primary] <ul style="list-style-type: none"> Includes 6 uRDN vs 0 Sham patients with missing ABPM, assumed to have no treatment effect 	69	67
Complete 2 Month ABPM Population <ul style="list-style-type: none"> Includes all patients with complete ABPM at 2 months 	63	67
ITT with Multiple Imputation <ul style="list-style-type: none"> Includes 6 uRDN patients vs 0 Sham patients with missing ABPM, multiple imputation used for missing data 	69	67

RADIANCE-TRIO: Primary Endpoint Results by Analysis Methods



Data for ITT and Complete ABPM populations presented as medians as change from baseline is non-normal;
Data for ITT with Multiple Imputation presented as baseline adjusted mean

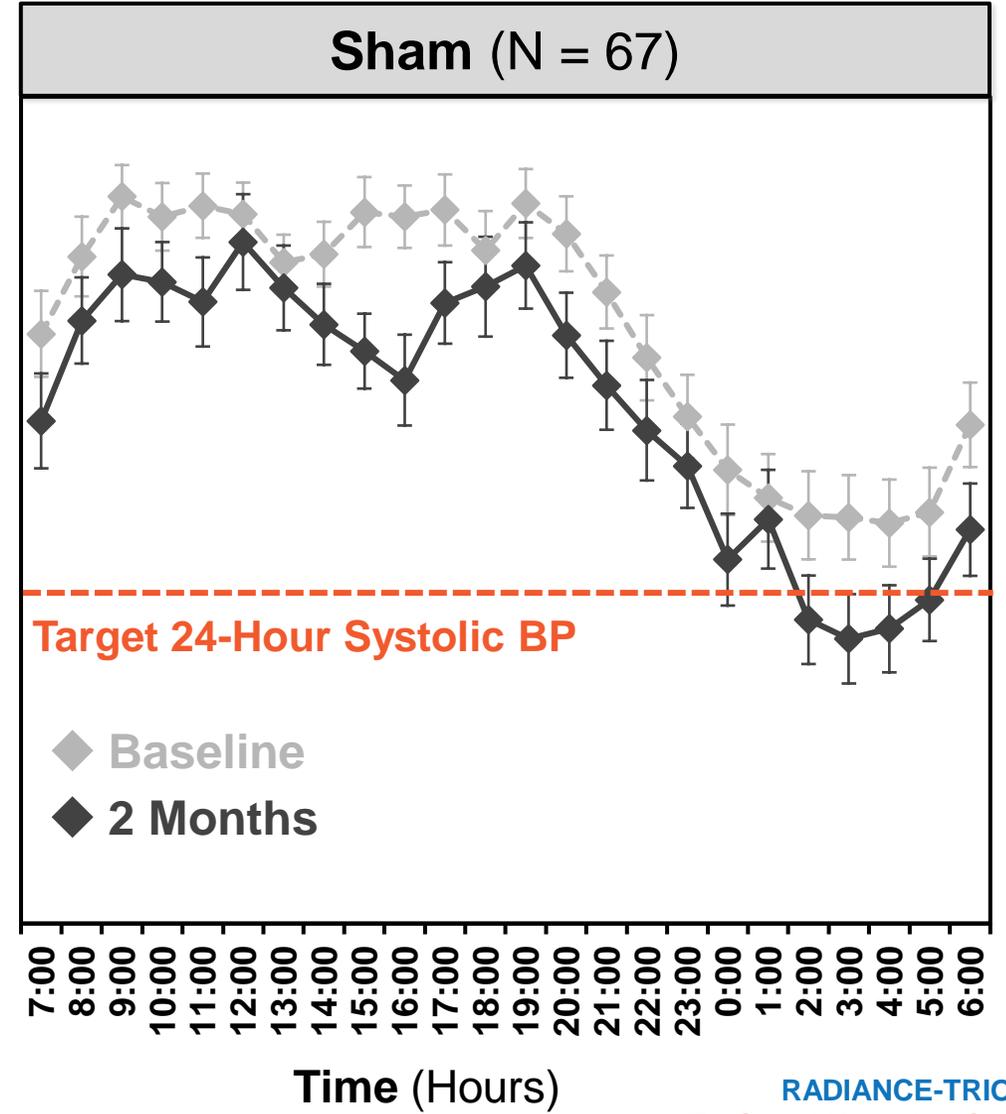
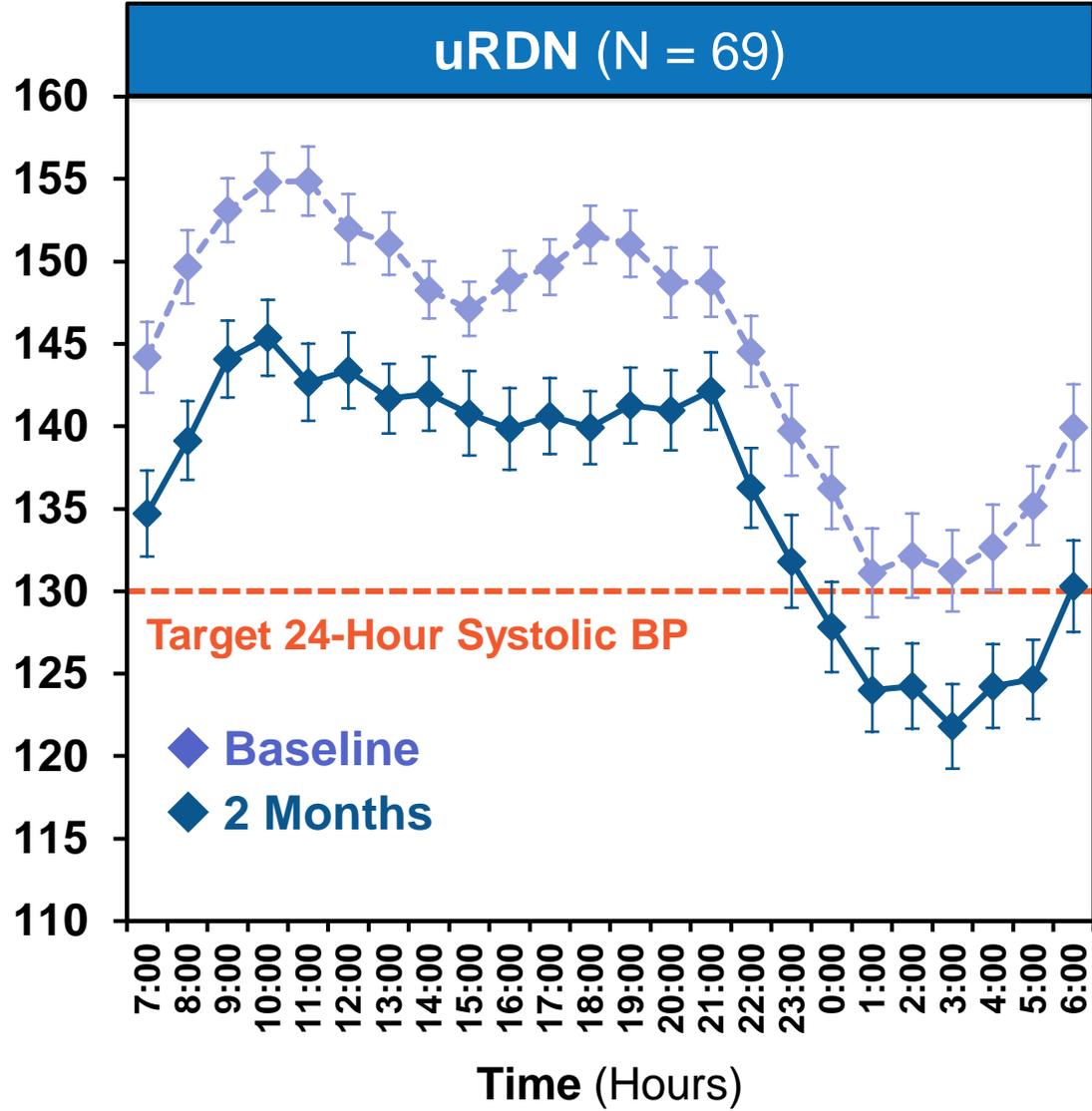
RADIANCE-TRIO: Observational Efficacy Assessment: Blood Pressure Reduction Magnitude



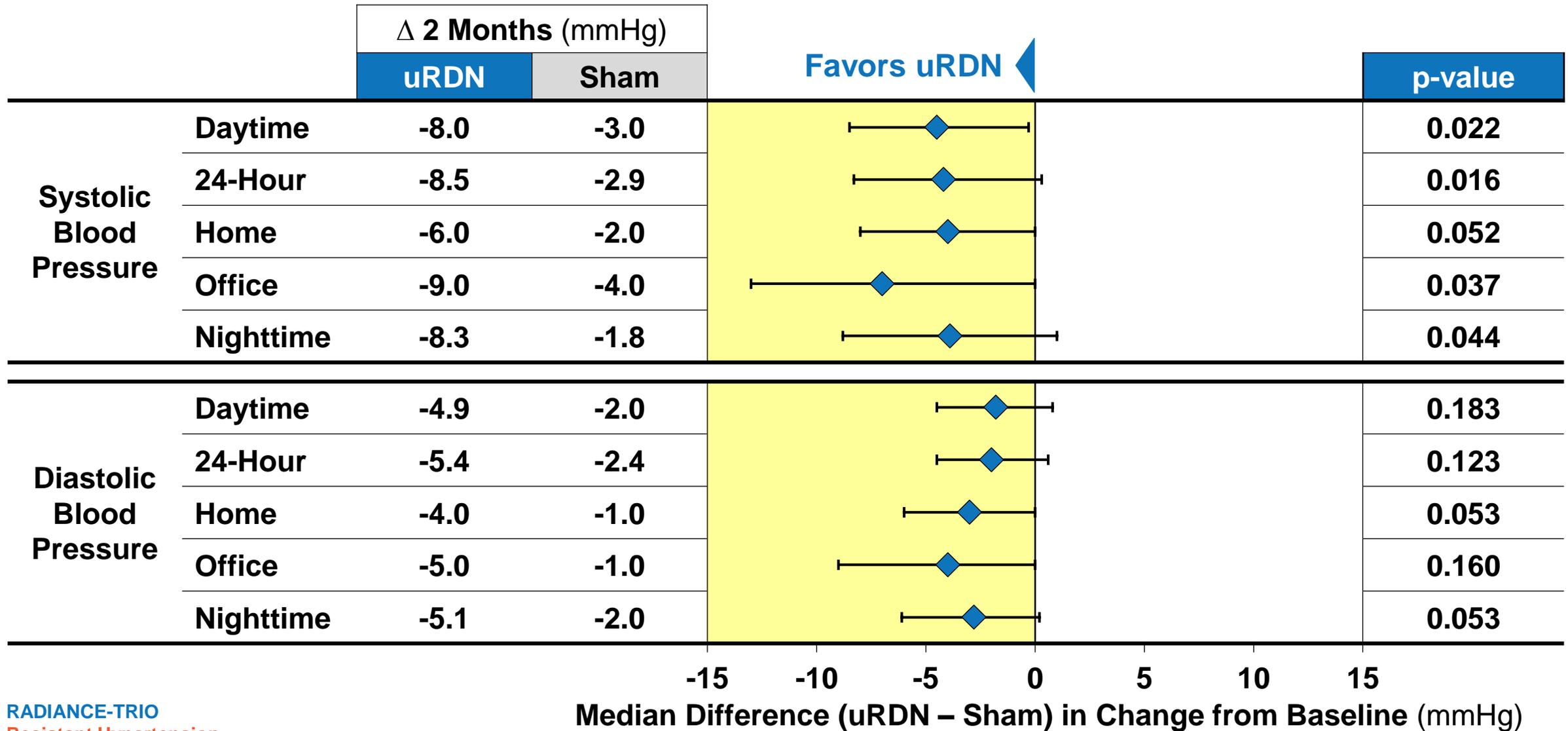
Daytime Ambulatory Systolic Blood Pressure Reduction

RADIANCE-TRIO: Paradise uRDN Provides Continuous Benefit Throughout 24-Hour Circadian Cycle

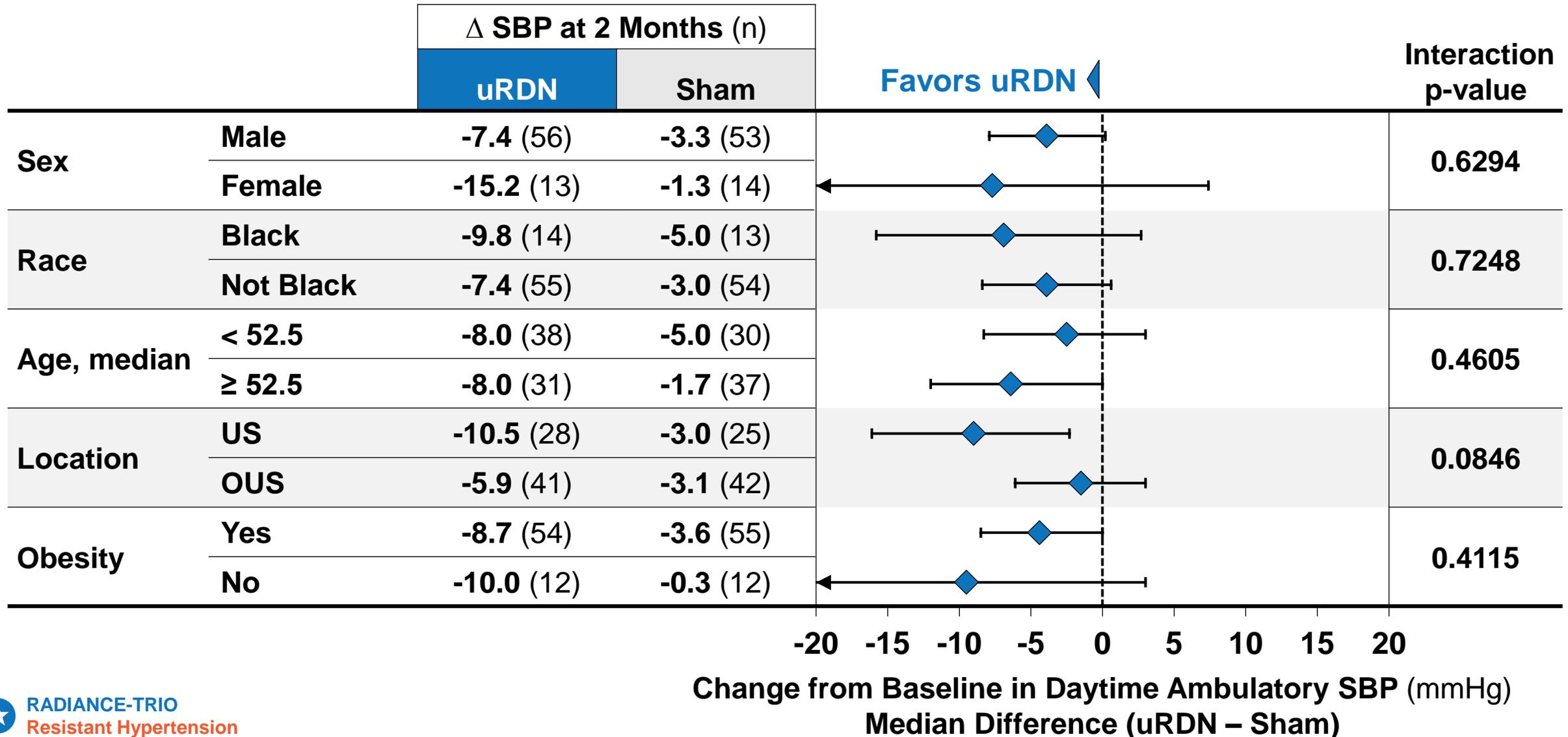
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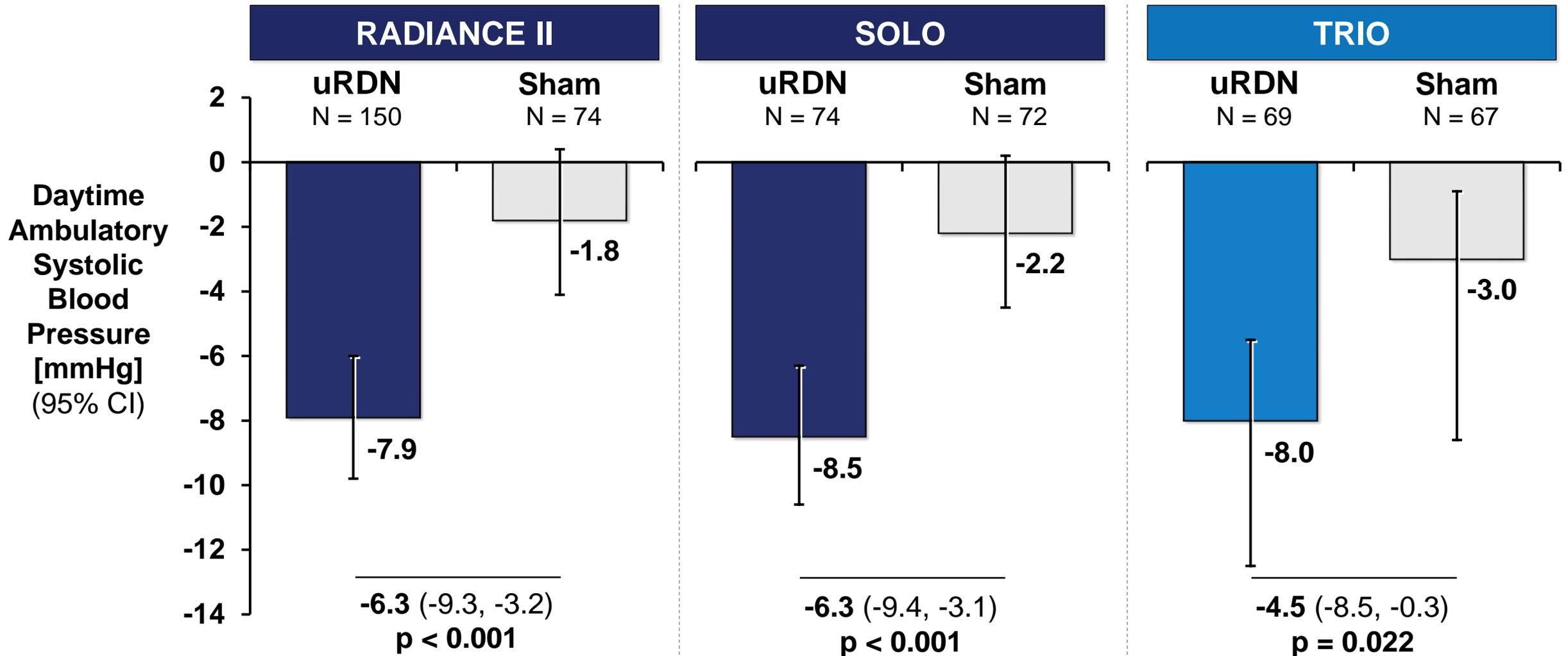
RADIANCE-TRIO: Consistent Benefit with uRDN Across BP Endpoints at 2-Months



RADIANCE-TRIO: Benefits of uRDN on Daytime Ambulatory Systolic BP Consistent by Patient Characteristics



Primary Endpoint Met in All Studies: uRDN Provided Statistically Significant BP Reductions vs Sham



RADIANCE II = Individual group changes based on observed values uRDN N=145 and Sham N=73

TRIO = Data is presented as medians and the p-value is from baseline-adjusted ANCOVA on the ranks as the change from baseline is non-normal

6 Month Efficacy

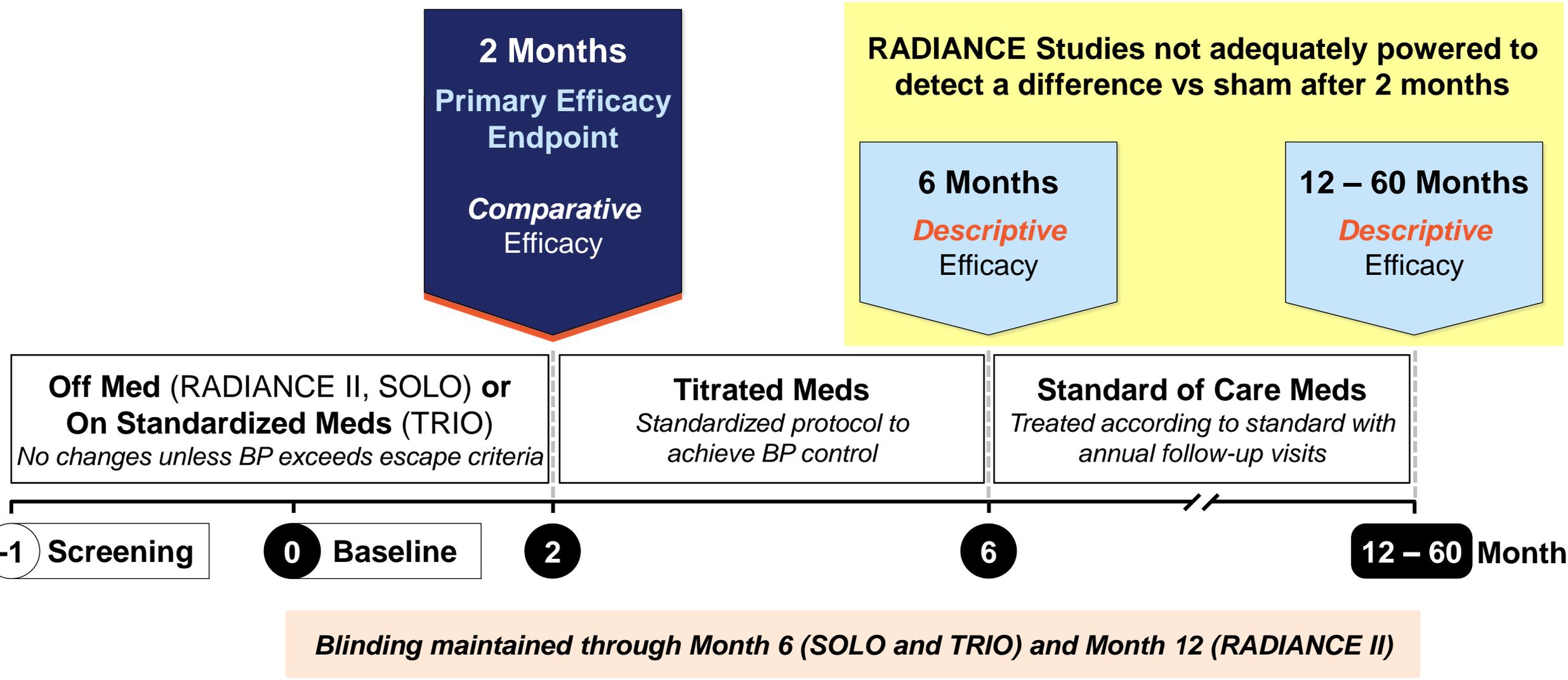
RADIANCE II, RADIANCE-HTN SOLO

Patients with Mild-Moderate Hypertension

RADIANCE-HTN TRIO

Patients with Resistant Hypertension

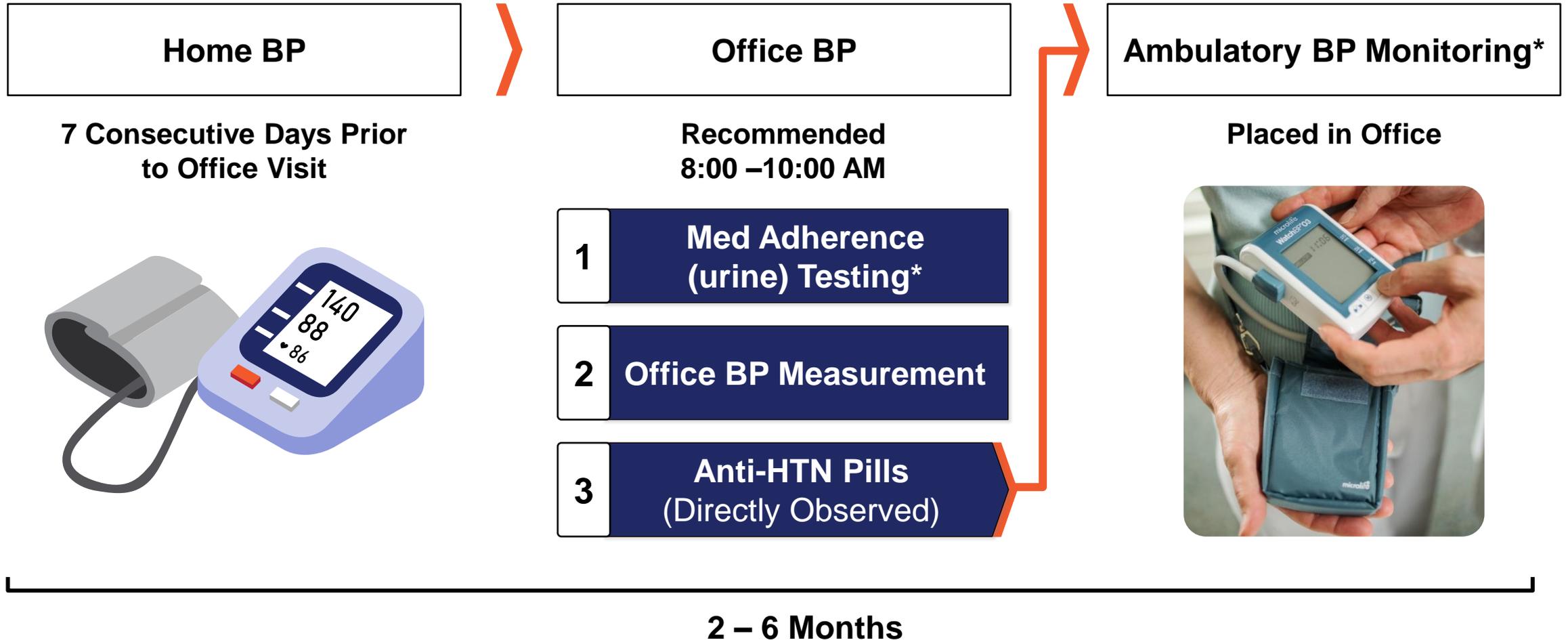
RADIANCE Studies Designed and Demonstrate Effects of uRDN on BP Lowering at 2 Months Compared with Sham



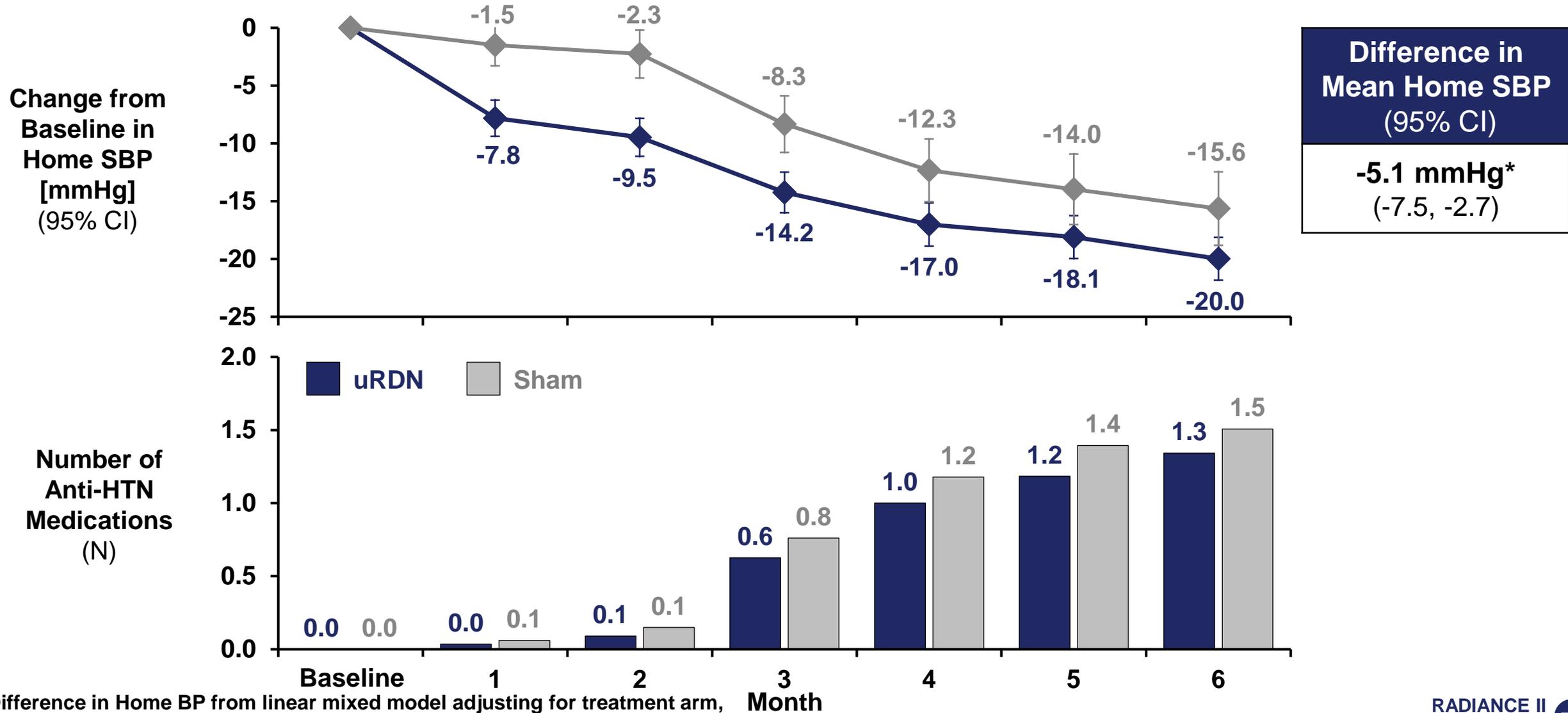
Standardized, Step-Wise Protocol for Adding Anti-HTN Medications Between Month 2 and 6

- Patients recorded home BP monthly between Month 2 and 6
- Home BP elevations ≥ 135 systolic or ≥ 85 mmHg diastolic and Office BP elevations ≥ 140 systolic or ≥ 90 mmHg diastolic
 - Protocol *recommended* one pre-specified medication be added per month with goal of achieving BP control

Blood Pressure Measurements at Follow-up Visits

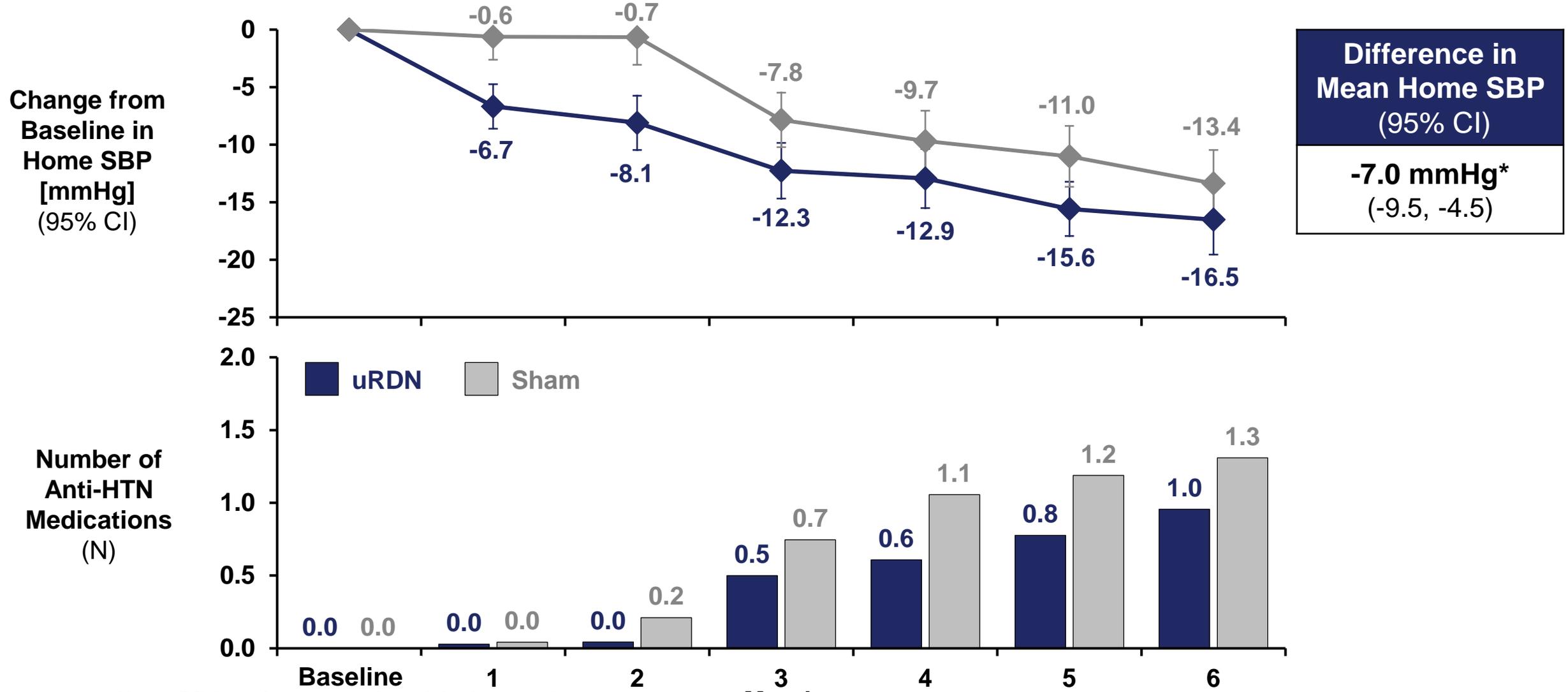


RADIANCE II: Lower Home Blood Pressure and Medication Burden with uRDN Through 6 Months



*Difference in Home BP from linear mixed model adjusting for treatment arm, visit, baseline blood pressure, number of medications at visit, and interaction term (treatment arm*visit)

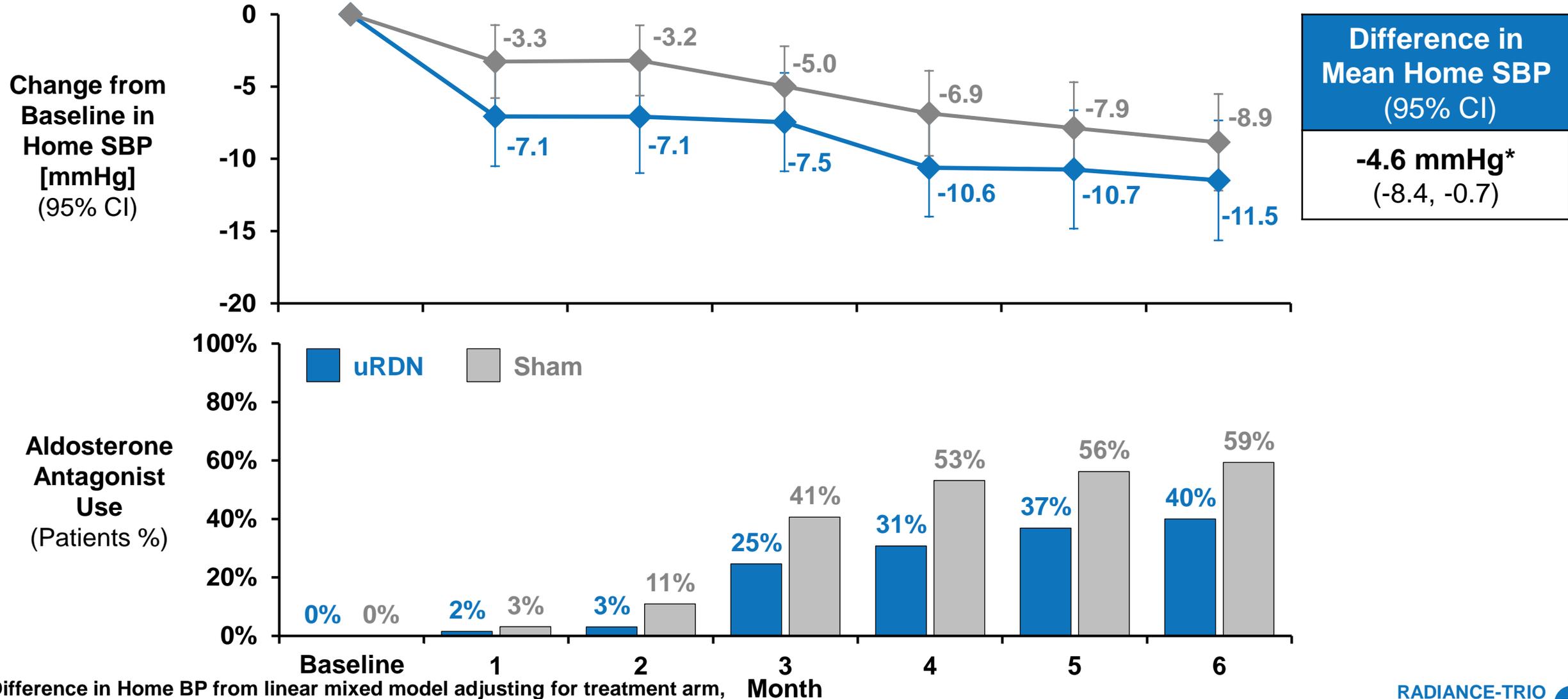
RADIANCE-SOLO: Home BP and Medication Burden Lower with uRDN Through 6 Months



Difference in Mean Home SBP (95% CI)
-7.0 mmHg*
(-9.5, -4.5)

*Difference in Home BP from linear mixed model adjusting for treatment arm, baseline blood pressure, and number of medications at visit.

RADIANCE-TRIO: Stepped Care Anti-HTN Regimen Decreased BP in Both Groups Through 6 Months



Long-Term Durability

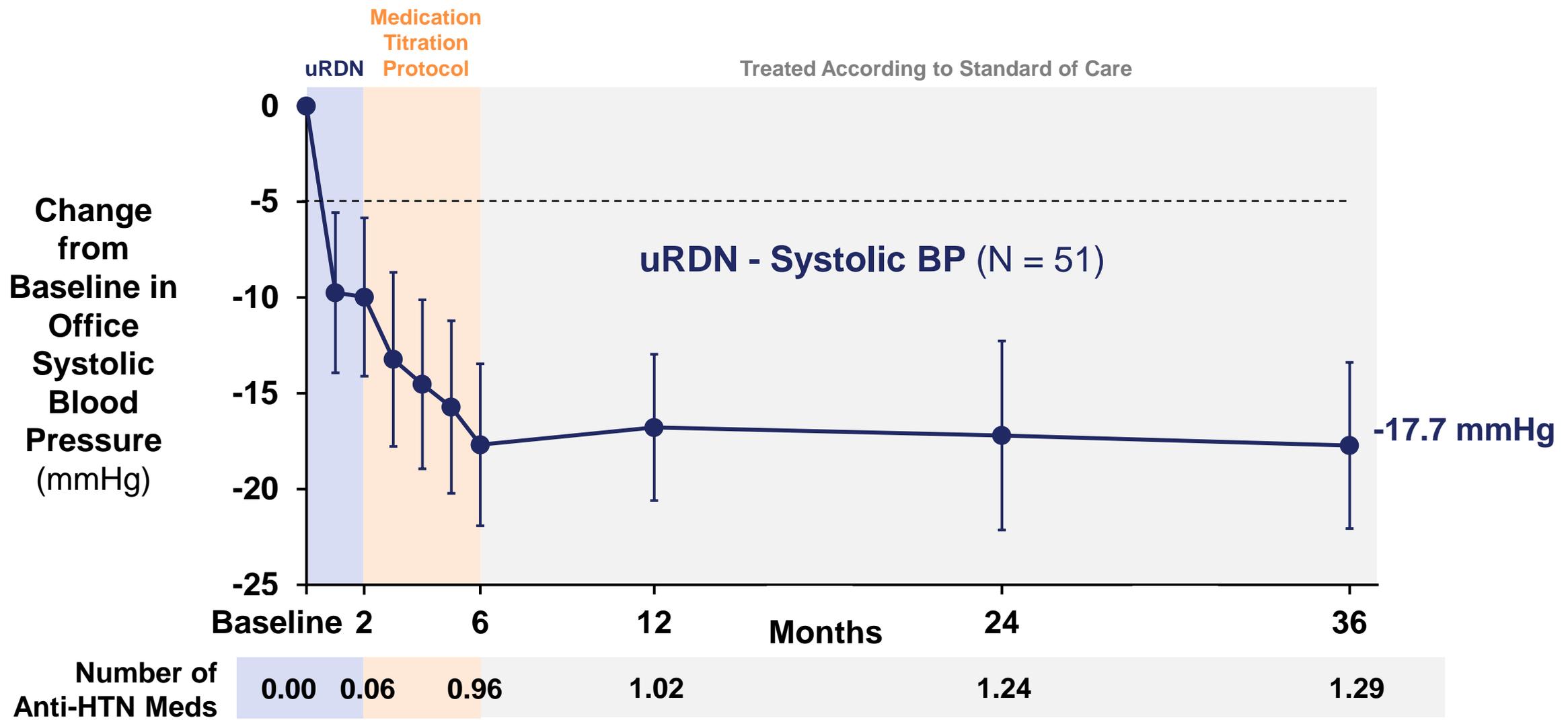
RADIANCE-HTN SOLO (36 Months)

Patients with Mild-Moderate Hypertension

RADIANCE-HTN TRIO (24 Months)

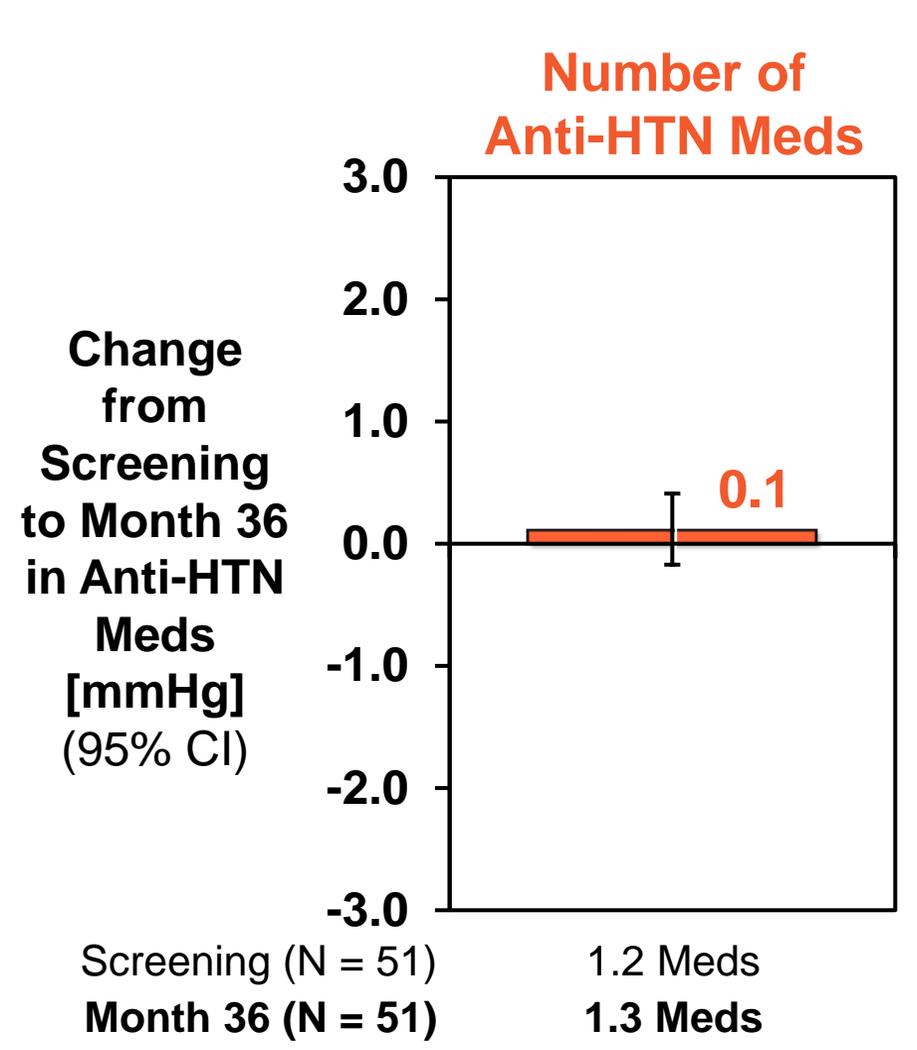
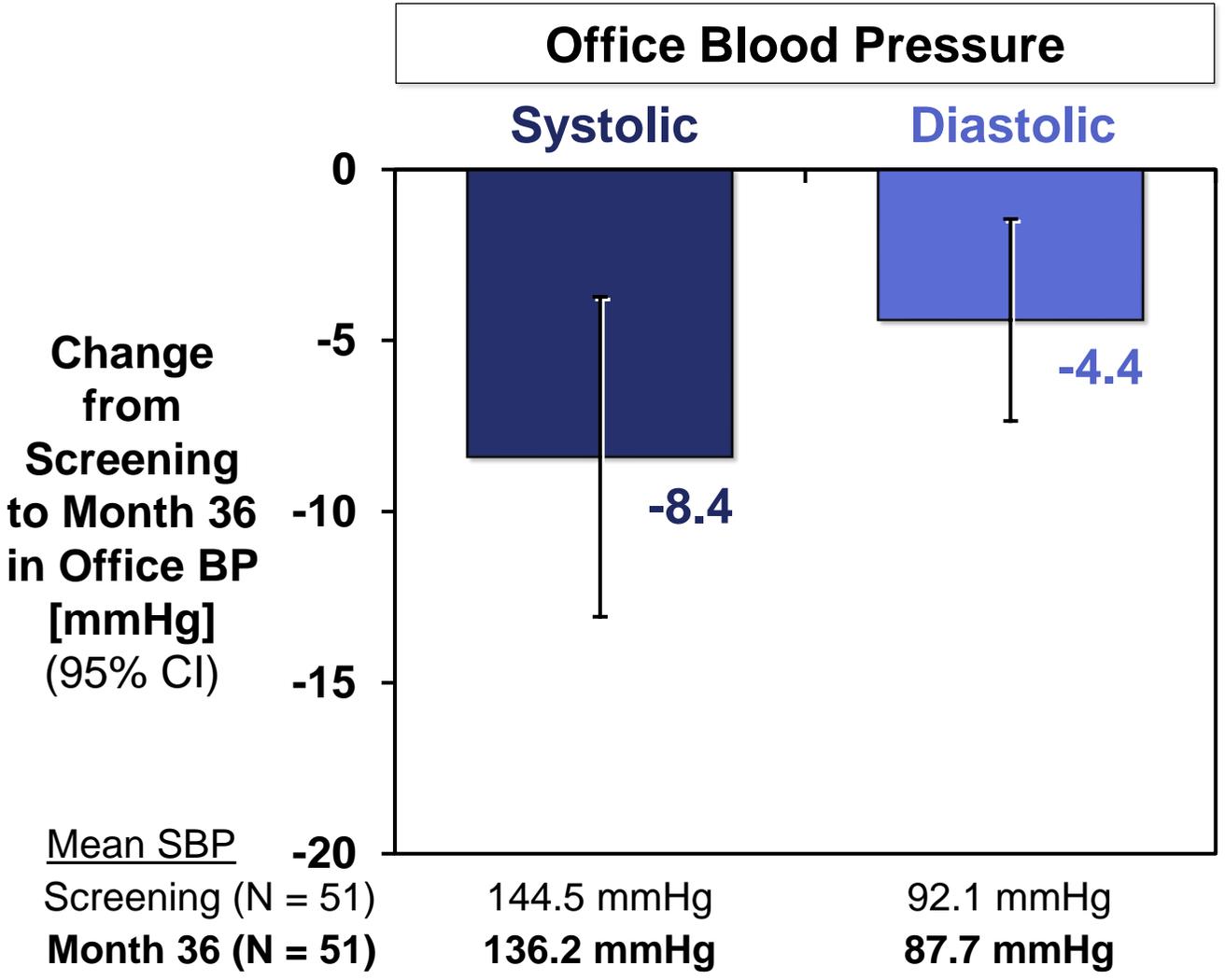
Patients with Resistant Hypertension

RADIANCE-SOLO: Reductions in Office Systolic BP with uRDN Sustained Through 36 Months

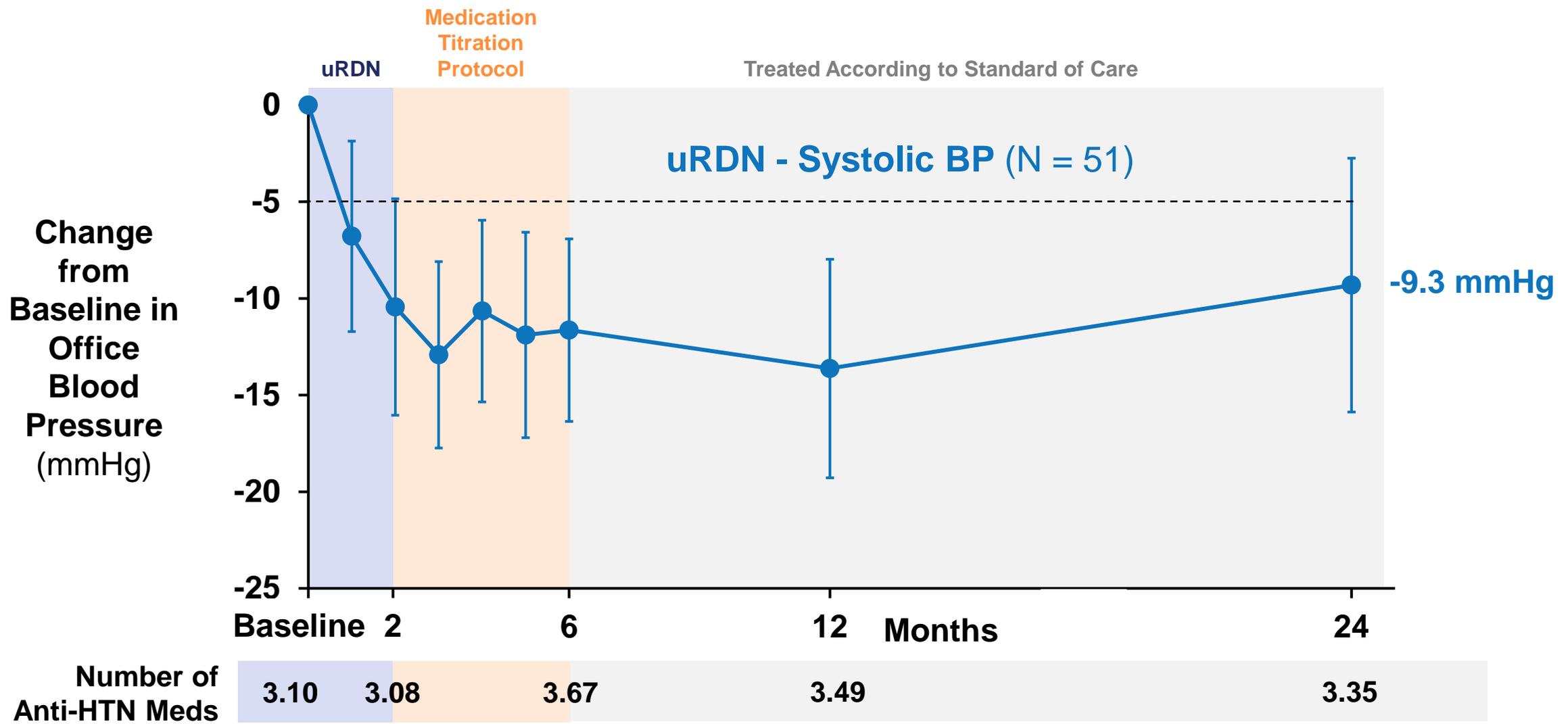


RADIANCE-SOLO: Improved BP with Similar Anti-HTN Meds

Screening to Month 36 – All Patients with Office BP at Screening



RADIANCE-TRIO: Supports Long-Term Durability of Paradise uRDN Treatment Effect Through 24 Months



RADIANCE-TRIO: Improved BP with Fewer Anti-HTN Meds

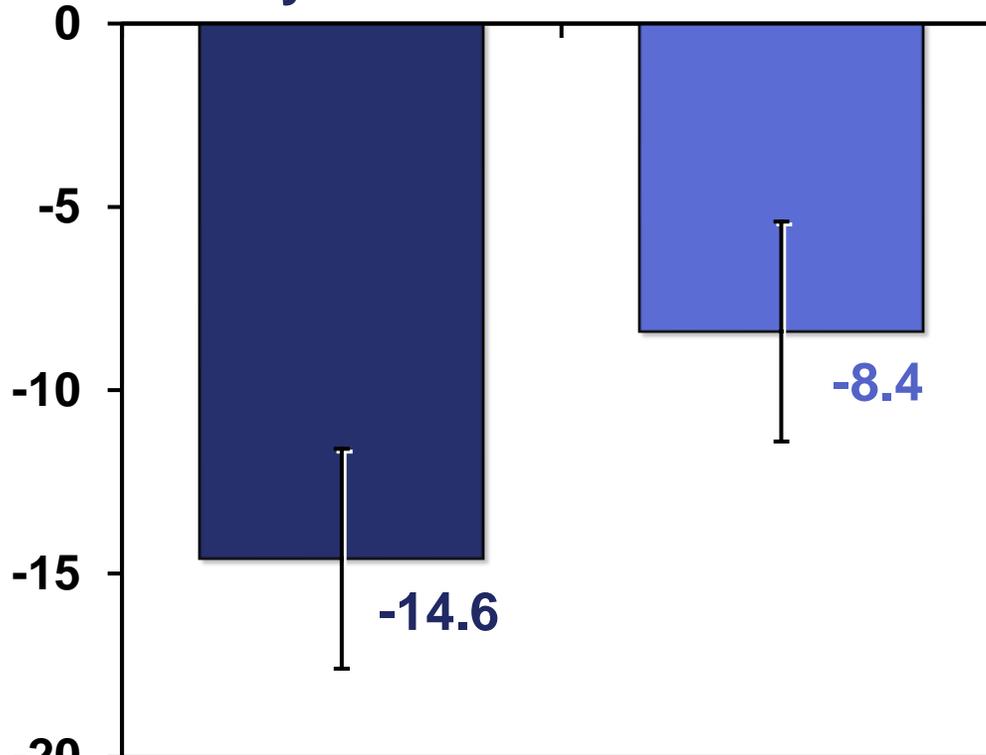
Screening to Month 24 – All Patients with Office BP at Screening

Office Blood Pressure

Systolic

Diastolic

Change from Screening to Month 24 in Office BP [mmHg] (95% CI)



Mean SBP

-20

Screening (N = 51)

159.8 mmHg

103.5 mmHg

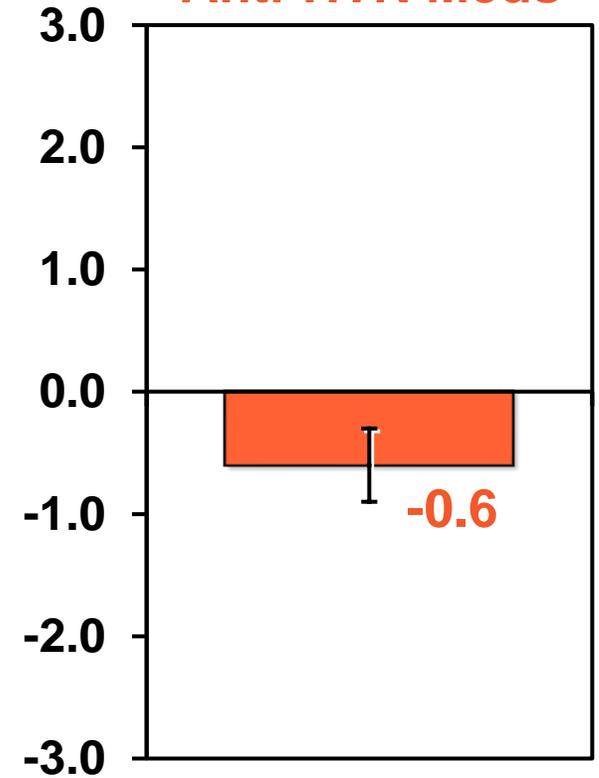
Month 24 (N = 51)

145.2 mmHg

95.1 mmHg

Change from Screening to Month 24 in Anti-HTN Meds [mmHg] (95% CI)

Number of Anti-HTN Meds



Screening (N = 51)

3.9 Meds

Month 24 (N = 51)

3.4 Meds

Efficacy Conclusions

- Met prespecified primary endpoint in all 3 studies
- Paradise uRDN provided statistically significant and clinically meaningful BP reductions
 - Consistent across secondary and observational endpoints
 - Demonstrates continuous benefit throughout 24-hour circadian cycle
- Clinically meaningful reductions sustained through long-term follow-up



Safety

Glenn Chertow, MD, MPH

Professor of Medicine
Stanford University

Adverse Clinical Events Consistently Collected Across RADIANCE Studies

RADIANCE II

RADIANCE-SOLO

RADIANCE-TRIO

- All events collected regardless of time to onset post-procedure
 - **AEs** adverse events
 - **ADEs** adverse device events
 - **SAEs** serious adverse events
 - **SADEs** serious adverse device events
- Events stratified by those occurring ≤ 30 days vs > 30 days post-procedure
- Relatedness to device or procedure determined by investigator
- Other events of interest pre-specified in protocol
 - Post-procedural pain
 - New onset orthostatic hypotension
 - Renal function (eGFR and creatinine)
 - New onset renal artery stenosis (post-procedure imaging of renal arteries)

RADIANCE II: Primary Safety Composite Endpoint 30-Day and 6-Month Post-Procedure MAEs

Events Occurring \leq 30 Days

- All-cause mortality
- New onset end-stage renal disease
- Significant embolic event
- Renal artery perforation
- Renal artery dissection
- Major vascular complications
- Hospitalization hyper/hypotensive crisis
- Hospitalization major CV events
- New onset stroke
- New onset myocardial infarction

Events Occurring at 6 Months

- New renal artery stenosis $>$ 70%
 - Confirmed by CT/MR angiography
- All events adjudicated by independent clinical events committee
- Composite event rate compared to pre-specified performance goal of 9.8%

RADIANCE II Met Prespecified Primary Safety Endpoint; No Patients had Major Adverse Event

		RADIANCE II	
		uRDN N = 150	Sham N = 74
Pre-specified Performance Goal		9.8%	
Overall Composite Endpoint		0% (0.0, 2.4)	0% (0.0, 4.9)
≤ 30 Days	All-cause Mortality	0	0
	New Onset End-stage Renal Disease	0	0
	Significant Embolic Event	0	0
	Renal Artery Perforation	0	0
	Renal Artery Dissection	0	0
	Major Vascular Complications	0	0
	Hospitalization Hyper/Hypotensive Crisis	0	0
	Hospitalization Major CV Events	0	0
	New Onset Stroke	0	0
	New Onset Myocardial Infarction	0	0
6 Months	New Renal Artery Stenosis > 70%	0	0

No Unexpected SADEs Reported

Events Occurring in ≥ 2 uRDN-Treated Patients

All Post-Procedure Events Patients % (Events)	RADIANCE II		SOLO		TRIO	
	uRDN N = 150	Sham N = 74	uRDN N = 74	Sham N = 72	uRDN N = 69	Sham N = 67
SADE	7%	1%	7%	0	4%	3%
Access Site Hematoma	2% (3)	0	0	0	1% (1)	0
Syncope	1% (2)	0	0	0	0	0
Bradycardia	0	0	3% (2)	0	0	0

- No other SADEs occurred in > 1 patient across the RADIANCE studies

8 Deaths Occurred During Clinical Development Program; Majority in Patients Receiving Sham

	RADIANCE II		SOLO		TRIO ¹	
	uRDN N = 150	Sham N = 74	uRDN N = 74	Sham N = 72	uRDN N = 69	Sham N = 67
Randomized Patients, N						
Deaths	1	1	0	1	2	2

- No deaths were determined by investigators or the CEC to be related to procedure or investigational device

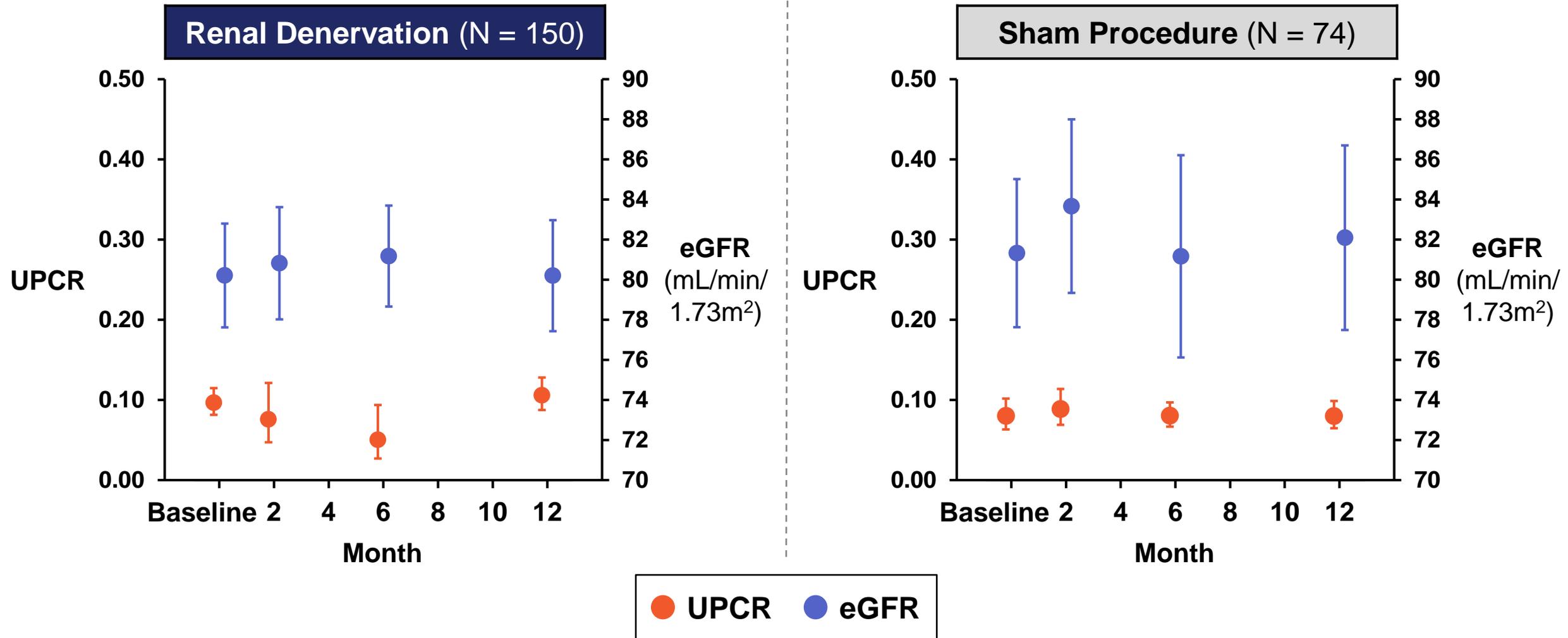
1. One additional death occurred during screening phase of TRIO, prior to randomization due to pancreatic cancer

Kidney Function and Vascular Safety

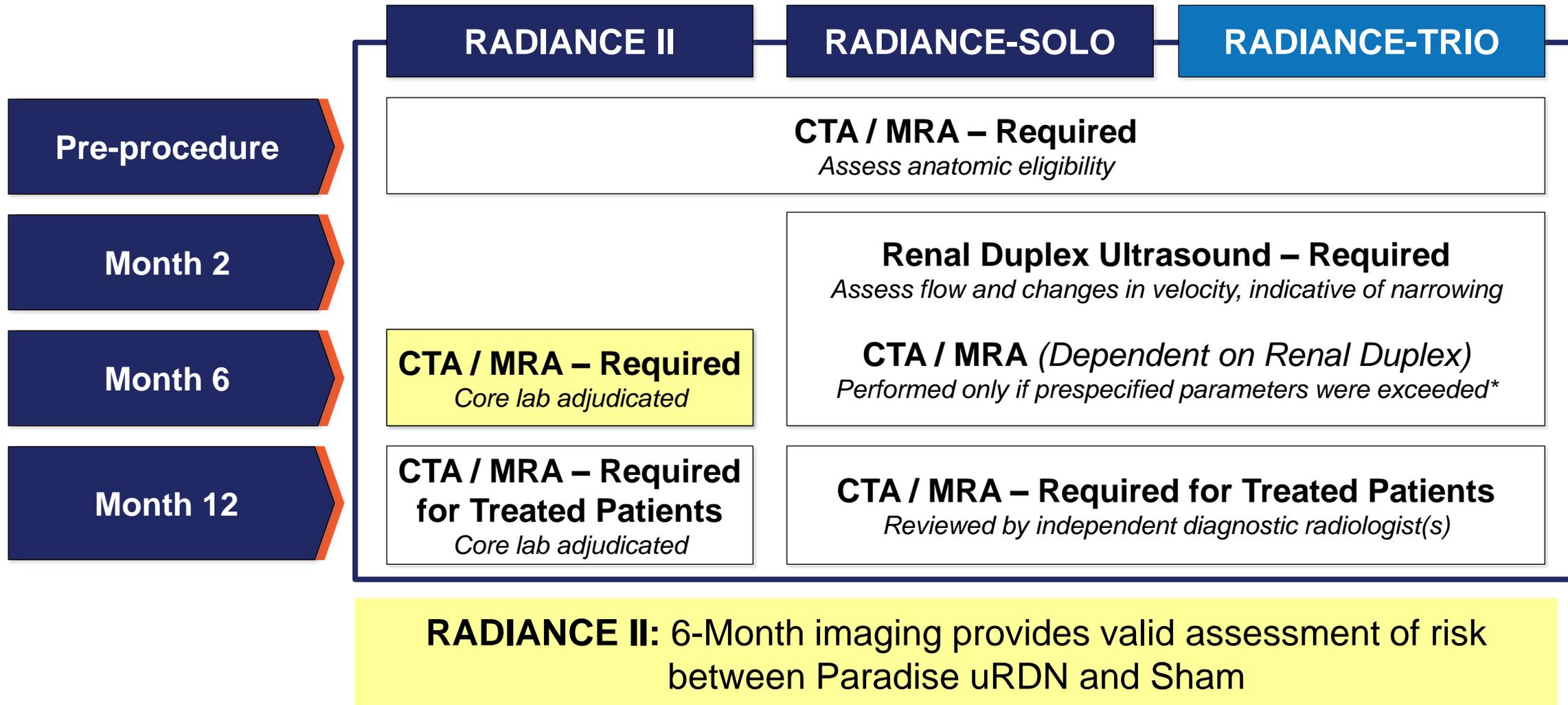
Serum creatinine / eGFR and proteinuria

Imaging of renal arteries

RADIANCE II: No Differences Observed in UPCR and eGFR Between Treatment Groups



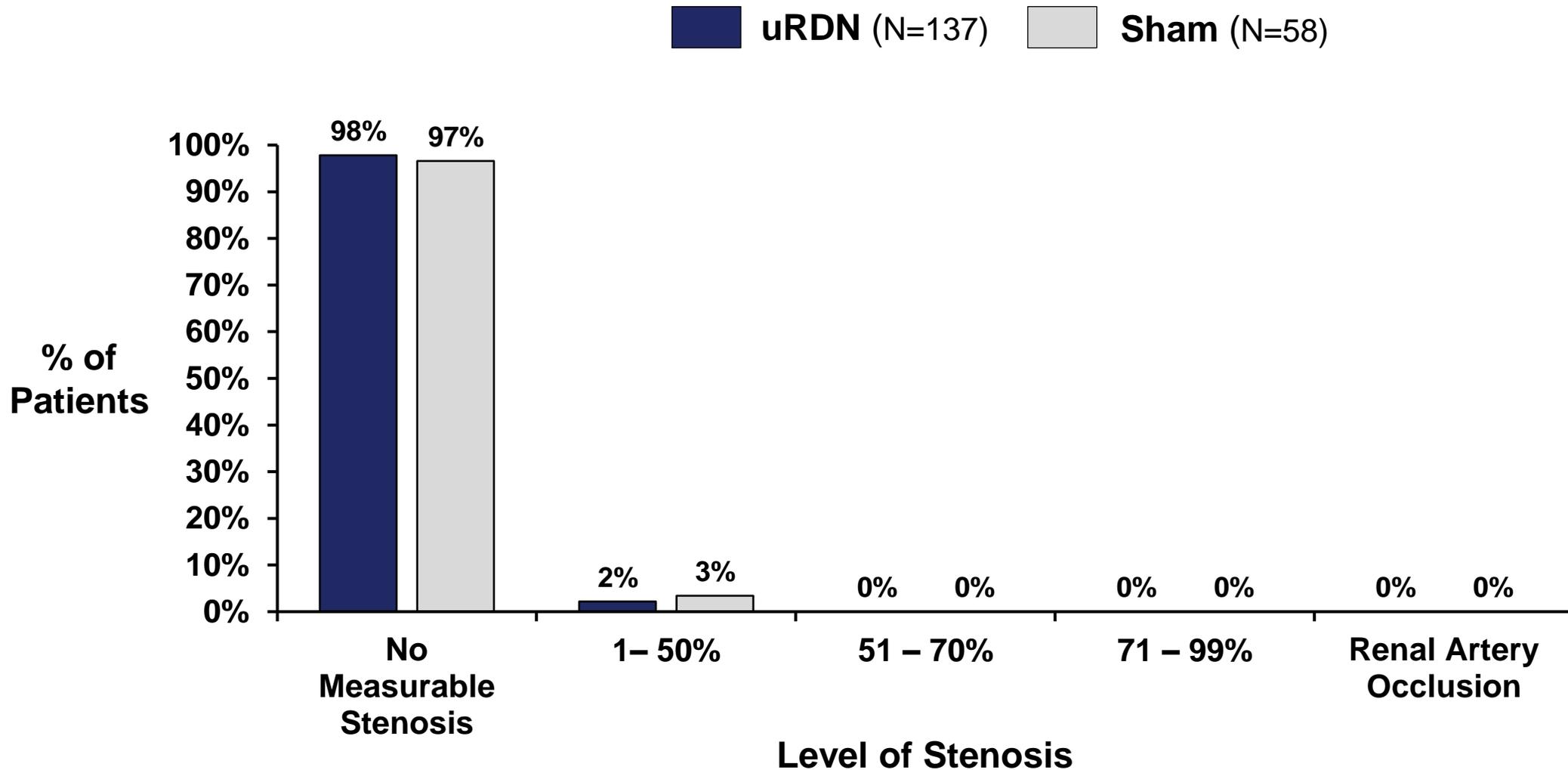
Imaging Conducted Across RADIANCE Studies to Evaluate Potential Renal Artery Injury



*Peak systolic velocity along any portion of the renal arteries > 180 cm/sec:

Renal to aortic peak systolic velocity ratio > 3.5 or complete lack of Doppler signal in any portion of the main or accessory renal artery

RADIANCE II: No Evidence of Clinically Significant Renal Artery Stenosis at 6 Months

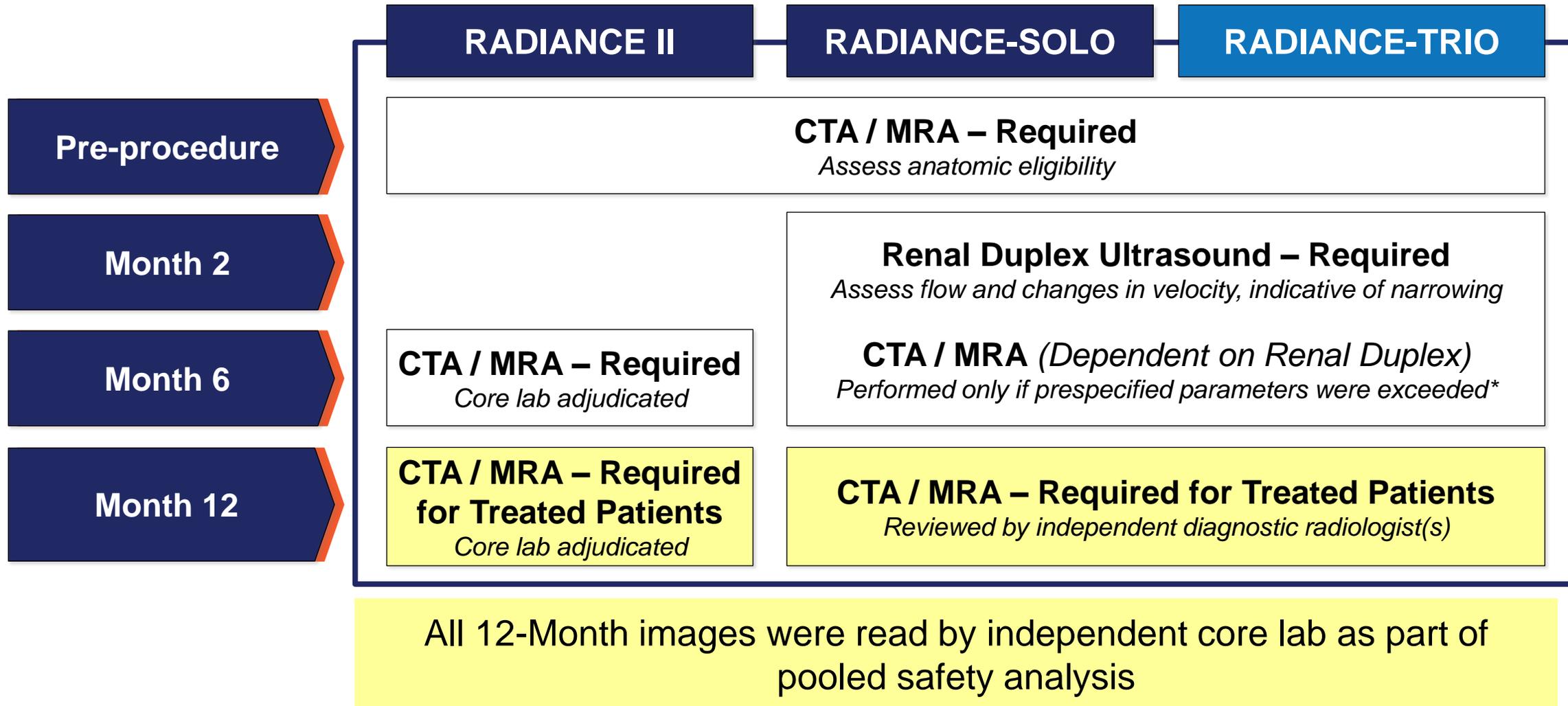


Pooled Safety

12-Month Imaging

Composite Safety Outcome

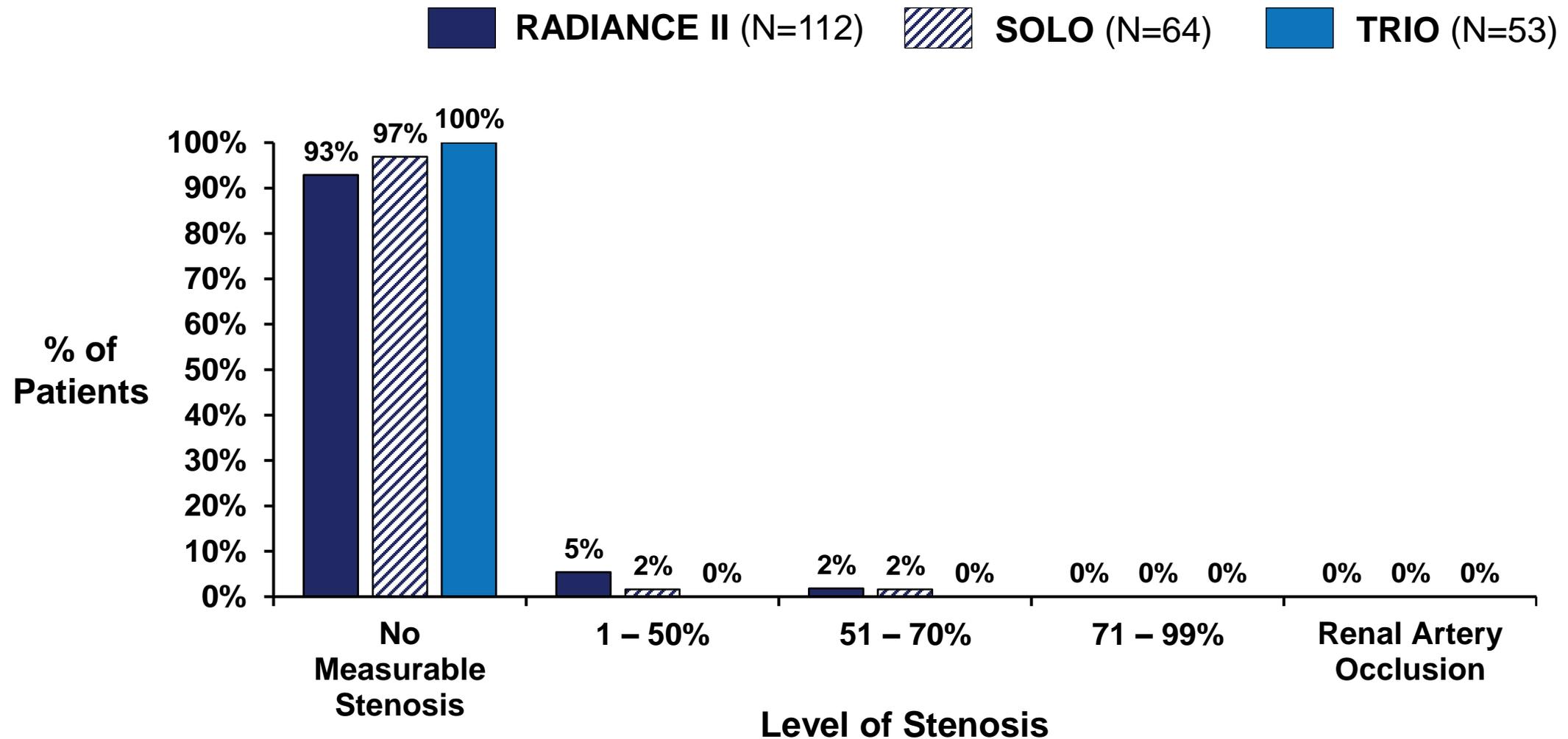
12-Month Imaging for All uRDN-Treated Patients Reviewed by Independent Core Lab



*Peak systolic velocity along any portion of the renal arteries > 180 cm/sec:

Renal to aortic peak systolic velocity ratio ≥ 3.5 or complete lack of Doppler signal in any portion of the main or accessory renal artery

No Evidence of Clinically Significant Renal Artery Stenosis at 12 Months



Pooled Safety Analysis Further Characterizes Safety Profile of Paradise uRDN

- Includes 367 patients treated with Paradise uRDN from RADIANCE Studies
- RADIANCE II primary safety composite endpoint used
 - Composite event rate compared to pre-specified performance goal of 9.8%
- All events were adjudicated by an independent CEC

Pooled Data: Summary of MAEs

- All events adjudicated unlikely / not related to uRDN

Pooled Data Set

uRDN
N = 367

Overall Composite Endpoint; Events (Rate); [95% CI]

6 (1.1%); [0.3, 2.8]

All-Cause Mortality

2 (0.5%)

New Onset End-stage Renal Disease

0

Significant Embolic Event

0

Renal Artery Perforation

0

Renal Artery Dissection

0

≤ 30 Days

Major Vascular Complications

2 (0.3%)

Hospitalization for Hyper/Hypotensive Crisis

1 (0.3%)

Hospitalization for Major CV Event

1 (0.3%)

New Onset Stroke

0

New Onset Myocardial Infarction

0

6 Months

New Renal Artery Stenosis > 70%

0

Safety Conclusions

- Favorable safety profile
- No increased risk for MAE over Sham
- Procedure-related events resolved with no long-term sequelae
- No evidence of acute or long-term kidney injury
- No evidence of renal artery injury or any clinically significant renal artery stenosis



Post Approval Study

Helen Reeve-Stoffer, PhD

Chief Clinical Officer

ReCor Medical

Post-Approval Study Proposal

1. Continue follow-up of patients enrolled in RADIANCE studies
 - Follow-up planned for up to 5 years
2. Initiate US arm of Global Paradise System (US-GPS) Registry
 - 700 patients needed to achieve ~500 evaluable at 5 years
 - Patients currently enrolled in the RADIANCE Continued Access Protocol
 - Minimum of 500 de novo patients to be enrolled and treated according to approved labelling
 - Up to 100 US clinical sites

Proposed Clinical Data Collection

- Primary effectiveness outcome measure = BP reduction
 - Telemetric Home BP as primary assessment method
 - Office BP will be collected at each in-clinic follow-up visit
 - Patient reported outcomes
- Safety focused on procedure and device related events
 - Additional assessments will include cardiovascular and hemodynamic clinical events and changes in renal function
 - Sample size will allow for 95% probability of detecting clinical events with an occurrence rate as low as 0.6%

Statistical Analyses and Subgroups

- Descriptive statistics for all outcomes including frequency, percentage and 95% confidence interval
- Analyses of targeted subgroups
 - Sex, race, age
 - Heart rate, obesity, BIM, eGFR, NYHA
 - Isolated systolic hypertension
 - Diabetes
 - Number and class of antihypertension medications

Diversity and Recruitment

- Recruitment initiatives will focus on increased diversity and inclusivity initiatives, particularly in under-represented populations
- Study leadership
 - Naomi Fisher, MD, Study Principal Investigator
 - Steering Committee will provide guidance
 - Expertise in Renal Denervation, Vascular Medicine, Hypertension, Interventional Cardiology, Nephrology and Pharmacology
 - Committee members confirmed to date:
 - Mohammad Ansari, MD, Texas Tech University Health System
 - Tiffany Randolph, MD, Cone Health
 - Hunter Nichols, PharmD, Brigham and Women's Hospital



Clinical Perspective

Naomi Fisher, MD

Director, Hypertension Service & Hypertension Specialty Clinic

Brigham and Women's Hospital

Associate Professor

Harvard Medical School

Achieving Blood Pressure Control Remains a Challenge for Physicians and Patients

Lifestyle Modification

Difficult for patients to achieve and sustain optimal blood pressure targets with lifestyle modifications alone

Antihypertensive Medications

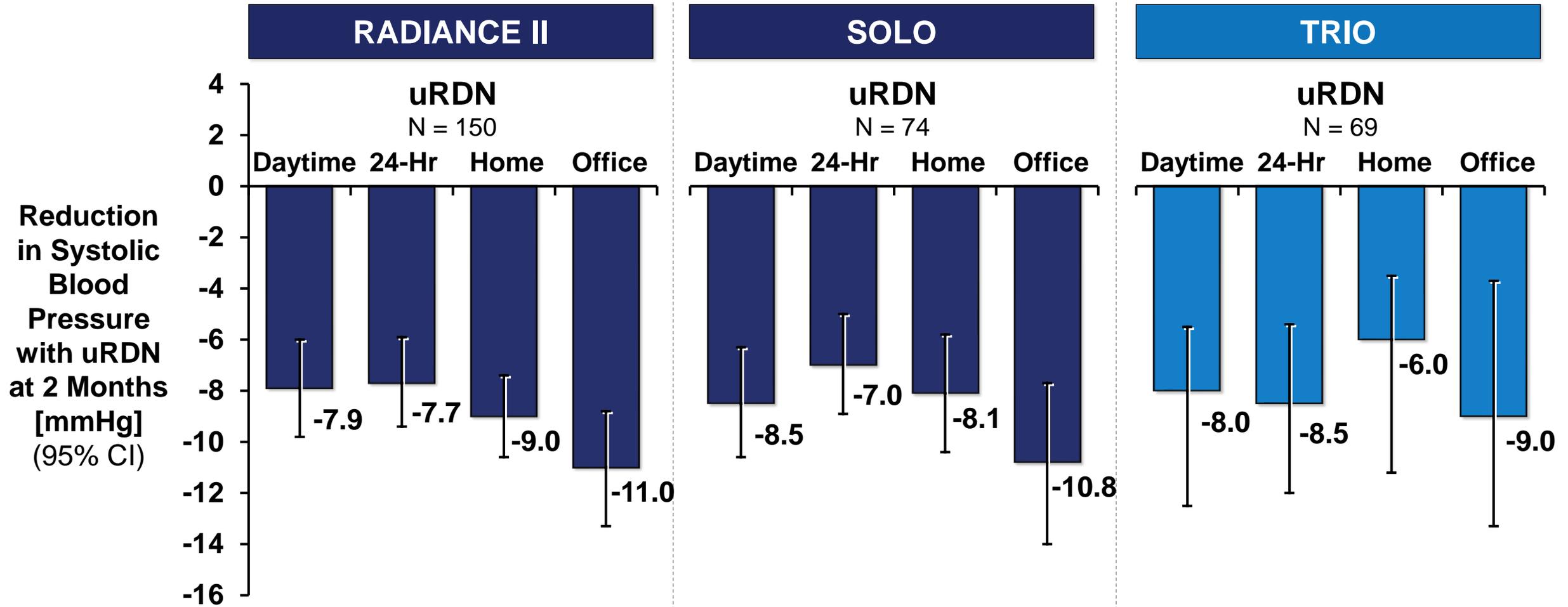
Multiple factors including adherence, tolerability, and drug resistance impact effectiveness

Blood pressure control remains a problem for many patients despite prolific availability of antihypertensive meds

Unmet Need

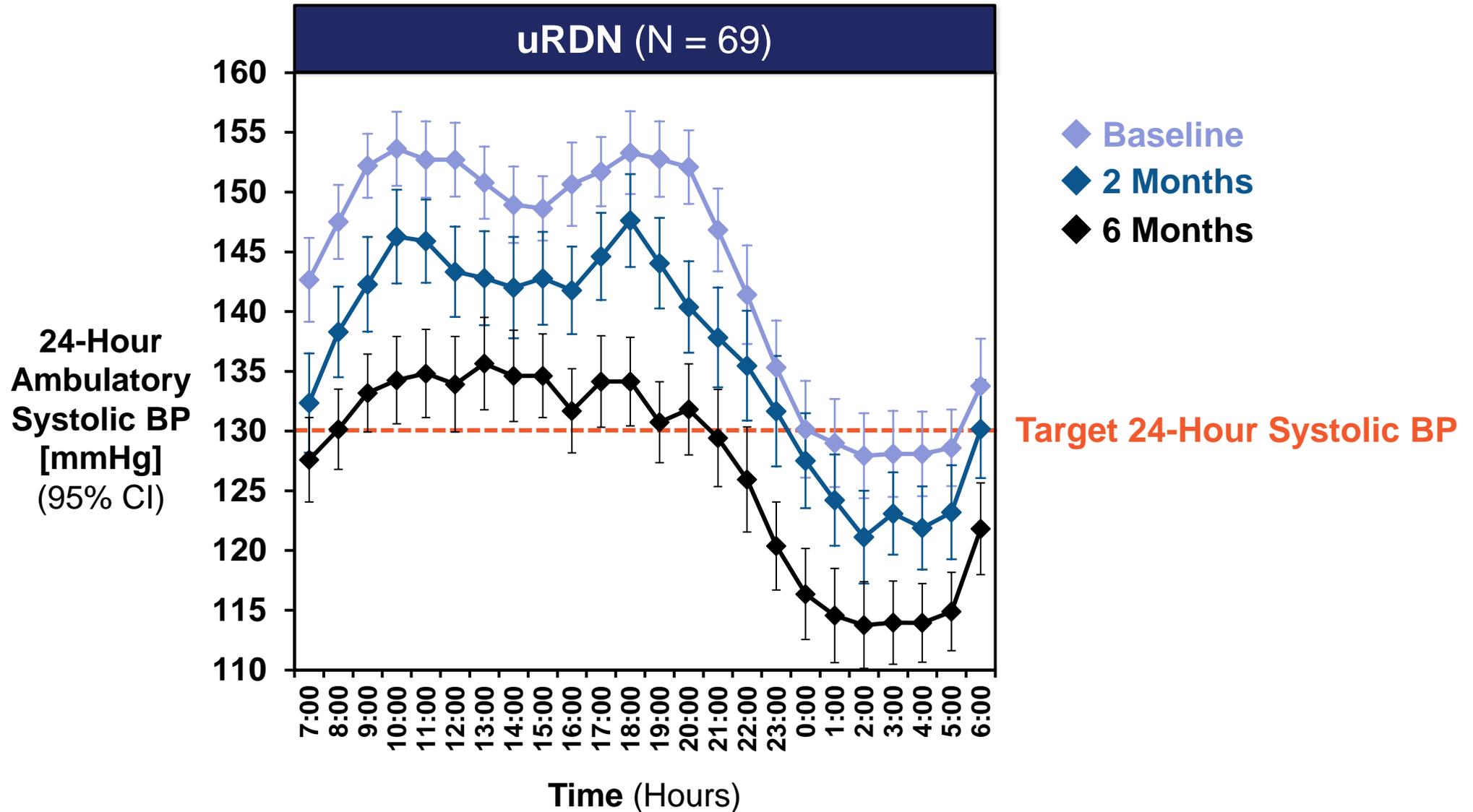
~74% of adults with hypertension fail to achieve blood pressure < 130/80 mmHg with standard medical therapy

Benefits Achieved at 2 Months with Paradise System Represent Robust Outcome for Patients



■ Average reduction in office SBP with effective antihypertensive medication is 10 mmHg¹

RADIANCE-SOLO: uRDN Provides “Always On” Therapy, Reducing Blood Pressure Throughout 24-Hour Circadian Cycle



RADIANCE Studies Support Paradise uRDN is Safe

- Procedure-related events were minor
- Long-term safety demonstrated through 36 months

Paradise uRDN Represents Important Treatment Option for Patients with Uncontrolled Hypertension

Lifestyle Modification

Difficult for patients to achieve and sustain optimal blood pressure targets with lifestyle modifications alone

Antihypertensive Medications

Multiple factors including adherence, tolerability, and drug resistance impact effectiveness

Blood pressure control remains a problem for many patients despite prolific availability of antihypertensive meds

Ultrasound Renal Denervation

Would allow patients to achieve reductions beyond what would be expected with medications alone

Fills a critical gap in care of patients with uncontrolled hypertension

Benefits of Paradise uRDN Outweigh Potential Risks

- Risks are minimal
- Substantial benefits achieved

**Paradise uRDN, as supplement to medical therapy,
would be a significant advancement for patients**

Paradise Ultrasound Renal Denervation (uRDN) System Reduces Blood Pressure in Patients with Uncontrolled Hypertension

August 22, 2023

Circulatory Systems Devices Panel

ReCor Medical