Results and Updates from the Vessix REINFORCE Program

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8 mins

Disclosure Statement of Financial Interest
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Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation / Financial Relationship	Company
• Grant / Research Support	Abbott, Boston Scientific, Edwards Lifescience, Medtronic
• Consulting Fees / Honoraria	Boston Scientific, Gore
• Shareholder / Equity	Cathworks, Elixir, GDS, Medinol, Valve Medical

Six Month Results of the REDUCE HTN:REINFORCE Study of Renal Denervation for the Treatment of Hypertension

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tct2018

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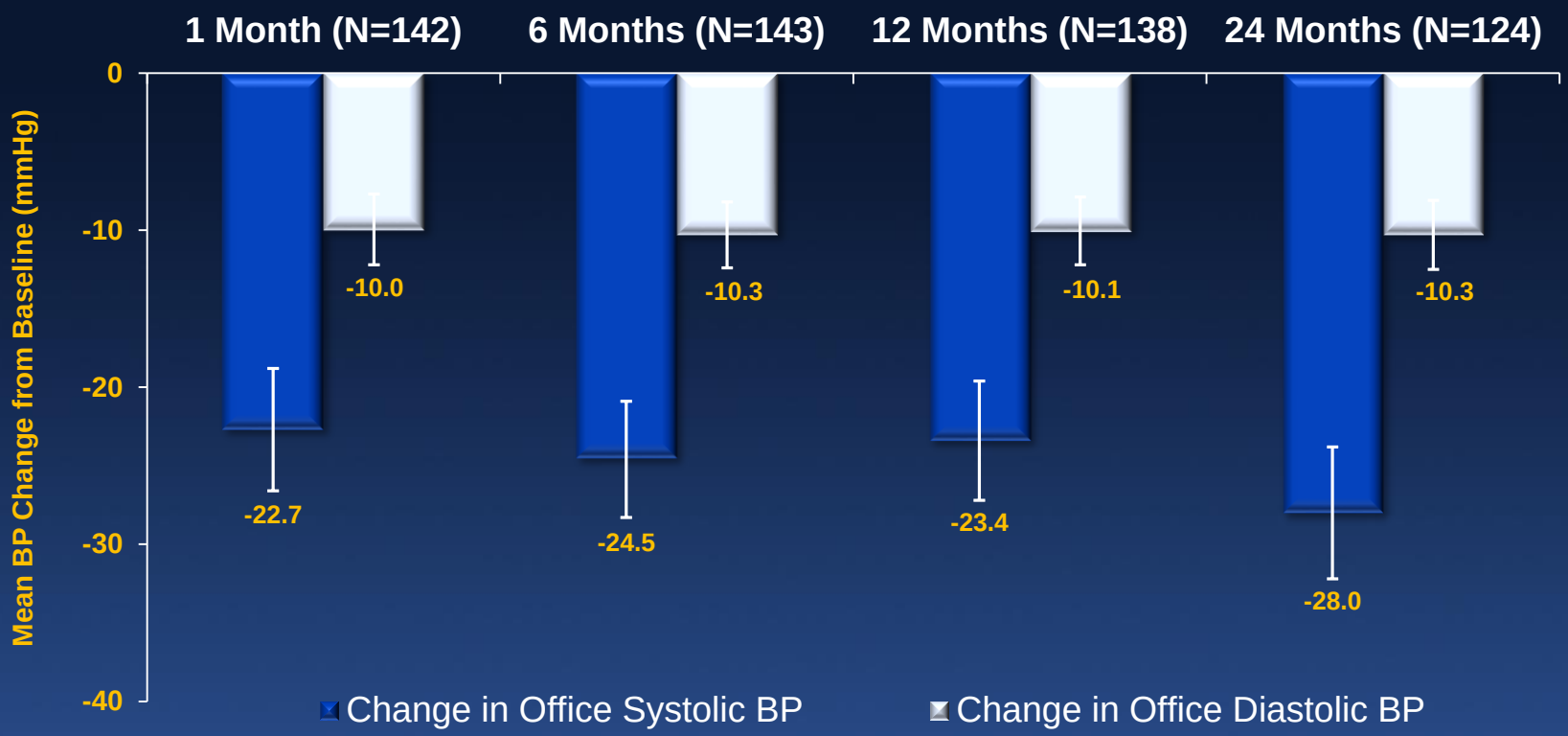
REDUCE-HTN FIM+PMS

Significant Office Blood Pressure Reductions Over Time



P<.0001 for each timepoint vs baseline. Error bars represent 95% confidence bounds.

Sievert , H. et al. J of Human Hypertension, (12 January 2017) | doi:10.1038/jhh.2016.82

The Vessix System is an investigational device and not available for sale in the US.

Single Center Experience with RDN: 57 Uncontrolled Hypertensive Patients Treated by One Operator (TF Lüscher)

Effects on Office Blood Pressure

		SBP/DBP (mmHg)			
Device	Number	Baseline	Δ at 6 Months	Δ at 12 Months	Δ at 24 Month
Vessix	19	155/87	-19/-8	-29/-7	-29/-13
Symplicity	24	173/89	-25/-5	-22/-4	-22/-2
EnligHTN	14	175/94	-29/-9	-36/-11	-42/-14

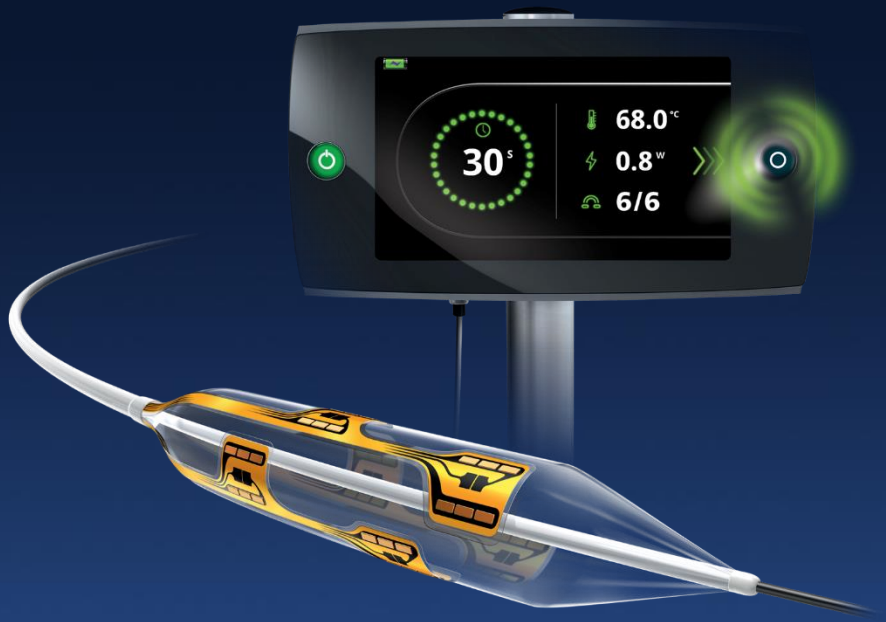
Denegri A, et al. J Clin Hypertens (Greenwich). 2018;20(4):627-633

The Vessix System is an investigational device and not available for sale in the US.

Investigational Device:

Vessix™ Renal Denervation System

- Balloon-based technology
  - 4 - 7 mm diameters
- Helical pattern of bipolar RF electrodes
- All electrodes are activated simultaneously
- 30 second treatment time
- Temperature-control algorithm for energy delivery at 68°C
- One-button operation
- 7F compatible (Vessix Reduce™ Catheter)



Rationale for Renal Denervation Study Designs

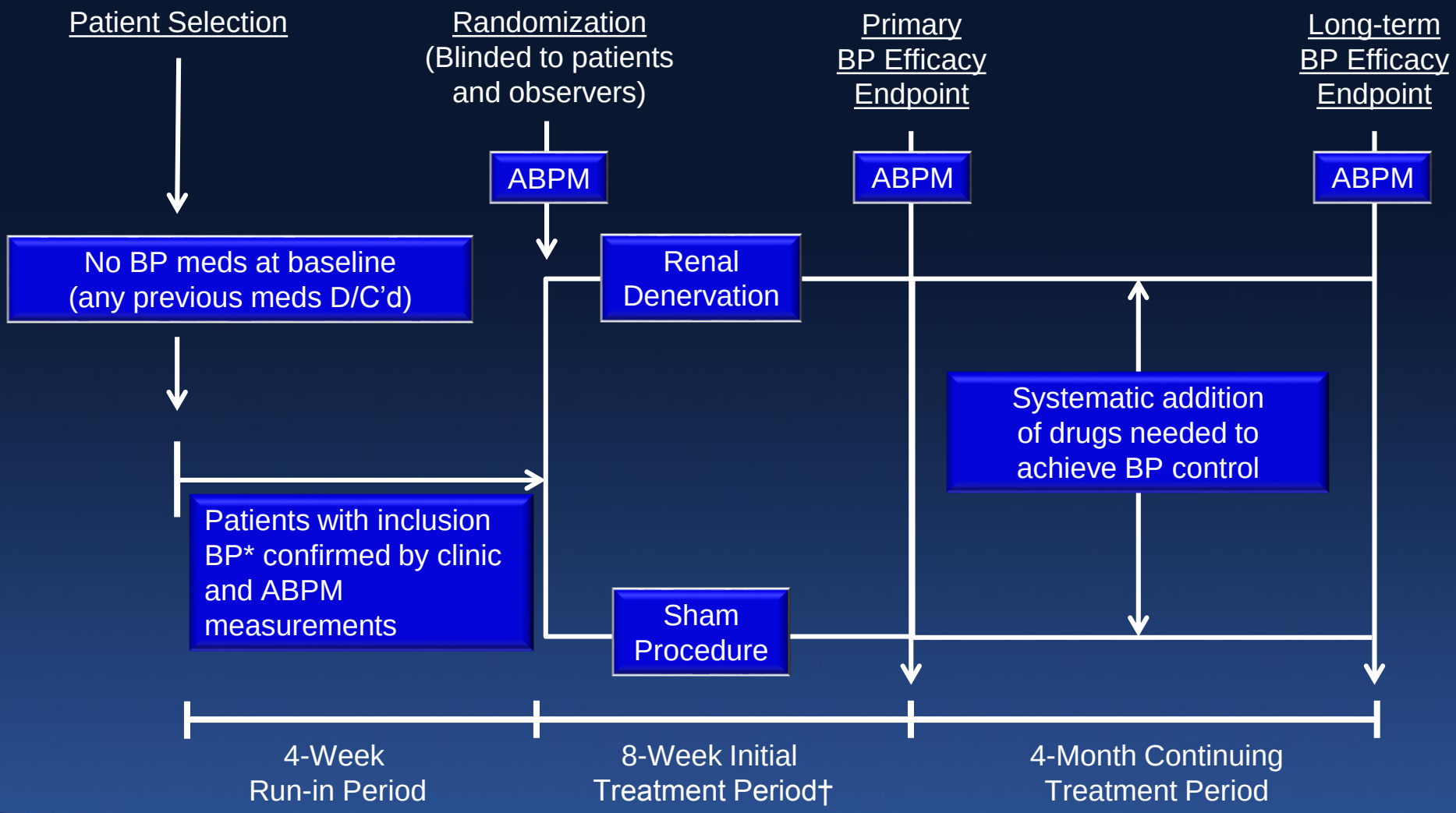
To justify renal denervation as a meaningful therapy for HTN, we must demonstrate:

1. **Renal denervation reduces BP more than placebo (sham)**
2. **The combination of renal denervation and drug therapy is significantly better than either therapy alone**

Courtesy of M. Weber

Focused Protocols for Renal Denervation:

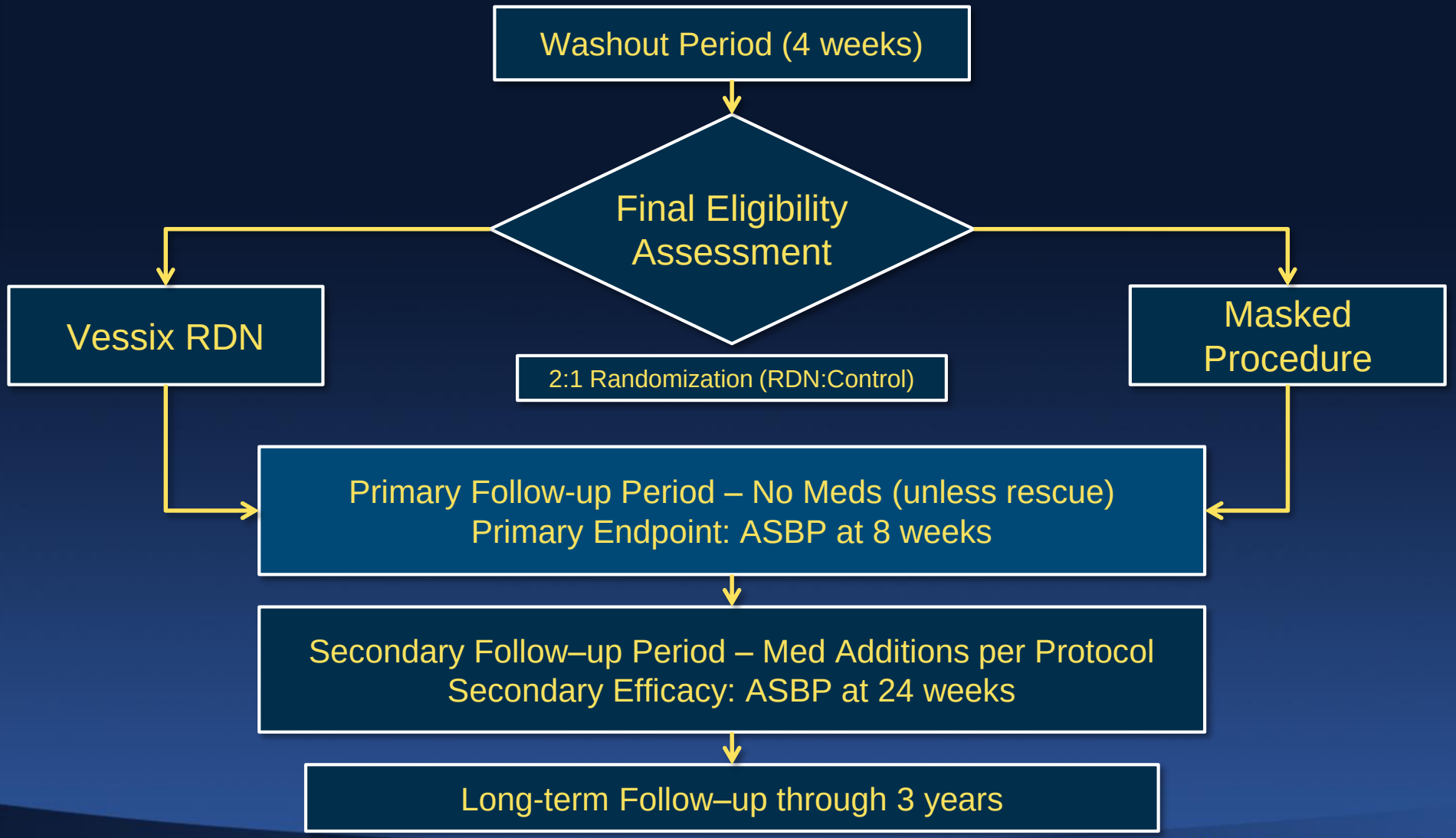
Patients Initially Off Drugs



- *Clinic systolic BP 150-180 mmHg and ABPM systolic BP 140-170 mmHg
- †Can be extended with careful patient oversight.
- From: Weber/ Kirtane/ Mauri/Townsend/Kandzari/Leon. CCI/ Clin Cardiol/ JCH 2015;17:743-750

REDUCE-HTN: REINFORCE

Study Overview (N=100, ≤20 US Sites)



REDUCE-HTN: REINFORCE

Study Overview (N=100, ≤20 US Sites)

Randomization	2:1 (Vessix:Control) Control: Masked Procedure (after renal angiogram)
Key Inclusion Criteria	• Age ≥18 and ≤75 • **OSBP ≥150 mmHg and ≤180 mmHg** • Average **24-hour ASBP ≥135 mmHg and ≤170 mmHg** • For each kidney, a **main renal artery, with or without accessory renal arteries, with diameter ≥3.0 mm and ≤7.0 mm and length ≥20.0 mm**
Primary Efficacy Assessment	**Reduction in average 24-hour ASBP at 8 weeks post randomization**

REDUCE-HTN: REINFORCE

Statistical Methods and Endpoints

Power	**93 patients required to give at least 80% power** to test primary endpoint (expected difference between groups 6 mmHg)
Primary Endpoint	Difference in **reduction of 24h ambulatory systolic BP** between intervention group and sham control **at 8 weeks**
Secondary Endpoints	At 8 weeks: • Reduction in office systolic and diastolic BPs • Proportion at target BP At 6 months: • Reduction of 24h and office systolic and diastolic BPs

Study Enrollment Cessation
The REDUCE-HTN: REINFORCE Trial
March 2018 (M Weber at CRT)

- Due to ongoing enrollment challenges, an interim analysis was conducted and reviewed by the Data Monitoring Committee (DMC) and Physician Steering Committee
- Futility: According to the interim analysis, pre-defined statistical decision rule definition for futility and confirmation by the DMC, it was determined that the trial could not achieve the primary endpoint at 8 weeks
- After careful consideration, the decision was made to end enrollment in this pilot trial, effective October, 2017
- The trial continues to follow subjects per protocol for those enrolled (N=51)

Baseline Characteristics

	Vessix Renal Denervation	Control
N	34	17
Age (y)	58.5±10.1	58.2±9.8
Male/Female	53%/47%	76%/24%
Race and Ethnicity		
Asian	6%	0%
Black, of African Heritage	18%	18%
Caucasian	79%	82%
Hispanic or Latino	3%	6%
Current Diabetes	18%	12%
Hyperlipidemia	38%	24%
Coronary Artery Disease	15%	18%
Myocardial Infarction	9%	6%
Office BP		
Systolic	166.3 ± 9.0	166.2 ± 8.8
Diastolic	94.9 ± 11.8	94.9 ± 11.1
24 h BP		
Systolic	148.3 ± 10.9	149.1 ± 7.2
Diastolic	85.7 ± 9.1	86.4 ± 9.8

Renal Artery Anatomy

	Vessix Renal Denervation (N=34)	Control (N=17)	Total (N=51)
Renal Artery			
Left Renal Artery	100%	100%	100%
Left Renal Accessory Artery	26%	18%	24%
Right Renal Artery	100%	100%	100%
Right Renal Accessory Artery	26%	41%	31%
Max Renal Diameter (mm)	6.5±1.8	6.4±1.6	6.5±1.7
Reference Renal Diameter (mm)	5.4±1.4	5.5±1.3	5.5±1.4
Renal Length (mm)	48.3±18.1	46.9±16.9	47.8±17.6
Percent Stenosis (%)	17.2±6.4	17.0±8.6	17.1±7.2

Safety through 6 months

- Of the safety endpoint events, only 1 hospitalization for hypertensive crisis occurred (CEC-confirmed)

	Vessix Renal Denervation (N=34)	Control (N=17)
All Cause Death	0%	0%
Renal Failure	0%	0%
Hypertensive Crisis	3% (1/34)	0%
Severe Hypotension/Syncope	0%	0%
Significant Embolic Event	0%	0%
Renal Artery Dissection or Perforation	0%	0%
Vascular Complications	0%	0%
Renal Artery Stenosis >70%	0%	0%

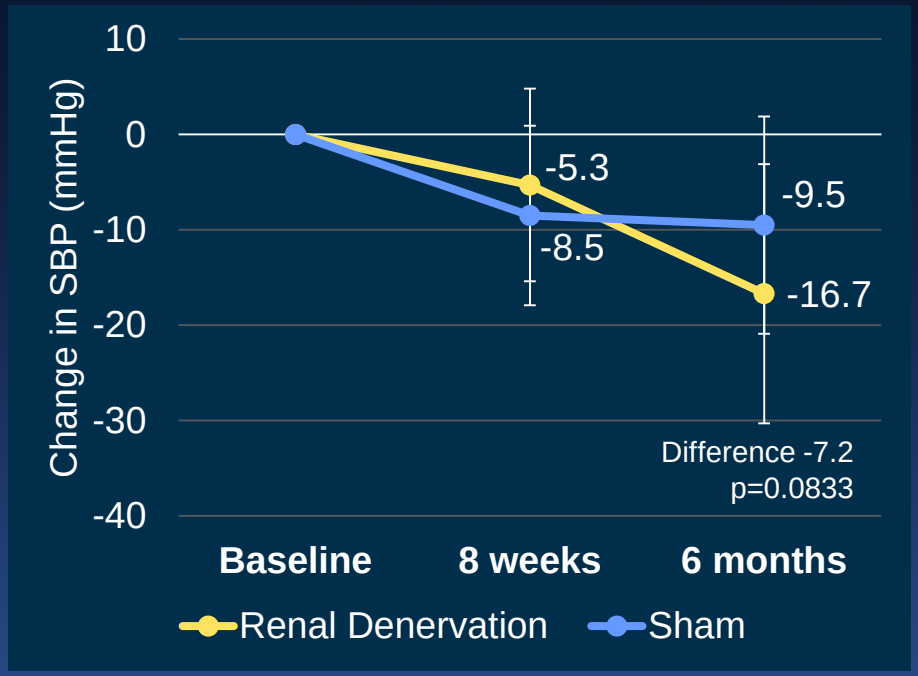
Antihypertensive Medication Usage

	Vessix Renal Denervation (N=34)	Control (N=17)
Baseline (post-washout)	0	0
6 Months		
On antihypertensive drug	79%	82%
Number of drugs	1.3±0.5	1.2±0.4

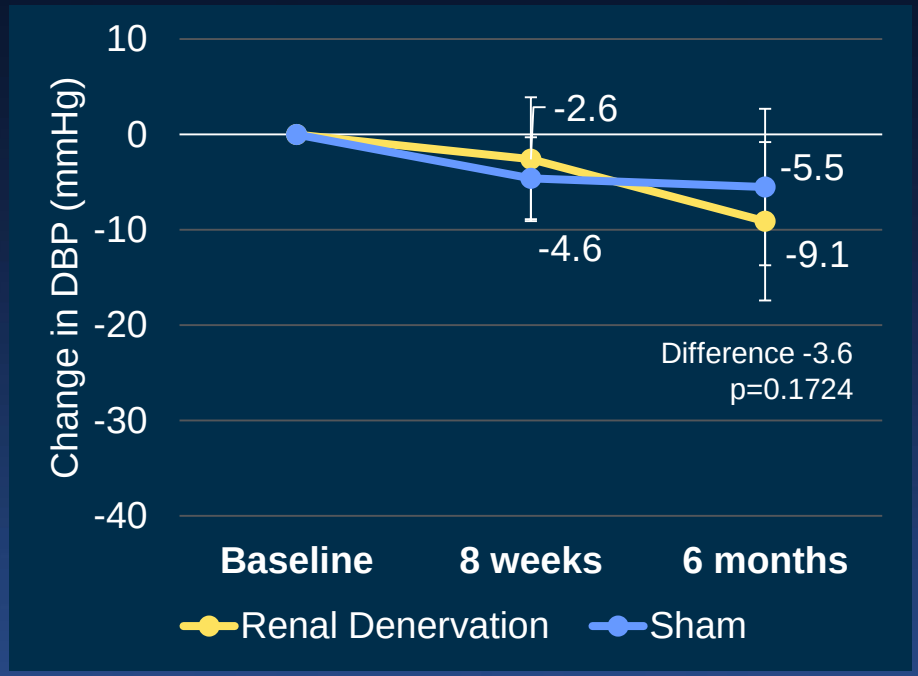
- **Medications could be initiated following the 8-week primary efficacy assessment, unless excessive BP increases necessitated earlier use**

Change in 24-Hour Blood Pressures

Baseline BP (mm Hg)	Systolic	Diastolic
Vessix	148.3±10.9	85.7±9.1
Control	149.1±7.2	86.4±9.8



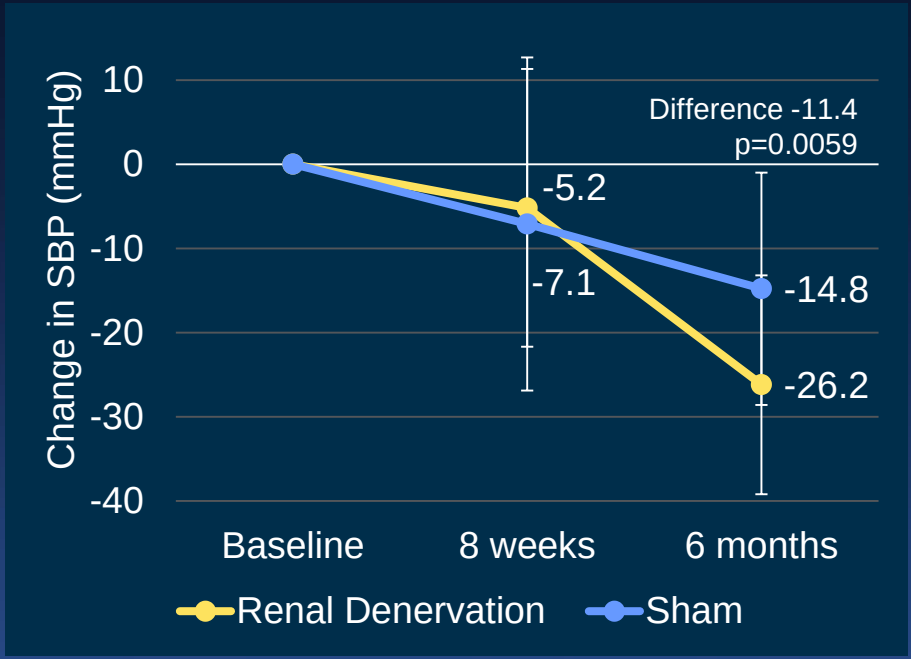
Systolic



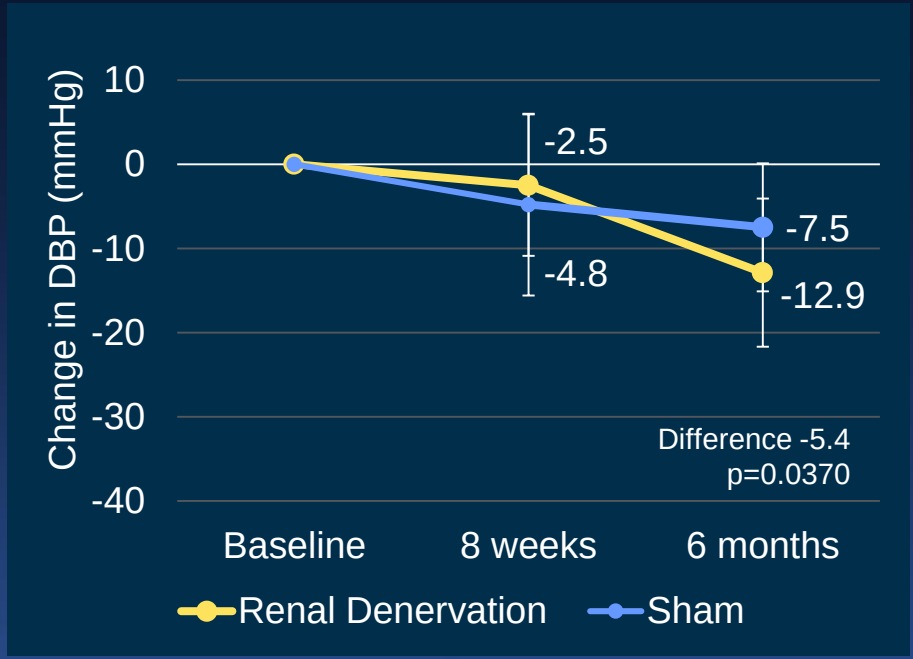
Diastolic

Change in Office Blood Pressures

Baseline BP (mm Hg)	Systolic	Diastolic
Vessix	166.3±9.0	94.9±11.8
Control	166.2±8.8	94.9±11.1



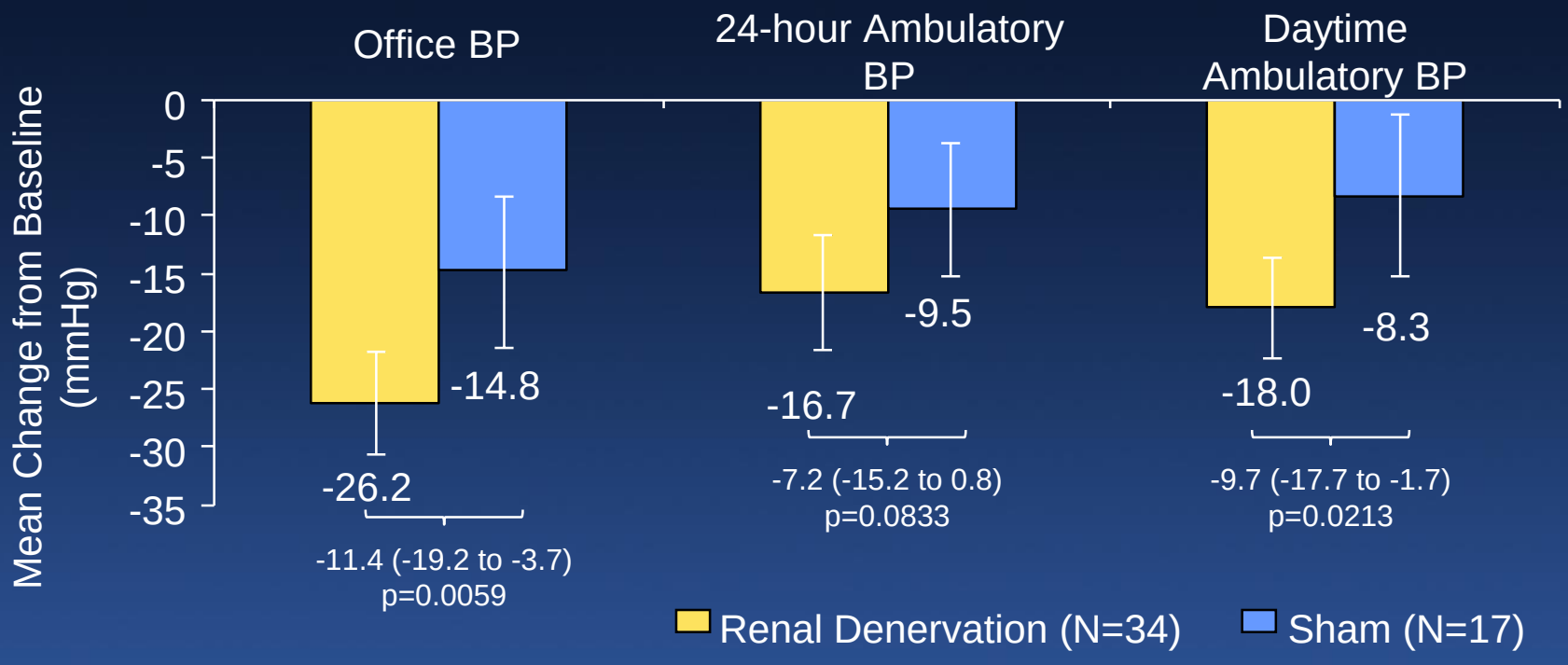
Systolic



Diastolic

Change in Blood Pressures at 6 Months

- **Systolic BP continued to decrease in the Vessix group, with a lesser decrease in the control group**



Conclusions

- No procedural or clinical safety concerns
- Primary BP endpoint at 8 weeks (in patients not taking BP meds) was no different in Vessix-treated vs. control patients
- However, at 6 months:
  - ~ 80% of patients in both groups were taking BP meds
  - *Ambulatory and office BP reduced significantly more in Vessix-treated vs. control patients*
- Late appearance of efficacy - ? due to slow onset of denervation on SNS afferent signals OR renal denervation is more effective in patients receiving BP meds

Conclusions

- ***Preliminary data from this small randomized sham-controlled trial suggest that the Vessix renal denervation catheter system may be of clinical value in treating hypertension.***