

New Generation

Barostim *neo*TM System

Preliminary Results and Discussion

Gerd Hasenfuss

Heart Center and Heart Research Center

University of Goettingen

Germany

Presenter Disclosure Information

Gerd Hasenfuss

DISCLOSURE INFORMATION:

The following relationships exist related to this presentation:

Servier

Honorarium for presentations

Consultant

CVRx

Honorarium for presentations

Impulse Dynamics

Honorarium for presentations

Autonomic Modulation Clinical Development

Approach	Disease States	Companies	Sympathetic Modulation	Parasympathetic Modulation
Baroreflex Activation	Hypertension Heart Failure	CVRx	Yes	Yes
Vagal Stimulation	Heart Failure	Biocontrol	No	Yes
Spinal Cord Stimulation	Heart Failure	MDT	No	Yes
Renal Nerve Ablation	Hypertension	MDT, BSX, St Jude, Kona, Cryomedix, Cryomend, Mercator, Northwind	Yes	No

Moving Forward: Barostim™ *neo*™ System

Single Sided 1mm Electrode

First Generation Lead (Bilateral)



Rheos

New Generation Lead
(Unilateral)



neo

Moving Forward: Barostim™ *neo*™ System

Smaller Pulse Generator with Longer Battery Life

First Generation



Rheos

New Generation



neo

Hypertension Verification Trial Design

- Single arm open label trial
 - 40 patients at 10 sites
 - Enrollment to be completed in September: 32 de-novo subjects and 8 subjects with renal nerves ablated
- Endpoints
 - Reduction in office cuff systolic blood pressure at 3 and 6 months with Barostim *neo* system
 - 30-day procedure safety of the Barostim *neo* system
- Key inclusion criteria
 - SBP \geq 140 mmHg within 14 days prior to implant
 - 2 measurements at least 24 hours apart
 - \geq 3 antihypertensive medications, including a diuretic
 - Medications optimized and stable for \geq 4 weeks prior to obtaining blood pressure measurements
 - Serum creatinine \leq 2.5 mg/dL and not being treated with dialysis

Trial Demographics

	Mean \pm SD or N (%)
Gender (N = 33)	16 Male (48.5%)
Age (yrs) (N = 33)	56.5 \pm 11.9
BMI (kg/m ²) (N = 33)	29.5 \pm 4.1
Number of meds (N = 26)	6.8 \pm 3
Systolic BP (mean mmHg \pm sd) (N = 33)	172.3 \pm 20.3
Diastolic BP (mean mmHg \pm sd) (N = 33)	100.2 \pm 14
Heart Rate (mean bpm \pm sd) (N = 33)	75.9 \pm 12.1

Trial Baseline Medications

	Baseline
Diuretic	77%
Beta Blocker	88%
Calcium Channel Blocker	69%
ACE Inhibitor	38%
ARB	65%
Alpha Blocker	35%
Sympatholytic	58%
Minoxidil	19%

n = 26

Safety Profile

- New smaller lead design
- Unilateral incision
- Shorter procedure time
- Conscious sedation sub-study

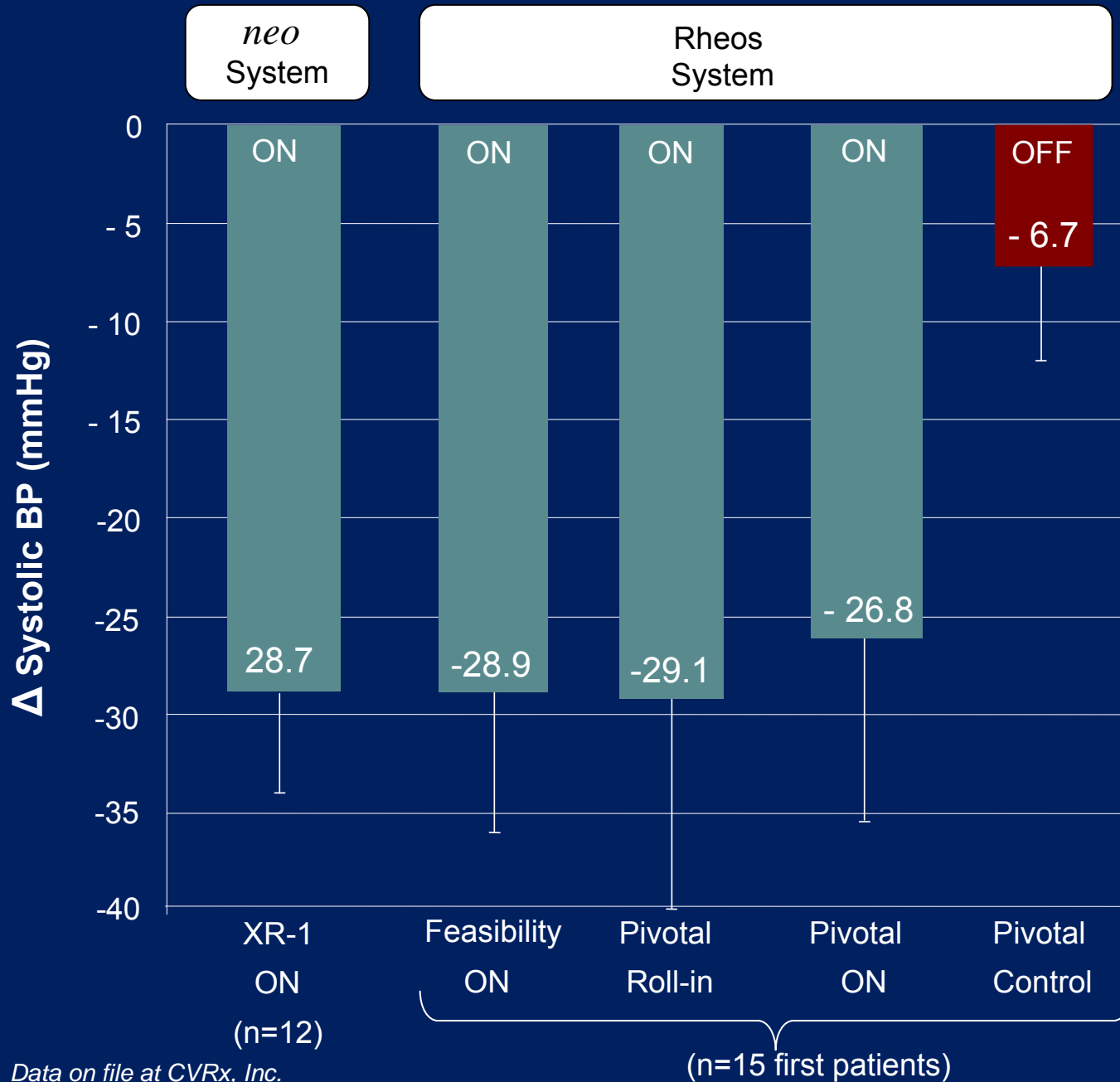


Substantially improved
procedure safety profile
as compared to first
generation

Complications

- 1 Hematoma resulting in swelling and pain in pocket area. Was resolved by draining.
- 1 wound complication (open wounds in neck and pocket). Was resolved by re-suturing.

Preliminary Efficacy Compared to Previous Trials



Barostim at:
 3 months for XR-1
 3 months for Feasibility
 6 months for Pivotal

Mean ± s.e

Data on file at CVRx, Inc.

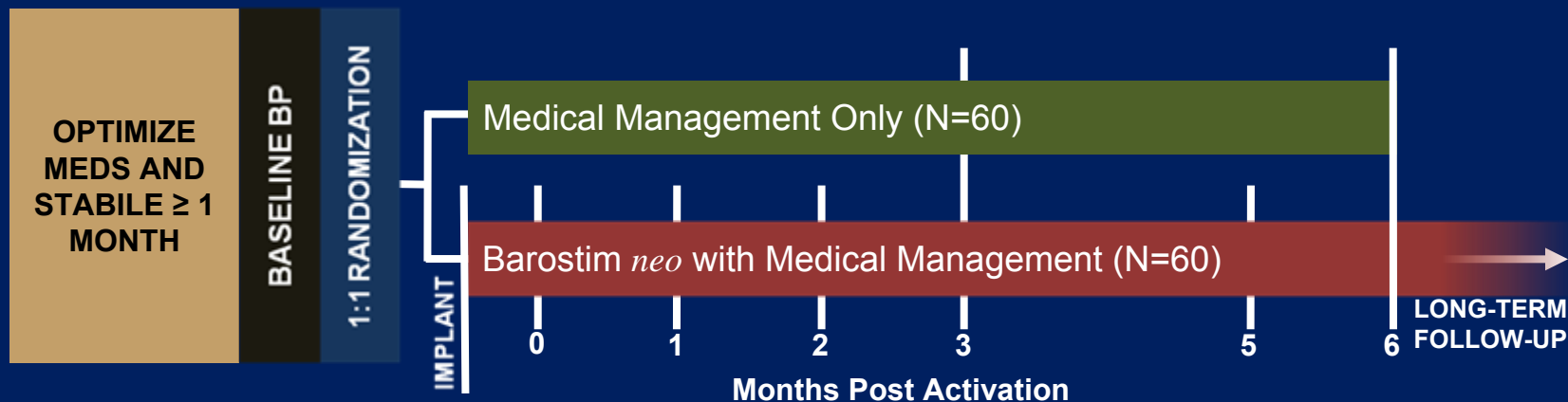
Hypertension Trial Design Randomized Phase

■ Randomized Controlled Trial

- 120 patients randomized 1:1 at 30 sites in Europe and Canada
- Status: enrollment ongoing

■ Endpoints

- Reduction in office cuff systolic blood pressure at 3 and 6 months with Barostim *neo* system
- Safety of the Barostim *neo* system through the 6-month visit



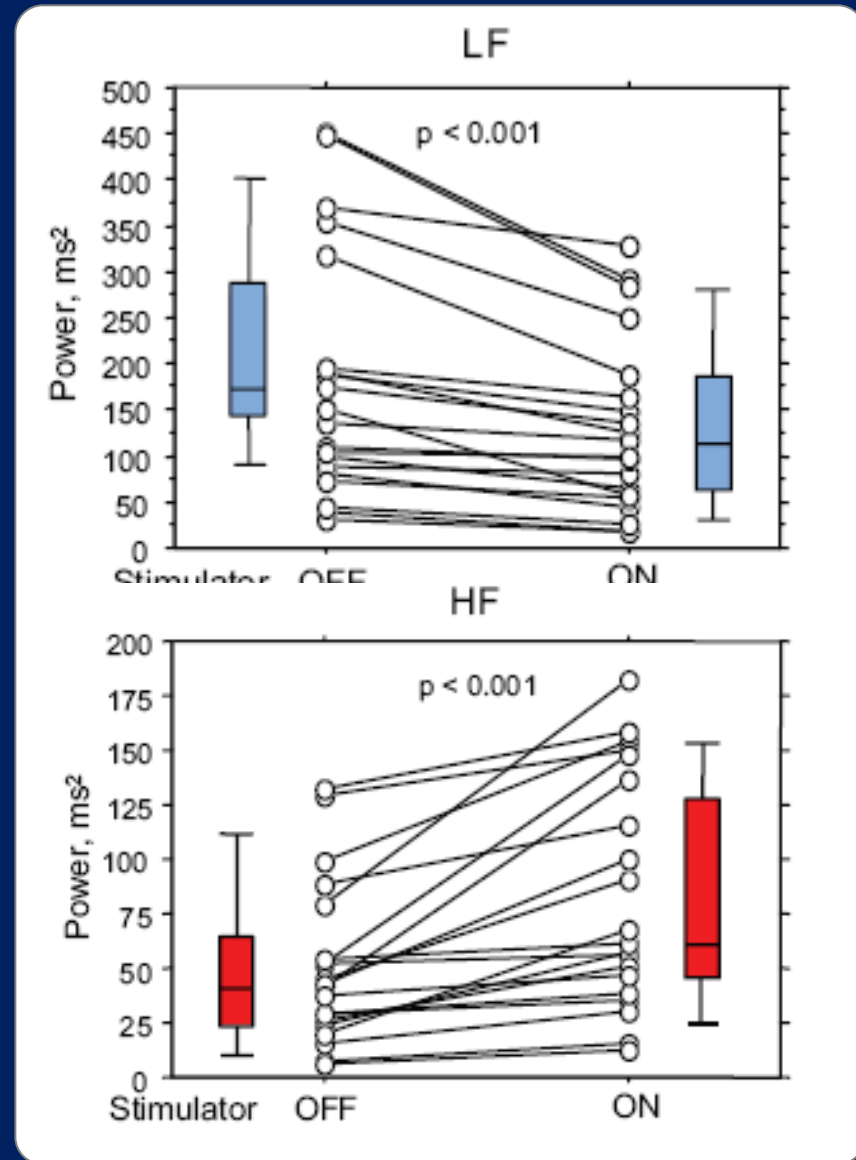
NOTE: Prior to randomizing subjects, 30 open-label subjects will be implanted and followed per the same visit schedule as the device arm

Key Inclusion Criteria

- **SBP \geq 140 mmHg within 14 days prior to implant**
- **2 measurements at least 24 hours apart**
- **\geq 3 antihypertensive medications, including a diuretic**
- **Medications optimized and stable for \geq 4 weeks prior to obtaining blood pressure measurements**
- **Serum creatinine \leq 2.5 mg/dL and not being treated with dialysis**

**Clinical Results
Motivating Further Study
Of Barostim for Heart Failure**

Heart Rate Variability and Turbulence After 3 Months of Continuous Barostim Therapy

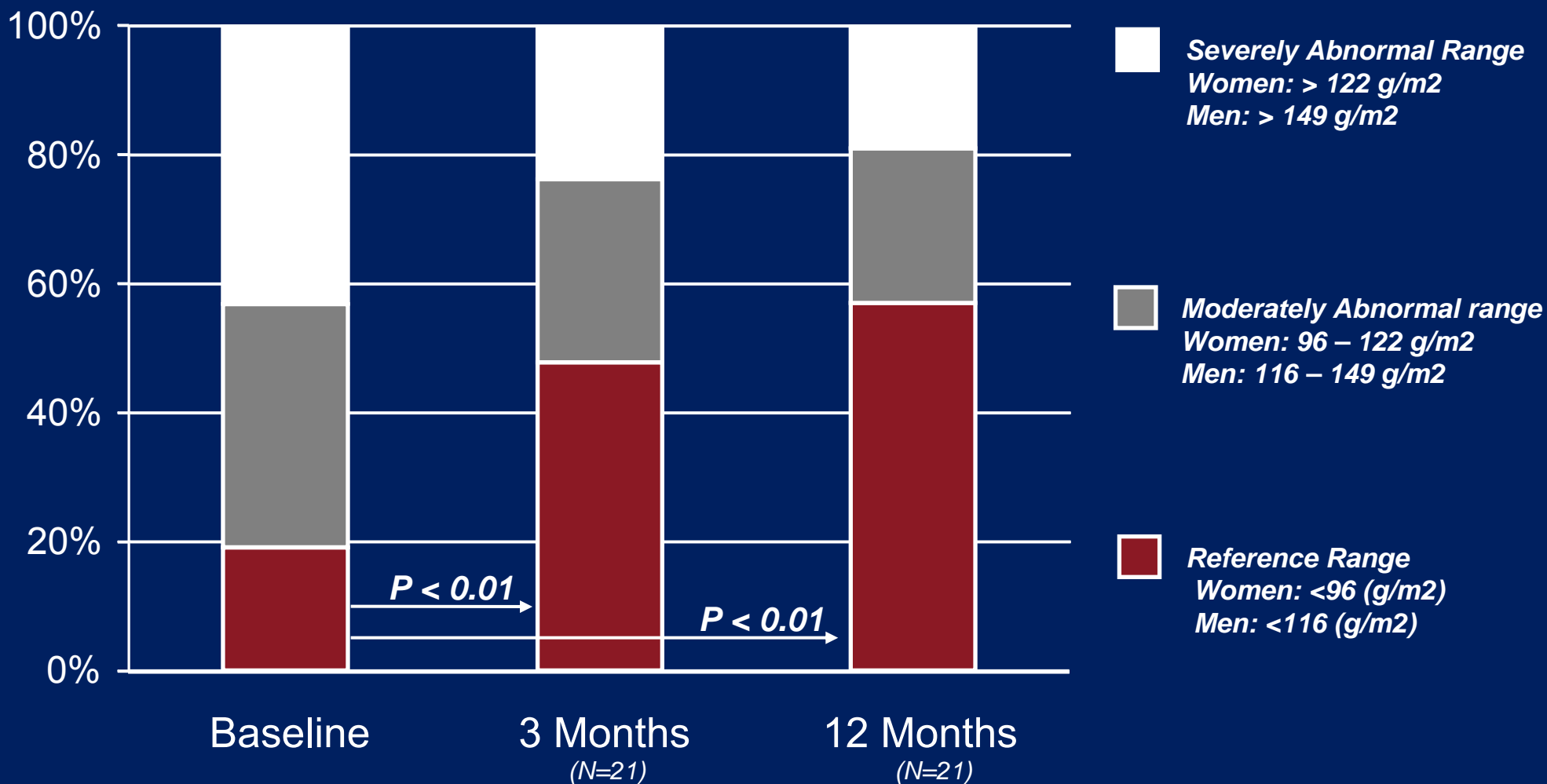


Variable	Stimulator Off	Stimulator On	P
Time-domain measures			
Heart rate, 1/min	81±11	76±10	0.001
R-R intervals, ms	743±182	818±107	0.002
SDNN, ms	89±20	95±23	0.2
SDNN index, ms	37±10	44±13	<0.001
pNN50, %	1.3 (2.2)	2.6 (4.8)	<0.001
RMSSD, ms	18.6±6.7	24.3±9.5	<0.001
Frequency-domain measures (FFT)			
HF power, ms ²	42 (59)	67 (105)	<0.001
LF power, ms ²	150 (196)	117 (135)	<0.001
Ratio LF:HF	2.78 (2.75)	2.24 (2.09)	<0.001
Turbulence Measures			
TO SVPD, % (n=17)	0.018	0.007	0.076
TS SVPD, ms per beat (n=17)	1.94	4.2	0.01
TO VPD, % (n=13)	-0.002	-0.015	0.004
TS VPD, ms per beat (n=13)	3.75	5.6	0.02

N = 21

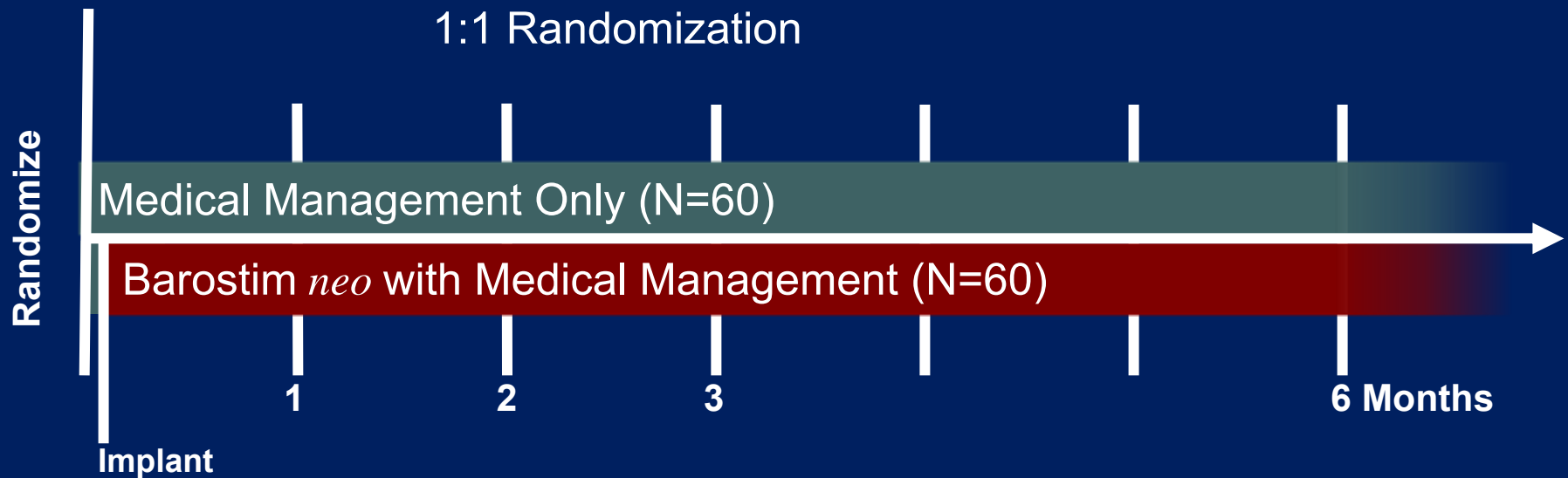
Barostim Reduces Left Ventricular Mass Index at 3 and 12 Months

12 months follow up of 21 pts. With resistant hypertension. Echo/Doppler



Decrease of LVMI by 18%
Decrease of LA diameter

Barostim *neo* Heart Failure Trial Overview



Open Label Phase

- First 10 patients treated open-label

Randomized Phase

- 120 patients randomized 1:1

Barostim *neo* Heart Failure Trial Overview

■ Primary Efficacy Objective

- To determine whether the Barostim *neo* system produces an increase in **Left Ventricular Ejection Fraction (LVEF)** from screening through 6 months of follow-up

■ Key Inclusion Criteria

- LVEF \leq 35%
- NYHA Class III
- On stable, guideline-directed heart failure therapy for at least 4 weeks
- Serum creatinine \leq 2.5 mg/dL and not being treated with dialysis

Secondary Objectives

To compare between the randomized groups 6-month changes in the following measures:

- Six-Minute Hall Walk
- NYHA Classification
- Quality of Life, using the Minnesota Living With Heart Failure Questionnaire
- NT-pro BNP
- Creatinine
- Central pressure and hemodynamic parameters
- Electrocardiographic parameters and indices of rhythm status derived from 24-hour Holter recordings
- Additional echocardiographic parameters

Summary

■ Barostim *neo* System For Hypertension

- Substantial improvement in safety profile and procedure duration
- Preliminary results suggest equivalent efficacy to first generation Rheos system
- Successfully completed conscious sedation procedures
- Preliminary results suggest Barostim effective in subjects with ablated renal nerves
- On-going XR-1 verification randomized controlled trial in Europe and Canada

■ Barostim *neo* System for Heart Failure

- Additional studies (Arrhythmias, HRV, PV Loops, Echo Cardiography, HFpEF case study) suggest cardio-protective effect of Barostim independent of blood pressure reduction
- On-going XR-1 Heart Failure randomized controlled trial in Europe and Canada