

The logo for HFSA 2023 is a stylized white graphic on the left, resembling a heart or a cross with rounded ends. To its right, the text "HFSA 2023" is written in a large, white, serif font. Below this, the words "ANNUAL SCIENTIFIC MEETING" are written in a bold, white, sans-serif font, enclosed within a white rectangular box. Underneath the box, the tagline "WHERE HEART FAILURE TEAMS GATHER" is written in a smaller, white, sans-serif font.

HFSA 2023
ANNUAL SCIENTIFIC MEETING
WHERE HEART FAILURE TEAMS GATHER

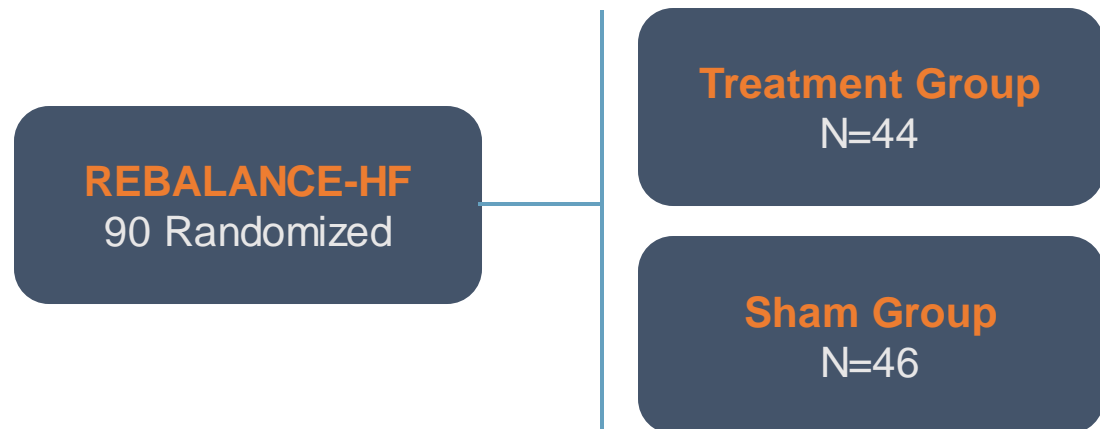
Huntington Convention Center, Cleveland, OH | October 6-9, 2023

REBALANCE-HF Study Design

Phase II, multi-center, double-blind, Sham-controlled feasibility trial

PURPOSE: Evaluate the safety and initial effectiveness of catheter-based unilateral ablation of the right greater splanchnic nerve (GSN) in subjects having heart failure with preserved ejection

POPULATION: Symptomatic HF, ongoing GDMT, age ≥ 40 , elevated PCWP at rest or exertion



PRIMARY ENDPOINT

Reduction in mean PCWP at 1-month follow-up evaluated as a repeated measure at legs-up and exercise (20W) as compared to the baseline PCWP

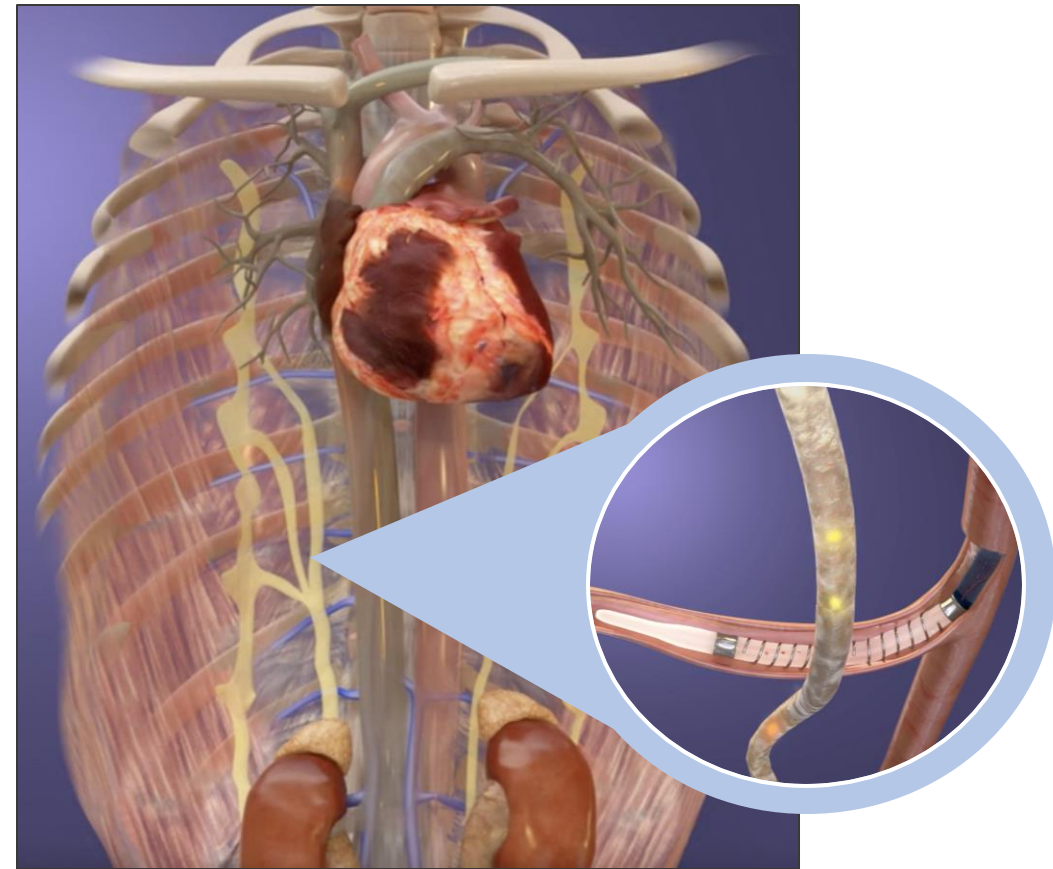
SECONDARY ENDPOINTS

- Change in KCCQ score over time from baseline
- Change in 6MWT score over time from baseline
- Incidence of HFH through 12-months
- Reduction in PCWP for each stage of exercise

Approach and Objectives

Splanchnic Ablation for Volume Management (SAVM)

- ▶ Unilateral ablation of the right greater splanchnic nerve (GSN)
- ▶ Transvenous femoral procedure
- ▶ Minimally invasive and implant free
- ▶ Unilateral procedure retains the body's sympathetic response for emergency use



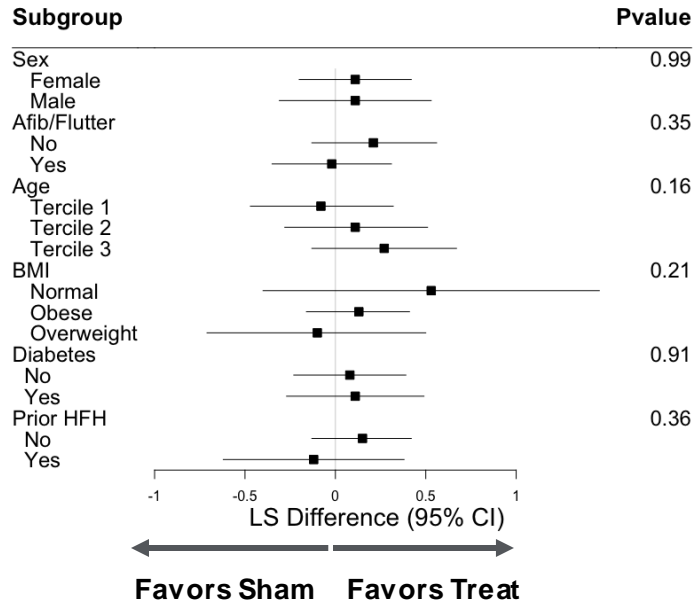
Conclusions from REBALANCE-HF Study



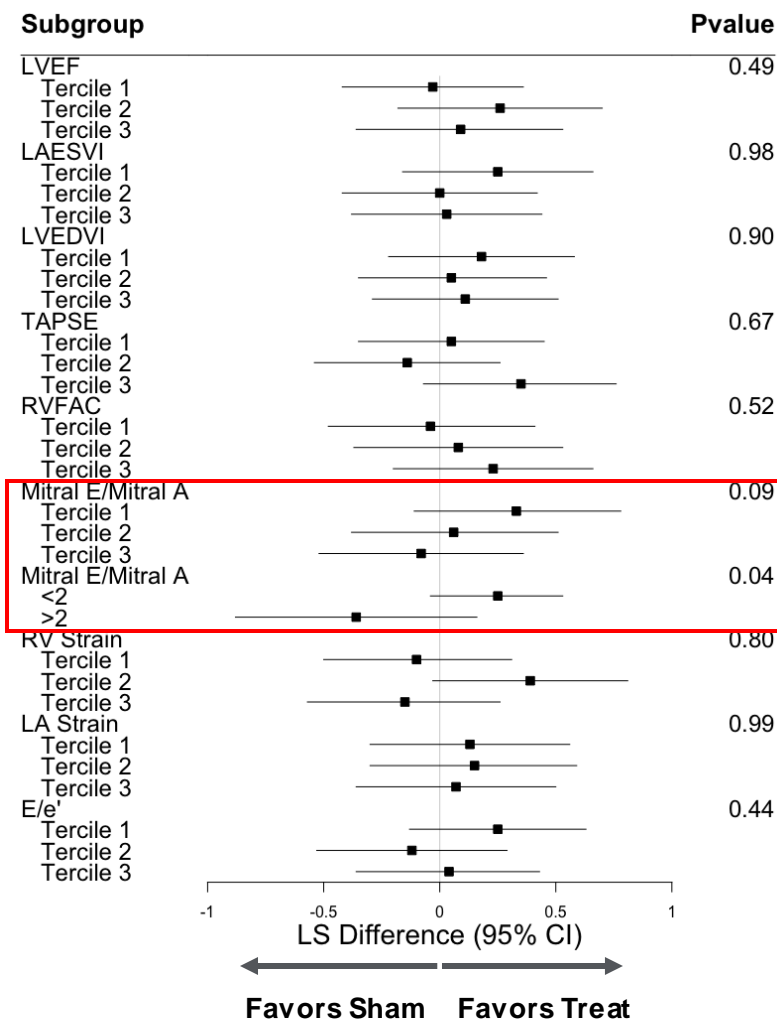
- SAVM (right-sided GSN ablation) is quick to perform and appears safe and well-tolerated
- In a broad population of patients with HFpEF, SAVM had limited impact on hemodynamics (at 1 month) or clinical outcomes (at 6 and 12 months)
- Potential responder group identified:
 - Rise in cardiac output when going from supine → standing position and during exercise
 - Not limited by chronotropic insufficiency
 - Not limited by advanced (structural/restrictive) heart disease
- Additional prospective clinical studies are needed to confirm the potential benefits of SAVM in the identified responder group

Z-score for composite endpoint: KCCQ, 6MWT, NTpro-BNP, PCWP

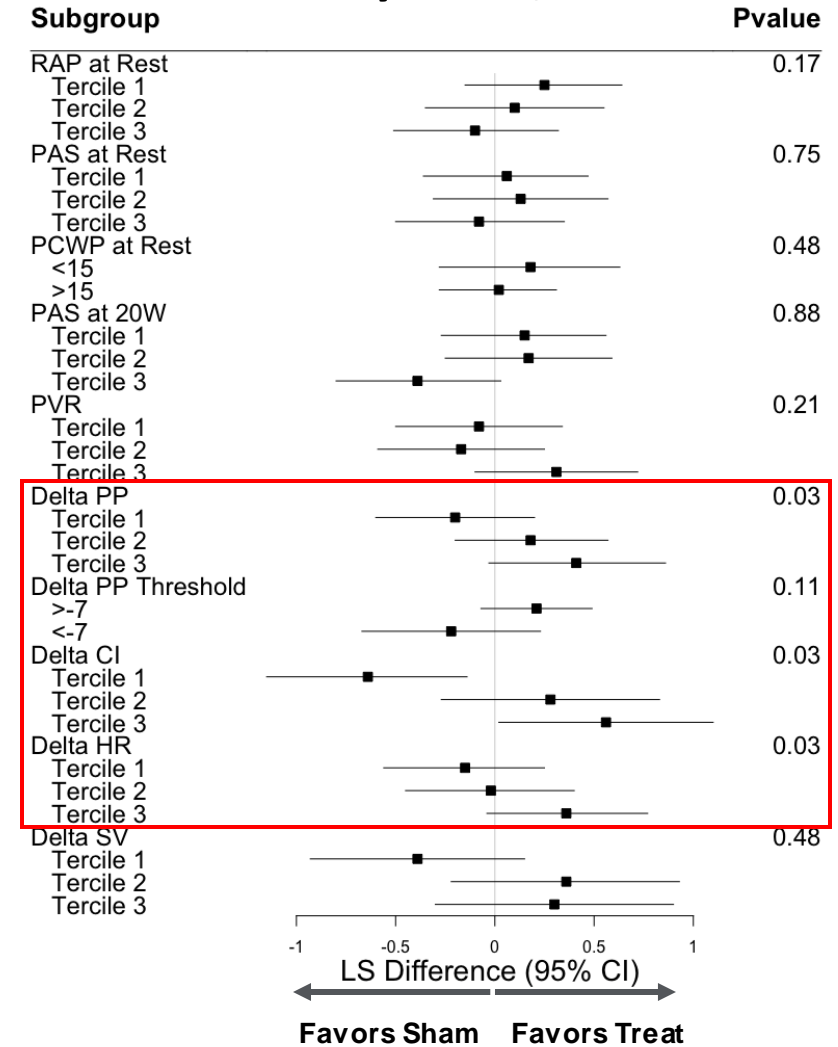
Clinical



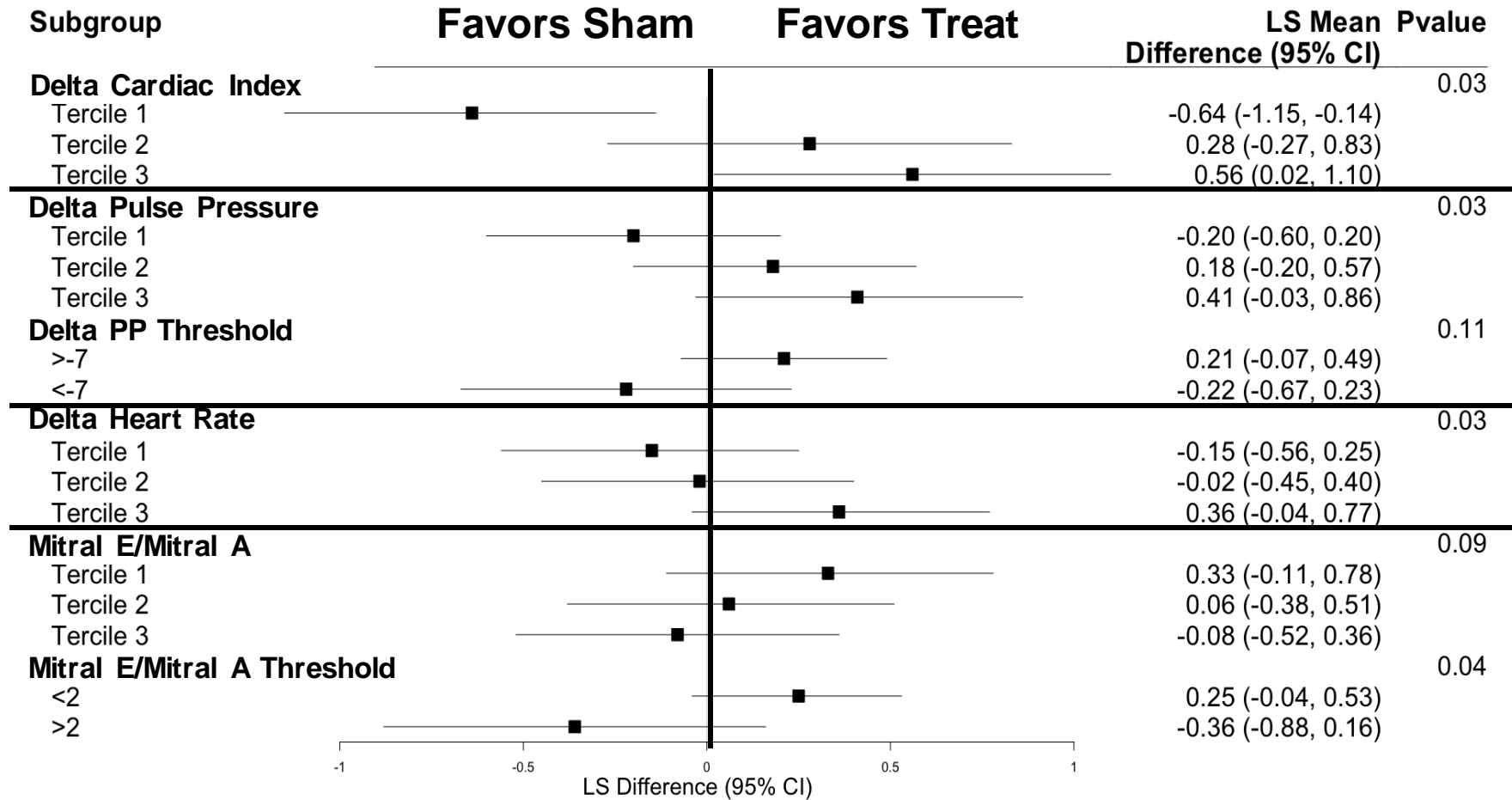
Echo



Hemodynamic/Stress



Z-score for composite endpoint: KCCQ, 6MWT, NTpro-BNP, PCWP



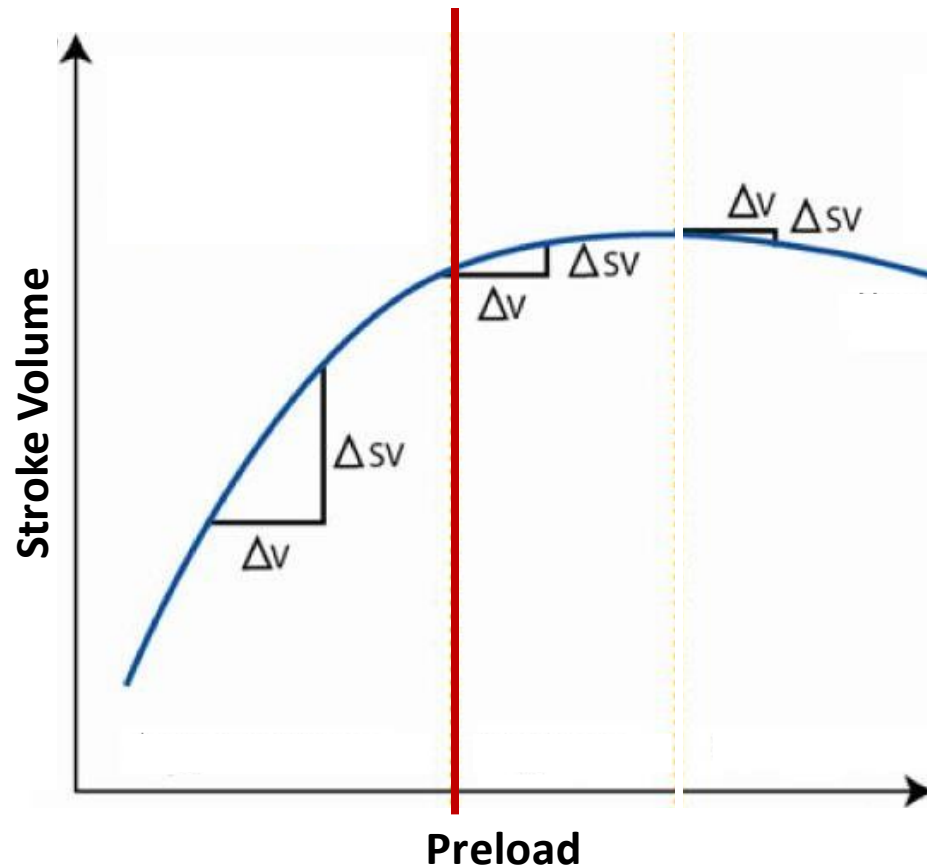
Excluded Group – E/A \geq 2.0 OR [PP \leq -7 AND HR < 15])

Responder Group Rationale

Stroke Volume (SV) is a critical component to CO Reserve

Non-Responder

Responder



Small changes in preload =
Large decreases in SV,
small change in pressure

Reducing venous return
reduces SV vs. pressure

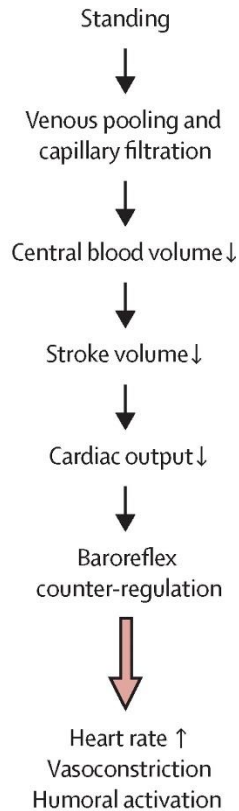
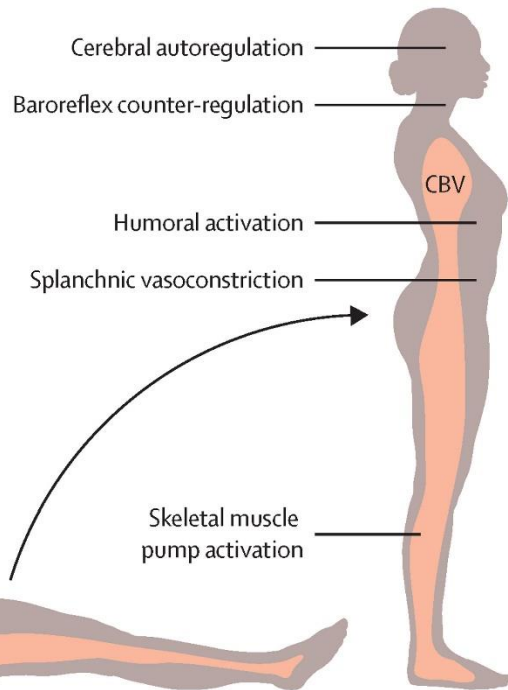
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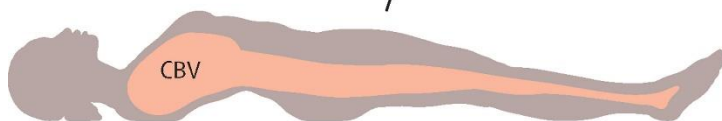
Orthostatic Pulse Pressure and Heart Rate



Upright position:
Blood volume
redistributed



Supine position:
Central blood
volume high



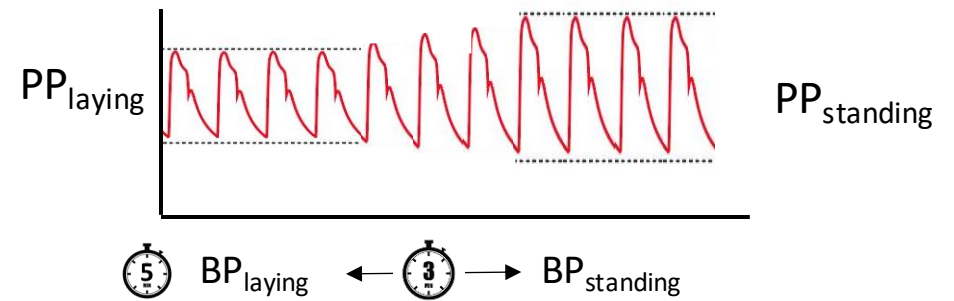
Pulse Pressure (PP):

Systolic Blood Pressure – Diastolic Blood Pressure

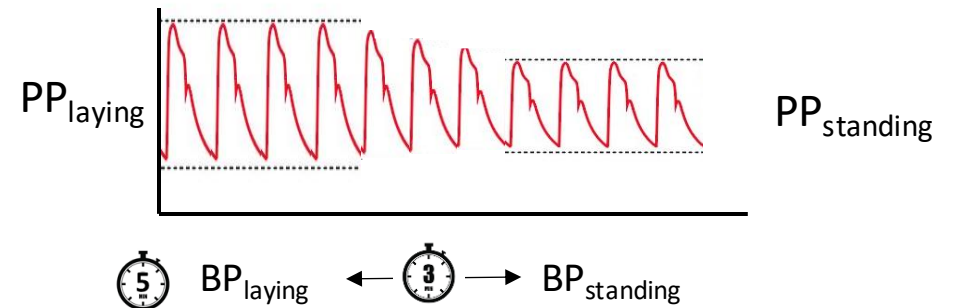
Orthostatic Pulse Pressure:

PP (post 3m standing) – PP (post 5m laying)

Increase PP (widening) ↑ Stroke Volume



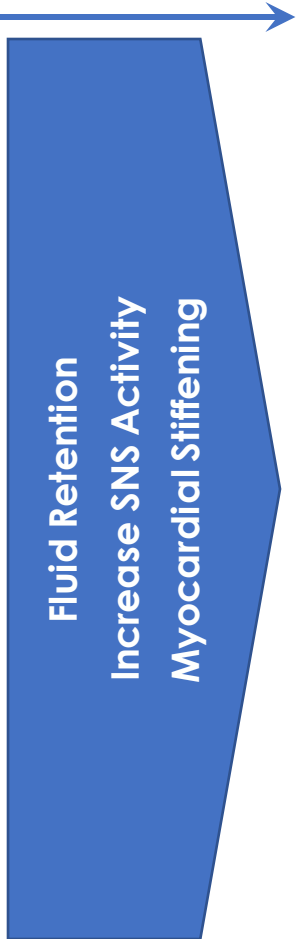
Decrease PP (narrowing) ↓ Stroke Volume



Diastolic Dysfunction – Mitral E/A

Precipitating Condition

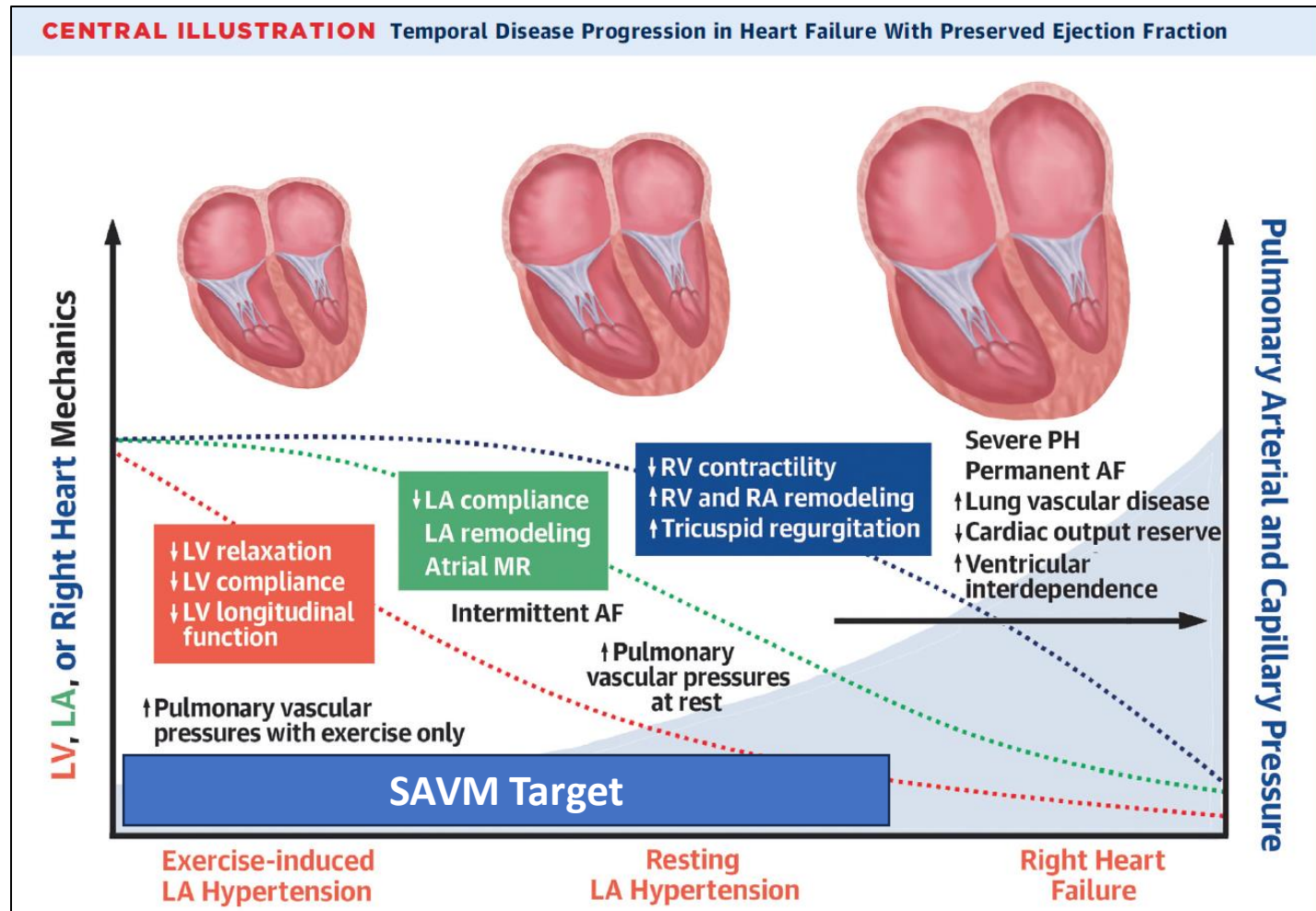
- Obesity
- Hypertension
- CKD
- Afib
- CAD



The problem is "pressure"

Remodeling

The problem is "structure"



Baseline Medical History: Responder vs Non-Responder

Variable	Responder N=48	Non-Responder N=41	P-Value
Age	69 (64, 78)	72 (63, 78)	>0.9
Female	71%	59% (24)	0.3
Race – White	88%	90%	0.4
BMI, kg/m ²	33.2 (29.9, 38.4)	34.6 (29.5, 37.8)	>0.9
Prior HFH	25%	22%	0.8
Comorbidities			
Sleep Apnea	65%	56%	0.5
Atrial Fibrillation	29%	76%	<0.001
Hypertension	90%	88%	>0.9
Diabetes	48%	32%	0.14
CKD	27%	24%	0.8
Therapies			
Coronary Revasc	40%	27%	0.3
Ablation for Afib	6.3%	54%	<0.001
Beta Blocker	58%	71%	0.3
MRA	63%	66%	0.8
Diuretic	88%	85%	>0.9
SGLT2i	44%	41%	>0.9

Baseline Hemodynamics and Function: Responder vs Non-Responder

Variable	Responder N=48	Non-Responder N=41	P-Value
Labs			
eGFR	60 (42, 75)	61 (55, 84)	0.094
Hemodynamics			
HR, bpm	74 (65, 80)	70 (65, 77)	0.3
BP systolic, mmHg	125 (118, 132)	125 (113, 137)	>0.9
RAP(resting), mmHg	8.0 (5.0, 11.0)	11.0 (8.0, 13.0)	0.014
PAD (resting), mmHg	17 (14, 20)	22 (17, 26)	<0.001
PAS (resting), mmHg	35 (30, 40)	45 (38, 52)	<0.001
PCWP (resting), mmHg	15 (11, 19)	21 (17, 26)	<0.001
PCWP (peak), mmHg	35 (31, 41)	39 (34, 47)	0.041
CO, L/min	5.40 (4.73, 7.00)	5.12 (4.50, 6.20)	0.4
CI, L/min/m ²	2.71 (2.34, 3.36)	2.49 (2.31, 3.00)	0.3
PVR (resting)	1.57 (1.08, 2.04)	1.55 (1.25, 2.68)	0.6
Prognosis			
NYHA III/IV	85%	98%	0.065
KCCQ-OSS	37 (27, 51)	46 (33, 53)	0.072
6MWD, m	273 (189, 342)	310 (248, 380)	0.089
NT-proBNP, pg/ml	254 (98, 427)	276 (177, 565)	0.2

Baseline Echo: Responder vs Non-Responder

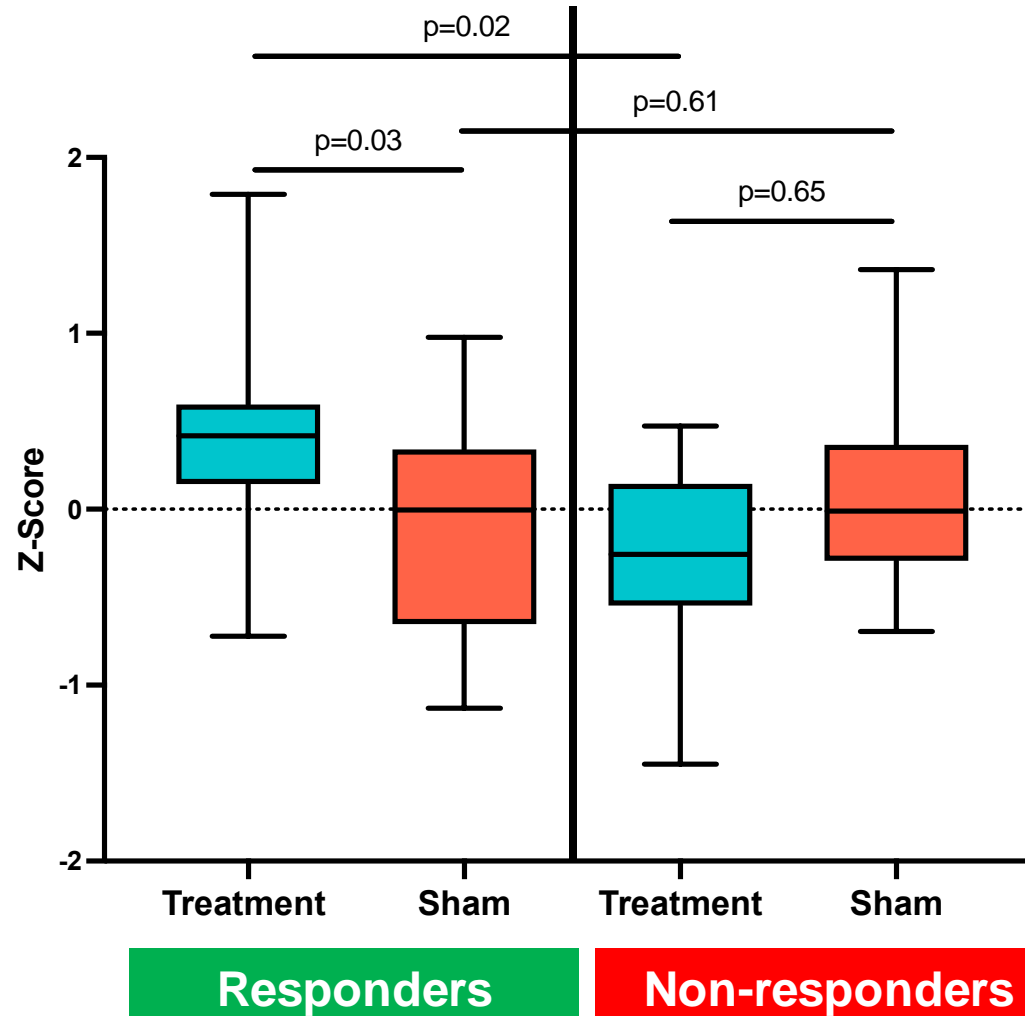


Variable	Responder N=48	Non-Responder N=41	P-Value
E/e' (septal)	11.7 (9.8, 13.2)	14.4 (11.3, 19.4)	0.008
LA end-diastolic volume index	14 (11, 19)	22 (16, 29)	<0.001
LA end-systolic volume index	26 (23, 34)	35 (27, 39)	0.006
Mitral E/Mitral A	0.87 (0.70, 0.99)	2.03 (0.93, 2.34)	<0.001
LA reservoir strain Biplane	26 (19, 30)	14 (9, 21)	<0.001
LVEF	60.0 (57.0, 62.0)	60.0 (57.0, 63.0)	>0.9
RVFAC	38.6 (35.3, 41.7)	36.3 (33.1, 39.7)	0.083
TAPSE, mm	1.89 (1.69, 2.23)	1.82 (1.62, 1.93)	0.2

Composite Efficacy Endpoint: Responders vs. Non-responders



Mean Z score, treatment (GSN ablation) vs. sham procedure in responders vs. non-responders



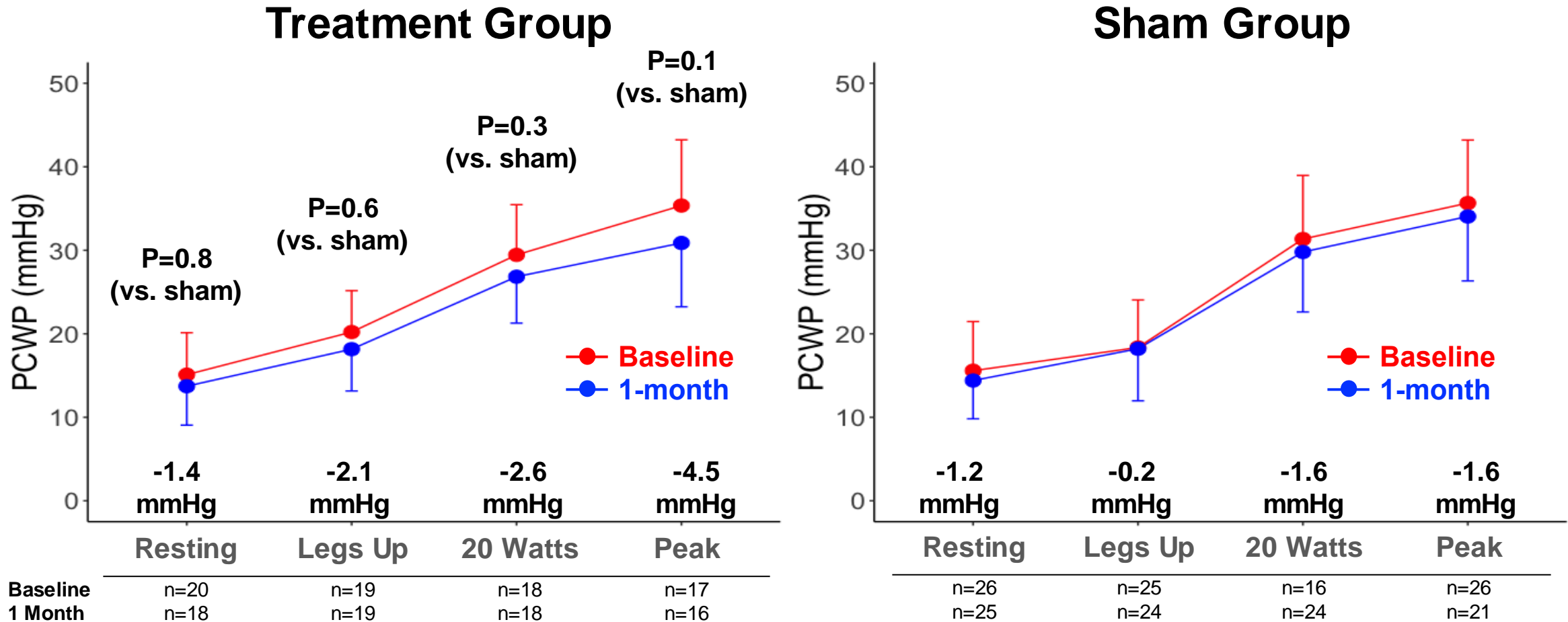
Responder and non-responder subgroups defined by:

- Mitral E/A
- Orthostatic PP
- Orthostatic HR

Significant difference between the treatment effect in responders vs. non-responders

No significant difference in sham group in responders vs. non-responders

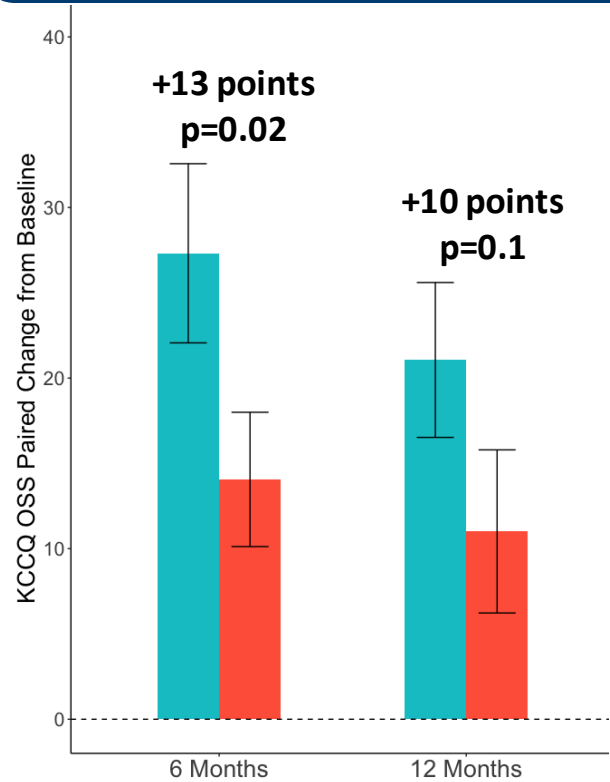
Primary Efficacy Endpoint: Responder Group



Δ -18 mmHg/W/kg (p=0.02) in Work Index PCWP
 Δ +95 seconds (p=0.02) exercise duration

Responder Patient Population Individual Outcomes

KCCQ Overall Summary Score



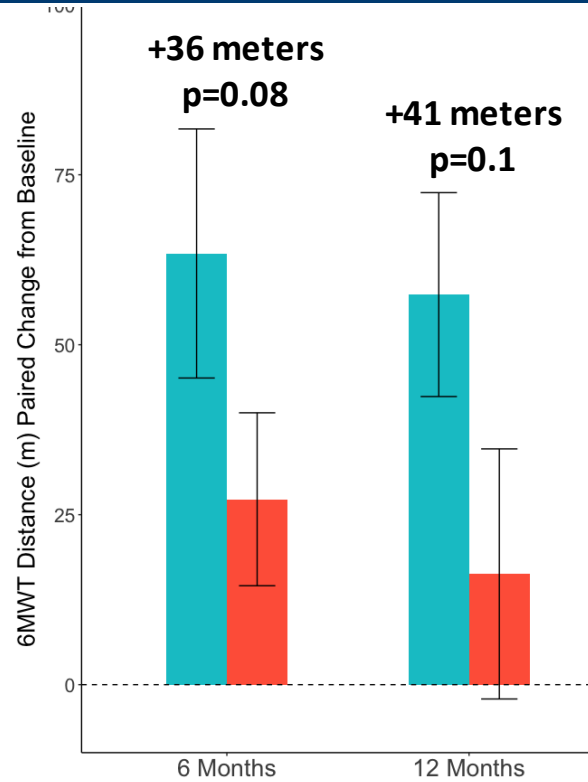
■ Treatment ■ Sham

6 Months 12 Months

Treatment
Sham

n=20	n=16
n=26	n=21

6 Minute Walk Test

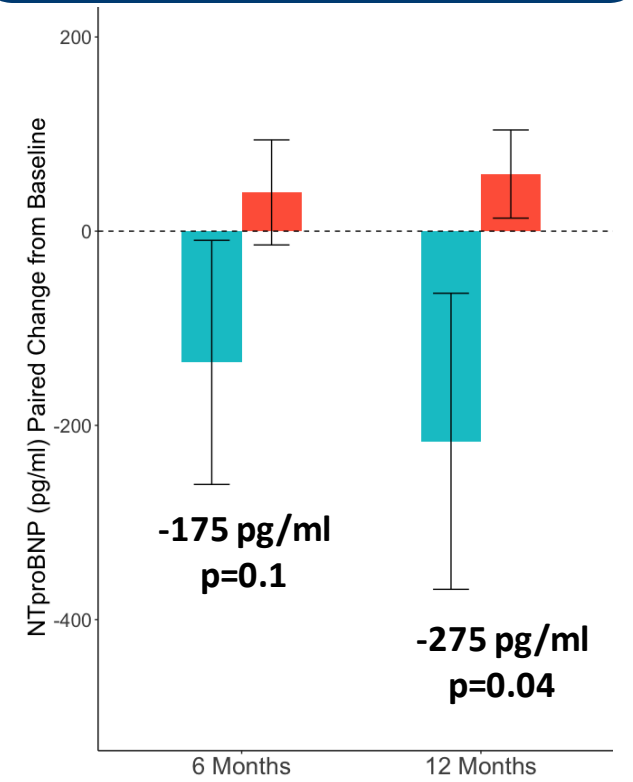


■ Treatment ■ Sham

6 Months 12 Months

n=19	n=16
n=26	n=21

NTproBNP



■ Treatment ■ Sham

6 Months 12 Months

n=20	n=16
n=26	n=19

Conclusions



- Identified responder group makes up ~55% of the population
- Responders can be easily identified using standard echo and orthostasis measurements
- Responders saw clinical and statistical improvements in KCCQ-OSS, NTproBNP, and 6MWT at 6-months and trending towards significance at 12-months
- Additional prospective clinical studies are needed to confirm the potential benefits of SAVM in the identified responder group