Pulmonary Artery Pressure-Guided Therapy for Ambulatory Heart Failure Patients in Clinical Practice: *1-Year Outcomes from the CardioMEMS Post-Approval Study*

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for the CardioMEMS PAS Investigators

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Registration: www.clinicaltrials.gov, NCT 02279888

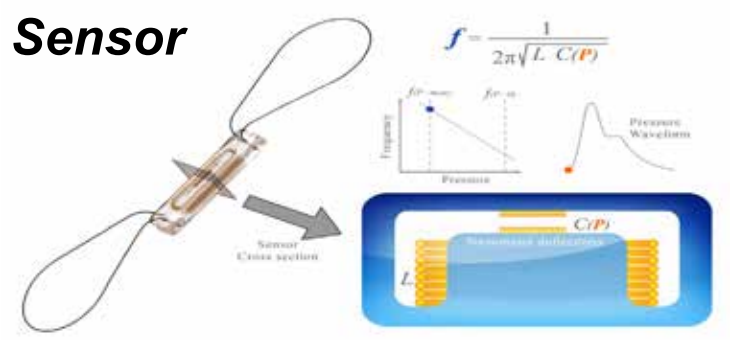
Background

- The burden of HF hospitalization (HFH) remains high despite increasingly effective medical therapy
- Most HFH occur because of ‘congestion’ or elevated cardiac filling pressures
- Increases in pulmonary artery (PA) pressures occur weeks in advance of the signs and symptoms that prompt HFH
- Therapy guided by PA pressures in the randomized CHAMPION study[1] resulted in a 37% reduction in HFH rates and all cause hospitalization (ACH)

[1]Abraham WT, et al. *Lancet* 2011:377:658-666.

CardioMEMS-HF system: Ambulatory Hemodynamic Monitoring with an Implantable PAP Sensor

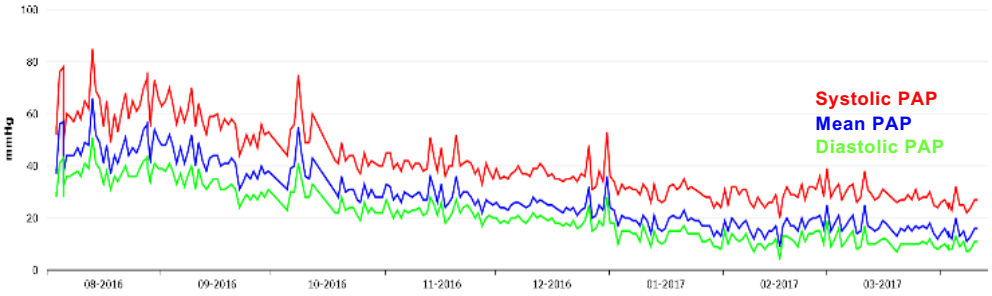
Sensor



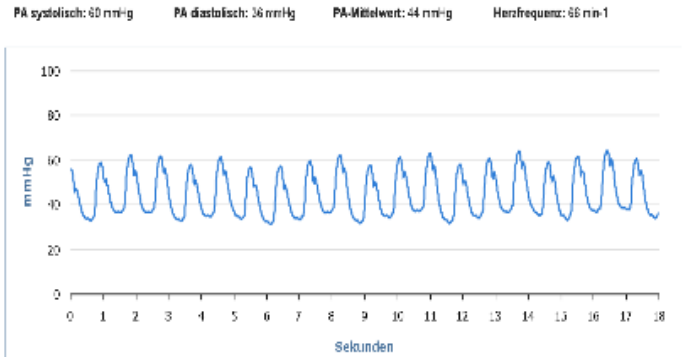
Home electronics unit

Database

PA pressure trend data

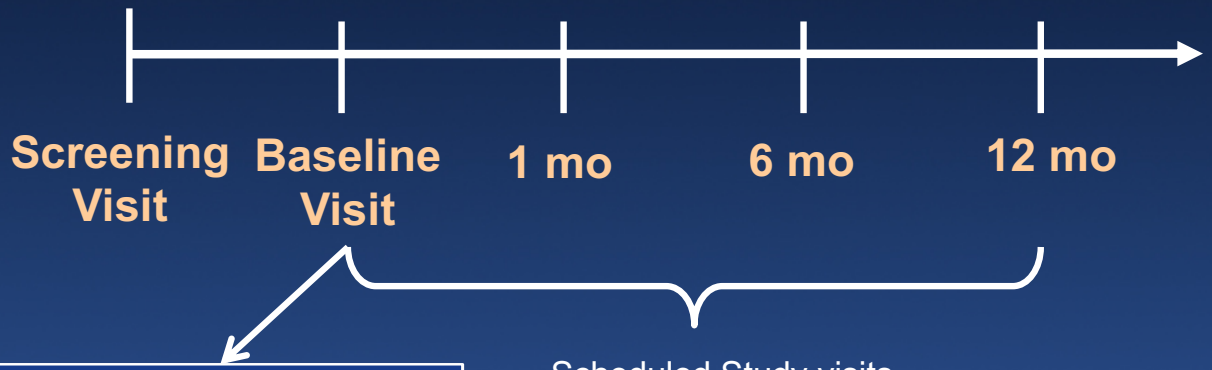


Daily PA measurement



CardioMEMS Post Approval Study (PAS): Study Design

A prospective, multi-center, open-label trial in ~1200 patients with NYHA Class III Heart Failure and a HFH within the prior 12 months



Right Heart Catheterization
Baseline Hemodynamics
PA Sensor Implantation

Scheduled Study visits

Patients instructed to transmit PA pressures daily

All hospitalizations submitted to CEC* for adjudication

Primary Efficacy Endpoint:
Reduction in rate of HFH at 1-year post-implant compared with the year prior to enrollment

Primary Safety Endpoints:
Freedom from DSRC** > 80% at 2 years
Freedom from Sensor Failure > 90% at 2 years

Supplemental Analysis:
HFH or death at 1 year
Death at 1 year
Patient compliance with pressure transmission
Outcomes in pre-specified subgroups

*CEC = Clinical Events Committee; **DSRC = Device and System Related Complications; HFH = Heart Failure Hospitalization

CardioMEMS Post Approval Study (PAS)

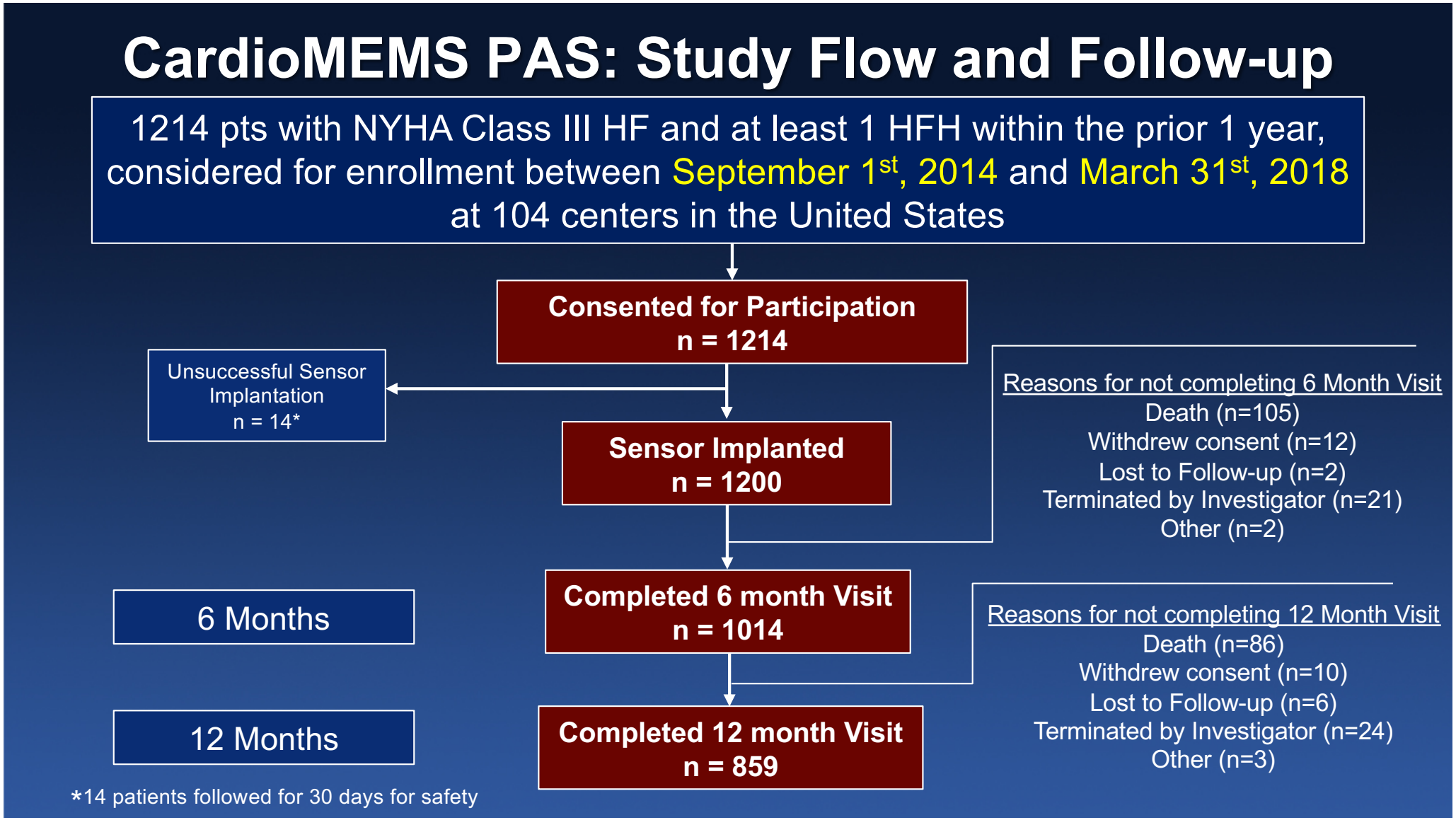
Inclusion Criteria

1. NYHA class III heart failure
2. At least 1 HFH within the previous 12 months
3. Patients with HFrEF should be receiving a beta blocker for 3 months and an ACE-I or ARB for 1 month unless in the investigator's opinion, the patient is intolerant to beta blocker, ACE-I or ARB
4. Patients with BMI > 35 required chest circumference (at mid axillary level) to be < 65 inches
5. PA branch diameter ≥ 7mm

Exclusion Criteria

1. Active infection
2. History of recurrent (> 1) pulmonary embolism or deep vein thrombosis
3. Inability to tolerate right heart catheterization
4. Major cardiovascular event (e.g., myocardial infarction, open heart surgery, cerebral vascular accident) within previous 2 months
5. CRT implanted within previous 3 months
6. GFR < 25 ml/min who are non-responsive to diuretic therapy or who are on chronic renal dialysis
7. Congenital heart disease or mechanical right heart valve
8. Likely to undergo heart transplantation or VAD within the next 6 months
9. Known coagulation disorders
10. Hypersensitivity or allergy to aspirin, and/or clopidogrel

CardioMEMS PAS: Study Flow and Follow-up



Baseline Characteristics

Characteristic	All Patients* (n=1200)
Age (years)	69 ± 12
Female sex	452 (38%)
Race/ethnicity	
White	993 (83%)
Black	172 (14%)
Asian	12 (1.0%)
Other	18 (1.5%)
Ischemic CM	496 (41%)
CRT/CRT-D or ICD	600 (50%)
GFR (mL/min/1.73 m^2)	53 ± 21
CKD stage 3 and stage 4	808 (68%)

*Two subjects did not submit EF at baseline.

Baseline Characteristics

Characteristic	All Patients* (n=1200)	EF < 40% (n=637;53%)
Age (years)	69 ± 12	67 ± 13
Female sex	452 (38%)	183 (29%)
Race/ethnicity		
White	993 (83%)	499 (78%)
Black	172 (14%)	114 (18%)
Asian	12 (1.0%)	8 (1.3%)
Other	18 (1.5%)	14 (2.2%)
Ischemic CM	496 (41%)	352 (55%)
CRT/CRT-D or ICD	600 (50%)	488 (77%)
GFR (mL/min/1.73 m^2)	53 ± 21	55 ± 22
CKD stage 3 and stage 4	808 (68%)	312 (49%)

*Two subjects did not submit EF at baseline.

Baseline Characteristics

Characteristic	All Patients* (n=1200)	EF < 40% (n=637;53%)	EF 41-50% (n=198;17%)
Age (years)	69 ± 12	67 ± 13	70 ± 11
Female sex	452 (38%)	183 (29%)	75 (38%)
Race/ethnicity			
White	993 (83%)	499 (78%)	171 (86%)
Black	172 (14%)	114 (18%)	26 (13%)
Asian	12 (1.0%)	8 (1.3%)	0 (0%)
Other	18 (1.5%)	14 (2.2%)	0 (0%)
Ischemic CM	496 (41%)	352 (55%)	78 (40%)
CRT/CRT-D or ICD	600 (50%)	488 (77%)	73 (37%)
GFR (mL/min/1.73 m^2)	53 ± 21	55 ± 22	53 ± 21
CKD stage 3 and stage 4	808 (68%)	312 (49%)	133 (68%)

*Two subjects did not submit EF at baseline.

Baseline Characteristics

Characteristic	All Patients* (n=1200)	EF < 40% (n=637;53%)	EF 41-50% (n=198;17%)	EF > 50% (n=363;30%)
Age (years)	69 ± 12	67 ± 13	70 ± 11	72 ± 10
Female sex	452 (38%)	183 (29%)	75 (38%)	194 (53%)
Race/ethnicity				
White	993 (83%)	499 (78%)	171 (86%)	321 (88%)
Black	172 (14%)	114 (18%)	26 (13%)	32 (9%)
Asian	12 (1.0%)	8 (1.3%)	0 (0%)	4 (1.1%)
Other	18 (1.5%)	14 (2.2%)	0 (0%)	2 (0.6%)
Ischemic CM	496 (41%)	352 (55%)	78 (40%)	64 (18%)
CRT/CRT-D or ICD	600 (50%)	488 (77%)	73 (37%)	38 (11%)
GFR (mL/min/1.73 m^2)	53 ± 21	55 ± 22	53 ± 21	50 ± 19
CKD stage 3 and stage 4	808 (68%)	312 (49%)	133 (68%)	261 (72%)

*Two subjects did not submit EF at baseline.

Baseline Medical Therapy

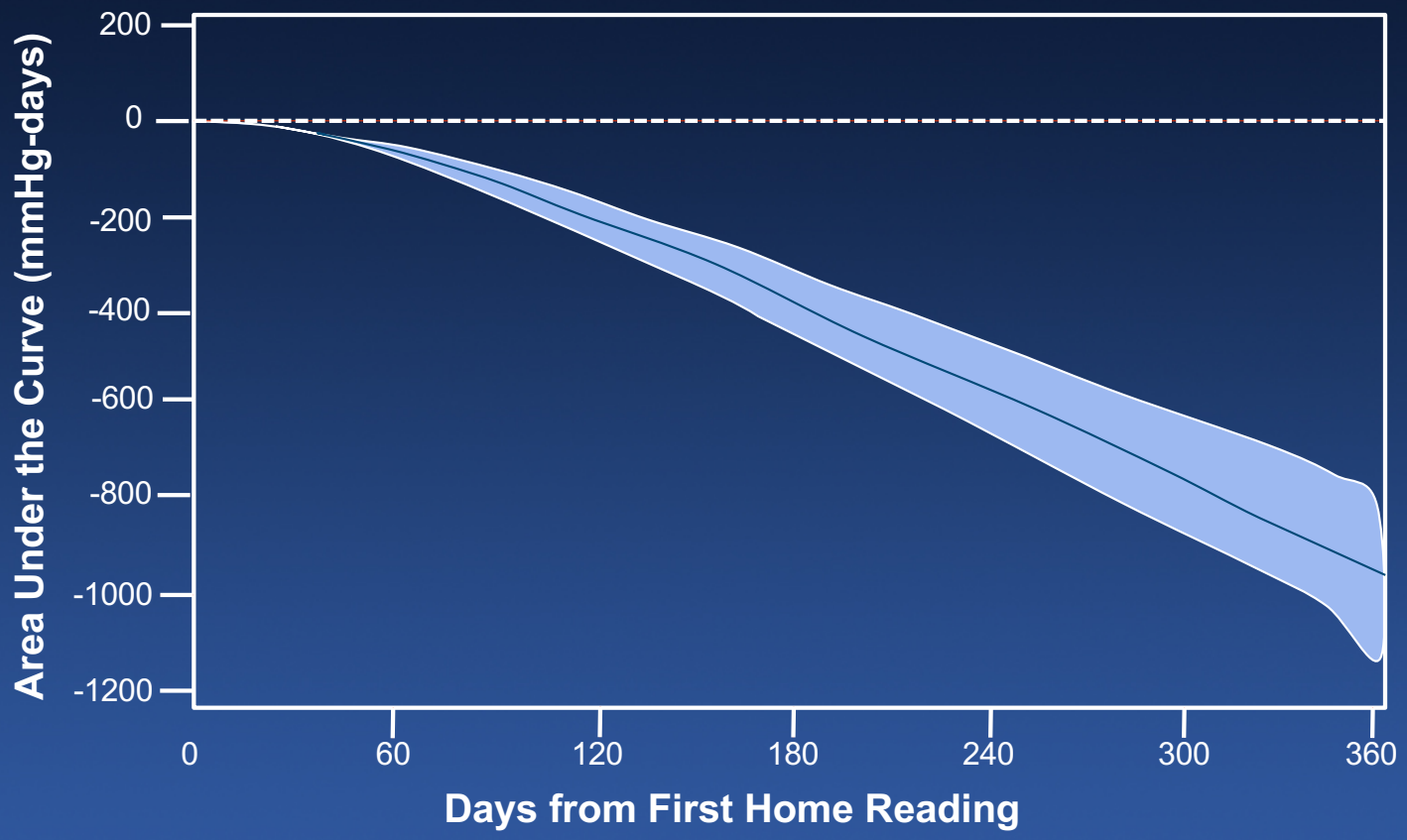
Characteristic	All Patients (n=1200)	EF < 40% (n=637)	EF 41-50% (n=198)	EF > 50% (n=363)
Medical Therapy				
Beta blocker	1046 (87%)	597 (94%)	172 (87%)	275 (76%)
ACE/ARB/ARNi	696 (58%)	444 (70%)	117 (59%)	134 (37%)
Beta blocker + ACE/ARB/ARNi	626 (52%)	416 (65%)	103 (52%)	106 (29%)
Aldosterone agonist	673 (56%)	426 (67%)	113 (57%)	133 (37%)
Loop diuretic	1136 (95%)	597 (94%)	187 (94%)	350 (96%)

Hemodynamics at PA Sensor Implant

Characteristic	All Patients (n=1200)	EF < 40% (n=637)	EF 41-50% (n=198)	EF > 50% (n=363)
Hemodynamics – Baseline				
Systolic blood pressure (mm Hg)	127 ± 22	121 ± 20	130 ± 24	134 ± 22
Pulmonary capillary wedge pressure (mm Hg)	20 ± 8	21 ± 9	18 ± 6.8	19 ± 7
PA systolic pressure (mm Hg)	48 ± 15	48 ± 15	45 ± 14	49 ± 15
PA diastolic pressure (mm Hg)	20 ± 8	20 ± 8	19 ± 7	20 ± 7
PA mean pressure (mm Hg)	31 ± 10	32 ± 10	29 ± 9	32 ± 9
Cardiac index (Lit/min/m^2)	2.2 ± 0.7	2.1 ± 0.6	2.3 ± 0.7	2.4 ± 0.8

Change in PA Pressure Over Time

Area Under the Curve (AUC) Method

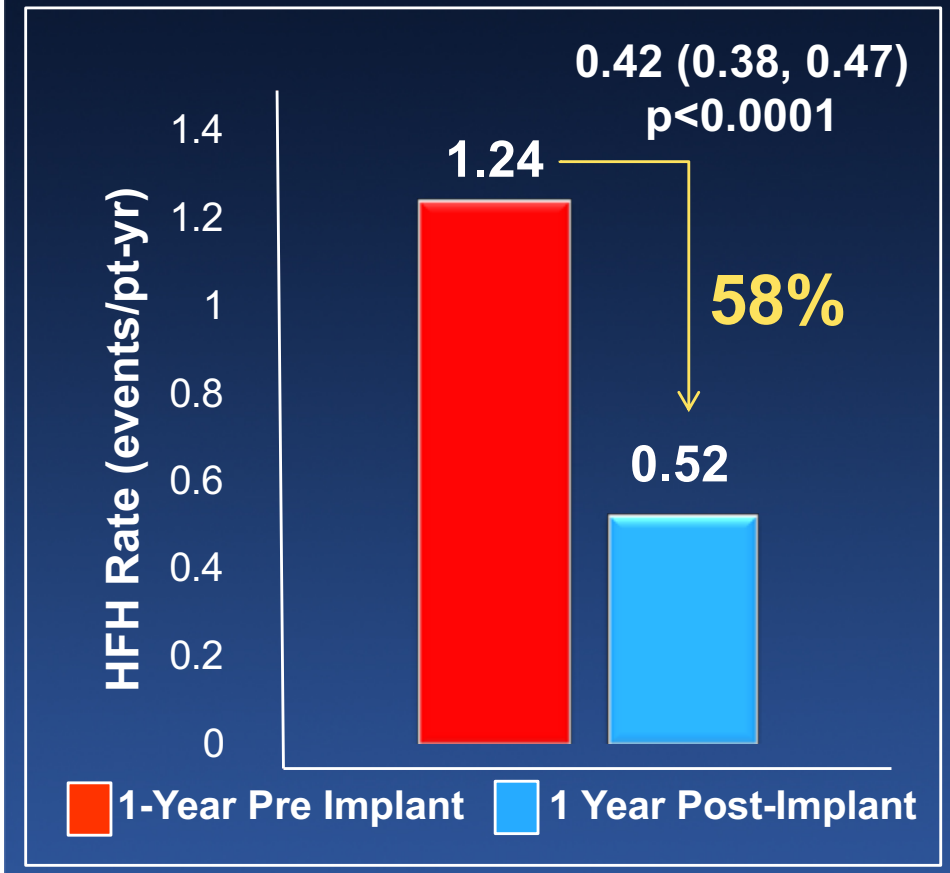


AUC method measures the frequency and duration of time that a patient spends at a pressure, lower or higher, than their baseline mean PA pressure in mmHg-days.

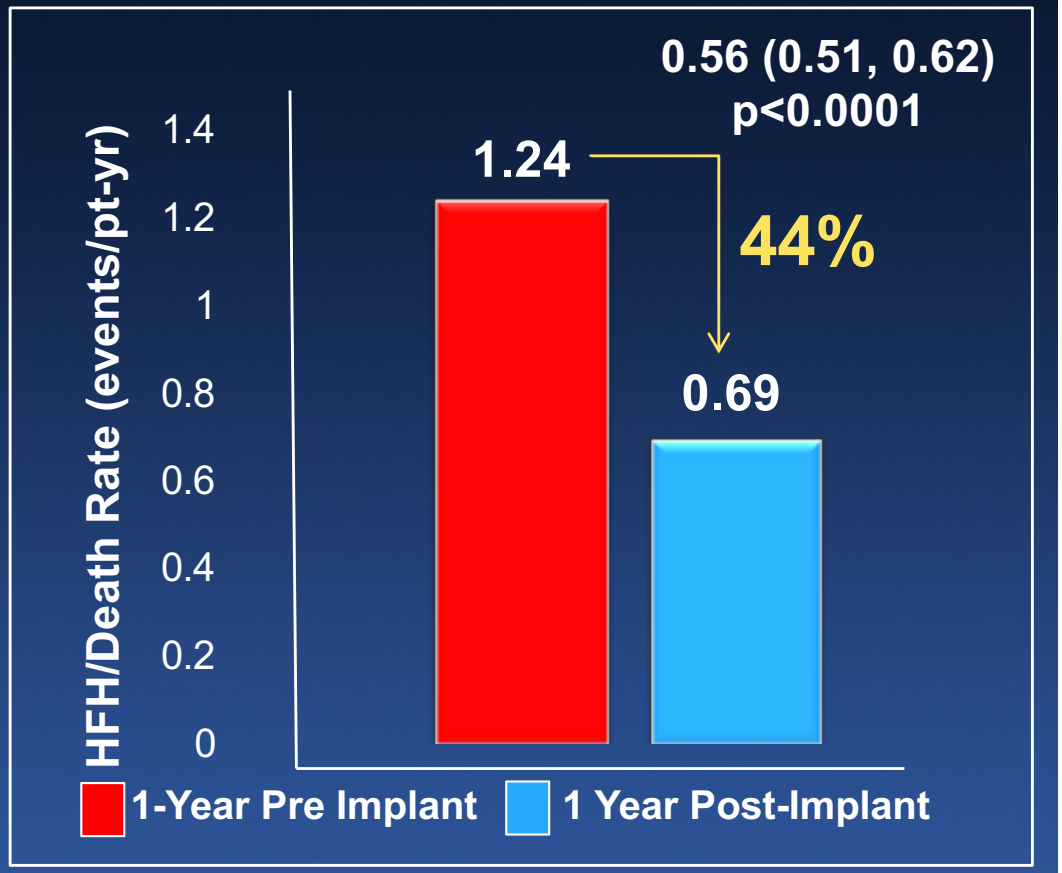
Pressure Transmission Compliance

	Mean±SD	Median
Daily	76±24%	85%
Weekly	92±16%	100%

Hospitalizations for HF Pre and Post-Implant

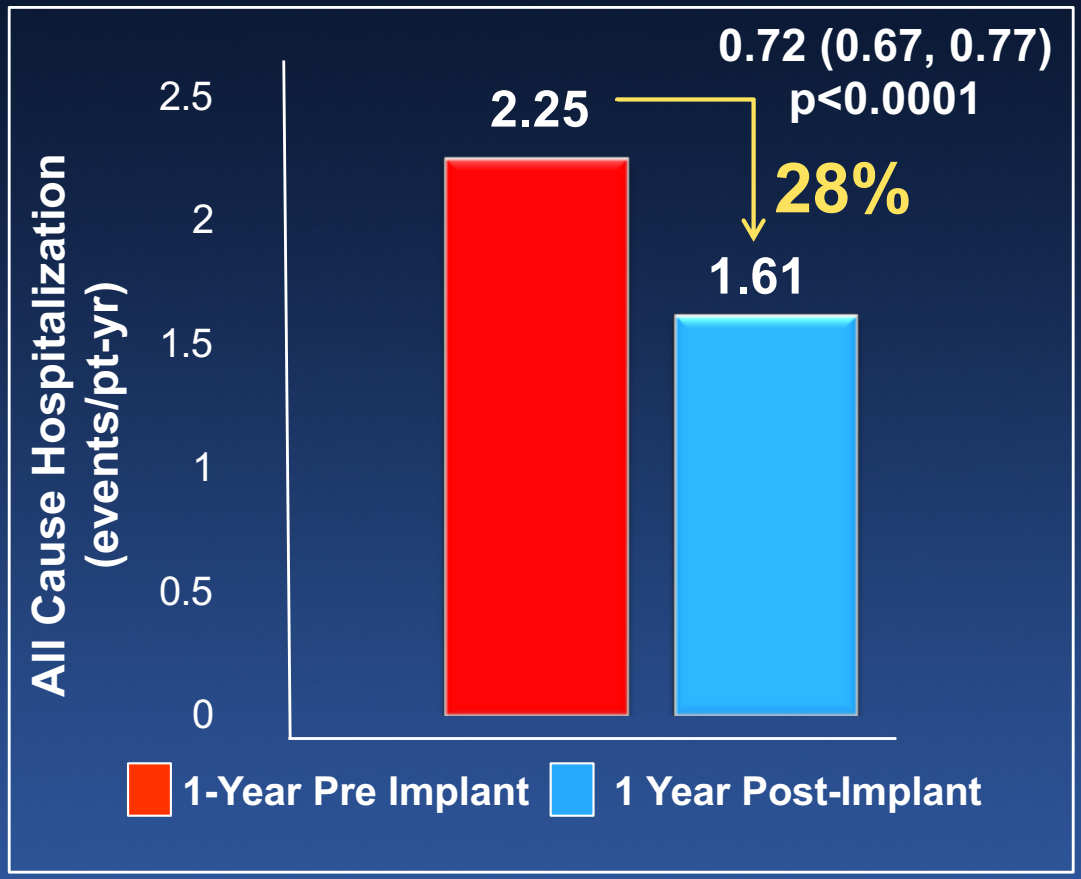


Hospitalizations for HF/Death Pre and Post-Implant



Hazard Ratio, 95% Confidence Interval and p-value estimated from the Anderson-Gill model.
All hospitalization events adjudicated by CEC.

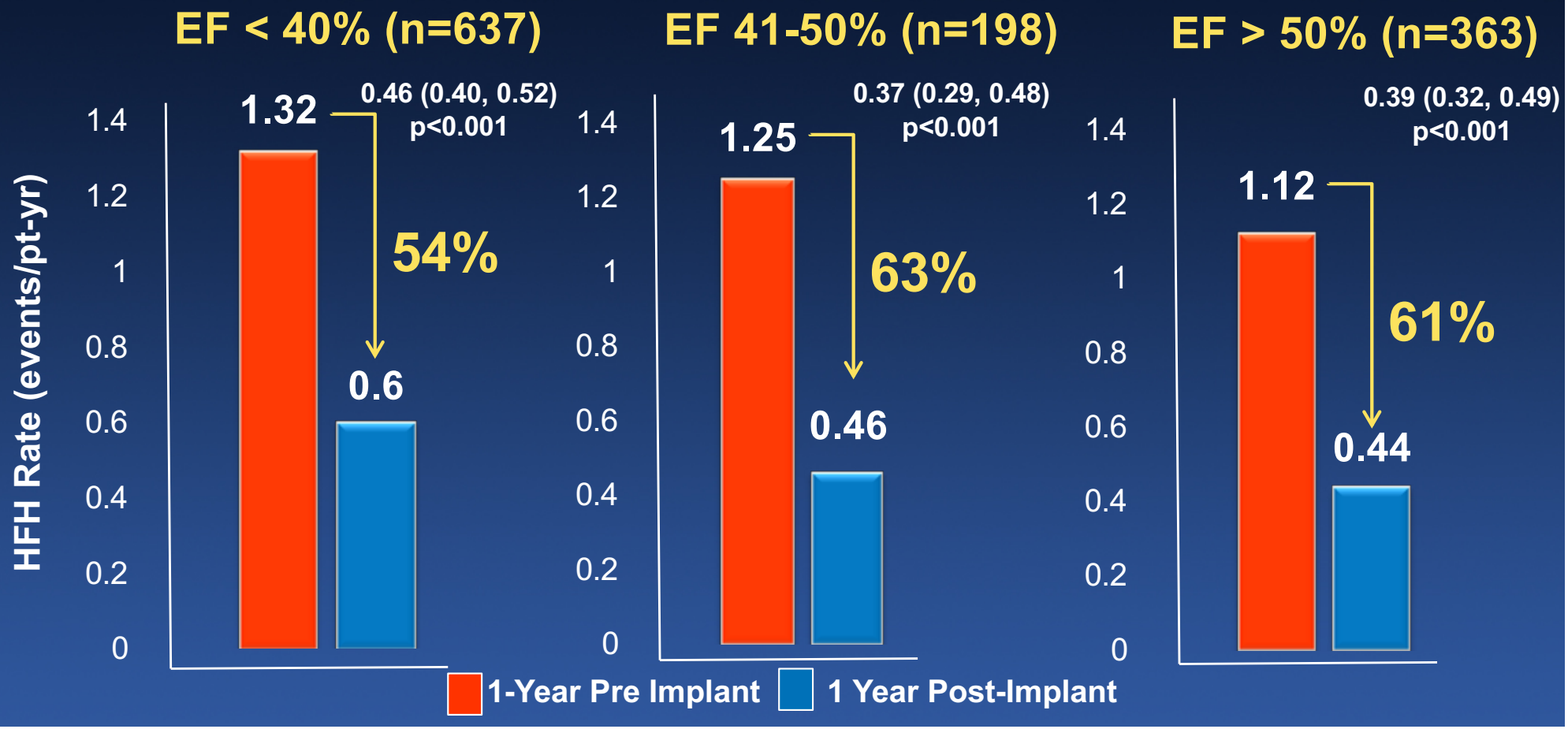
All Cause Hospitalizations Pre and Post-Implant



Hazard Ratio, 95% Confidence Interval and p-value estimated from the Anderson-Gill model.
All hospitalization events adjudicated by CEC.

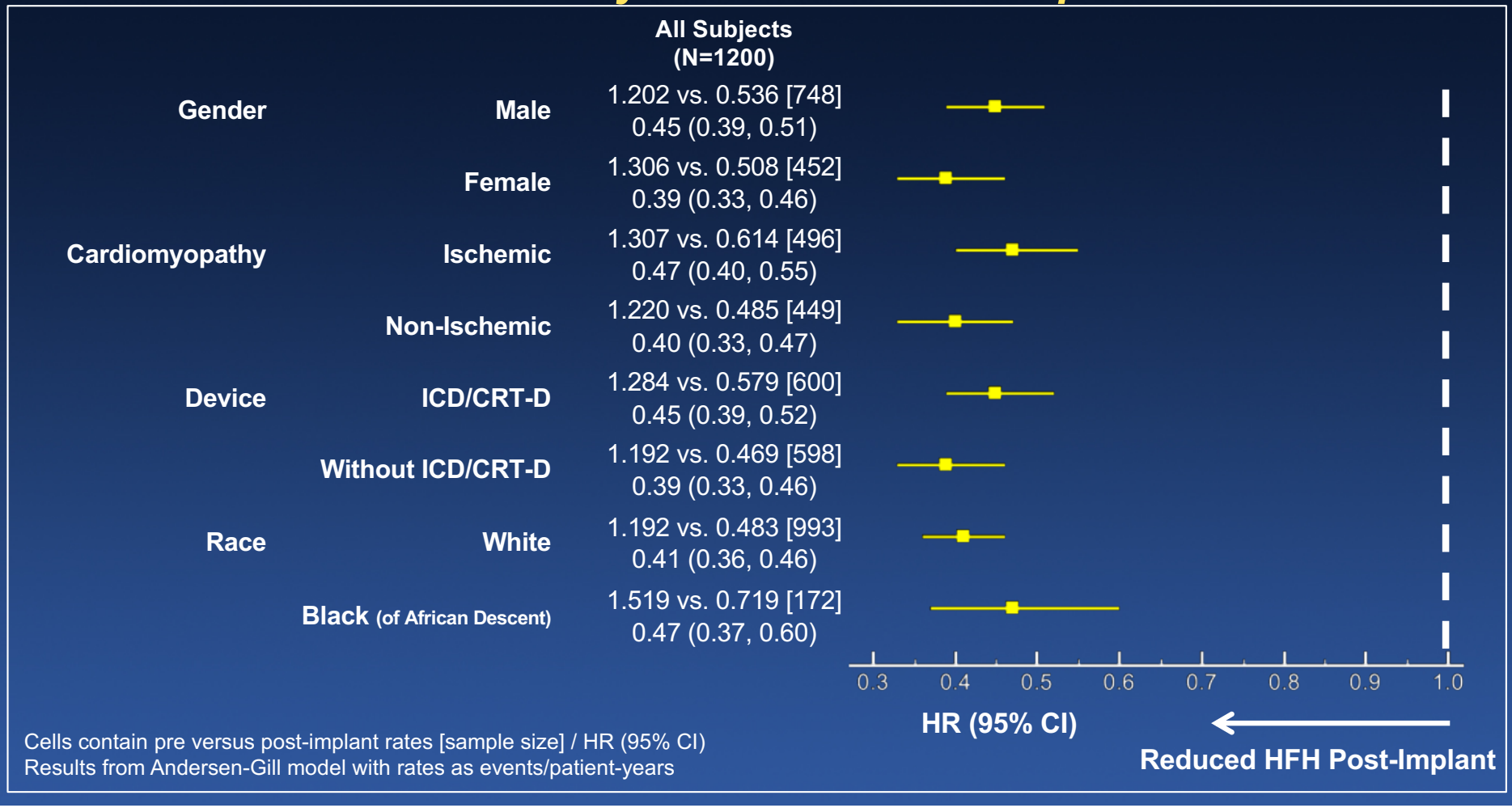
Hospitalizations for Heart Failure: Pre and Post-Implant

Stratified by Ejection Fraction



Heart Failure Hospitalizations: Pre Implant vs Post-Implant

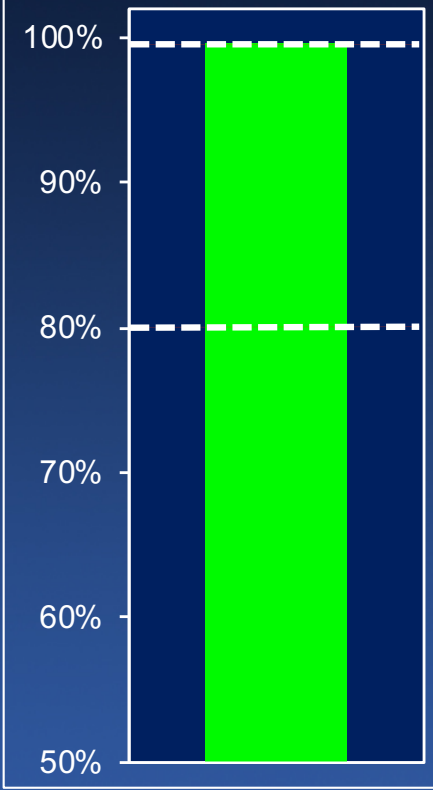
Stratified by Planned Sub-Groups



Cells contain pre versus post-implant rates [sample size] / HR (95% CI)
Results from Andersen-Gill model with rates as events/patient-years

Primary Safety Endpoints

Freedom from Device/System Related Complications at 1 year



99.7%

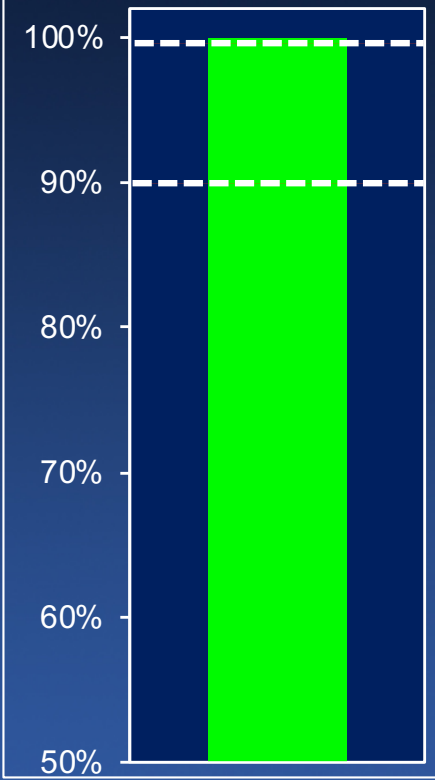
80% OPC

Device/System Related Complications 4/1214 (0.3%)

Device/System Related Complications: Adverse event that is possibly related to the system and has at least 1 of the following: treated with invasive means (other than IM medication or RHC), results in death of subject or results in explant of device.

OPC = objective performance criteria

Freedom from Sensor Failure at 1 year



99.9%

90% OPC

Sensor Failure 1/1200 (0.1%)

Sensor Failure: No readings can be obtained after troubleshooting system to rule out any problems with external electronics

OPC = objective performance criteria

Limitations

- Single arm study with prior to and post-enrollment comparisons
- Likely underestimation of HFH events prior to enrollment due to incomplete recall of events (information bias)
- Censoring at the time of death may have resulted in survivor bias, however:
  - HFH/death for the entire cohort reduced 44%
- PAS enrolled high risk patients: baseline HFH ~ 2x higher than CHAMPION
- Comparable efficacy to prior studies:
  - CHAMPION → Open Access Study: HFH reduced 48%
  - PAS: HFH reduced 58%

Conclusions

- In the commercial setting, PA pressure-guided therapy for HF:
  - Decreased PA pressures
  - Decreased HF Hospitalizations
    - across sex and race
    - across all EF ranges
    - on top of best medical and rhythm device therapies
  - Decreased All-Cause Hospitalizations
- PA pressure-guided therapy was safe with few device/system related complications and a low rate of pressure sensor failure

CardioMEMS PAS Leadership

- **Steering Committee**
  - Lynne W. Stevenson (Chair), William T. Abraham, Robert C. Bourge, Maria Rosa Costanzo, Akshay S. Desai, J. Thomas Haywood, Lisa D. Rathman, Nirav Raval, David M. Shavelle, Richard Shlofmitz
- **Clinical Events Committee**
  - Alan Miller, Chair — University of Florida
  - Peter Carson — Georgetown University
  - Eugene Chung — Christ Hospital
  - Edward Michael Gilbert — University of Utah
  - Paul Hauptman — University of Tennessee
  - Wayne Levy — University of Washington
  - John Teerlink — UC San Francisco
- **Sponsor**
  - Abbott, Santa Clara, CA