Remote Management of Sitting Pulmonary Artery Pressures Tested Against a Performance Goal of Reduced HF Hospitalizations and All-cause Mortality in a Prospective Multi-Center Open Label PROACTIVE-HF Trial in NYHA Class III Heart Failure

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Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

Nature of Financial Relationship	Ineligible Company
Grant/Research Support	Ancora Heart, Axon Therapies, Edwards, Impulse Dynamics, V-Wave Medical, Zoll
Consultant Fees/Honoraria	Abbott, Boston Scientific, Medtronic
Individual Stock(s)/Stock Options	
Royalties/Patent Beneficiary	
Executive Role/Ownership Interest	
Other Financial Benefit	

All relevant financial relationships have been mitigated.
Faculty disclosure information can be found on the app

Background

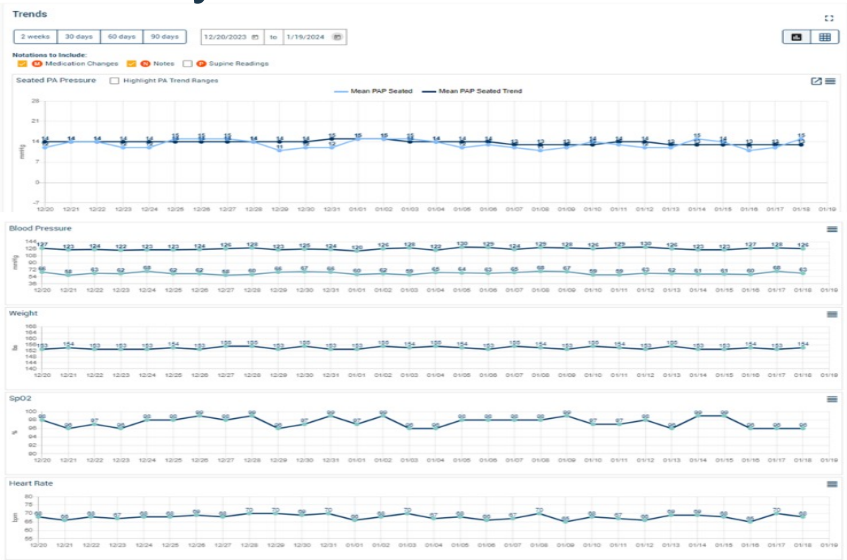
- Monitoring supine PA pressures to guide HF management has reduced HF hospitalizations in select patients[1,2,3]

- PROACTIVE-HF: evaluate the effect of remote management of seated PA pressures with the Cordella PA sensor, in addition to BP, HR, weight on outcomes in patients with chronic HF

1. Abraham W et al. Lancet. 2011;377:658-666
2. Lindenfeld JA et al. Lancet. 2021;398:991-1001
3. Brugts JJ et al. Lancet. 2023;401;2113-2123

Background

- Cordella PA sensor: wireless MEMS sensor implanted in the right PA via RHC[1]
- Seated PAP measurements: enabled by a handheld reader

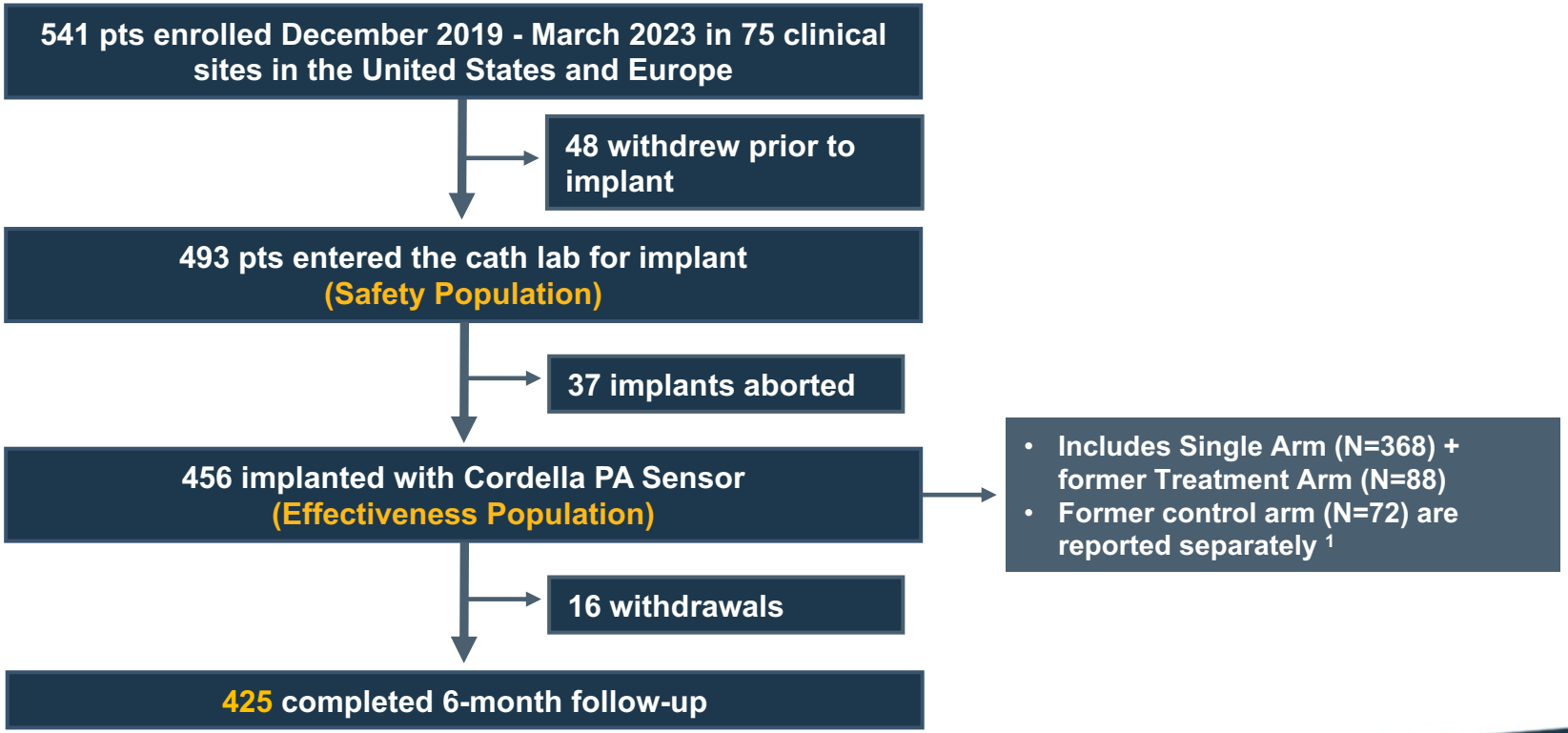


1. Guichard J et al. *J Invasive Cardiol.* 2023;35:E75-E83

PROACTIVE-HF

- **DESIGN:** Following GUIDE-HF, with FDA input, PROACTIVE-HF was changed from a randomized, single-blind design to a single-arm, open label design with blinded endpoint assessment and pre-specified safety and effectiveness endpoints defined from previous hemodynamic monitoring trials
- **OBJECTIVE:** Evaluate the safety and effectiveness of the Cordella PA Sensor System
- **PATIENTS:** NYHA III symptoms, recent HF hospitalization and/or elevated NT proBNP.

PROACTIVE-HF: Patient Flow



1. Cowger et al. *J Card Fail.* Under review for publication

PROACTIVE-HF Endpoints

Primary Effectiveness: 6-month incidence of HF hospitalization or all-cause mortality compared to a performance goal

Primary Safety: 6-month freedom from device or system-complications (DSRC) and pressure sensor failure

Secondary Endpoints:

- Combined outcome of HF hospitalizations, IV diuretic visits, and all-cause mortality
- KCCQ-OSS (Kansas City Cardiomyopathy Questionnaire) at 6 months
- 6MWT (six-minute walk test) at 6 months
- Change in seated mean PA pressure at 6 months
- Cumulative change in HF medications
- Patient and clinic compliance

Baseline Characteristics

Characteristic	All Subjects N = 456
Age (years), Mean (SD)	64 (13)
Female	40%
Black	18%
BMI (kg/m^2), Mean ± SD	36 (9)
LVEF ≥ 50%	44%
Number of HFH in previous year, Mean ± SD	1.4 ± 1
Hypertension	88%
Chronic obstructive pulmonary disease	20%
Chronic kidney disease	43%
Atrial fibrillation	52%
eGFR, Mean ± SD	55 ± 19
NT-proBNP, Mean ± SD	1731 ± 3013
KCCQ, Mean ± SD	53 ± 23
6MWT, Mean ± SD	260 ± 121

Characteristic	All Subjects N = 456
Supine pulmonary artery pressure, Mean ± SD	28 ± 10
Pulmonary capillary wedge pressure, Mean ± SD	17 ± 9
Systolic blood pressure, Mean ± SD	122 ± 19
Angiotensin receptor-neprilysin inhibitor	44%
Angiotensin II receptor blocker	18%
ACE Inhibitor	7%
Beta blocker	87%
Aldosterone Antagonist	68%
SGLT2 inhibitor	58%
Loop Diuretic	97.4%
Enrollment: HFH criteria only	33%
Enrollment: NT-proBNP criteria only	20%
Enrollment: HFH + NT-proBNP criteria	47%
Subjects with HFH prior to implant	80%

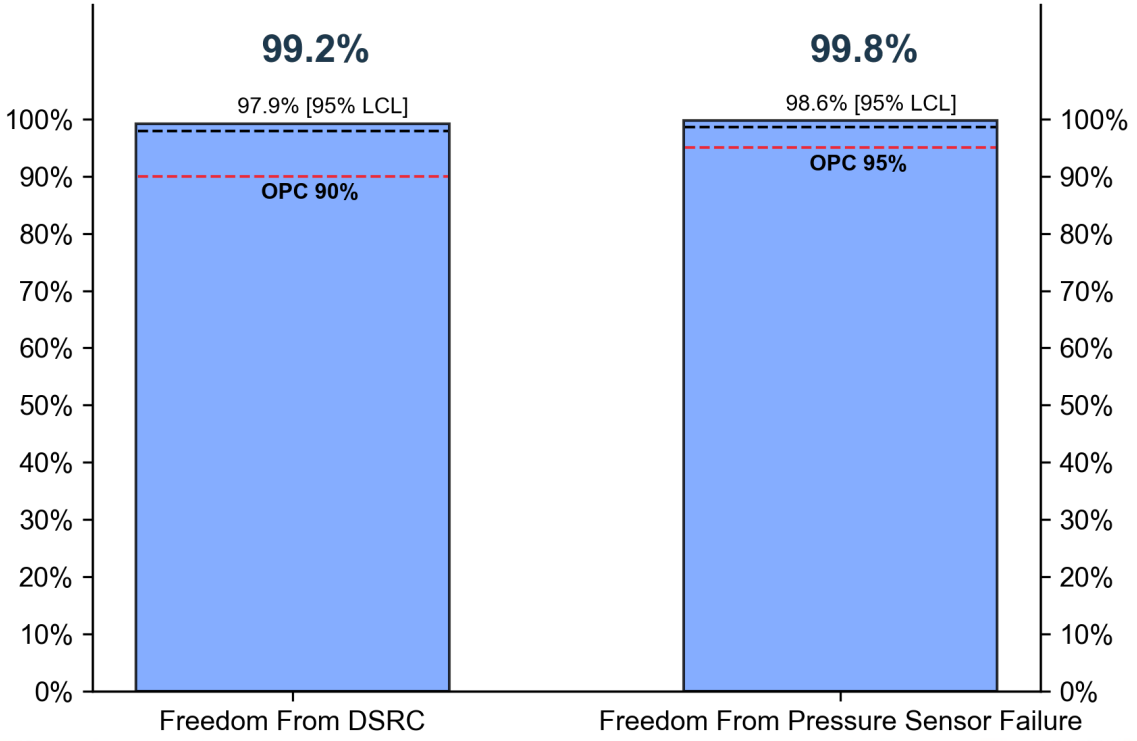
Baseline Characteristics

Characteristic	PROACTIVE-HF Treatment (N=456)	GUIDE-HF Treatment NYHA III (N=322)	GUIDE-HF All Treatment (N=497)	CHAMPION Treatment (N=270)	MONITOR-HF Treatment (N=176)
Age	64 ± 13	69 ± 11	69 ± 11	61 ± 13	69 (61-75)*
Female	40%	40%	38%	28%	22%
Non-White	24%	19%	19%	27%	NR
BMI (kg/m^2)	36 ± 9	34 ± 8	33 ± 8	31 ± 7	27 (24-32)*
LVEF > 40%	54%	47%	45%	23%	27%
HFH in prior year	80%	56%	54%	100%	100%
SGLT2i	58%	1%	<1%	0%	7%
eGFR (mL/min)	55 ± 19	54 ± 21	54 ± 21	60 ± 23	48 (35-60)*
NT-proBNP (pg/mL)	1731 ± 3013	2258 ± 3316	2460 ± 3701	NR	2377 (837-5153)*
RHC mPAP (mmHg)	28 ± 10	NR	29 ± 10	29 ± 10	33 ± 11
PCWP (mmHg)	17 ± 9	17 ± 8	17 ± 8	18 ± 8	NR
KCCQ-OS (points)	53 ± 23	50 ± 23	55 ± 24	NR	55.8 ± 23.3
6MWT (m)	260 ± 121	219 ± 116	235 ± 120	NR	NR

*Reported as Median (IQR); NR = Not Reported

Primary Safety Endpoints

Freedom from DSRC & pressure sensor failure at 6 months



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Primary Effectiveness Endpoint

Performance goals

Primary Effectiveness Success Criteria

1. Upper confidence bound of the event rate required to be < 0.43 events/patient/6-month
2. Or equivalently, the event rate compared to 0.43 p-value is <0.025
3. Event rate is required to be <0.37 (***assumed 50% SGLT2i***)

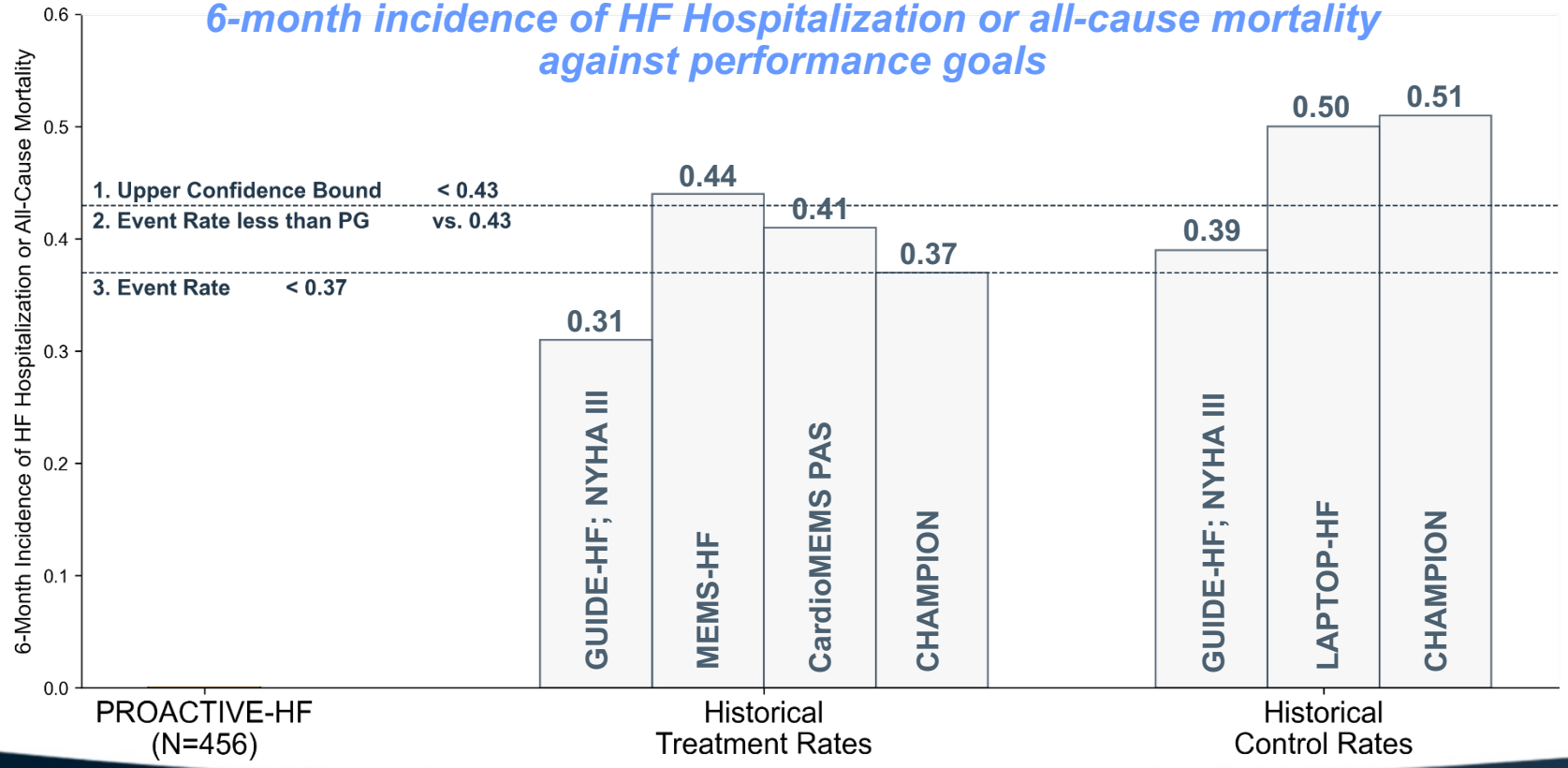
Historical Treatment Rates

Performance goals are within the confidence intervals of treatment rates from prior hemodynamic-guided HF management trials

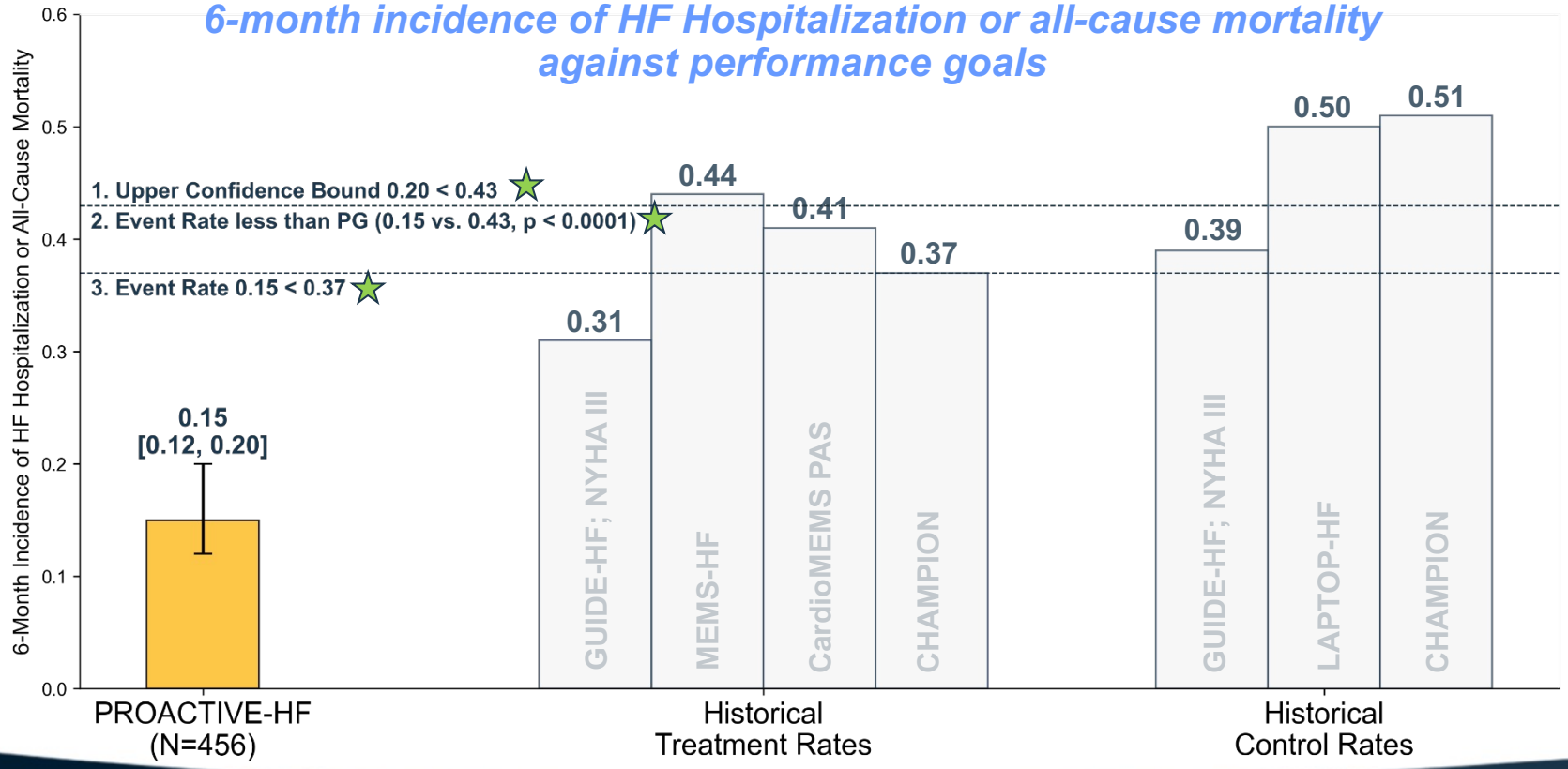
Historical Control Rates

Performance goals are lower than the control rates from prior hemodynamic-guided HF management trials

Primary Effectiveness Endpoint

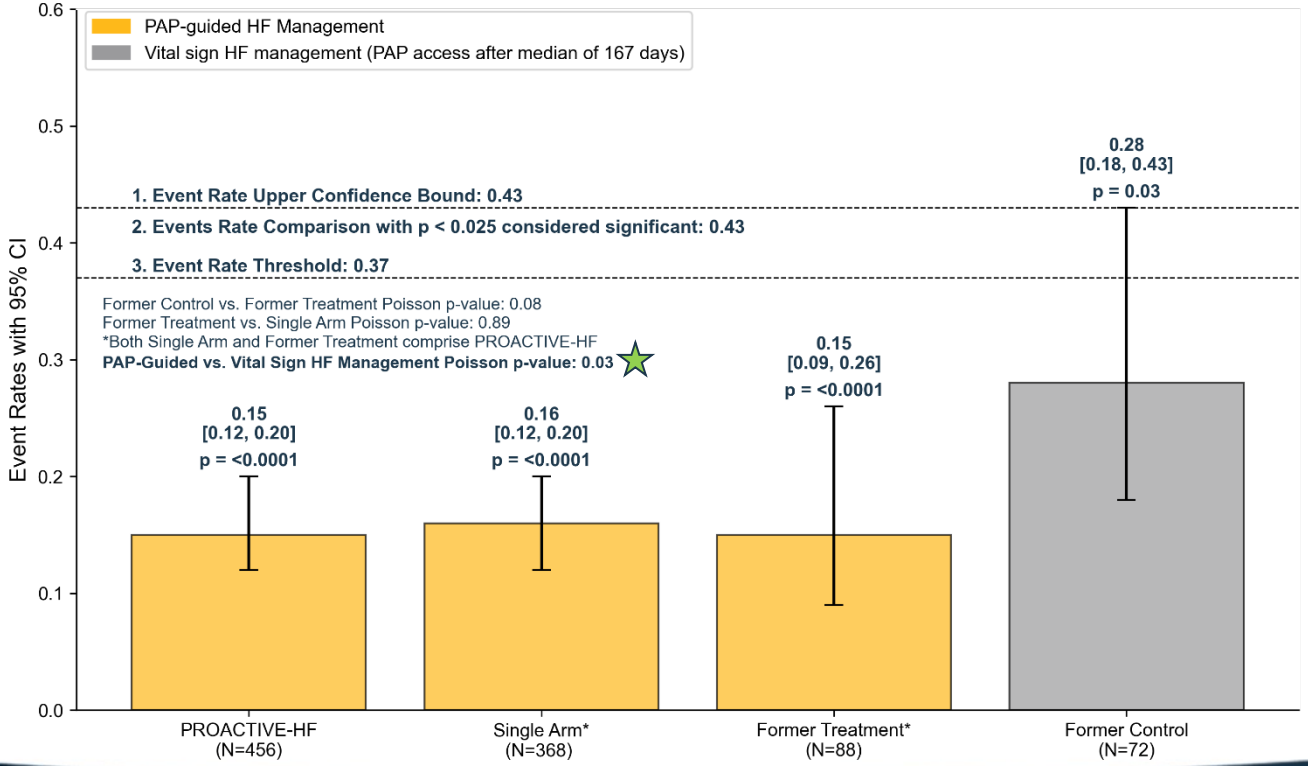


Primary Effectiveness Endpoint



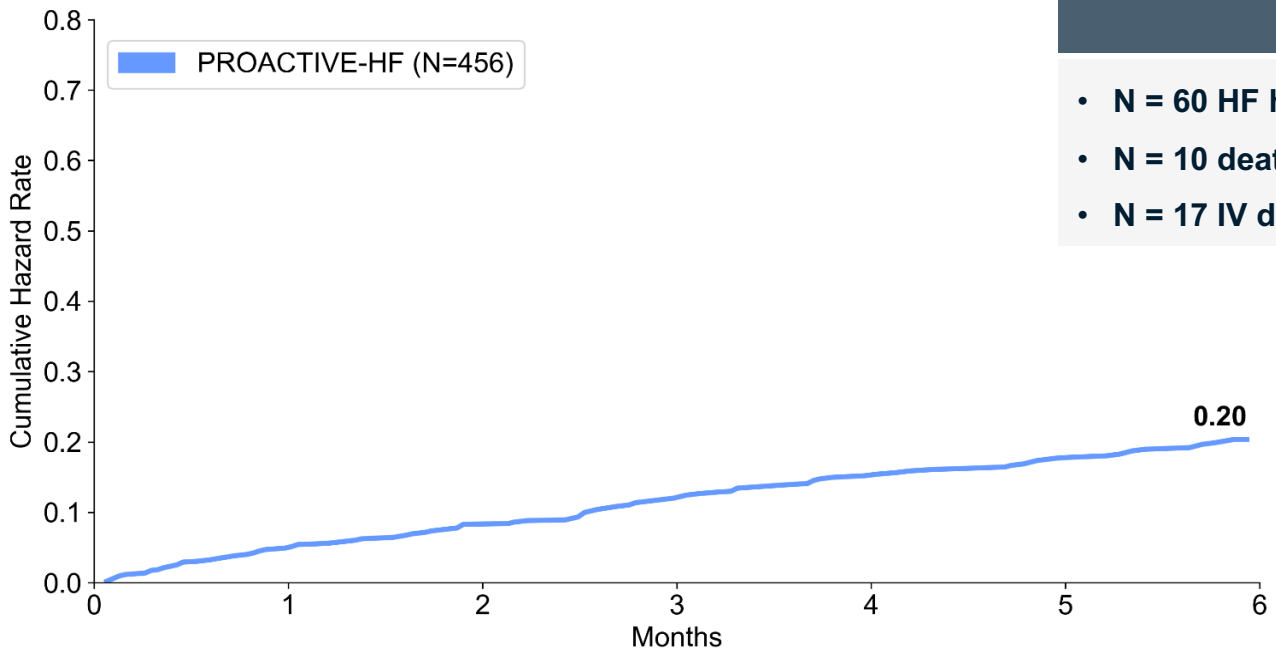
Primary Effectiveness Endpoint

Enrollment cohorts



Key Secondary Endpoints

HF Hospitalizations, IV diuretic visits, or all-cause mortality



Events

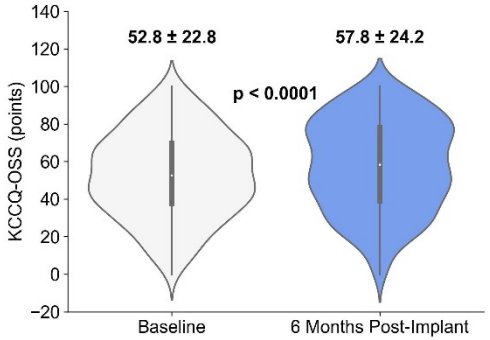
- **N = 60 HF hospitalizations in 48 patients**
- **N = 10 deaths**
- **N = 17 IV diuretic visits in 14 patients**

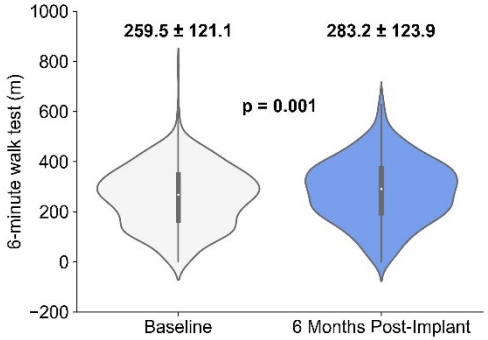
Key Secondary Endpoints

Quality of life, functional capacity, NT-proBNP

KCCQ-OSS

+ 5.0 points



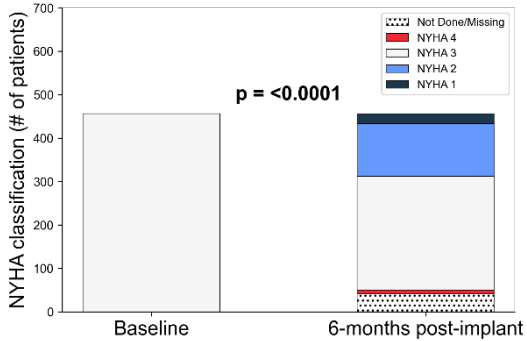


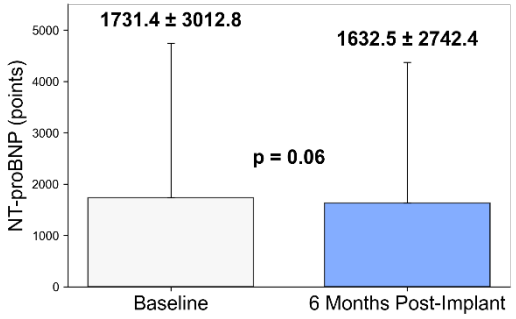
6MWT

+ 23.7 meters

NYHA

32% improved





NT-proBNP

-98.9 pg/ml

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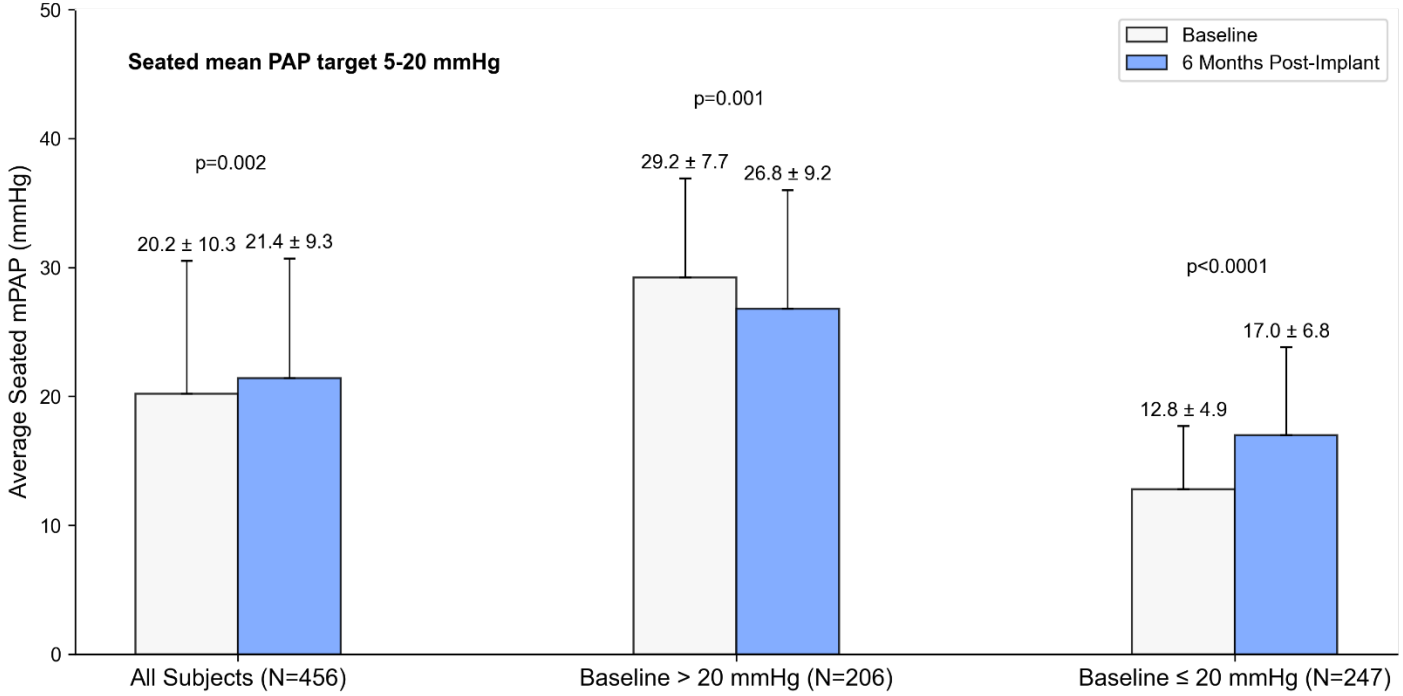
Key Secondary Endpoints

Change in seated mean PA pressure

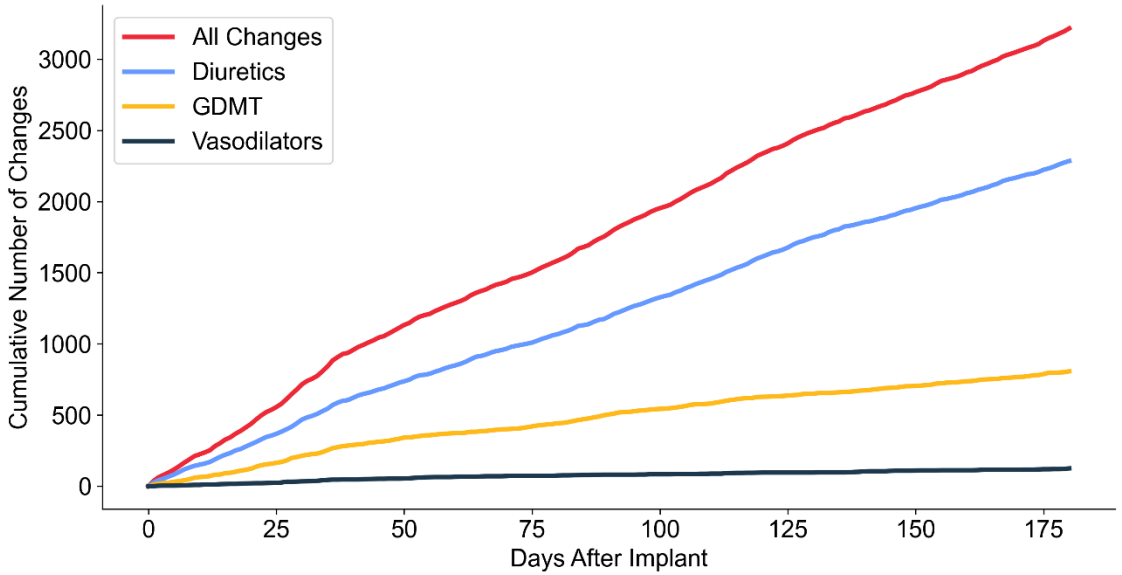


Secondary Effectiveness Endpoints

Cumulative HF medication changes

% changes per class

- 25% GDMT
  - RAS-I, Beta blocker, MRA, SGLT2i
- 71% Diuretic
- 4% Vasodilators

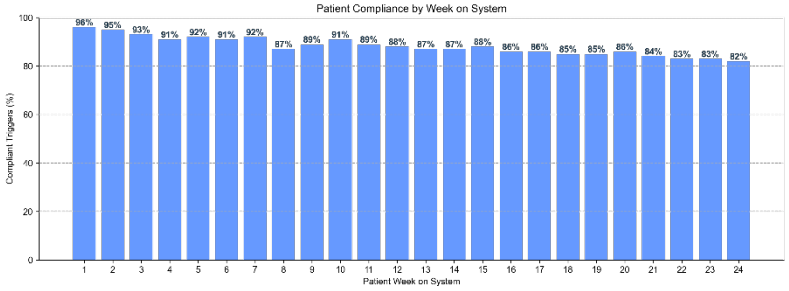


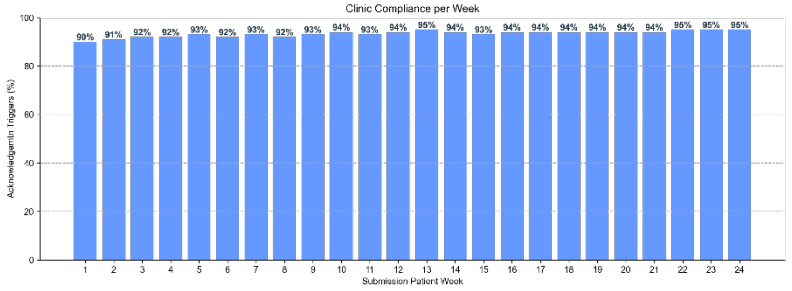
Secondary Effectiveness Endpoints

Compliance through 6 months

Patient Compliance: data transmission at least 5 out of 7 days (not need to be consecutive)

Clinic Compliance: Site checks patient data at least 2 times/week with maximum 4 days between





Average of 6.2 submissions/week

Average of 2.2 days between checks

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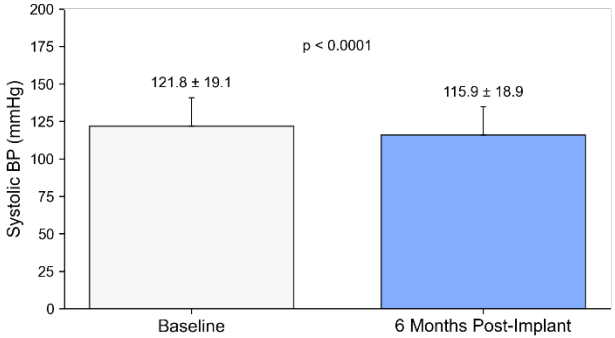
Vital Signs

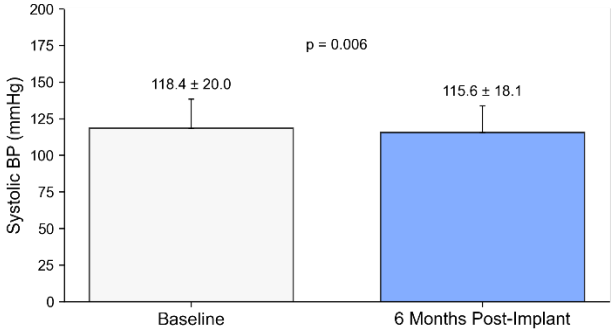
In-Office sBP

- 5.9 mmHg



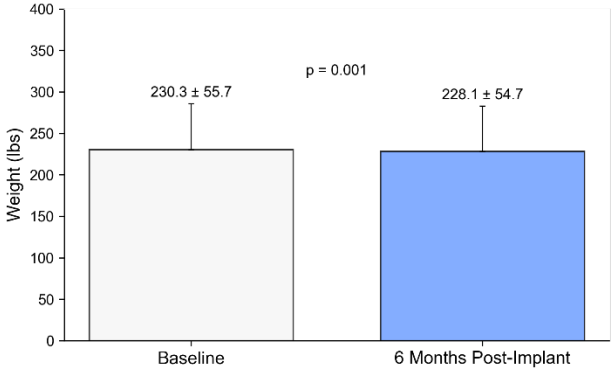
At-Home sBP

- 2.8 mmHg



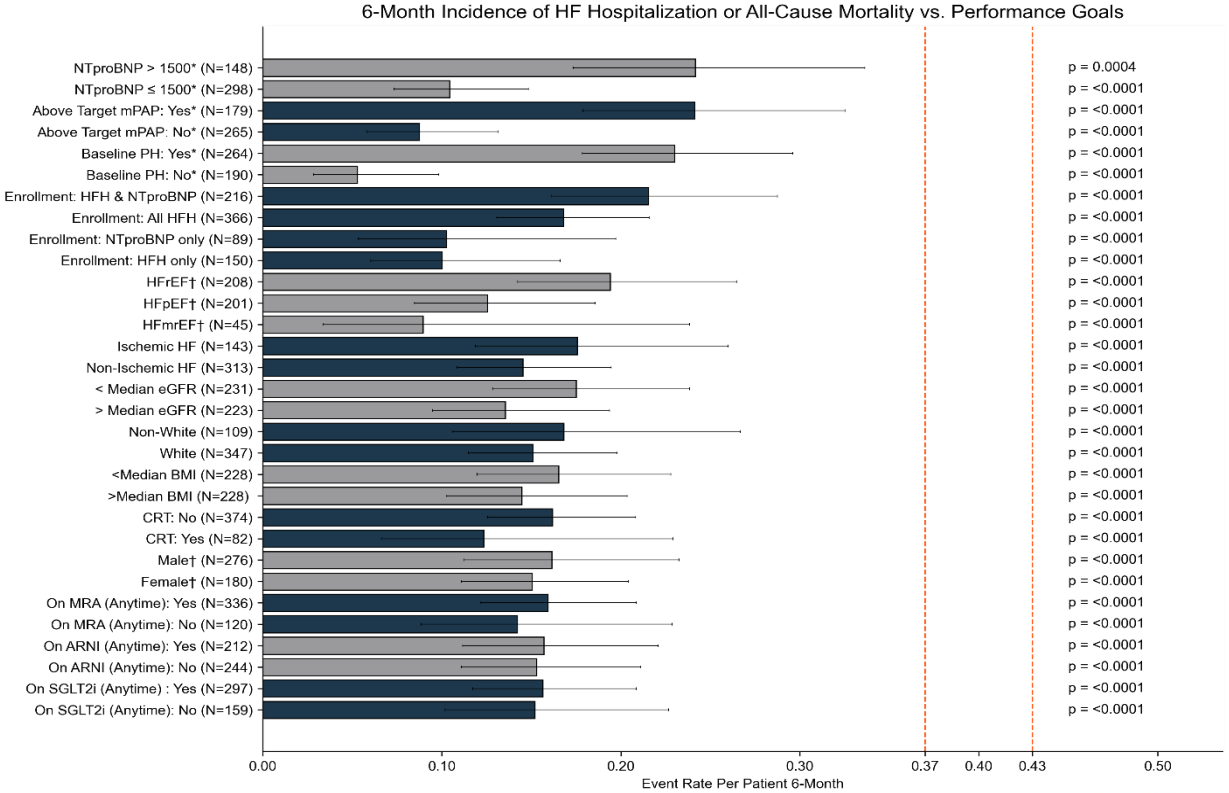
Weight

- 2.2 lbs



Subgroup Analysis

All subgroups analyzed compared favorably to the performance goals



Subgroup analyses were exploratory and hypothesis generating. There were no adjustments for multiple comparisons.

Conclusions

- For HF patients with NYHA class III symptoms:
  - Cordella PA sensor and HF system was safe, improved QOL and functional capacity
  - Cordella enabled significant reductions in PA pressure for patients with PAP elevated at baseline

- The markedly low event rates may relate to high patient compliance and engagement, high rates of baseline GDMT, and proactive interventions guided by integration of daily vital signs with seated mean PA pressure (may be more relevant than supine PA pressure alone for management of ambulatory HF patients)