ABBOTT HEART FAILURE

Longer-term effects of hemodynamic monitoring on outcomes: a combined data analysis of HFrEF patients in CHAMPION, GUIDE-HF and LAPTOP-HF

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Introduction

- Hemodynamic-guided management using left atrial pressure (LAP) or pulmonary artery pressure (PAP) results in a reduction in elevated pressures and heart failure hospitalizations (HFH)
- Both HFH and elevated PAP are associated with increased mortality
- Three separate randomized controlled trials (RCTs) with patient-level data available provided a unique opportunity to evaluate the impact of hemodynamic monitoring on HFH and survival
- We hypothesized that hemodynamic-guided management would reduce mortality in patients with heart failure with reduced ejection fraction (HFrEF)

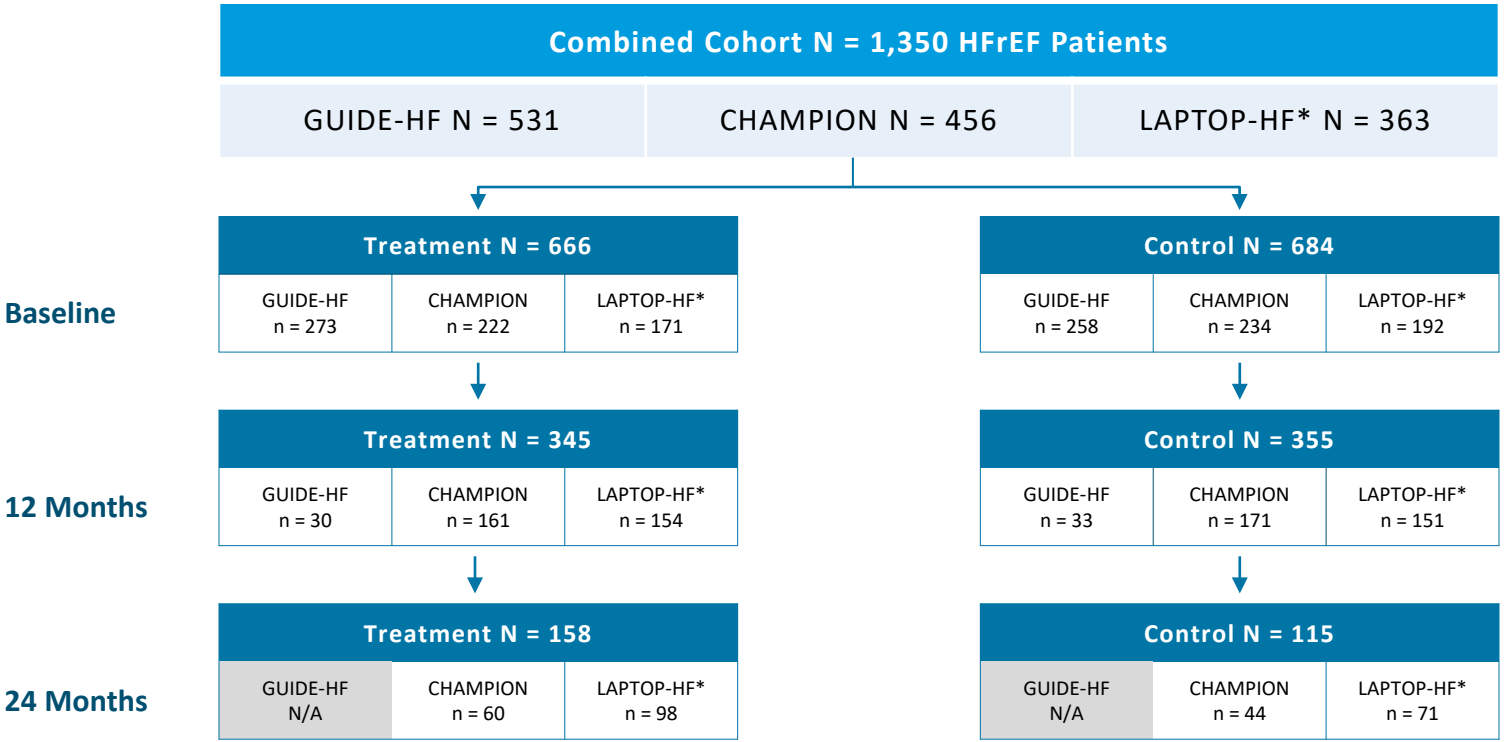
This analysis is focused on HFrEF because

- A previous study suggested a mortality benefit in patients with HFrEF in the CHAMPION trial[1]
- The majority of patients in all three trials had HFrEF (n = 1,350), with n = 700 with 1 year and n = 273 with 2 or more years of follow-up
- There were far fewer patients with heart failure with preserved ejection fraction (HFpEF) (n = 533) and even fewer with 1 year (n = 154) and 2 or more years (n = 48) of follow-up
- Mortality in HFrEF is primarily cardiovascular (88% in DAPA-HF), whereas in HFpEF about 50% is cardiovascular (48% in DELIVER)

Study comparisons

	CHAMPION[2,3] N = 456	LAPTOP-HF[4] N = 363	GUIDE-HF[1] N = 531
Trial Design	Prospective, multicenter, randomized, controlled, single-blinded evaluation of the CardioMEMS™ HF System	Prospective, multicenter, randomized, controlled evaluation of the LAP monitoring system	Prospective, multicenter, randomized, controlled, single-blinded evaluation of the CardioMEMS HF System
Management Strategy	Pulmonary artery pressure via CardioMEMS HF System	Left atrial pressure via a transseptal lead	Pulmonary artery pressure via CardioMEMS HF System
Trial Dates	Sep 2007–Dec 2014	Jun 2010–Apr 2015	Mar 2018–Jan 2021
Duration	Continued follow-up until last subject at 6 months	Continued follow-up until last subject at 12 months	12 months follow-up
Primary Endpoint	Heart failure (HF) hospitalizations at 6 months	HF major acute cardiovascular and neurological events at overall follow-up	Composite of HF hospitalizations, urgent HF visits and all-cause mortality at 12 months
Geography	United States	United States and New Zealand	United States and Canada
Inclusion	New York Heart Association (NYHA) Class III with prior HF hospitalization	NYHA Class III with prior HF hospitalization or persistently elevated brain natriuretic peptide (BNP) level	NYHA Class II/III/IV with prior HF hospitalization or elevated BNP or N-terminal pro b-type natriuretic peptide (NT-proBNP) level

Study designs and subject disposition



*For GUIDE-HF, only follow-up occurring prior to the COVID-19 pandemic (March 13, 2020) is included. For LAPTOP-HF, follow-up is only included for the as-treated population.

Statistical methods

- Follow-up data was limited to HFrEF (ejection fraction ≤ 40% at baseline) patients and included:
  - GUIDE-HF 12-month follow-up occurring prior to COVID-19 (March 13, 2020)
  - CHAMPION follow-up through 24 months
  - LAPTOP-HF as-treated population follow-up through 24 months
- Heart failure hospitalizations and composite analyses were evaluated using the Andersen-Gill extension of the Cox proportional hazards model with randomized group as a covariate
- Survival analyses were conducted using Kaplan-Meier estimates of freedom from all-cause mortality

HFrEF patient demographics by study

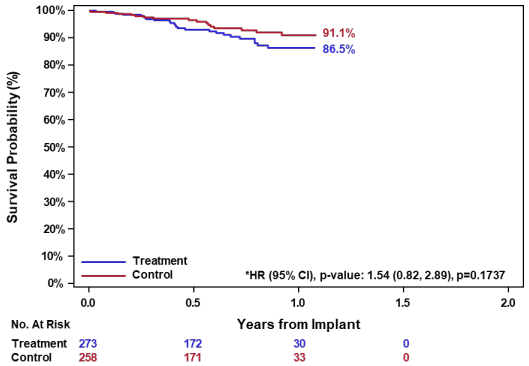
	All Subjects (N = 1,350)	GUIDE-HF (N = 531)	CHAMPION (N = 456)	LAPTOP-HF (N = 363)
Age — Year	63.5 ± 12.6	67.2 ± 11.4	60.7 ± 12.8	61.7 ± 12.7
Female Sex	25.3% (342)	29.2% (155)	24.3% (111)	20.9% (76)
Caucasian Race	71.1% (960)	73.6% (391)	71.3% (325)	67.2% (244)
NYHA Class II	13.6% (183)	31.6% (168)	0.0% (0)	4.1% (15)
NYHA Class III	84.1% (1,136)	62.5% (332)	100.0% (456)	95.9% (348)
NYHA Class IV	2.3% (31)	5.8% (31)	0.0% (0)	0.0% (0)
Ischemic Etiology	54.5% (736)	50.5% (268)	62.9% (287)	49.9% (181)
Diabetes	48.9% (660)	49.0% (260)	47.8% (218)	50.1% (182)
LVEF — %	24.9 ± 8.1	25.9 ± 8.3	24.3 ± 8.0	24.3 ± 7.7
BMI — kg/m²	31.1 ± 7.0	31.4 ± 7.4	30.1 ± 6.3	32.0 ± 7.1
PA Diastolic Pressure — mmHg	19.4 ± 8.7	19.3 ± 8.9	19.4 ± 8.4	N/A
PCWP — mmHg	18.3 ± 8.7	17.8 ± 9.0	18.8 ± 8.3	N/A
Left Atrial Pressure — mmHg*	19.7 ± 10.1	N/A	N/A	19.7 ± 10.1*
Cardiac Output — L/min	4.48 ± 2.05	4.52 ± 2.46	4.44 ± 1.43	N/A
Estimated GFR — mL/min/1.73 m²	57.8 ± 23.2	54.4 ± 22.8	61.7 ± 23.1	N/A
Previous CRT	38.8% (524)	40.5% (215)	37.9% (173)	37.5% (136)
ACE Inhibitor or ARB or ARNI	77.6% (1,048)	75.1% (399)	78.1% (356)	80.7% (293)
Beta Blocker	94.7% (1,278)	95.1% (505)	93.4% (426)	95.6% (347)
Mineralocorticoid Receptor Antagonist	52.3% (706)	51.0% (271)	45.2% (206)	63.3% (229)
Diuretic	95.1% (1,284)	94.2% (500)	93.0% (424)	99.2% (360)

Continuous variables presented as mean ± standard deviation. Categorical variables presented as percentage (counts).
*Left atrial pressure only available in treatment group subjects within the LAPTOP-HF trial.
ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor-neprilysin inhibitor; BMI = body mass index; CRT = cardiac resynchronization therapy; GFR = glomerular filtration rate; LVEF = left ventricular ejection fraction; PA =pulmonary artery; PCWP = pulmonary capillary wedge pressure

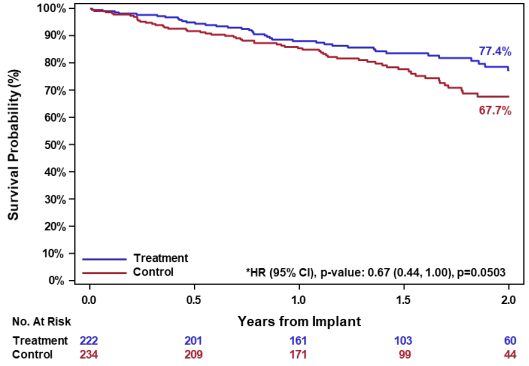
Survival at 2 years by study in HFrEF patients

Improved survival becomes apparent at follow-up time > 1 year

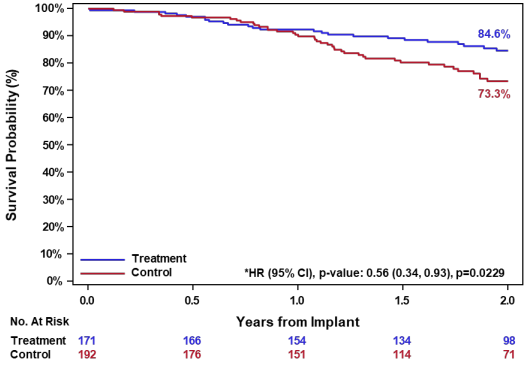
GUIDE-HF



CHAMPION



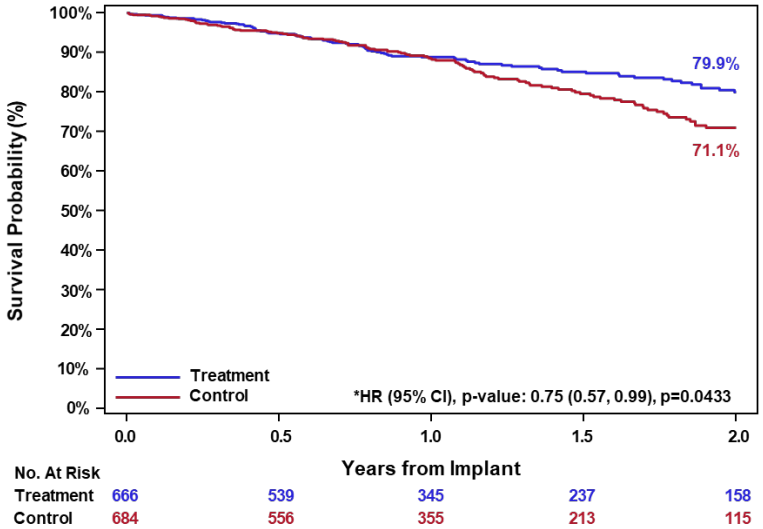
LAPTOP-HF



GUIDE-HF data includes follow-up prior to COVID-19 only. LAPTOP-HF cohort is the as-treated population. Kaplan-Meier survival estimate at 2 years. Hazard ratio and 95% confidence interval estimated from the Cox proportional hazards model and P value from log-rank test.

Results: survival at 2 years in HFrEF patients

25% reduction in mortality at 2 years in treatment group relative to control

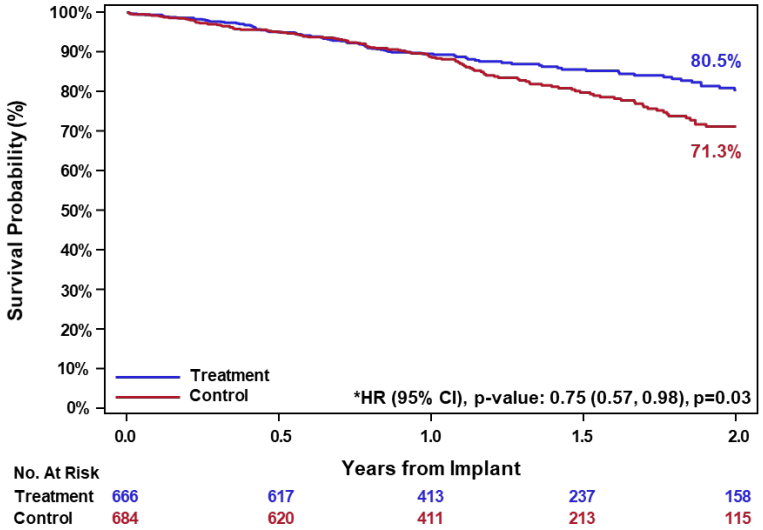


25%
Reduction in mortality

GUIDE-HF data includes follow-up prior to COVID-19 only. LAPTOP-HF cohort is the as-treated population. Kaplan-Meier survival estimate at 2 years. Hazard ratio and 95% confidence interval estimated from the Cox proportional hazards model and P value from log-rank test.

Survival at 2 years in HFrEF patients — full GUIDE-HF

Same 25% reduction in mortality at 2 years in treatment group relative to control



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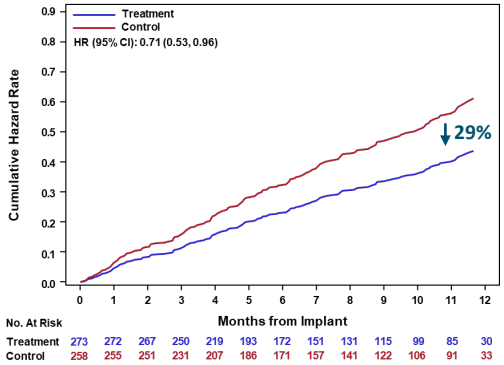
GUIDE-HF data includes follow-up prior to COVID-19 only. LAPTOP-HF cohort is the as-treated population. Kaplan-Meier survival estimate at 2 years. Hazard ratio and 95% confidence interval estimated from the Cox proportional hazards model and P value from log-rank test.

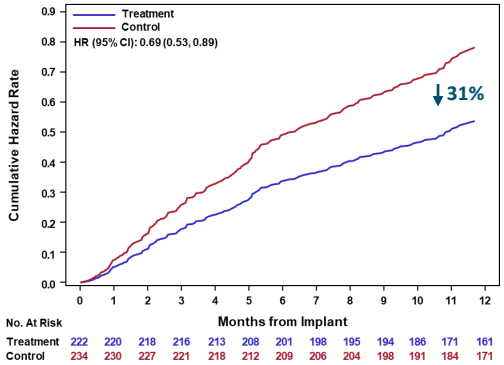
HF hospitalizations at 12 months by study in HFrEF patients

Significant reduction in heart failure hospitalizations at 12 months across trials

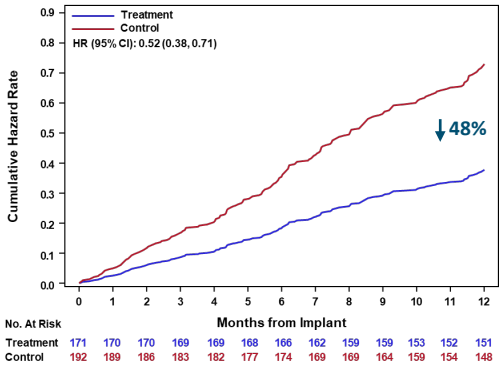
GUIDE-HF



CHAMPION



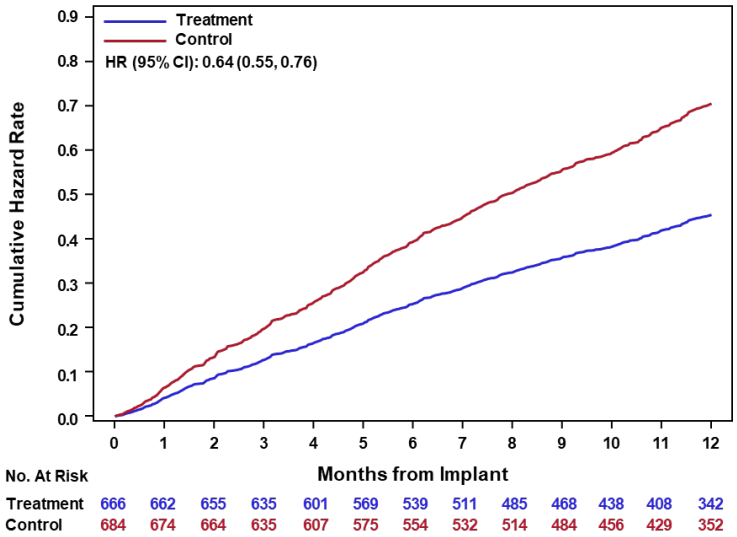
LAPTOP-HF



GUIDE-HF data includes follow-up prior to COVID-19 only. LAPTOP-HF cohort is the as-treated population. Hazard ratio and 95% confidence interval estimated from the Cox proportional hazards model and P value from log-rank test.

HF hospitalizations at 12 months in HFrEF patients

36% reduction in HF hospitalizations at 12 months in treatment group relative to control



36%
Reduction in HF hospitalizations

GUIDE-HF data includes follow-up prior to COVID-19 only. LAPTOP-HF cohort is the as-treated population. Hazard ratio and 95% confidence interval estimated from the Cox proportional hazards model and P value from log-rank test.

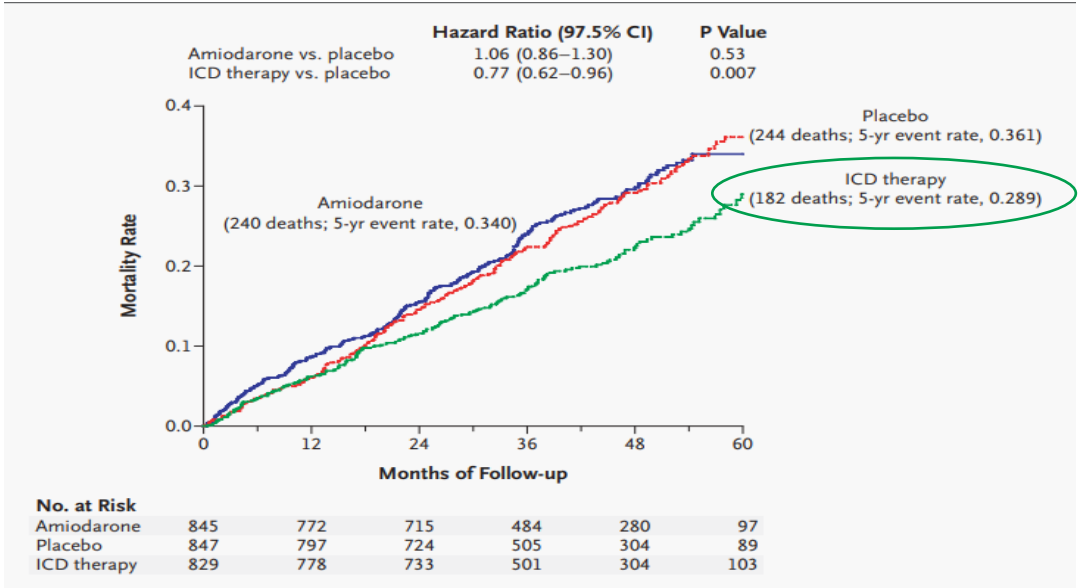
Conclusions

LONG-TERM USE OF PRESSURE-GUIDED MANAGEMENT SHOWS SURVIVAL BENEFIT

- This patient-level meta-analysis of **HFrEF** patients over 2 years of follow-up demonstrates that remote hemodynamic monitoring improves all-cause mortality and reduces heart failure hospitalizations
- Consistency was observed across trials with different devices, different time periods and evolving GDMT
- A longer follow-up period (> 1 year) is required to observe improved survival with hemodynamic monitoring than is required to demonstrate a reduction in heart failure hospitalizations

Why does it take longer to show a mortality benefit?

Longer follow-up period required to show improved survival for implantable cardioverter defibrillators versus controls



Implications for clinical practice

- New results from a robust long-term meta-analysis of three RCTs continue to support that pressure-guided management with Abbott devices such as the CardioMEMS™ HF System improves survival in HFrEF patients
- Hemodynamic management of HFrEF patients significantly reduces mortality risk by 25% at 2 years
- This meta-analysis further validates the ability of hemodynamic management to disrupt the progression of heart failure by significantly decreasing HF hospitalization and improving survival

In conclusion, hemodynamic monitoring with the CardioMEMS HF System improves survival in heart failure patients[5-7]

References

1. Lindenfeld J, Zile MR, Desai AS, et al. Haemodynamic-guided management of heart failure (GUIDE-HF): a randomized controlled trial. *Lancet*. 2021;398(10304):991-1001. doi:10.1016/S0140-6736(21)01754-2
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3. Abraham WT, Stevenson LW, Bourge RC, et al. Sustained efficacy of pulmonary artery pressure to guide adjustment of chronic heart failure therapy: complete follow-up results from the CHAMPION randomised trial. *Lancet*. 2016;387(10017):453-461.
4. Abraham WT, Adamson PB, Costanzo MR. Hemodynamic monitoring in advanced heart failure: results from the LAPTOP-HF trial. *J Card Fail*. 2016;22(11):940. doi:10.1016/j.cardfail.2016.09.012
5. Givertz MM, Stevenson LW, Costanzo MR, et al; CHAMPION Trial Investigators. Pulmonary artery pressure-guided management of patients with heart failure and reduced ejection fraction. *J Am Coll Cardiol*. 2017;70(15):1875-1886. doi:10.1016/j.jacc.2017.08.010
6. Abraham J, Bharmi R, Jonsson O, et al. Association of ambulatory hemodynamic monitoring of heart failure with clinical outcomes in a concurrent matched cohort analysis [published correction appears in JAMA Cardiol. 2019;4(6):601]. *JAMA Cardiol*. 2019;4(6):556-563. doi:10.1001/jamacardio.2019.1384
7. Lindenfeld J, on behalf of the GUIDE-HF, CHAMPION and LAPTOP-HF Investigators. Longer-term effects of hemodynamic monitoring on outcomes: a combined data analysis of patients with HFrEF in CHAMPION, GUIDE-HF and LAPTOP-HF. Presented at: Technology and Heart Failure Therapeutics (THT) Conference; March 21, 2023; Boston, MA.

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Rx Only
Brief Summary: Prior to using these devices, please review the Instructions for Use for a complete listing of indications, contraindications, warnings, precautions, potential adverse events and directions for use.

CardioMEMS™ HF System Indications and Usage: The CardioMEMS™ HF System is indicated for wirelessly measuring and monitoring pulmonary artery pressure and heart rate in NYHA Class II or III heart failure patients who either have been hospitalized for heart failure in the previous year and/or have elevated natriuretic peptides. The hemodynamic data are used by physicians for heart failure management with the goal of controlling pulmonary artery pressures and reducing heart failure hospitalizations.

CardioMEMS™ HF System Contraindications: The CardioMEMS HF System is contraindicated for patients with an inability to take dual antiplatelet or anticoagulants for one month post implant.

CardioMEMS™ HF System Potential Adverse Events: Potential adverse events associated with the implantation procedure include, but are not limited to, the following: air embolism, allergic reaction, infection, delayed wound healing, arrhythmias, bleeding, hemoptysis, hematoma, nausea, cerebrovascular accident, thrombus, cardiovascular injury, myocardial infarction, death, embolization, thermal burn, cardiac perforation, pneumothorax, thoracic duct injury and hemothorax.

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