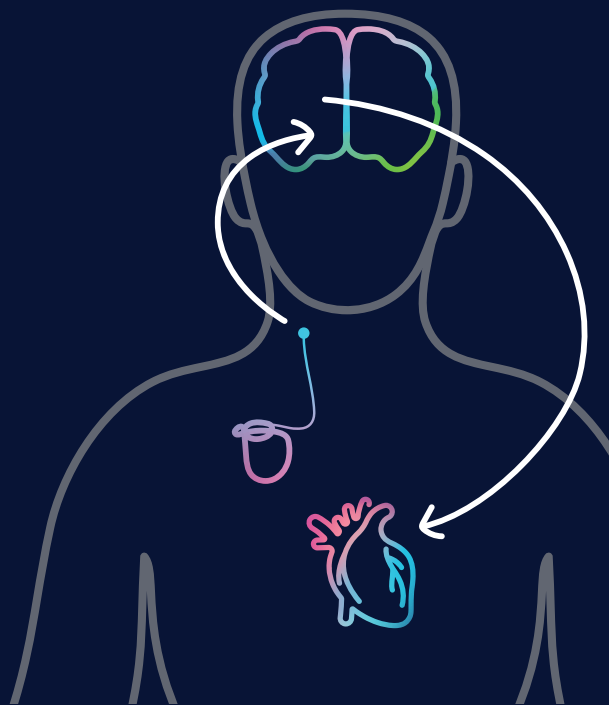
BeAT-HF Clinical Trial Summary

- Pre-market approval in 2019 based on symptomatic improvements and reductions in NT-proBNP
- Sustained and significant symptomatic improvements and safety at long-term follow-up
- Reductions in all-cause death, LVAD or transplant
- Improvement in the hierarchical composite (win ratio) of CV mortality, HF morbidity and QOL
- No statistically significant difference in the primary endpoint of CV mortality and HF morbidity



Trial design

Design

- Prospective, multicenter, randomized 2-arm parallel-group, open-label with blinded evaluation
- 73 US centers and 1 United Kingdom center
- Randomized arms
  - Barostim (BAT) plus GDMT (Barostim arm)
  - GDMT alone (Medical management arm)

Eligibility criteria

- NYHA Class III or Class II (with a recent history of Class III)
- Left ventricular EF ≤ 35%
- 6MHW 150 – 400 m
- HF Hospitalization or NT-proBNP> 400
- Stable optimal management ≥ 4 weeks
- No class I indication for CRT
- NT-proBNP < 1600 pg/ml

BeAT-HF two-phase clinical trial

Pre-Market Phase as Breakthrough Device[1]

Met safety and all effectiveness endpoints

- ✓ Safety
- ↑ 6-month symptom improvement
- ↓ NT-proBNP at 6 months

FDA approval 2019 — Published 2020

Post-Market Phase for Labeling Expansion[2]

Confirmed safety and effectiveness endpoints of Pre- Market Phase. Primary endpoint of CV death and hospitalization was not met. Additional effective analysis suggest favorable effect of Barostim therapy

- ✓ Safety
- ↑ 6,12,24-month symptom improvement
- ↔ CV death and HF hospitalization
- ↑ All-cause death, LVAD or transplant
- ↓ Win ratio - mortality, morbidity & QOL

FDA labeling expansion 2023

Baseline demographics

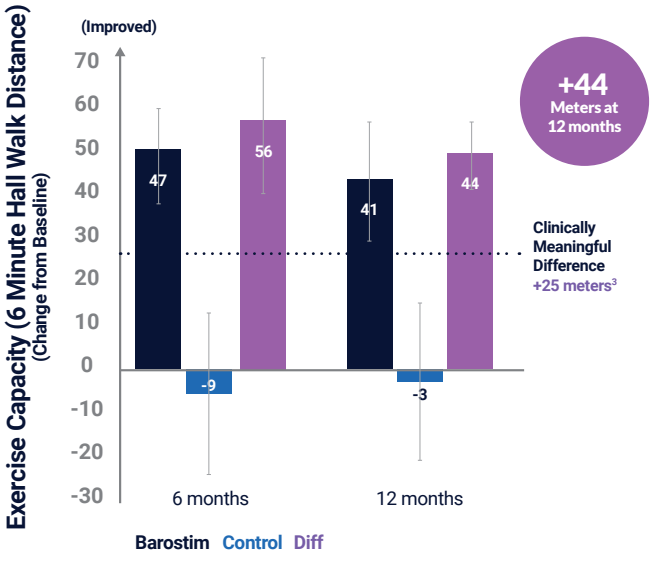
	Barostim (n=163)	Control (n=160)
Demographics		
Age at Screening (years)	63 ± 11	63 ± 10
Gender (Female)	28 (17.2%)	35 (21.9%)
Race (Caucasian)	120 (73.6%)	116 (72.5%)
Heart failure and physical status		
SBP (mmHg)	120 ± 16	121 ± 16
DBP (mmHg)	74 ± 10	73 ± 10
HR (bpm)	75 ± 10	75 ± 11
BMI (kg/m2)	31 ± 5	31 ± 5
eGFR	62.5 ± 16.3	61.1 ± 18.9
NYHA: Class III	155 (95.1%)	151 (94.4%)
LVEF (%)	27 ± 6	28 ± 6
6 Minute Walk (m)	314 ± 66	300 ± 71
QOL	53 ± 24	51 ± 24
NT-proBNP (pg/mL)	736 (474, 1057)	704 (442, 1044)
LBBB	4 (2.5%)	2 (1.3%)
>=1 HF Hospitalization	66 (40.5%)	79 (49.4%)
Number of HF Hospitalizations	0.6 ± 0.9	0.7 ± 0.8

	Barostim (n=163)	Control (n=160)
Co-Morbidities		
Coronary Artery Disease	104 (63.8%)	107 (66.9%)
Atrial Fibrillation	53 (32.5%)	66 (41.3%)
Stroke or TIA	29 (17.8%)	37 (23.1%)
Chronic Kidney Disease	45 (27.6%)	43 (26.9%)
Type II Diabetes	74 (45.4%)	80 (50.0%)
Heart failure treatment		
Number of Meds	4.0 ± 1.3	4.1 ± 1.5
ACE-I / ARB / ARNI	143 (88%)	129 (81%)
ARNI	57 (35%)	43 (27%)
Beta-Blocker	152 (93%)	147 (92%)
MRA	74 (45%)	64 (40%)
Diuretic	138 (85%)	139 (87%)
Ivabradine	4 (2.5%)	9 (5.6%)
ICD	125 (77%)	127 (79%)

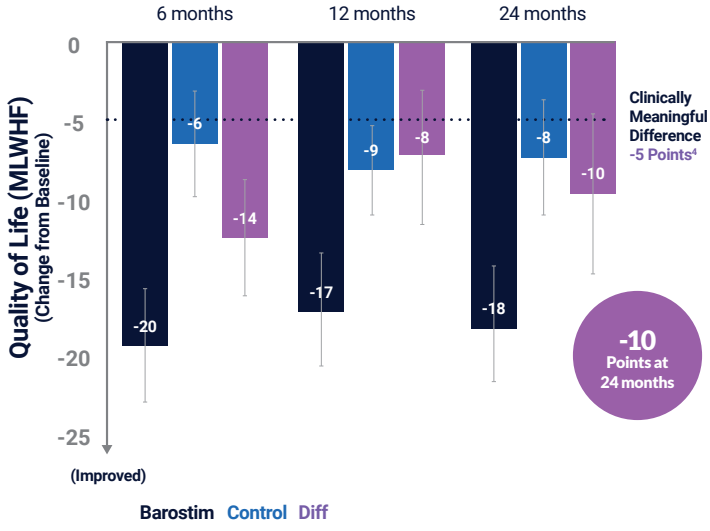
No significant difference between BAT and Control

Sustained symptomatic improvement & safety

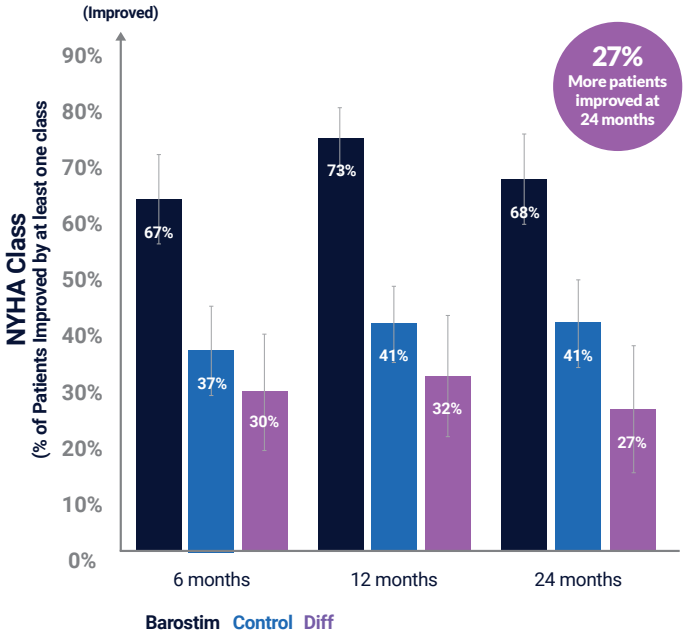
Exercise capacity (6MHW)[2]



Quality of life (MLWHF)[2]



Functional status (NYHA Class)[2]

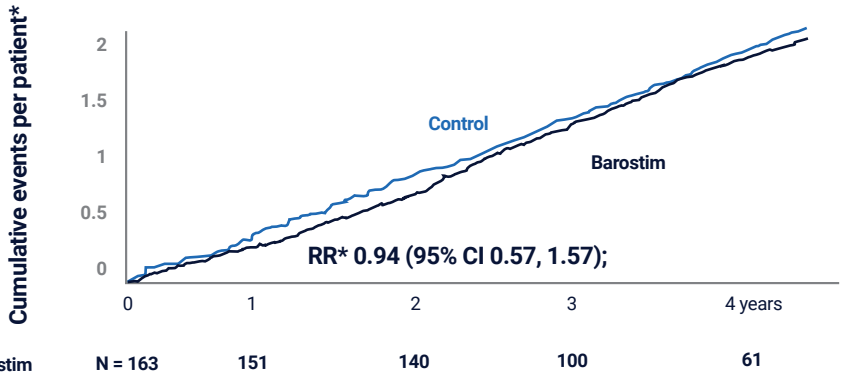


Safety profile: MANCE[2]

97%

Freedom from major adverse neurological or cardiovascular system or procedure-related event rate in the Barostim arm

Primary composite endpoint: CV mortality & HF morbidity[5]

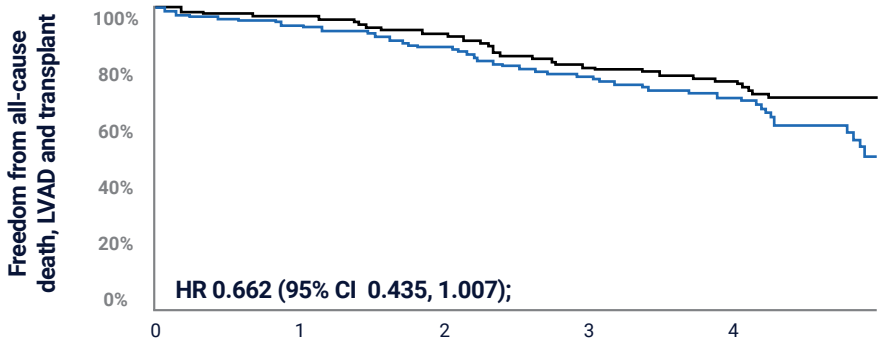


Barostim	N = 163	151	140	100	61

No statistically significant difference between BAT and Control

*Cumulative events per patient and rate ratio (RR) of treatment / control and 95% confidence interval estimated by negative binomial method

Freedom from all-cause death, LVAD, and transplant[2]



Barostim	N = 163	151	140	100	61
Control	N = 160	141	121	87	51

-34%
Relative reduction

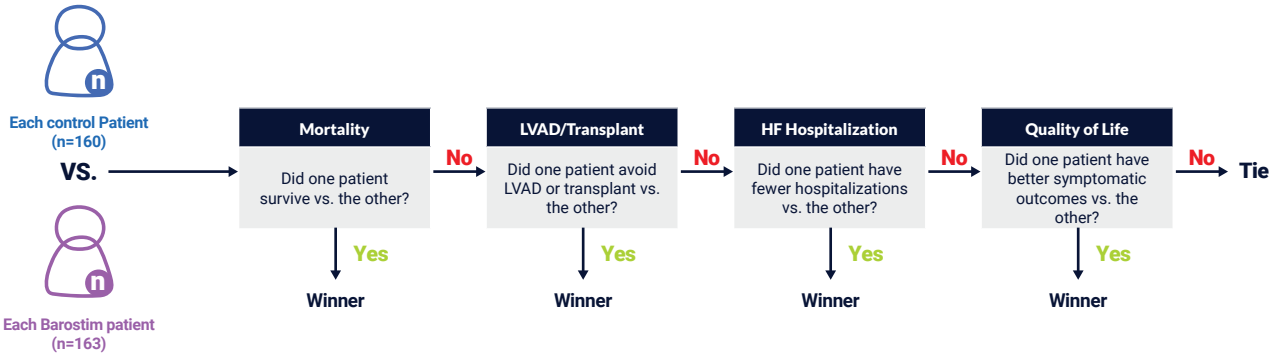
Patients in the Barostim arm had a 34% reduction in all-cause death or the use of LVAD or heart transplant at > 4 years follow-up

* Curves estimated using Kaplan-Meier method. Hazard ratio and p-value from Cox proportional hazards model.

Hierarchical composite using win ratio analysis[2]

Rationale:

- CV Mortality + HF Morbidity: 40% of patients contributed to the endpoint
- Win ratio: 100% of patients contribute to the endpoint



= 26,080 pairs

Win Ratio = Total wins for treatment arm / Total wins for control arm

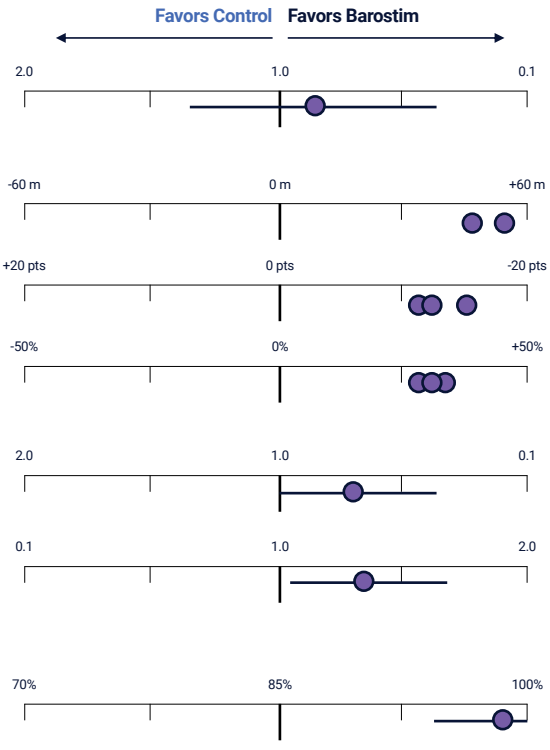
1.26

HR 1.26 (95% CI 1.02, 1.58)

26% more patients in the Barostim arm had better outcomes as evaluated by hierarchical composite of CV mortality, LVAD/transplant, HF hospitalization and quality of life

BeAT-HF summary of key evidence[5]

Primary Endpoint	**CV Mortality and HF Morbidity**	Rate Ratio = 0.94	
Long-term Symptom Improvement	**Exercise Capacity – 6MHW** (6 / 12-month improvement vs. control)	+55 / +44	
	Quality of Life – MLWHF (6 / 12 / 24-month improvement vs. control)	-13 / -8 / -10	
	Functional Status – NYHA Class % Improved (6 / 12 / 24-month improvement vs. control)	30% / 32% / 27%	
Additional Endpoints	**All-cause Mortality*** (6 / 12 / 24-month improvement vs. control)	Hazard Ratio = 0.66	
	Hierarchical Win Ratio* (CV mortality, HF morbidity, QOL)	Win Ratio = 1.26	
Long-term Safety	**Related MANCE-free Rate** (Major Adverse Neurologic and Cardiac Events)	96.9%	



1. Zile MR, et al. J Am Coll Cardiol. 2020;76(1):1-13; 2. Instructions for Use 900133-001 Rev. D available at www.cvrx.com/ifu; 3. Gremeaux V, et al. Arch Phys Med Rehabil. 2011;92(4):611-619; 4. Rector TS, et al. J Card Fail. 1995;1(3):201-216; 5. Zile M, Presented at THT 2023, March 21, 2023.

Important Safety Information

CAUTION: Federal law restricts this device to sale by or on the order of a physician. See System Reference Guide 900120-001 or 900133-001 for a complete instruction for use and a description of indications, contraindications, warnings, precautions and adverse events.

Barostim™ Brief Summary for Physicians
The Barostim™ System is indicated for the improvement of symptoms of heart failure—quality of life, six-minute hall walk and functional status—for patients who remain symptomatic despite treatment with guideline-directed medical therapy, are NYHA Class III or Class II (who had a recent history of Class III), have a left ventricular ejection fraction ≤ 35%, a NT-proBNP < 1600 pg/ml and excluding patients indicated for Cardiac Resynchronization Therapy (CRT) according to AHA/ACC/ESC guidelines.

Patients are contraindicated if they have been assessed to have bilateral carotid bifurcations located above the level of the mandible, baroreflex failure or autonomic neuropathy, uncontrolled symptomatic cardiac bradyarrhythmias, carotid atherosclerosis that is determined by ultrasound or angiographic evaluation greater than 50%, ulcerative plaques in the carotid artery as determined by ultrasound or angiographic evaluation, known allergy to silicone or titanium.

Warnings include: only trained physicians may use this system, prescribing physicians should be experienced in the diagnosis and treatment of heart failure and should be familiar with the use of this system, monitor blood pressure and heart rate during Carotid Sinus Lead placement and when adjusting stimulation parameters intra-operatively, post-implantation, program the system to avoid the following: heart rate falls below 50 beats per minute (BPM), or systolic pressure falls below 90 mmHg, or diastolic blood pressure falls below 50 mmHg, or problematic adjacent tissue stimulation is noted, or undesirable interaction indicated by monitoring of any other implanted electrical device (see "Device Interaction Testing" in Section 10), or any other potentially hazardous patient responses are observed. Improper system implantation could result in serious injury or death. Do not use diathermy therapy including shortwave, microwave, or therapeutic ultrasound diathermy on patients implanted with the system. Patients should be counseled to stay at least 15 cm (6 inches) away from devices with strong electrical or magnetic fields such as strong magnets, loudspeaker magnets, Electronic Article Surveillance (EAS) system tag deactivators, arc welders, induction furnaces, and other similar electrical or electromechanical devices. This would include not placing items such as earphones in close proximity to the implanted pulse generator. The IPG may affect the operation of other implanted devices such as cardiac defibrillators, pacemakers, or neurological stimulation systems. For patients who currently have an implanted electrical medical device, physicians must verify compatibility with the implanted device during implantation of the system. Contralateral implant of the Barostim System may help to reduce potential interactions. Interactions are more likely in devices that contain a sensing function, such as an implantable cardiac defibrillator or pacemaker. If an interaction is observed, the Barostim System should be programmed to reduced therapy output settings in order to eliminate the interaction. If necessary, change settings in the other implant only if the changes are not expected to negatively impact its ability to perform its prescribed therapy. During the implant procedure, if device interactions cannot be eliminated the Barostim System should not be implanted.

Precautions include: the system should be implanted and programmed carefully to avoid stimulation of tissues near the electrode or in the area of the IPG pocket. Such extraneous stimulation could involve the following: the regional nerves, causing laryngeal irritation, difficulty swallowing, or dyspnea, the cervical musculature, causing intermittent contraction, skeletal muscles, causing intermittent contraction around the IPG pocket. Proper sterile technique during implantation should be practiced and aggressive pre-operative antibiotics are recommended. Infections related to any implanted device are difficult to treat and may necessitate device explantation.

It is anticipated that subjects will be exposed to operative and post-operative risks similar to related surgical procedures involving the neck and/or a pacemaker implant. These risks and potential risks of chronic device based baroreflex activation may include, but are not limited to: stroke, transient ischemic attack (TIA), systemic embolization, surgical or anesthetic complications, infection, wound complications, arterial damage, pain, nerve damage/stimulation, hypotension, hypertensive crisis, respiratory, exacerbation of heart failure, cardiac arrhythmias, tissue erosion/IPG migration, injury to baroreceptors, fibrosis, allergic reaction, general injury to user or patient, need for reoperation, secondary operative procedure, and death. Patients implanted with the system may receive Magnetic Resonance Imaging (MRI) only when all MR Conditional safety parameters are met as listed in the instructions for use.

For a list of all potential benefits and risks go to www.cvrx.com/benefit-risk-analysis/

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