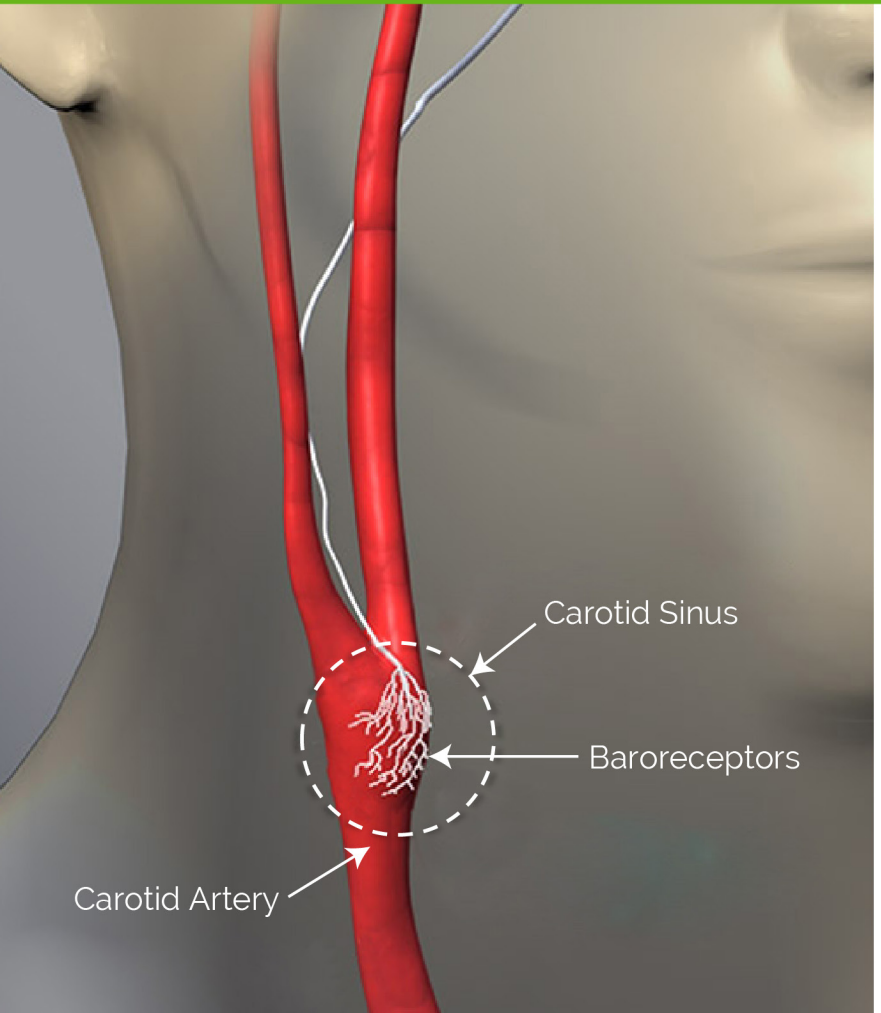
BAROSTIM THERAPY™

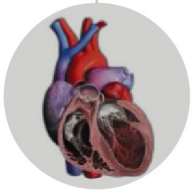
Images

BAROSTIM NEO™ MECHANISM OF ACTION



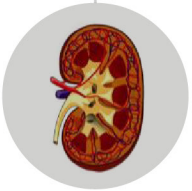
Carotid Baroreceptor Stimulation
Afferent Signaling

Integrated Autonomic Nervous System Response
Inhibits Sympathetic Activity
Enhances Parasympathetic Activity



↓ Heart Rate
↓ Remodeling

↑ Vasodilation
↓ Elevated BP



↑ Diuresis
↓ Renin Secretion

BAROSTIM NEO™ MECHANISM OF ACTION

3. Brain

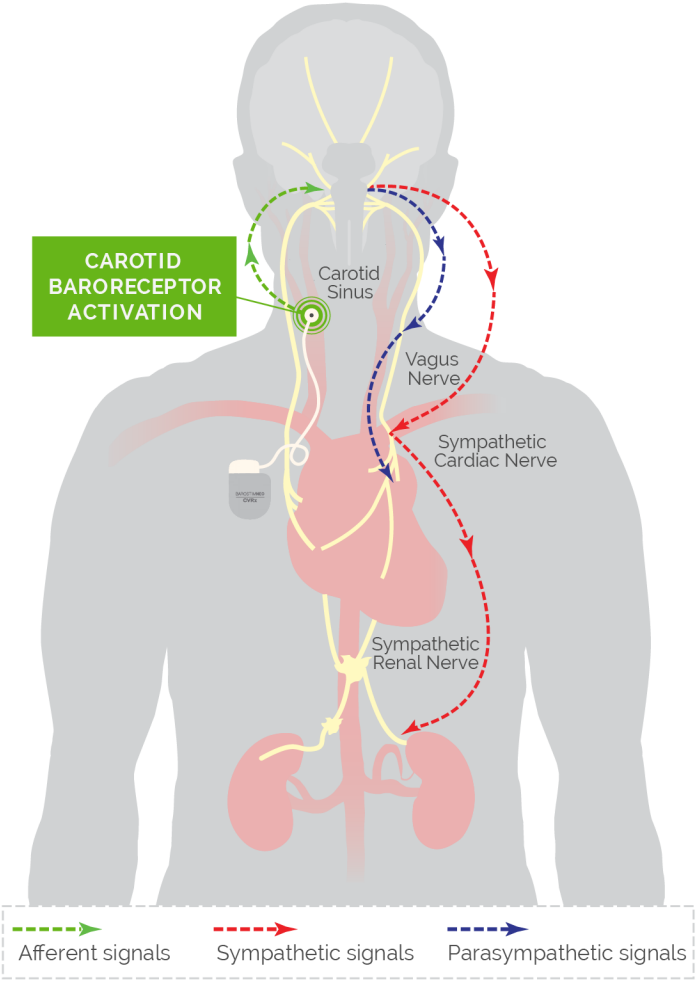
- Control board for autonomic nervous system
- Achieves autonomic balance by reducing sympathetic activity while increasing parasympathetic activity

2. Baroreceptors

- Sensors that provide information to the central nervous system, which are used in autonomic reflexes and act as part of the baroreflex
- Stimulated by BAROSTIM THERAPY™

1. BAROSTIM NEO

- A single electrode delivering continuous stimulation that is powered by a novel pulse generator
- Activates the baroreflex



4. Heart

↓ HR ↓ Remodeling

- Reduces myocardial work
- Reduces oxygen consumption

5. Blood Vessels

↑ Vasodilation ↑ Venous capacitance

- Reduces cardiac afterload
- Reduces pulmonary congestion

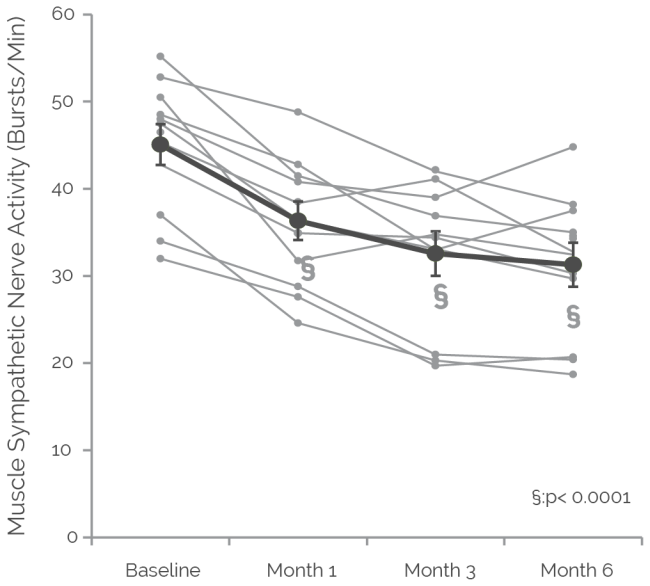
6. Kidneys

↑ Diuresis ↓ Renin secretion

- Reduces neurohormonal stimulus
- Reduces fluid retention

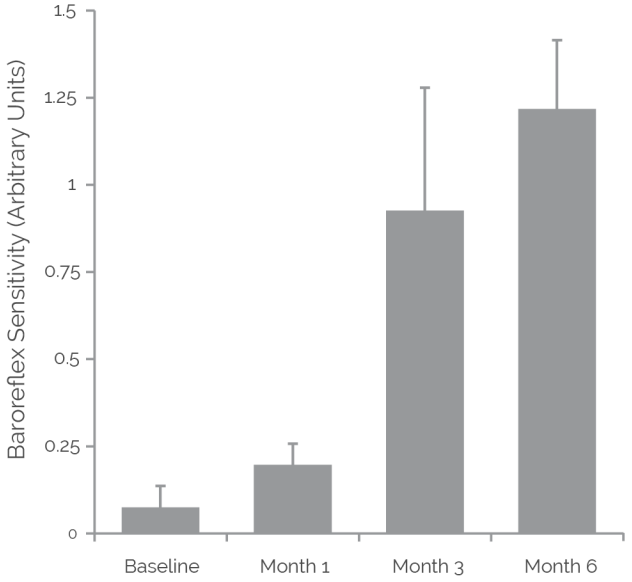
PHASE I: BAT-HF TRIAL DEMONSTRATES MECHANISM OF ACTION

Sympathetic Activity



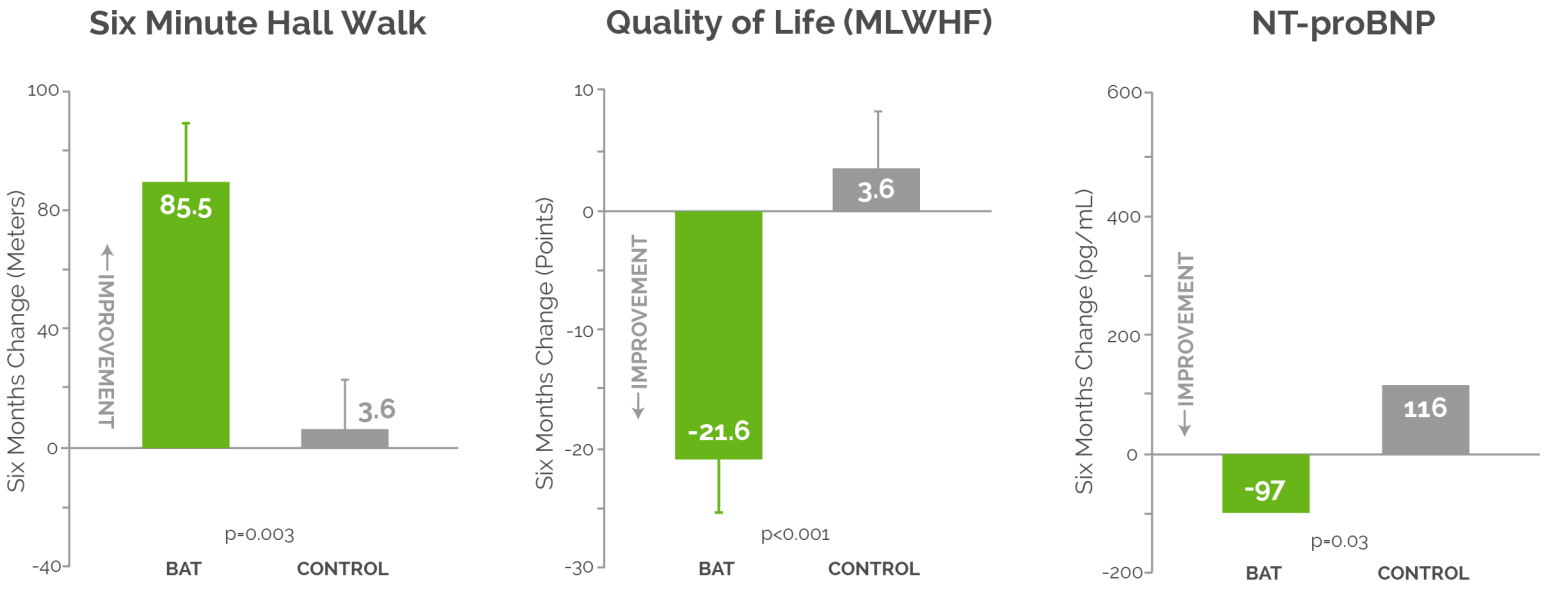
Gronda E, et al., EJHF 2014

Parasympathetic Activity



BAROSTIM THERAPY™ restores the sympatho-vagal balance
by decreasing sympathetic activity and increasing parasympathetic activity.

PHASE II: HOPE4HF TRIAL DEMONSTRATES IMPROVEMENT IN 6MHW, QOL AND NT-PROBNP

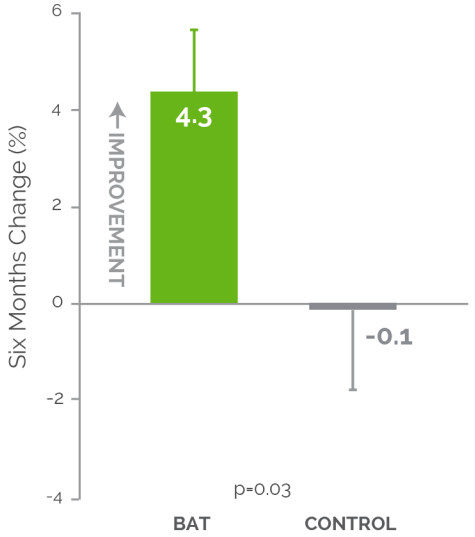


Zile MR, et al. Eur J Heart Fail 17: 1066-1074, 2015.

The HOPE4HF Trial demonstrates six month improvement between the arms in Six Minute Hall Walk of 82 meters (p=0.003), Minnesota Living with Heart Failure Quality of Life of 25 points (p<0.001) and NT-proBNP of 318 pg/mL (p=0.03).

PHASE II: HOPE4HF TRIAL DEMONSTRATES IMPROVEMENT IN LVEF AND HF HOSPITALIZATION

Left Ventricular Ejection Fraction



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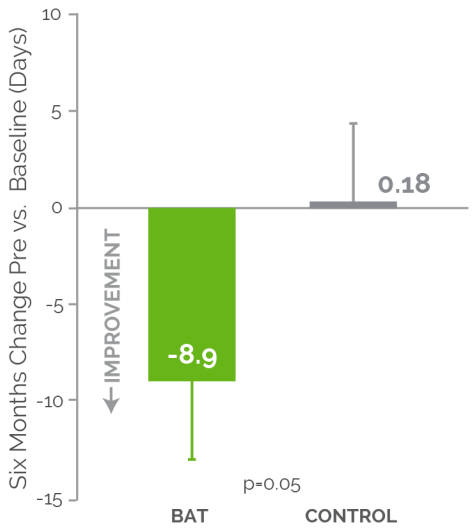
Heart Failure Hospitalization Days



The HOPE4HF Trial demonstrated improvement in LVEF of 4.4% (p=0.03) between the arms at six months and a decrease between the arms of almost 9 days of hospitalization for heart failure comparing six months before BAT implant to six months after BAT implant (p=0.05).

PHASE III: BEAT-HF BASELINE CHARACTERISTICS

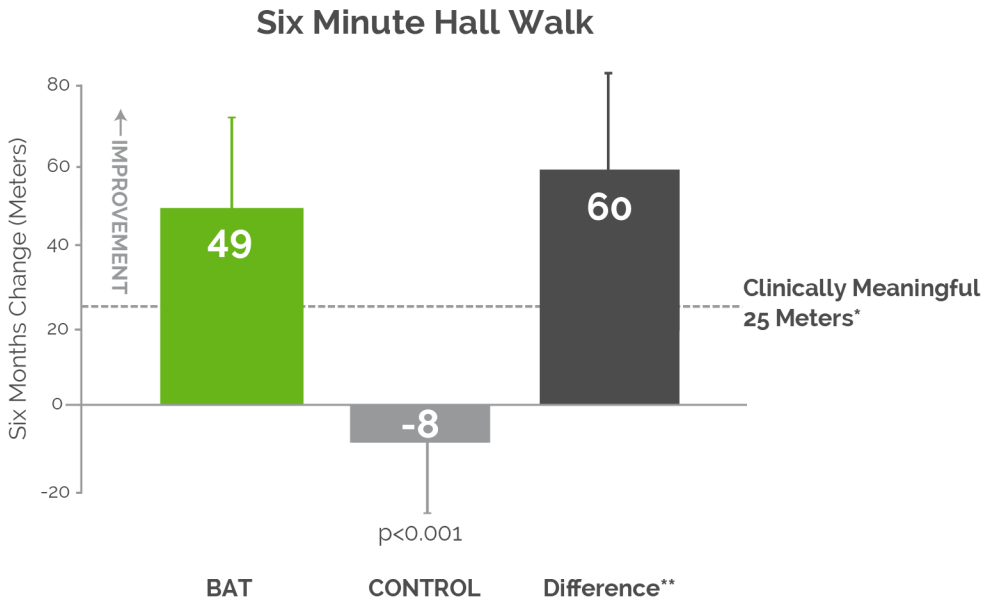
BeAT-HF Baseline Demographics

VARIABLE	BAT (n=130)	CONTROL (n=134)
DEMOGRAPHICS		
Age (years)	62 ± 11	63 ± 10
Gender: Female	19%	22%
Race: Caucasian	75%	72%
HEART FAILURE AND PHYSICAL STATUS		
NYHA: Class III	93%	95%
MLWHF QOL Score	53 ± 24	52 ± 24
6 Minute Hall Walk Distance (m)*	316 ± 68	294 ± 73
HR (bpm)	75 ± 10	75 ± 11
SBP (mmHg)	120 ± 17	121 ± 16
DBP (mmHg)	73 ± 10	73 ± 10
LVEF (%)	27 ± 7	28 ± 6
NT-pro BNP (pg/mL, Median [IQR])	731 [475, 1021]	765 [479, 1052]
eGFR (mL/min)	64 ± 17	62 ± 20
QRS Interval	109 ± 18	110 ± 26
Previous HF hospitalization	42%	51%

BeAT-HF Baseline Therapies

VARIABLE	BAT (n=130)	CONTROL (n=134)
CO-MORBIDITIES		
Coronary Artery Disease	80%	92%
Atrial Fibrillation	38%	57%
Stroke or TIA	24%	30%
Chronic Kidney Disease	31%	33%
Diabetes Type II	58%	68%
HEART FAILURE TREATMENT		
Number of Meds	3.9 ± 1.2	4.1 ± 1.4
ACE-I/ARB/ARNI	89%	84%
Beta-Blocker	95%	95%
MRA	49%	42%
Diuretic	85%	87%
Ivabradine	2%	5%
ICD	78%	79%

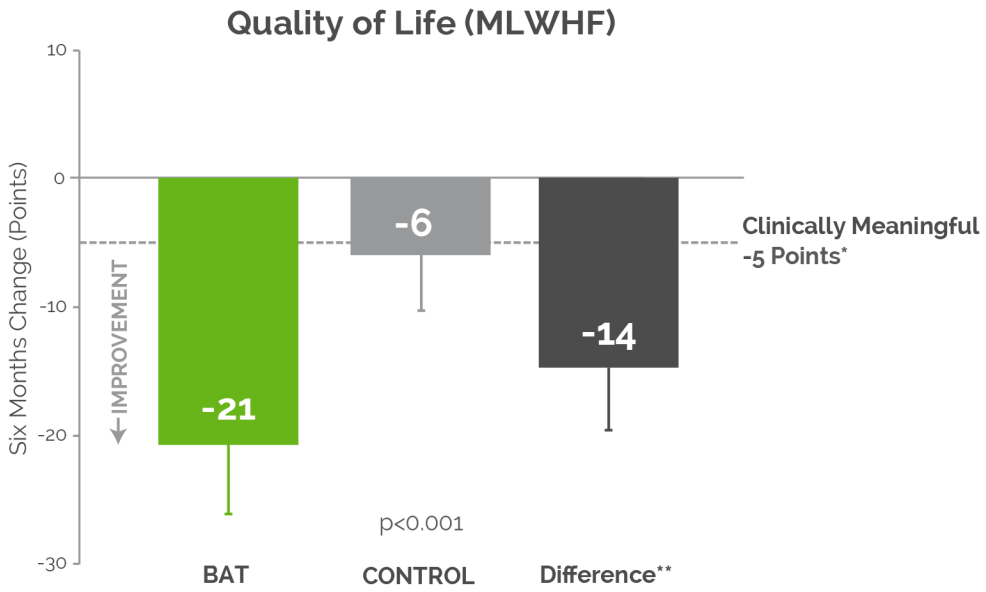
PHASE III: BEAT-HF TRIAL DEMONSTRATES IMPROVEMENT IN EXERCISE CAPACITY



Zile MR, et al. JACC 2020;76 (1):1-13.
*Gremeaux V, et al. Arch Phys Med Rehabil 2011 Apr;92(4):611-9.
**Mean + 95% confidence interval. Differences analyzed by ANCOVA adjusted for baseline values.

The BeAT-HF trial demonstrated improvement at six months in exercise capacity of 60 meters ($p<0.001$) as measured by the six-minute hall walk test. This observed improvement is more than twice the clinically meaningful amount of 25 meters.

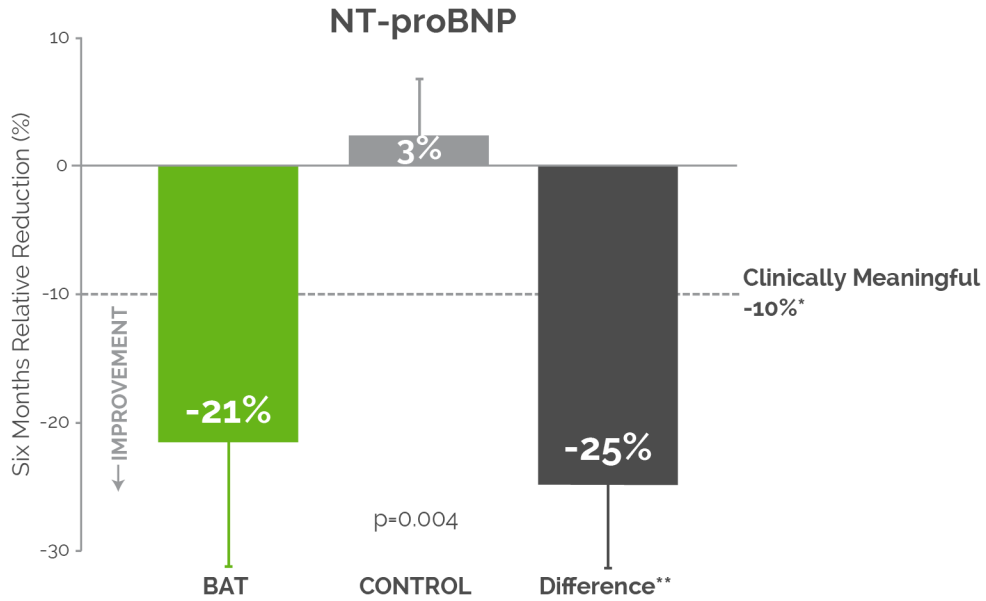
PHASE III: BEAT-HF TRIAL DEMONSTRATES IMPROVEMENT IN QUALITY OF LIFE



Zile MR, et al. JACC 2020;76 (1):1-13.
*Rector TS, et al J Cardiac Failure 1995;1:201-206.
**Mean + 95% confidence interval. Differences analyzed by ANCOVA adjusted for baseline values.

The BeAT-HF trial demonstrated improvement at six months in quality of life of 14 points (p<0.001) as measured by the Minnesota Living with Heart Failure questionnaire. This observed improvement is almost three times the clinically meaningful amount of 5 points.

PHASE III: BEAT-HF TRIAL DEMONSTRATES IMPROVEMENT IN NT-PROBNP



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*Zile MR, et al. JACC 2016;68 (22)2425–2436.
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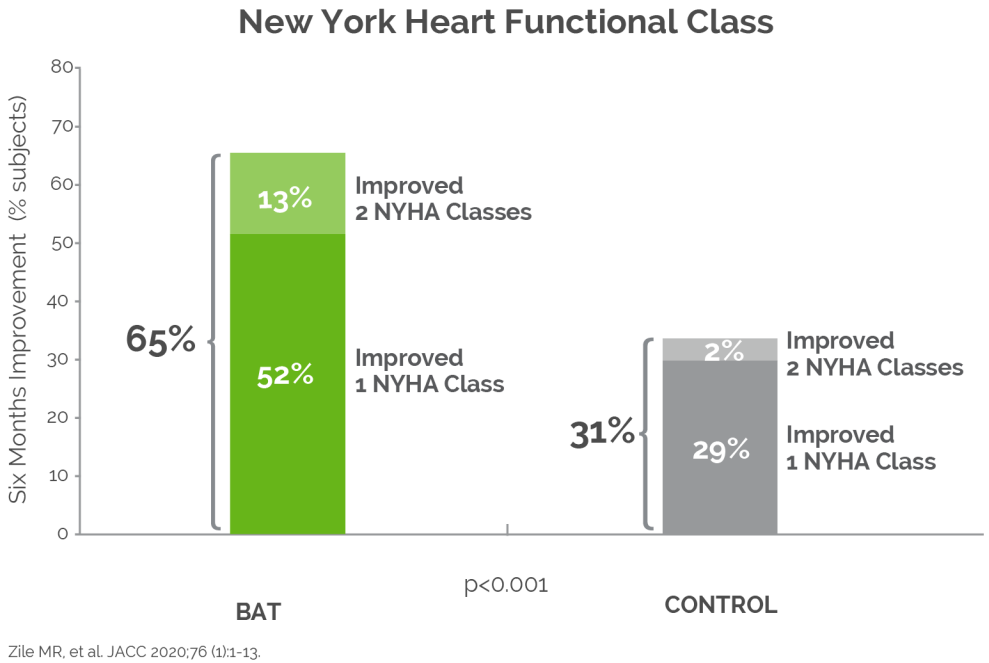
The BeAT-HF trial demonstrated improvement at six months in NT-proBNP of a 25% relative reduction (p=0.004). This observed improvement is more than twice the clinically meaningful amount of a 10% relative reduction.

PHASE III: BEAT-HF TRIAL DEMONSTRATES IMPROVEMENT IN FUNCTIONAL STATUS

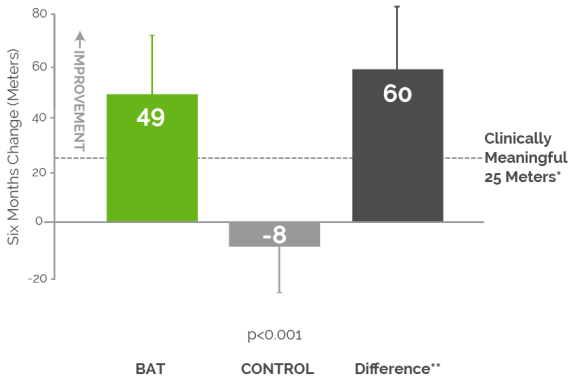


Zile MR, et al. JACC 2020;76 (1):1-13.

The BeAT-HF trial demonstrated improvement at six months in New York Heart Class with 65% of the subjects in the BAROSTIM THERAPY arm improving at least one class compared to 31% in the control arm (p<0.001). Thirteen percent (13%) of the BAROSTIM THERAPY arm improved 2 classes compared to 2% of the control arm.

PHASE III: BEAT-HF TRIAL DEMONSTRATES SYMPTOMATIC IMPROVEMENT AT SIX MONTH

Six Minute Hall Walk



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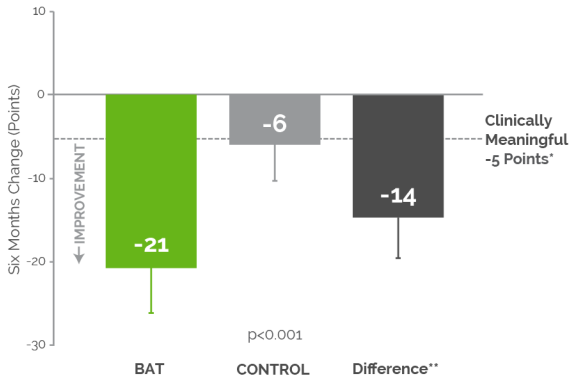
Quality of Life (MLWHF)



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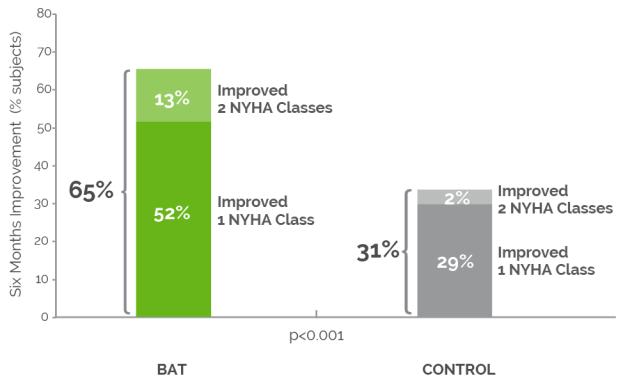
New York Heart Functional Class



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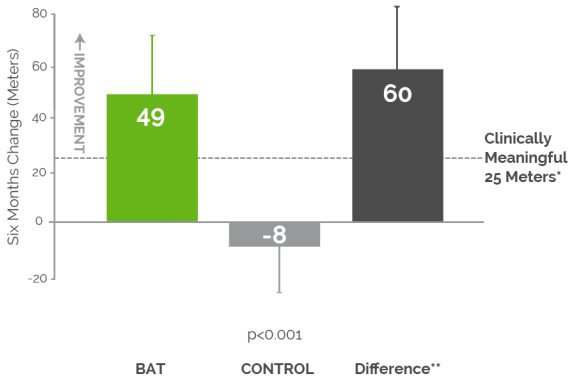
PHASE III: BEAT-HF TRIAL DEMONSTRATES IMPROVEMENT AT SIX MONTH

Six Minute Hall Walk



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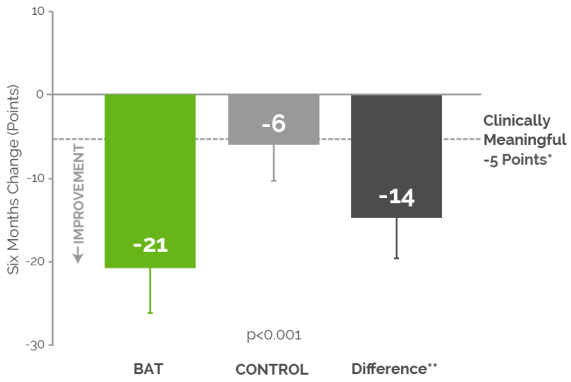

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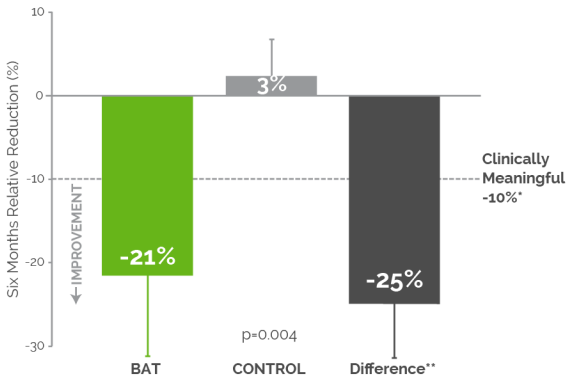
NT-proBNP



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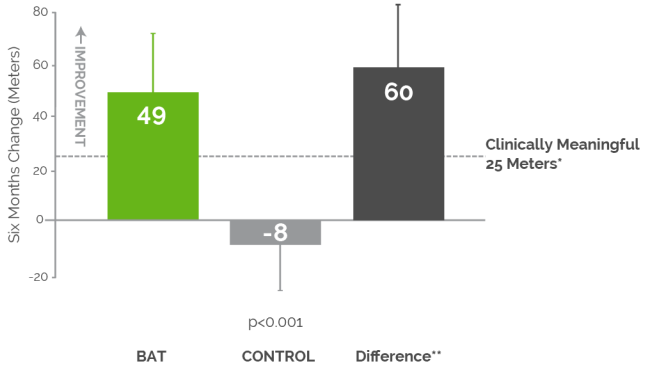
PHASE III: BEAT-HF TRIAL DEMONSTRATES IMPROVEMENT AT SIX MONTH

Six Minute Hall Walk



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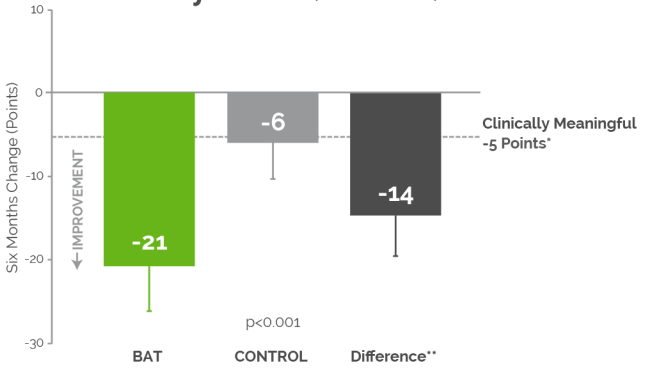

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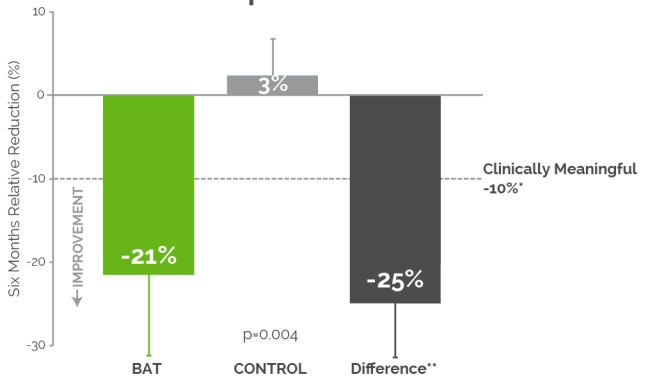
NT-proBNP



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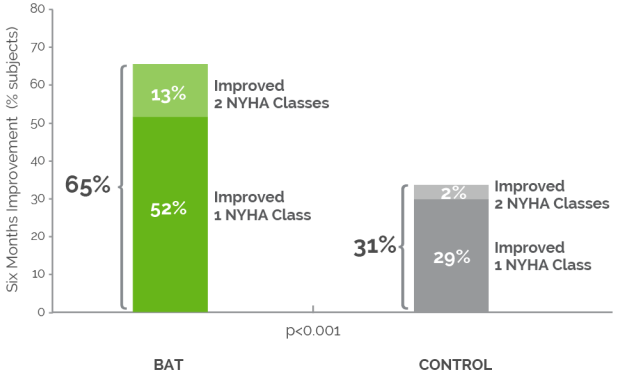
New York Heart Functional Class



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