A Randomized, Controlled Trial of Baroreflex Activation Therapy (BAT) in Patients with Heart Failure and Reduced Ejection Fraction (HFrEF)

BeAT-HF

(ClinicalTrial.gov Identifier: NCT02627196)

The BeAT-HF Executive Steering Committee

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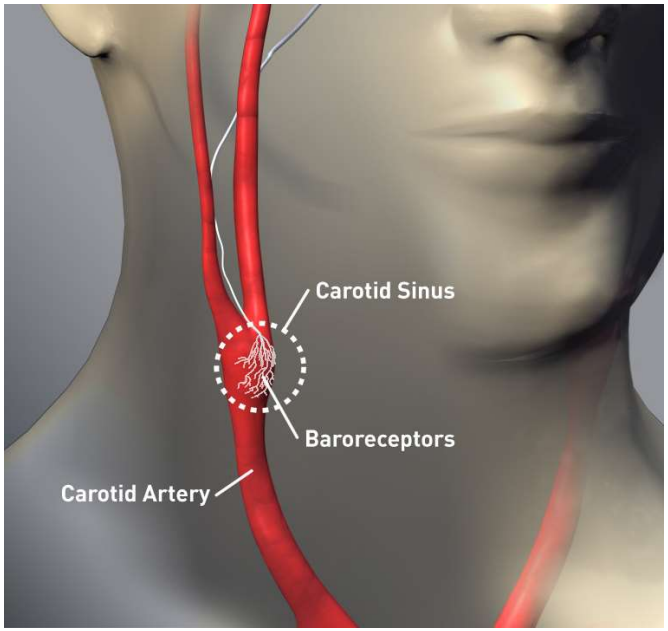
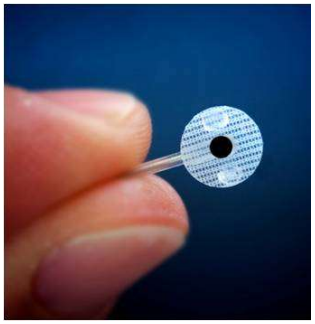
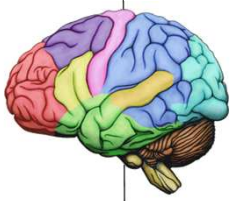
Sponsor
CVRx, Inc.

Mechanism of BAT in HFrEF





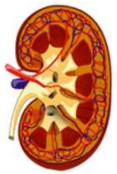
Carotid Baroreceptor Stimulation
Afferent Signaling



Integrated Autonomic Nervous System Response
Inhibits Sympathetic Activity
Enhances Parasympathetic Activity

↓ **Heart Rate**
↓ **Remodeling**

↑ **Vasodilation**
↓ **Elevated BP**



↑ **Diuresis**
↓ **Renin secretion**

BeAT-HF Pivotal Study

Purpose:

- Demonstrate safety and effectiveness of BAT in HFrEF patients using the FDA Breakthrough Devices Program

Design:

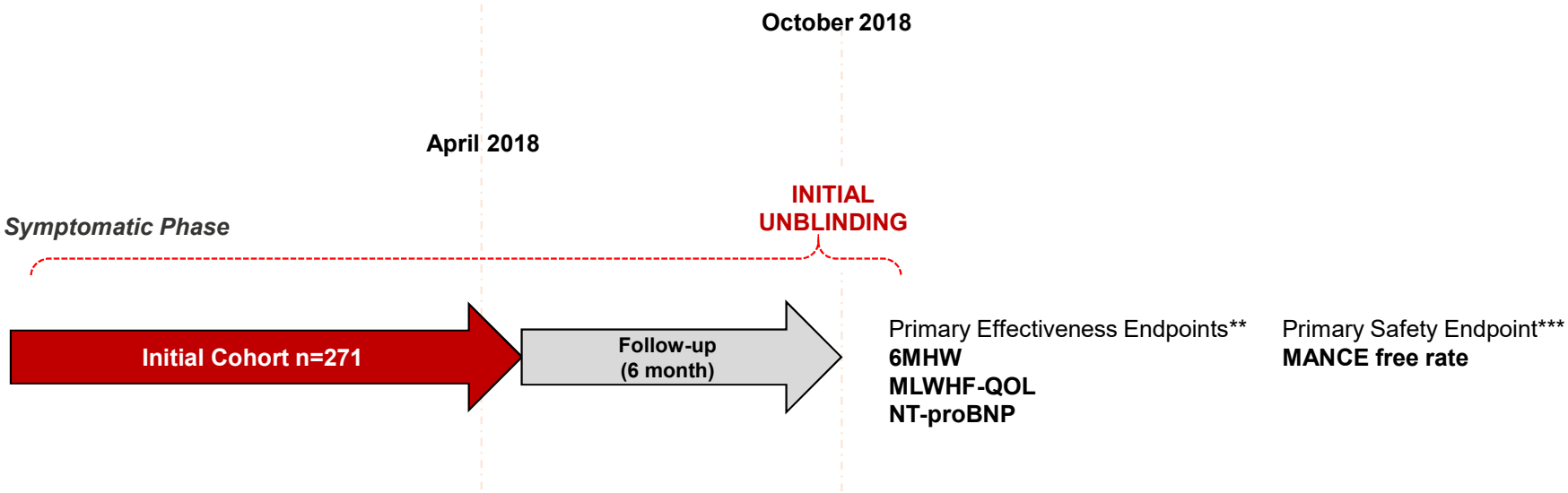
- Multicenter, prospective, randomized controlled trial
- Randomized 1:1 to receive BAT plus optimal medical management (“BAT”) or optimal medical management alone (“Control”)

BeAT-HF Key Eligibility Criteria

- NYHA Functional Class III
- Left ventricular ejection fraction ≤ 35%
- Six-minute hall walk distance (6MHW) 150 – 400 m
- Elevated NT-proBNP or previous Heart Failure Hospitalization
- Stable optimal medical therapy ≥ 4 weeks
- CRT-eligible subjects are excluded

No restriction on AF, QRS width or concomitant devices

BeAT-HF Trial Design*

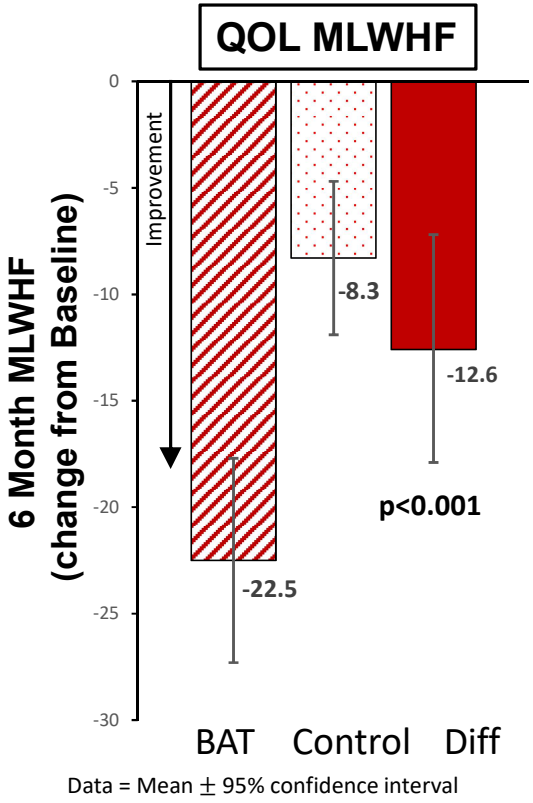


*Developed collaboratively with FDA
**Measured as changes from baseline to 6 months
***Major Adverse Neurological and Cardiovascular Event free rate, compared to a performance criteria of 85%

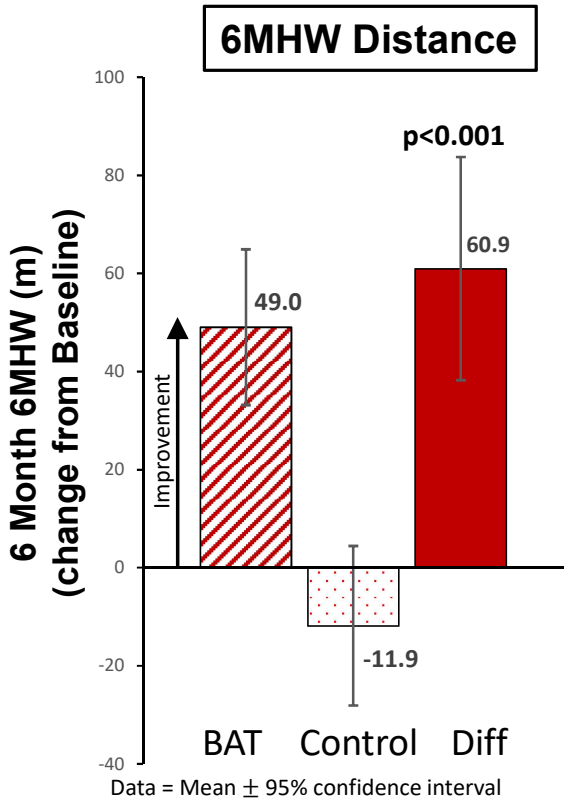
BEAT-HF Initial Cohort: Safety Endpoint Met And 2 of 3 Primary Efficacy Endpoints Met

MANCE

- MANCE-free rate : **94%** (118/125)
- Exceeded performance criteria of 85% with p-value < 0.001



Data = Mean ± 95% confidence interval



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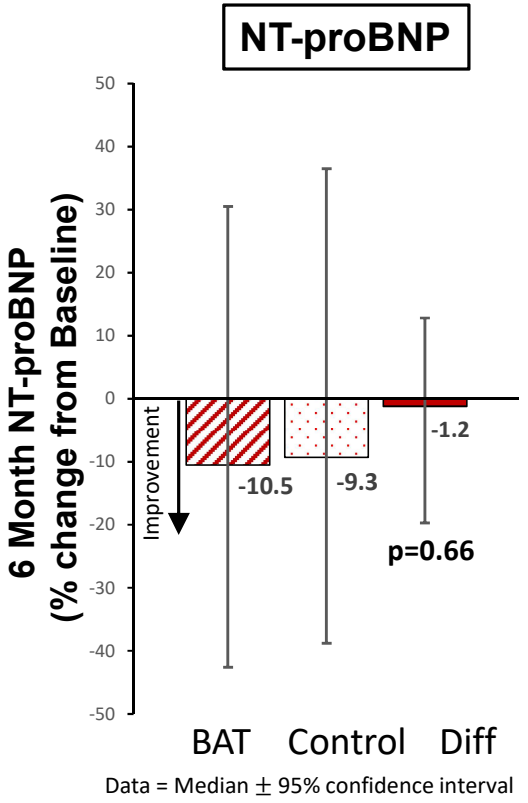
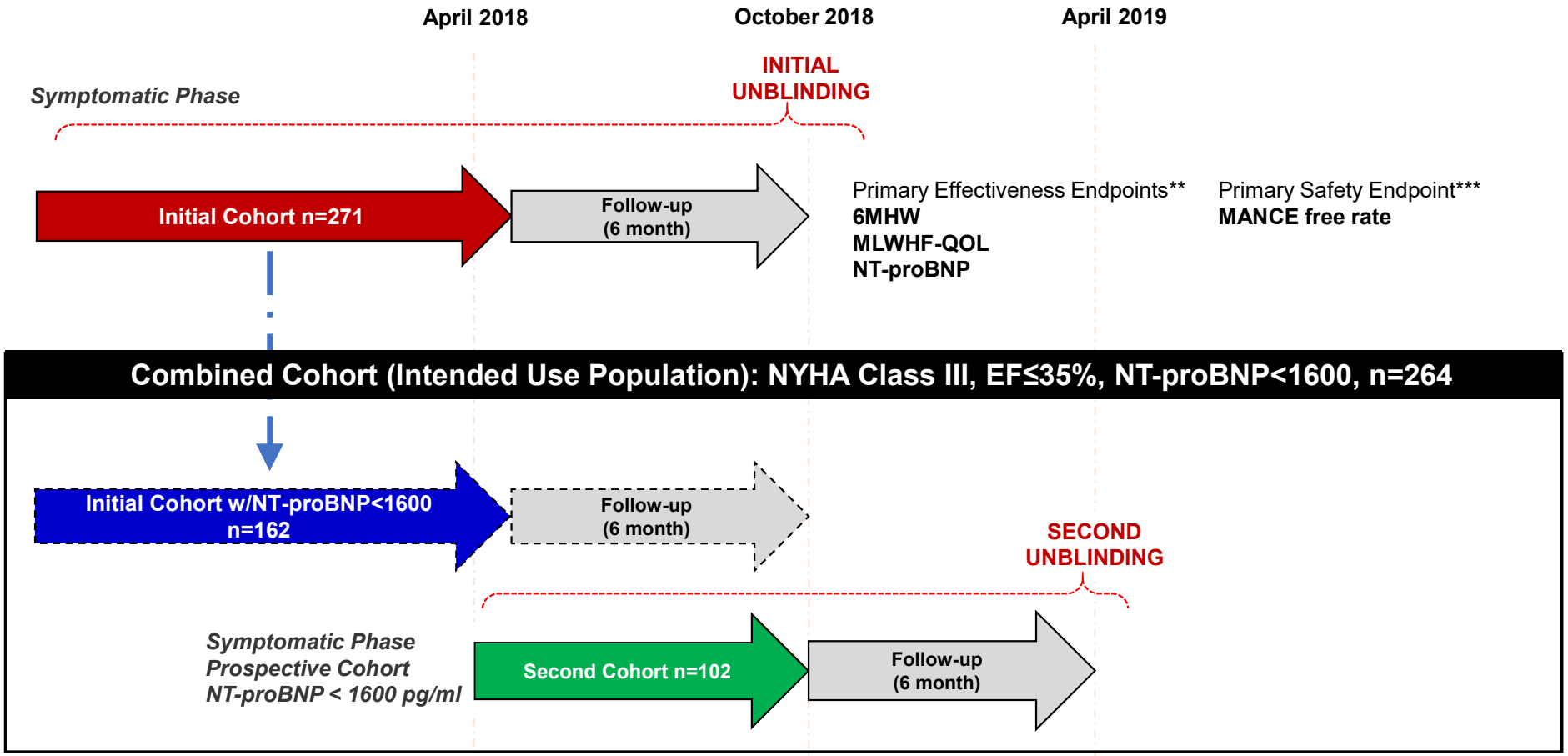


Data = Median ± 95% confidence interval

BeAT-HF Final Trial Design*



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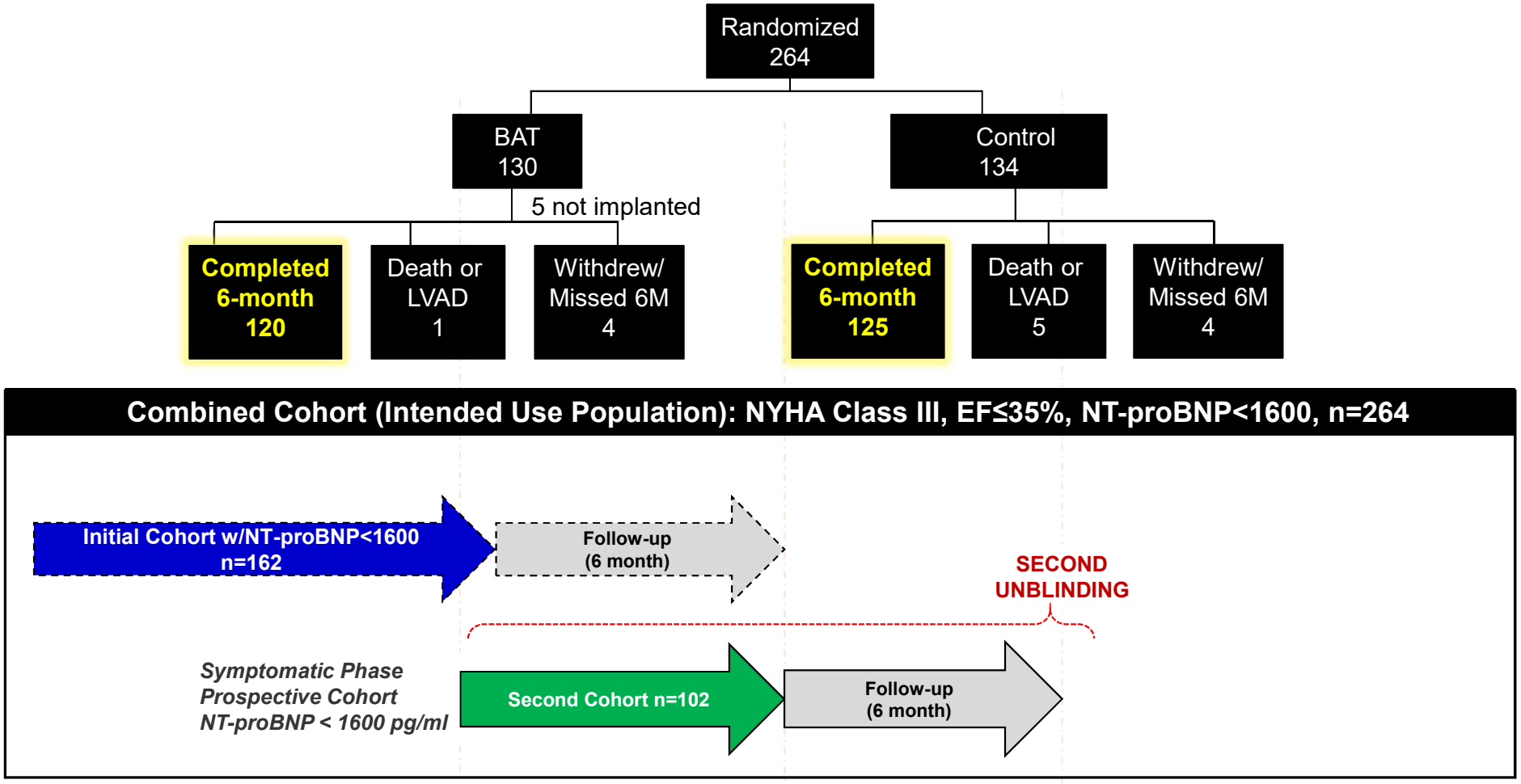
BeAT-HF Final Trial Design*



*Developed collaboratively with FDA

BeAT-HF Baseline Demographics for Combined Cohort

Variable	BAT (n=130)	Control (n=134)
Age (years)	62 ± 11	63 ± 10
Gender: Female	19%	22%
Race: Caucasian	75%	72%
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
History of Atrial Fibrillation	29%	42%
History of Coronary Artery Disease	62%	69%
Previous HF hospitalization	42%	51%

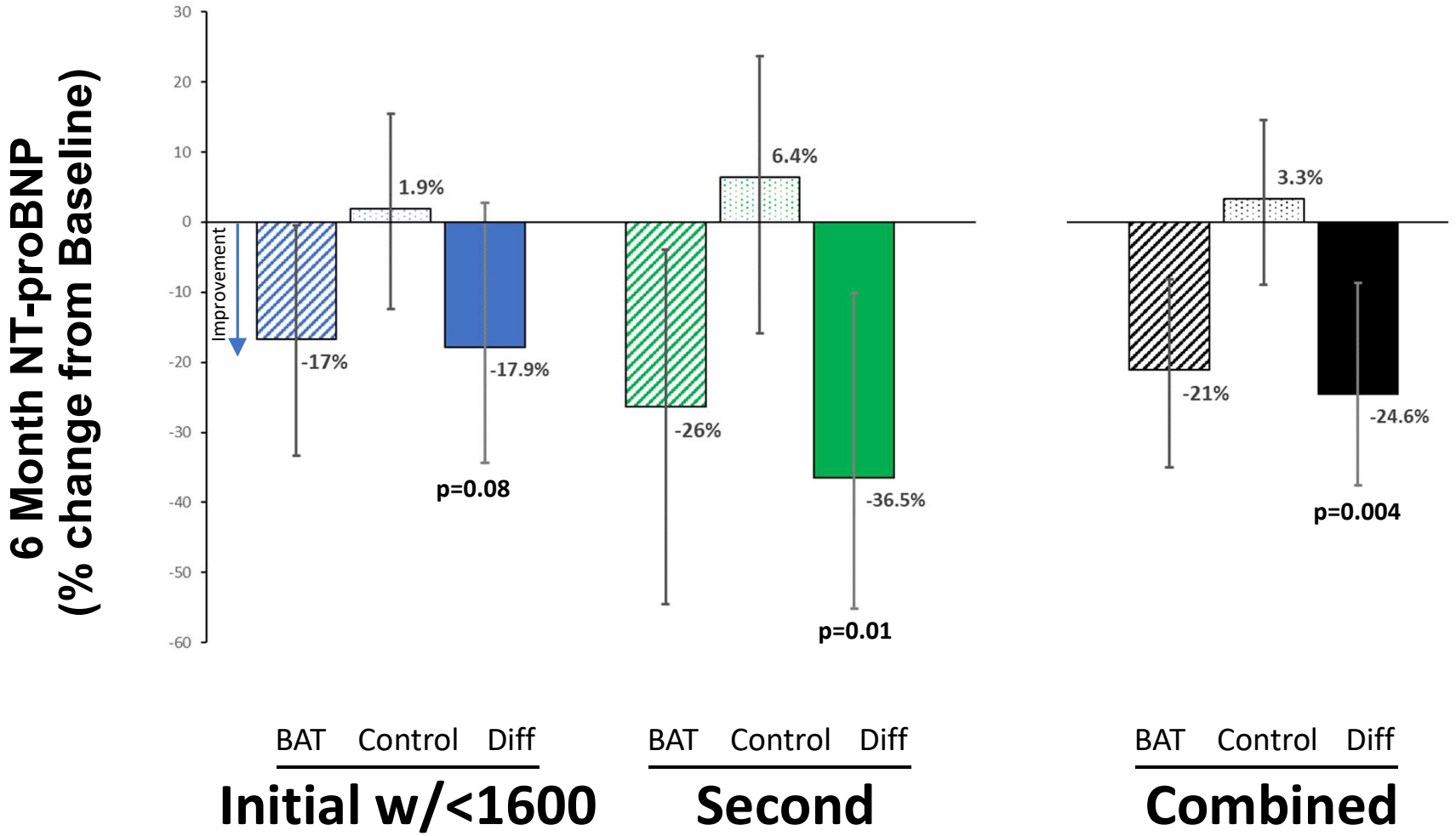
No significant difference between BAT and Control: none below 0.01, 6MHW p=0.015, AF p=0.03, all others > 0.05

BeAT-HF Baseline Therapies for Combined Cohort

Variable	BAT (n=130)	Control (n=134)
Number of Meds	3.9 ± 1.2	4.1 ± 1.4
ACE-I/ARB/ARNI	89%	85%
Beta-Blocker	95%	95%
MRA	49%	42%
Diuretic	85%	87%
Ivabradine	2%	5%
ICD	78%	79%

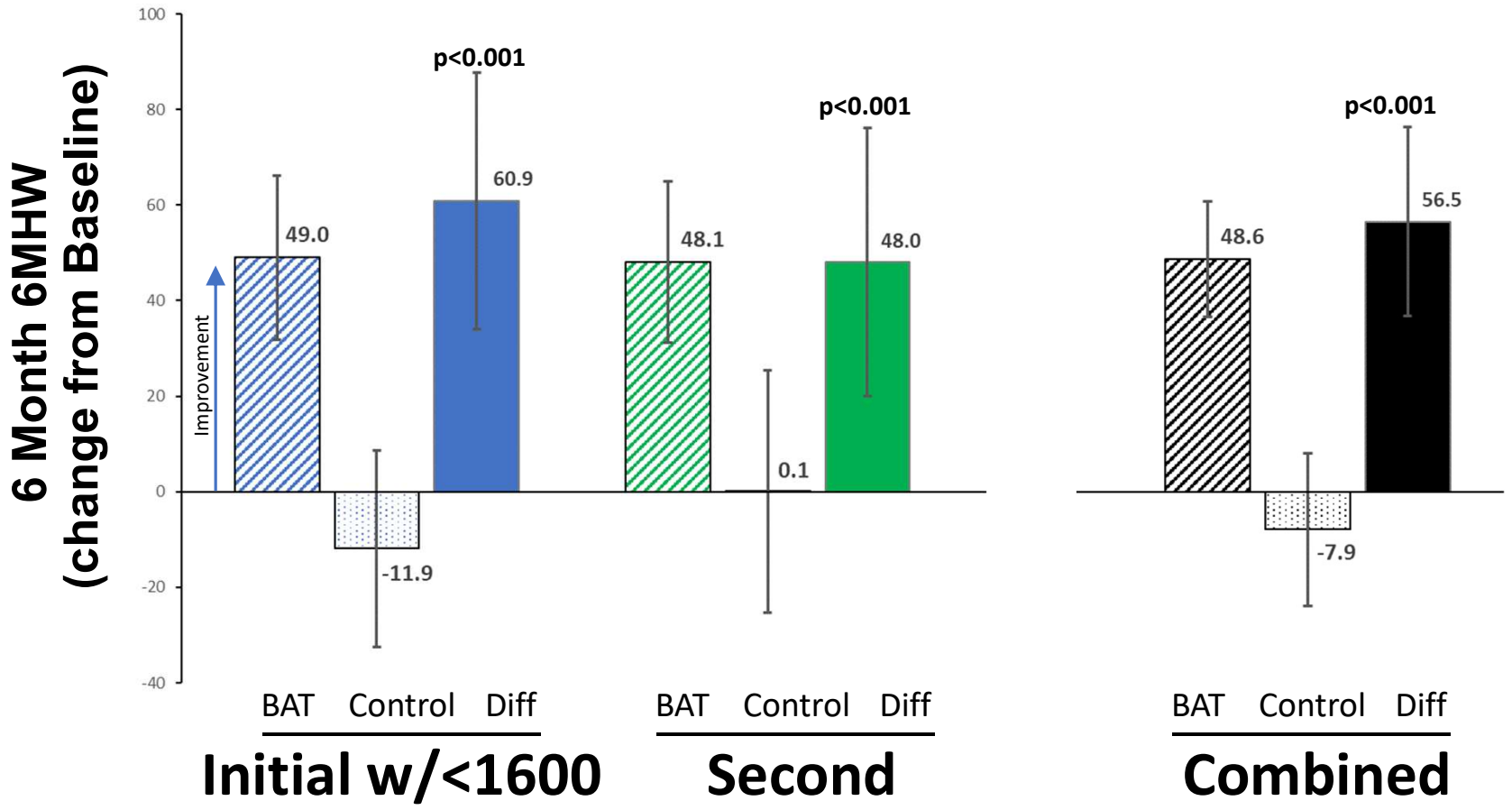
No significant difference between BAT and Control

BAT Significantly Reduces NT-proBNP



Data = Mean ± 95% confidence interval, all differences analyzed using Log10 transformed NT-proBNP by ANCOVA adjusted for baseline values
Zile MR, et al. LBCT01-04, Heart Rhythm Society Annual Scientific Sessions, May 2019

BAT Significantly Improves Functional Capacity



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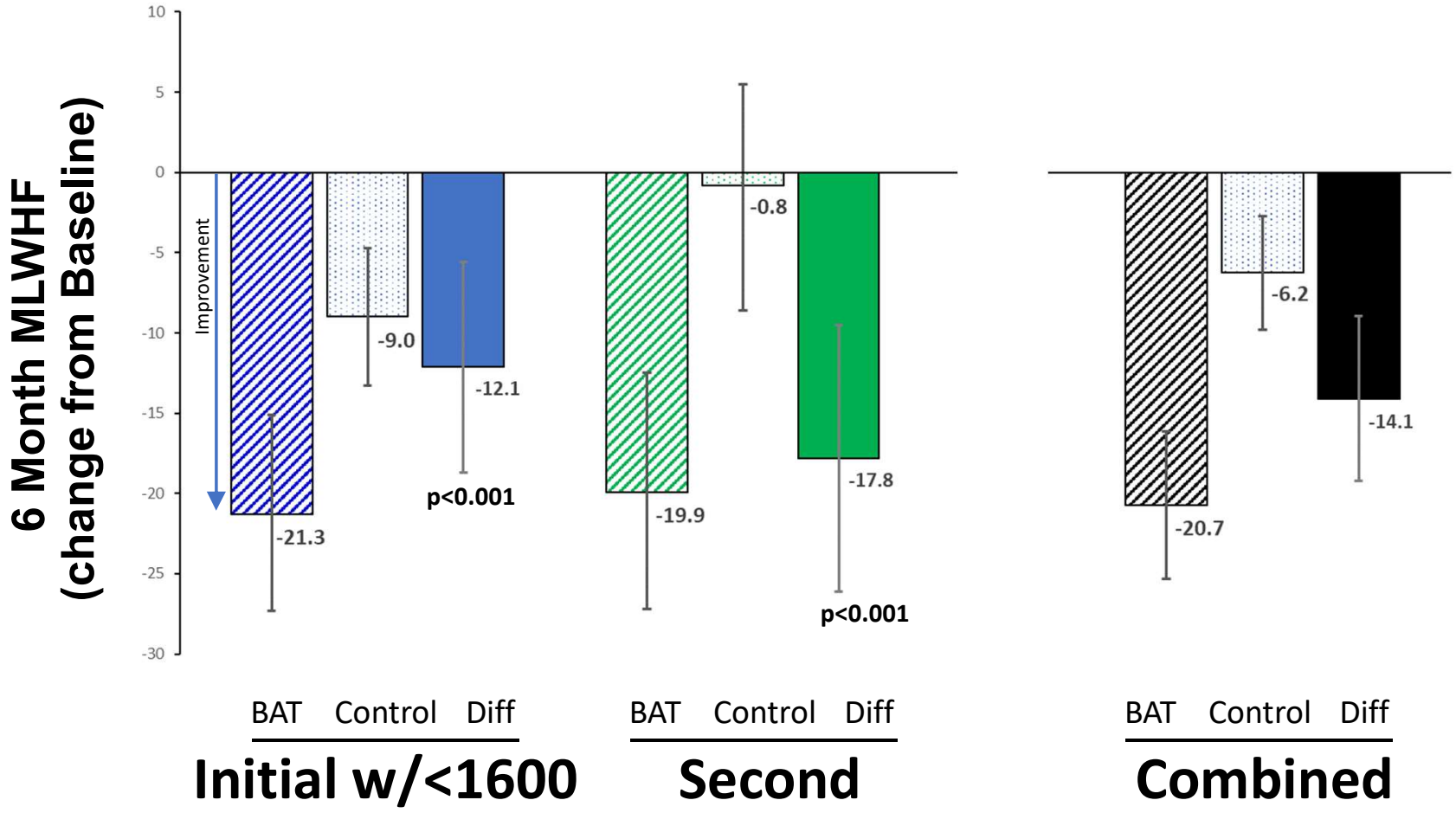
BAT Significantly Improves Quality of Life



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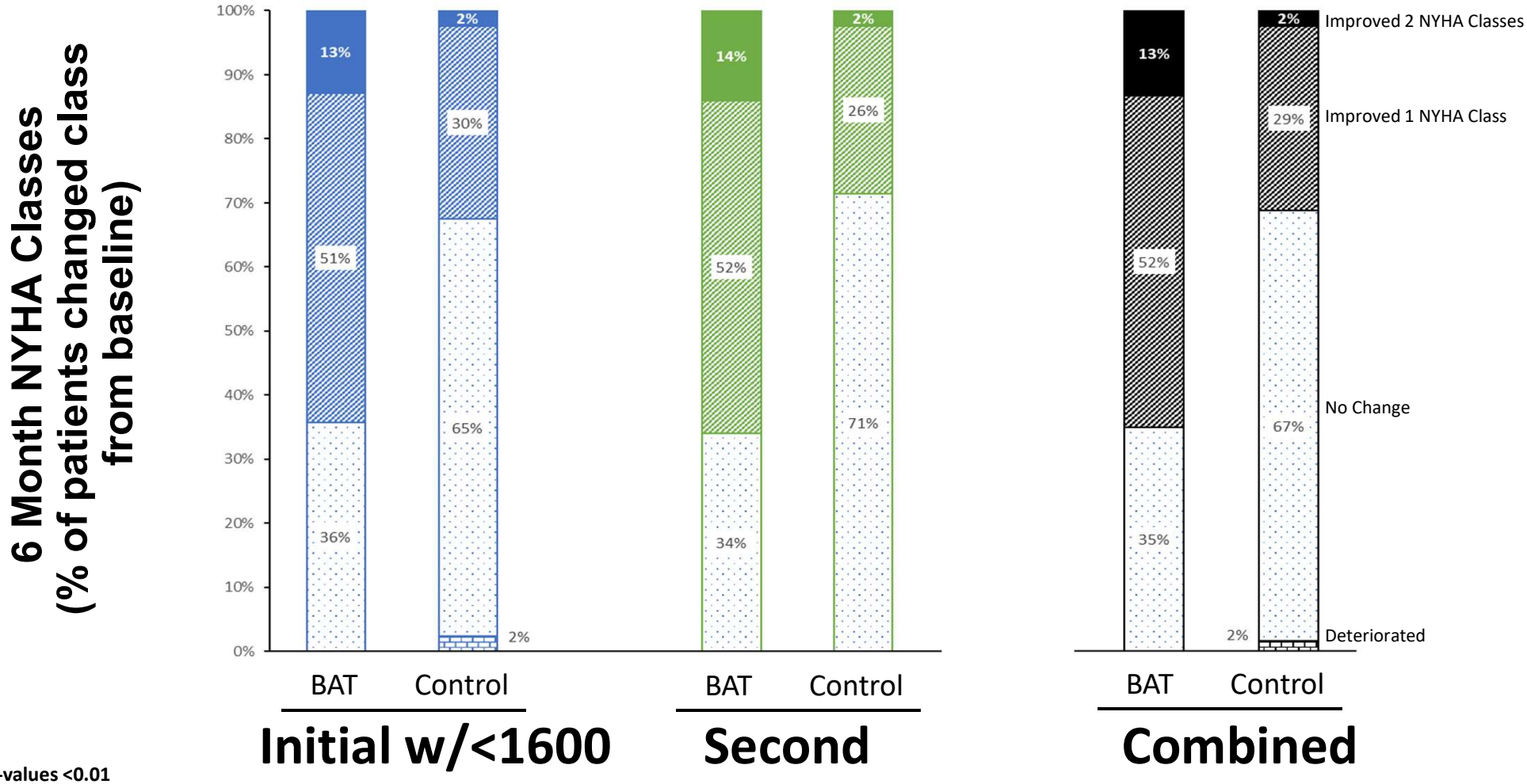
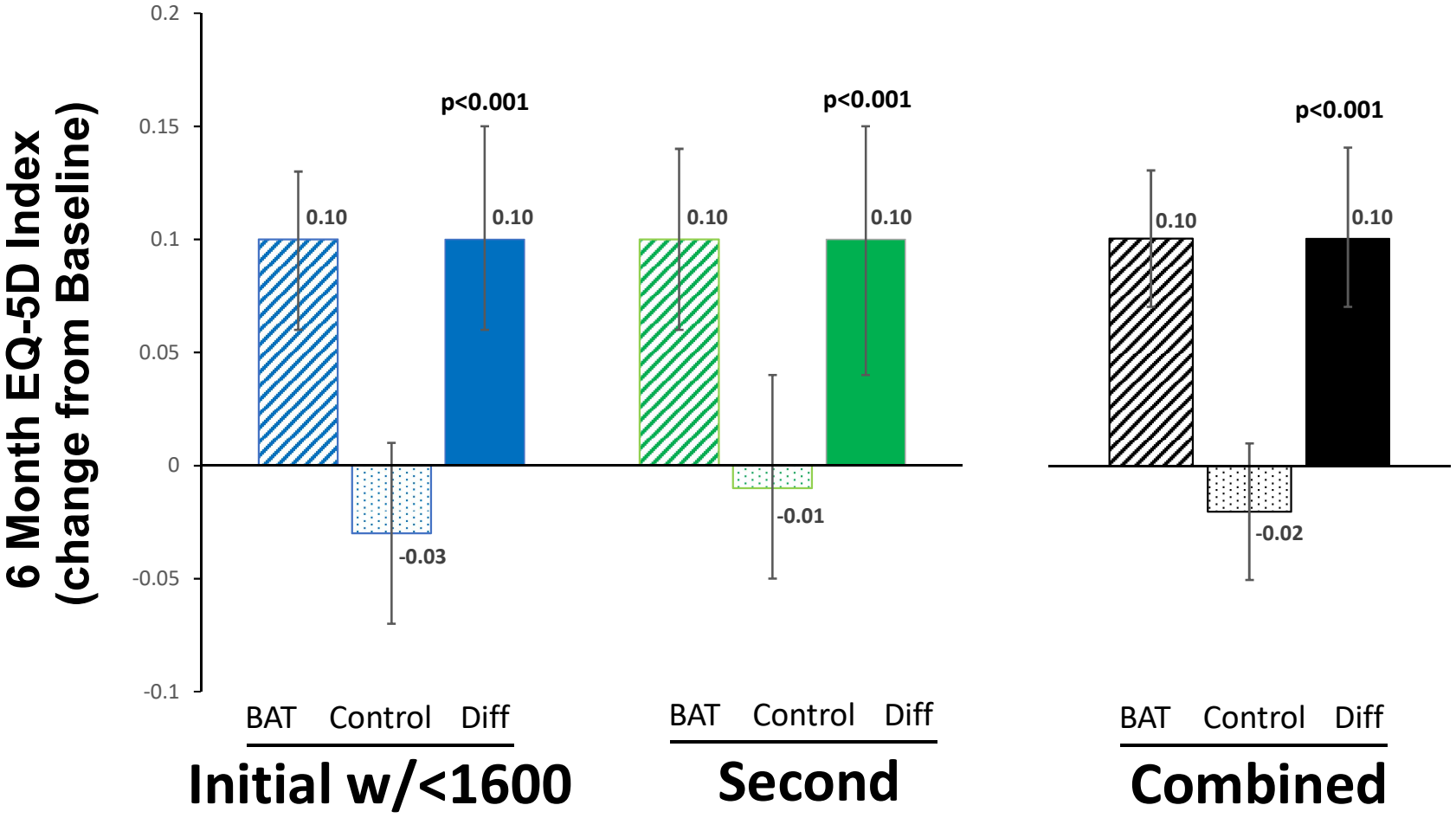
BAT Significantly Improves Functional Status

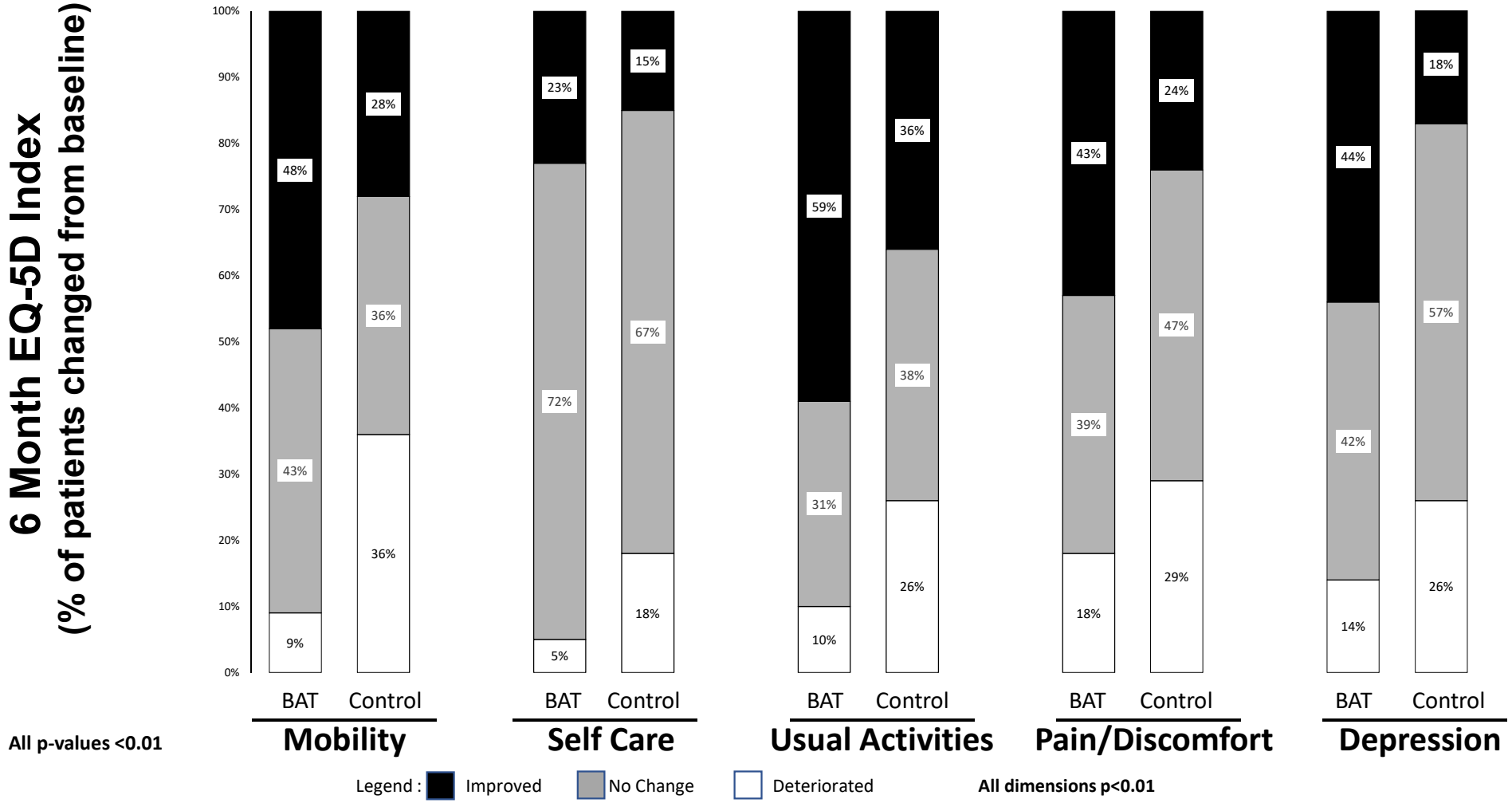


All p-values <0.01

BAT Significantly Improves EQ-5D Index



BAT Significantly Improves EQ-5D Dimensions Combined Cohort



All p-values <0.01

All dimensions p<0.01

BAT Reduces Cardiovascular Events
in Intended Use Population

- Heart Failure Hospitalization data remains blinded to support the on-going post-market outcome phase
- Observation of other cardiovascular events suggests a reduction between arms

Adverse Events	BAT (n=130)	Control (n=134)	Reduction of Events
Arrhythmias	8	18	54%
Angina / Acute MI	5	10	50%
Pre-syncope / Syncope	2	6	66%
Total	*15*	*35*	*55%* *(p-value = 0.023)*

BeAT-HF Medication Changes for Combined Cohort

- These significant differences in treatment effect were observed despite an increase in the number medication in the control arms

Variable	BAT (N=120)	CONTROL (N=125)	Increase in Control
Subjects with new classes of drugs added	21 (18%)	36 (29%)	+11%
Subjects with newly added ARNI	5 (4%)	20 (16%)	+12%

The number of subjects used (BAT N=120 and Control N=125) is the number of subjects who completed their 6-month visits

BeAT-HF Conclusions

- Baroreflex Activation Therapy is safe in HFrEF patients.
- BAT significantly improves patient-centered symptomatic endpoints
  - quality of life score (MLWHF and EQ-5D)
  - exercise capacity.
- These results are supported by objective evidence of significant reduction of NT-proBNP.
- These significant differences in treatment effect were observed despite an increase in the number of medications in the control arm.
- To our knowledge, this is the first successful pivotal trial of a device-based neuromodulation therapy in HFrEF patients.

BAT Ongoing Activities

- Continue enrollment for the post-market outcome phase to expand the indication to include reduction of heart failure hospitalizations and cardiovascular mortality
- Continue enrollment in Germany for the post-market companion study: **B**arostim Therapy **I**mproves Cardiac **R**emo**D**eling in **H**eart **F**ailure (BiRD-HF), to assess cardiac remodeling in HFrEF patients.
- Implement non-surgical approach for implantation in electrophysiology labs

This slide was added to the slide deck after the Presentation

The BAROSTIM NEO™ System is CE Marked and approved for sale for heart failure patients in the European Union (EU). It is also CE Marked and approved for sale for hypertension patients in the EU.

CAUTION: Investigational device. Limited by Federal (or United States) law to investigational use.

For a list of all potential benefits and risks go to:
www.beathf.com/risksbenefits/