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Title: Baroreflex activation therapy (BAT) in patients with heart failure and reduced ejection fraction: responder rates and quality of life measures analyzed by gender
Topic: Chronic Heart Failure – Treatment

Type of Submission: LATE-BREAKING CLINICAL TRIAL:
Full Title of Study: Barostim neo® - Baroreflex Activation Therapy® for Heart Failure
Acronym: BeAT-HF
On Behalf of: BeAT-HF Steering Committee and Investigators
Short title: BeAT-HF Symptomatic Results by Gender
Funding acknowledgements: None
Expected date of trial completion: Q1 2022
Data previously submitted as an abstract to the Heart Failure 2020: Yes
Nevertheless, simultaneous publication is authorised. I have submitted / I will submit my data for simultaneous publication: TBD

Presenter: Joanne Lindenfeld, M.D.
Principal Investigator: BeAT-HF Executive Steering Committee (Chair: Michael Zile, M.D.)
Multicenter: Yes, 106
Purpose: The purpose of this clinical trial is to develop valid scientific evidence for safety and effectiveness of Baroreflex Activation Therapy™ with the Barostim neo system in subjects with heart failure, defined as New York Heart Association functional Class III, LVEF ≤ 35% and NT-proBNP < 1600 pg/ml despite being treated with the appropriate heart failure guideline directed therapy, excluding subjects eligible for or with a CRT device.
Total number of subjects: 264 randomized
Total number of groups: 2 (1:1 randomization)
Population studied: New York Heart Association (NYHA) functional Class III, left ventricular ejection fraction (LVEF) ≤ 35% and NT-proBNP < 1600 pg/ml despite being treated with the appropriate heart failure guideline directed therapy, excluding subjects eligible for or with a Cardiac Resynchronization Therapy (CRT) device.
Intervention: Barostim Activation Therapy vs Guideline Directed Medical Management
Primary endpoint: Six Minute Hall Walk, Quality of Life and NT-proBNP
Secondary endpoint: NYHA Class, EQ-5D
Multicenter: Yes
Randomized: Yes
Prospective: Yes
Double-blind: No
Clinical Outcome as endpoint: Yes
Mortality as endpoint: No

Baroreflex activation therapy (BAT) in patients with heart failure and reduced ejection fraction: responder rates and quality of life measures analyzed by gender

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BACKGROUND. Heart failure with a reduced ejection fraction (HFrEF) affects over a million people in the United States and is associated with poor life expectancy, frequent heart failure (HF) hospitalizations, poorer quality of life (QoL), and substantial limitation in exercise capacity. Some device-based HF therapies have been reported to have different responses to symptomatic endpoints, including QoL, in men vs women with HFrEF.

PURPOSE: We hypothesized that use of Baroreflex Activation Therapy (BAT) will improve HF symptoms and QoL in both male and female patients with HFrEF who are on guideline-directed medical and device therapy (GDMT).

METHODS. A novel trial randomized subjects with an unmet clinical need to ongoing GDMT (Control) or ongoing GDMT plus BAT. HFrEF patients with New York Heart Association (NYHA) Class III or II (with recent Class III) and LVEF≤ 35% despite treatment with the

appropriate heart failure GDMT, N-terminal pro-brain natriuretic peptide (NT-proBNP) < 1600 and not indicated for cardiac resynchronization therapy were enrolled. The six month symptomatic effectiveness endpoints included changes in 6-min hall walk (6MHW), NYHA and QoL questionaires. QoL questionnaires included the Minnesota Living with HF Questionnaire (MLWHF) and the EuroQol 5-Dimension Long (EQ-5D) tool. From the MLWHF questionnaire, both a physical and an emotional dimension was analyzed using subsets of the 21 questions. From the EQ-5D, the five individual dimensions and the overall health status (0-100, where 100 is best) was analyzed. Clinically relevant responders were defined by 6-month improvement in 6MHW>10%, MLWHF>5 points or improvement in at least one NYHA class. Super responders were defined by 6-month improvement in 6MHW>20%, MLWHF >10 points or improvement to NYHA class I.

RESULTS. Of the 264 subjects randomized, as shown in the table below, at six months (n=245) BAT provided significant improvement in 6MHW, NYHA class and QoL elements. These improvements were observed in both women (n=49, 20%) and men (n=196, 80%) with no interaction by gender. Both physical and emotional domains of the MLWHF were improved as were overall health status and mobility

CONCLUSION. In symptomatic HFrEF patients, BAT improves multiple measures of functional status and is associated with very high responder rates in both men and women, supporting its use in indicated patients.

Six Month Symptomatic Endpoint Results Overall and by Gender

Endpoint Results		All			Women			Men			Interaction p-value
		BAT (N=120)	Control (N=125)	Difference	BAT (N=23)	Control (N=26)	Difference	BAT (N=97)	Control (N=99)	Difference	
Overall Results	6MHW	48.6 ± 66.3	-7.9 ± 88.4	60*	44.2 ± 45.0	-32.2 ± 118.0	81*	49.7 ± 70.7	-1.5 ± 78.3	55*	0.33
	MLWHF QoL Score	-20.7 ± 25.4	-6.2 ± 20.1	-14*	-34.2 ± 27.4	-9.0 ± 22.8	-23*	-17.5 ± 24.0	-5.5 ± 19.3	-12*	0.10
Clinically Relevant Responder	6MHW>10%	62%	31%	31%*	70%	20%	50%*	60%	34%	26%*	0.13
	QOL>5 Points	68%	44%	24%*	78%	54%	24%***	66%	41%	25%*	0.87
	NYHA Improve≥1 Class	65%	31%	34%*	70%	27%	43%*	64%	32%	32%*	0.46
	Clinically relevant response in ≥ 2	72%	29%	43%*	87%	28%	59%*	68%	29%	39%*	0.15
	Clinically relevant response in all 3	30%	8%	22%*	35%	4%	31%*	28%	9%	19%*	0.31
Super Responder	6MHW>20%	34%	18%	16%*	39%	20%	19%	33%	18%	15%**	0.84
	QOL>10 Points	61%	36%	25%*	78%	42%	36%**	57%	34%	23%*	0.34
	NYHA Improve to Class I	16%	2%	14%*	22%	4%	18%***	14%	2%	12%**	0.91
	Super response in ≥ 2	28%	10%	18%*	43%	8%	35%*	24%	11%	13%**	0.21
	Super response in all 3	4%	0%	4%**	4%	0%	4%	4%	0%	4%**	1.00
	Physical (8 Questions)	-8.8 ± 11.8	-3.3 ± 9.0	-5.3*	-15.4 ± 12.0	-4.2 ± 9.8	-10.2*	-7.2 ± 11.2	-3.0 ± 8.8	-4.1*	0.05

Endpoint Results		All			Women			Men			Interaction p-value
		BAT (N=120)	Control (N=125)	Difference	BAT (N=23)	Control (N=26)	Difference	BAT (N=97)	Control (N=99)	Difference	
Minnesota Living with HF QoL	Emotional (5 Questions)	-4.8 ± 7.2	-1.0 ± 6.2	-3.8*	-8.9 ± 7.5	-2.5 ± 6.5	-5.4*	-3.8 ± 6.8	-0.6 ± 6.1	-3.4*	0.28
EuroQol 5-Dimension	Overall health today	16.3 ± 19.6	5.3 ± 19.2	10.0*	24.4 ± 19.5	9.2 ± 22.7	11.5**	14.3 ± 19.2	4.3 ± 18.2	9.5*	0.59
	Mobility (% improved)	48%	28%	20%*	52%	42%	10%	46%	24%	22%*	0.36
	Self-Care (% improved)	23%	15%	8%	39%	12%	27%**	20%	16%	4%	0.10
	Usual Activities (% improved)	59%	36%	23%*	70%	23%	47%*	57%	39%	18%**	0.06
	Pain/Discomfort (% improved)	43%	24%	19%*	48%	27%	21%	42%	23%	19%*	0.97
	Anxiety / Depression (% improved)	44%	18%	26%*	70%	19%	51%*	38%	17%	21%*	0.12

**** p-value <0.01; **p-value<0.05; ***p-value<0.10***