Baroreflex Activation Therapy™ for Heart Failure Study

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Background

- Heart failure is characterized by a hyperadrenergic state with suppressed parasympathetic tone and secondary deleterious neurohormonal effects
- Despite improved guideline adherence and targeted medical therapy, outcomes in reduced-ejection fraction heart failure (HFrEF) remain unsatisfactory
- BAROSTIM THERAPY™ is a unique treatment option for HFrEF that delivers electrical stimulation to the carotid sinus to activate the baroreflex and reduce sympathetic activity while restoring parasympathetic activity
- Phase 1 (n=11) and Phase 2 (n=146) studies of BAROSTIM THERAPY in HFrEF patients have demonstrated that chronic baroreflex activation significantly:
  - Improves autonomic balance and reduces neurohormonal activation
  - Improves six minute walk (6MHW), Minnesota Living With HF Quality of Life (MLWHF), and NYHA functional class
  - Reduces heart failure hospitalization burden
- BAROSTIM THERAPY is particularly effective in patients who are not eligible for cardiac resynchronization therapy (CRT), a population in need of new therapeutic options

Relevant Clinical Experience

In non-CRT patients, results at six months showed that symptoms, functional capacity, and cardiovascular function were significantly improved, while heart failure hospitalization days were reduced in those who received Baroreflex Activation Therapy (BAT) compared to those in the control arm (BAT n=47; Control n=48) 3

The BAROSTIM NEO™ System

Implantable Pulse Generator (IPG) implanted under the skin below the collarbone. Provides control and delivery of activation energy from the IPG to the baroreceptors on the carotid artery.

Carotid Sinus Lead One thin lead wire implanted on the carotid artery and connected to the device. Conducts activation energy from the IPG to the baroreceptors on the carotid artery.

Wireless Programmer System An external system used to adjust and customize therapy settings via wireless communication.

Study Design & Objectives

The BAROSTIM NEO device for this study patient population has received Expedited Access Pathway designation from FDA. This designation is for medical devices that demonstrate the potential to address unmet medical needs for patients with life threatening or irreversibly debilitating diseases. Improvement in intermediate endpoints, which is of value to these patients, has been incorporated into the study design to support evaluation of safety and efficacy.

Safety:
  - Event-free rate of all system- and procedure-related Major Adverse Neurological and Cardiovascular Events occurring within 6 months post-implant

Efficacy:
  - Six Minute Hall Walk, Minnesota Living with Heart Failure Quality of Life, NT-proBNP
  - Cardiovascular mortality and worsening heart failure (M&M)

Key Eligibility Criteria

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<tr>
<th>Inclusion</th>
<th>Exclusion</th>
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<td>Symptomatic NYHA Class III</td>
<td>Currently implanted, or currently have, a Class 1 indication according to AHA/ACC guidelines for a cardiac resynchronization therapy device</td>
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<td>Left ventricular ejection fraction ≤ 35%</td>
<td>Known or suspected baroreflex failure or autonomic neuropathy</td>
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<td>Heart failure defined as:</td>
<td>AHA/ACC Stage D heart failure</td>
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<td>• BNP ≥ 400 OR NT-proBNP ≥ 1600</td>
<td>• Heart failure secondary to a reversible cause</td>
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<td>• BNP ≥ 100 OR NT-proBNP ≥ 4000 AND prior hospitalization for heart failure within 12 months.</td>
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<td>On optimal, stable, Guideline Directed Medical Therapy for the treatment of heart failure</td>
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<td>• Six-minute hall walk ≥ 150 m AND ≤ 400 m</td>
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Center Requirements

- Large heart failure population
- Large cardiology practice
- Strong collaboration with vascular surgery
- Electronic medical records
- Prior experience with randomized device studies
- Significant patient recruitment in previous heart failure studies
- Dedicated research coordinator

Centers interested in participating in BeAT-HF should contact Liz Galle, Senior Director of Clinical Research: lgalle@cvrx.com

References

2. Abraham WT et al., JACC: Heart Failure. 2015;3:487-496

The BAROSTIM NEO system is CE Marked and approved for sale for heart failure patients in Europe. It is also CE Marked and approved for sale for hypertension patients in Europe. Caution: BAROSTIM NEO is investigational device and is limited by United States law to investigational use. CVRx, BAROSTIM NEO, Baroreflex Activation Therapy and BAROSTIM THERAPY are all trademarks of CVRx, Inc. © 2016 CVRx, Inc. All rights reserved.