ONLINE SUPPLEMENT

Chronic Lowering of Blood Pressure by Carotid Baroreflex Activation: Mechanisms and Potential for Hypertension Therapy

By

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Short Title: Carotid Sinus Stimulation and Blood Pressure

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Table S1. CVRx Clinical Trials

ClinicalTrials.gov Identifier	Trial Name	Sample Size	Description	Primary Outcome Measures	Population	No. of Sites	Status
NCT00710294	DEBuT - HET: Device Based Therapy in Hypertension Extension Trial: Long-Term Follow-Up Trial for Patients Who Completed the DEBuT-HT Study	45	A chronic, prospective, non-randomized, self-controlled registry of safety and blood pressure reduction efficacy in patients with refractory hypertension who in course of the DEBuT-HT trial have been implanted with the CVRx Rheos™ System for the electrical activation of the baroreflex.	Describe the safety of Rheos Baroreflex Hypertension Therapy System by evaluating all adverse events and estimating the system and procedure related adverse event rate until and including the 13-month follow-up	Resistant hypertension defined as: Blood pressure greater than or equal to 160 mmHg systolic and/or greater than or equal to 90 mmHg diastolic despite two months of full therapy with at least three anti-hypertensive medications, of which at least one must be a diuretic.	9	Active, Not Recruiting
NCT01077180	Rheos Feasibility Trial	16	A clinical feasibility investigation designed to assess safety, device performance, and protocol parameters of the CVRx Rheos Baroreflex Hypertension Therapy System in patients with severe hypertension that are refractory to full drug therapy.	To summarize the efficacy of the Rheos System by estimating the reduction of systolic blood pressure associated with activation of the Rheos System at 4 and 13 months post implant when compared to baseline (1-month post implant). To describe the safety of the Rheos Sytsem by summarizing all system related adverse events and estimating the serious system related event-free rate through 4 and 13 months post-implant.	Resistant hypertension defined as: Blood pressure greater than or equal to 160 mmHg systolic despite one month of full therapy with at least three anti-hypertensive medications, of which at least one must be a diuretic.	6	Completed
NCT00718939	Rheos Diastolic Heart Failure Trial	3	A prospecive trialto evaluate the safety and efficacy of the Rheos System in a Diastolic Heart Failure population.	To describe the effects of the Rheos Baroreflex Activation Therapy System on the left ventricular mass index (LVMI) at six months	Symptomatic Heart Failure with LVEF ≥ 45%, and cuff systolic blood pressure ≥140 mmHg	2	Active, Not Recruiting
NCT00710190	DEBuT-HT: Device Based Therapy in Hypertension Trial	45	A chronic, prospective, non-randomized, self-controlled registry of safety and blood pressure reduction efficacy in patients with refractory hypertension.	To demonstrate the safety and efficacy of the Rheos Baroreflex Hypertension Therapy System in patients with refractory hypertension.	Resistant hypertension defined as: Blood pressure greater than or equal to 160 mmHg systolic and/or greater than or equal to 90 mmHg diastolic despite two months of full therapy with at least three anti-hypertensive medications, of which at least one must be a diuretic.	9	Completed

Table S1. CVRx Clinical Trials

Table S1 cont'd

NCT00957073	Health Outcomes Prospective Evaluation for Heart Failure With EF ≥ 40% (HOPE4HF)	540	The CVRx Health Outcomes Prospective Evaluation for Heart Failure with EF ≥ 40% (HOPE4HF) is a prospective, randomized trial. Subjects will be randomized in a 2:1 ratio to receive a Rheos system plus medical management (Device Arm) or to receive medical management alone (Medical Management Arm). The trial will utilize a phased enrollment process. Phase I of the study will be limited to 30 subjects randomized (20 implanted) at up to 10 U.S. sites.	1. Cardiovascular death or heart failure event 2. Assess safety by evaluating all system or procedure-related complications	Symptomatic heart failure with EF > 40%, and Office cuff systolic blood pressure ≥ 140 mmHg and ≤ 180 mmHg , despite being prescribed to at least three antihypertensive medications, including a diuretic	70 US, 20 OUS	Recruiting
NCT00442286	Rheos® Pivotal Trial	326	A randomized, double-blind, parallel-group trial. All subjects are implanted with the Rheos System. Therapy is programmed OFF for the first month following the implant. Subjects are then randomized 2:1 to receive active therapy for the first six months or have the device turned off for the first 6-month follow-up period. After 6-months, subjects in the OFF arm will have their Rheos system turned on.	1. To demonstrate a clinically significant reduction of office cuff systolic blood pressure at six months. 2. To demonstrate a sustained response to therapy through 12 months. 3. System and procedure related adverse event free rate in the first 30 days. 4. Hypertension-related adverse event and serious device-related adverse event free rate more than 30 days post-implant to 13 months. 5. Serious therapy-related adverse event free-rate through 6 months.	Resistant hypertension defined as: Office cuff systolic blood pressure greater than or equal to 160 mmHg and have a diastolic blood pressure greater than or equal to 80 mmHg as well as a 24-hour ambulatory systolic blood pressure greater than or equal to 135 mmHg despite at lest one month of maximally tolerated therapy with at least three anti-hypertensive medications, of which at least one must be a diuretic.	42	Active, Not Recruiting