SMI-001 Results Summary

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Relaxis™ is equivalent to the Symphony™ Counter-stimulation Device used in the study below

Study Number: SMI-001
Title: A Randomized, Double-blind, Sham-controlled, Multicenter Study of the Symphony™ Counter-stimulation Device in Restless Legs Syndrome
Indication: Restless Legs Syndrome
Coordinating Physician: Fred Burbank, MD, San Clemente, California
Rationale: Patients with moderate to severe RLS spontaneously apply various forms of counter-stimulation to diminish the painful somatic sensations that characterize RLS. They rub their legs, they flex and extend their knees and ankle joints, and they wiggle. While these counter-stimuli may provide brief relief from unpleasant sensations, the patient must be awake to apply them and, consequently, these counter-stimuli usually fail to allow the patient to fall asleep quickly. Usually, the patient has to become fully awake, get out of bed, and walk about. The unique design of the Symphony™ device allows the patient to apply vibratory stimulation (VS), a form of counter-stimulation, while in bed, allowing them to return to sleep quickly, improving sleep efficiency.
Objectives: The primary objective was to evaluate the safety and efficacy of the Symphony™ Counter-stimulation Device and a sham device in reducing the symptoms and/or signs associated with moderate to severe primary Restless Legs Syndrome (RLS). The secondary objective was to assess patient-reported outcomes.
Methodology: Prospective, randomized, double-blind, multicenter, 4-Wk study
Primary Endpoints: The primary effectiveness endpoints were the mean change from baseline in the International Restless Legs Scale (IRLS) total score. The primary safety endpoint was the incidence of adverse device effects.
Secondary Endpoints: The two secondary endpoints were the mean change from baseline to 4 weeks on the Johns Hopkins Restless Legs Syndrome Quality of Life questionnaire (RLS-QOL) and on the MOS (Medical Outcomes Study) Sleep Problems Index II (MOS-II).
Statistical Methods: The study population was randomized 1:1, Symphony:Sham. The primary endpoint null hypothesis of no difference in mean IRLS score change from baseline to Wk 4 was tested by t-test at the alpha = 0.05 level. Secondary endpoint hypotheses were tested at alpha levels adjusted for mulitiplicity using a bootstrap / permutation method that took into account correlation among the three endpoints.
Investigational Device: Symphony™ Device, Models 09-0002-01, 09-0003-01, and 09-0004-01 (pad size small, medium, large)
Sham Device: The sham pads were physically identical to the vibrating pads producing a variable, audible hum as loud as vibrating pads, and were, therefore, referred to as “sound sham pads.” Through a knob on the controller, patients could vary the loudness of sound in the sham pads in a manner identical to varying the intensity of vibration in the investigational device.
Study Period: April 20, 2009 to August 7, 2009
Study Population: Males or females aged ≥ 18 years old and < 80 years, with RLS diagnosed by a score of 15 or greater on the IRLS scale. Patients on FDA-approved RLS drugs could remain on their medication but could not change dosage. Subjects suffering from signs of secondary RLS were excluded.
Safety Population: All randomized patients who received a study device and had any follow-up.

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Number of Subjects	**Sham**	**Symphony**	**Total**
Treated (N)	38	39	77
Withdrawn due to AE (N)	0	0	0
Withdrew, other reasons (N)	0	1	1
Completed (N)	38	38	76
Patient Demographics:	**Sham**	**Symphony**	
Age, years, Mean (SD)	55.1 (15.0)	50.5 (15.5)	
Gender, N (%)			
Female	27 (71.1)	29 (74.4)	
Male	11 (28.9)	10 (25.6)	
Race, N (%)			
Caucasian	37 (97.4)	35 (89.7)	
African-American	0 (0.0)	1 (2.6)	
Asian	1 (2.6)	0 (0.0)	
Hispanic	0 (0.0)	2 (5.1)	
Other	0 (0.0)	1 (2.6)	
Primary Efficacy Results:			
IRLS Scale - Total Scores	Sham	Symphony	
Baseline, N	38	39	
Mean (SD) Score at Baseline	23.76 (5.01)	25.59 (5.43)	
Change from Baseline (SD) to Wk 4	-6.24 (6.90)	-7.11 (7.82) *Note: Wk 4 N=38*	
Treatment Difference	-0.87		
95% Confidence Interval	-2.50, 4.24		
P-value for Treatment Difference	0.6094		
Secondary Outcome Variable(s):			
RSL-QOL Scale - Total Scores	Sham	Symphony	
Baseline, N	38	39	
Mean (SD) Score at Baseline	65.86 (17.39)	58.01 (19.84)	
Mean Change from Baseline (SD) to Wk 4	7.43 (12.17)	12.70 (20.65) *Note: Wk 4 N=38*	
Treatment Difference	5.26		
95% Confidence Interval	-2.49, 13.01		
P-value for Treatment Difference (multiplicity adjustment)	0.1810		
MOS Scale MOS-II Scores	Sham	Symphony	
Baseline, N	38	38	
Mean Score at Baseline (SD)	46.39 (16.40)	55.33 (14.07)	
Mean Change from Baseline (SD) to Wk 4	-5.34 (15.89)	-15.83 (22.71) Note: Wk 4 N = 37	
Treatment Difference	-10.49		
95% Confidence Interval	-19.55, -1.43		
P-value for Treatment Difference (multiplicity adjustment)	0.0230		
Safety Results	**Sham N(%)**	**Symphony N (%)**	**Total N (%)**
Subjects with any AEs leading to study withdrawal	0 (0)	0 (0)	0 (0)
Subjects with device-related AEs	0 (0)	6 (15.4)	6 (7.8)
Subjects with any AEs	4 (10.5)	8 (20.5)	12 (15.6)

Conclusions:

By analysis of (i) any adverse event, (ii) adverse events related to the Symphony™ device, and (iii) adverse events leading to study withdrawal, at $p > 0.05$ the Symphony™ vibrating pads were as safe as sham pads.

On all outcome scales (IRLS, RLS-QoL, and MOS-II), patients treated with the Symphony™ device had greater average improvement than patients treated with sham pads. Improvement for IRLS and RLS-QoL scales was not statistically significant at $p \leq 0.05$. Improvement in the MOS-II scale was significant at $p \leq 0.02$. When MOS-II improvement scores were corrected for correlated endpoints by the Westfall and Young procedure, the p-value remained significant at $p \leq 0.04$.