SMI-002 Results Summary

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

Study Number: SMI-002
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-week study
Primary Endpoints: The primary efficacy endpoint was the mean change from baseline to 4 weeks 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 2:1, Symphony:Sham. The primary endpoint null hypothesis of no difference in mean IRLS score change from baseline to week 4 was tested by t-test at the alpha = 0.05 level.
Investigational Device: Symphony™ Device, Models 09-0002-01, 09-0003-01, and 09-0004-01 (pad sizes small, medium, large)
Sham Device: The sham pads were physically identical to the vibrating pads except that the sham pads did not vibrate. Instead, a light-emitting diode was incorporated into the pad and was visible at the top of the sham pad. When covered by a patient's legs, the light was not visible. Being diodes, the light did not produce heat. These sham pads were referred to as "light sham pads." By turning a knob on the controller, patients could vary the intensity of light in the sham pads in a manner identical to varying the intensity of vibration in the investigational device.
Study Period: October 13, 2009 to March 16, 2010
Study Population: Males or females aged ≥ 18 years and < 80 years, with symptomatic RLS and 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. Patients with 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)	29	52	81
Withdrawn due to Adverse Events	0	1	1
Withdrew, due to other reasons	1	1	2
Completed (N)	28	50	78
Patient Demographics:	**Sham**	**Symphony**	
Age, years, Mean (SD)	52.4 (15.3)	54.5 (14.2)	
Gender, N (%)			
Female	20 (69.0)	31 (59.6)	
Male	9 (31.0)	21 (40.4)	
Race, N (%)			
Caucasian	27 (93.1)	41 (78.8)	
African-American	1 (3.7)	8 (15.4)	
Asian	0 (0.0)	1 (1.9)	
Hispanic	1 (3.7)	2 (3.8)	
Other	0 (0.0)	0 (0.0)	
Primary Efficacy Results:			
IRLS Scale - Total Scores	Sham	Symphony	
Baseline, N	29	52	
Mean Score at Baseline (SD)	24.0 (6.5)	23.7 (4.4)	
Mean Change from Baseline (SD) to Wk 4	-6.6 (8.4) *Note: Wk 4 N=28*	-6.4 (6.9) *Note: Wk 4 N=50*	
Treatment Difference	+0.2		
95% Confidence Interval	(-3.3, 3.8)		
P-value for Treatment Difference	0.8887		
Secondary Outcome Variable(s)::			
RSL-QoL Scale Total Scores	Sham	Symphony	
Baseline, N	29	52	
Mean Score at Baseline (SD)	63.8 (18.4)	63.9 (18.1)	
Mean Change from Baseline (SD) to Wk 4	6.4 (19.4) *Note: Wk 4 N=28*	10.0 (15.8) *Note: Wk 4 N=50*	
Treatment Difference	2.4		
95% Confidence Interval	(-6.0, 10.9)		
P-value for Treatment Difference	0.5932		
MOS Scale – MOS-II Scores	Sham	Symphony	
Baseline, N	29	52	
Mean Score at Baseline (SD)	48.9 (18.4)	48.6 (15.6)	
Mean Change from Baseline (SD) to Wk 4	-7.4 (15.6) *Note: Wk 4 N=28*	-11.4 (17.1) *Note: Wk 4 N=50*	
Treatment Difference	-4.1		
95% Confidence Interval	(-11.8, 3.7)		
P-value for Treatment Difference	0.3040		

Safety Results	**Sham N (%)**	**Symphony™ N (%)**	**Total N (%)**
Subjects with any AEs leading to study withdrawal	0 (0.0)	1 (1.9)	1 (1.2)
Subjects with device-related AEs	2 (6.9)	4 (7.7)	6 (7.4)
Subjects with any AEs	2 (6.9)	6 (11.5)	8 (9.9)

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 the IRLS scale, improvement for patients in the Symphony™ group was similar to sham group improvement. On the RLS-QoL and MOS-II scales, patients treated with the Symphony™ device had greater improvement than patients treated with sham pads, but the differences were not statistically significant at $p \leq 0.05$.