Vagus Nerve Stimulation Improves Left Ventricular Function in Heart Failure: Results of a 6 Month Investigation with a Cross-over Design in Dogs with Experimental Heart Failure

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INTRODUCTION

Autonomic imbalance is a feature of chronic heart failure. This imbalance manifests as a high sympathetic and low parasympathetic drive.

We have previously shown that chronic (3 months) “open-loop” electrical Vagus nerve stimulation (VS) improves LV function and prevents progressive LV remodeling in dogs with heart failure.
OBJECTIVE

This study tested the hypothesis that 6 months of right Vagus nerve stimulation (VS), improves LV function and prevents progressive LV dilation in dogs with chronic heart failure.
METHODS

Studies performed in 26 dogs with intracoronary microembolization-induced heart failure (EF~35%).

Surgical implantation of bipolar cuff electrode on right cervical vagus nerve and connected to implantable pulse generator.

Dogs were randomized to one of four groups: no therapy (Control, n=7) active therapy (VS, n=7), no therapy crossed-over to therapy (Control x VS, n=6) or therapy crossed-over to no therapy (VS X Control, n=6). All dogs were maintained for 6 months and cross-overs occurred at 3 months.

Active “open-loop” VS delivered for 10 sec of every minute (Parameters: 20 Hz, 0.3 msec pulse width) Current amplitudes ranged from 0.6 to 1.9 mA and represent the highest tolerable dose as titrated over a 1 month period.
STUDY DESIGN

Baseline

Microembolizations to Induce Heart Failure*

VS System Implantation

- 1 mo.

Randomization
2D Echo
Blood Draw
48-hr. Holter
Hemodynamics
Ventriculography

Pre

Monthly
2D Echo

3 mo.

VS Therapy Titration (only 1st month post-device activation)

Study Midpoint
(Cross-over)
2D Echo
Blood Draw
48-hr. Holter
Hemodynamics
Ventriculography

End of Study
2D Echo
Blood Draw
48-hr. Holter
Hemodynamics
Ventriculography
Histology

6 mo.

Primary Study Endpoints
LV EDV and ESV
LV Ejection Fraction

* Model creation time may vary
6 Month Results - Ventriculography

**LV End Diastolic Volume (ml)**

- Control
- VS Therapy

**LV End Systolic Volume (ml)**

- Control
- VS Therapy

*\( p \leq 0.05 \) vs. Pre-treatment
6 Month Results - Ventriculography

LV Ejection Fraction (%)

* p≤0.05 vs. Pre-treatment

Control

VS Therapy

- Pre-treatment
- 3 Months
- 6 Months
Cross-over Results - Ventriculography

LV End Diastolic Volume (ml)

Control x VS

VS x Control

LV End Systolic Volume (ml)

Control x VS

VS x Control

* p≤0.05 vs. Pre-treatment
† p≤0.05 vs. 3 Months
Cross-over Results - Ventriculography

LV Ejection Fraction (%)

- Pre-treatment
- 3 Months
- 6 Months

* p≤0.05 vs. Pre-treatment; † p≤0.05 vs. 3 Months

Control x VS

VS x Control
Ventriculography – All study groups

LV Ejection Fraction (%)

Pre-treatment 3 Months 6 Months

Control VS Therapy Control x VS VS x Control

70% 80% 90% 100% 110% 120% 130%

LV Ejection Fraction as a % of Pre-treatment

Pre-treatment 3 Months 6 Months

Control VS Therapy Control x VS VS x Control
CONCLUSIONS

Heart Right VS delivered for 6 months continues to improve systolic LV function and prevent progressive LV remodeling in dogs with moderate heart failure.

Heart Dogs initially assigned to VS respond well to the therapy. However, when VS therapy was withdrawn the LV function tended to decrease over the following 3 month period.
CONCLUSIONS

These results favor the continued development of VS therapy as an adjunct treatment regimen of patients with chronic heart failure.
NECTAR–HF Clinical Feasibility Trial

NEuroCardiac TherApy for Heart Failure (NECTAR-HF)

96 patient, 18 month randomized clinical trial in Europe

Patients:
NYHA III, EF ≤35%, QRS ≤ 130ms

Principal Investigator:
Faiez Zannad, MD, PhD

Recently opened first sites in France and Spain for enrollment

Visit www.clinicaltrials.gov for more details