Supplementary Online Content

Ikramuddin S, Blackstone RP, Brancatisano A, et al. Effect of reversible intermittent intra-abdominal vagal nerve blockade on morbid obesity: the ReCharge randomized clinical trial. *JAMA*. doi:10.1001/jama.2014.10540/

This supplementary material has been provided by the authors to give readers additional information about their work.

Inclusion Criteria

1. Informed consent

2. Body mass index (BMI) ≥ 40 kg/m^2 to 45 kg/m^2 or BMI ≥ 35 kg/m^2 to 39.9 kg/m^2 with at least one obesity related co-morbid condition. Co-morbid conditions may include one or more of the following and will be documented on the appropriate case report form:

    - Type 2 diabetes mellitus as defined in inclusion criterion #3 (limited to 10% of randomized subjects)

    - Hypertension as defined by systolic pressure > 140 mm Hg and/or diastolic pressure >90 mm Hg

    - Treated or untreated with systolic ≥140 mmHg and/or diastolic pressure >90 mm Hg

    - Treated with systolic <140 mm Hg and/or diastolic <90 mm Hg

    - Dyslipidemia as defined by total cholesterol >200 or LDL >130

    - Treated or untreated with total cholesterol ≥200 or LDL ≥130

    - Sleep apnea syndrome (confirmed by overnight pO2 studies)

    - Obesity related cardiomyopathy

3. 18-65 years of age inclusive

4. Males or females. Note: females of child-bearing potential must have a negative urine pregnancy test at screening and also within 14 days of implant procedure followed by physician-approved contraceptive regimen for the duration of the study period

5. Type 2 diabetes mellitus subjects with:

    - Glycosylated hemoglobin (HbA1c) 7.0-10% inclusive at screening visit (Undiagnosed subjects that are found to have a HbA1c 7-10% at screening must see their primary physician for diagnosis and medical treatment before continuing in trial);

    - Onset: 12 years or less since initial diagnosis;

- Currently not using insulin therapy, GLP-1 receptor agonists (e.g., exenatide), for diabetes treatment and have not been on these treatments in the past 6 months;

- Creatinine within normal reference range;

- No history peripheral neuropathy; autonomic neuropathy; coronary artery disease; or peripheral vascular disease

6. Failure to respond to a supervised diet/exercise programs in which the subject was engaged within the last five years

7. Ability to complete all study visits and procedures

Exclusion Criteria

1. Concurrent chronic pancreatic disease

2. History of Crohn's disease and/or ulcerative colitis, bariatric surgery, fundoplication, gastric resection or major upper-abdominal surgery (acceptable surgeries include cholecystectomy, hysterectomy), pulmonary embolism or blood coagulation disorders

3. Clinically significant hiatal hernias (>5 cm) known from subject's medical record or determined by barium swallow (upper GI x-ray) or upper endoscopy per PI discretion prior to implant.

4. Current cirrhosis, portal hypertension and/or esophageal varices.

5. Intra-operative exclusion: hiatal hernia requiring surgical repair or extensive dissection at esophagogastric junction at time of surgery

6. Treatment with prescription weight-loss drug therapy within the prior three months and the use of prescription drug therapy or the use of over-the-counter weight loss preparations for the duration of the trial

7. Smoking cessation within the prior six months

8. Known genetic cause of obesity (e.g., Prader-Willi Syndrome)

9. Weight loss of more than 10% TBL in the previous 12 months

10. Physician-prescribed pre-operative weight loss program prior to surgery. Note: Study subject may continue any personal eating plan they were on prior to study enrollment.

11. Current type 1 diabetes mellitus

12. Current or recent history (within 12 months) of ongoing bulimia

13. Current alterations in treatment for thyroid disorders (stable treatment regimen for prior three months acceptable)

14. Current alterations in treatment for epilepsy (stable treatment regimen for prior six months acceptable)

15. Current treatment for peptic ulcer disease (previous history acceptable)

16. Chronic treatment (more than 4 weeks of daily use) with narcotic analgesic drug regimens (treatment with non-steroidal anti-inflammatory drugs acceptable)

17. Current alterations in treatment regimens of anti-cholinergic drugs, including tricyclic antidepressants (stable treatment regimen for prior six months acceptable)

18. Current medical condition that, in the opinion of the investigator, would make subject unfit for surgery under general anesthesia or that would be exacerbated by intentional weight loss. Some examples include diagnosis of cancer, recent heart attack, recent stroke, or recent serious trauma.

19. Presence of permanently implanted electrical powered medical device or implanted gastrointestinal device or prosthesis (e.g., pacemakers, implanted defibrillators, neurostimulators etc.)

20. Planned or contemplated use of Magnetic Resonance Imaging (MRI) or oncologic radiation during the course of the trial

21. Psychiatric disorders (including untreated severe depression, schizophrenia, substance abuse, bulimia nervosa, etc.) or limited intellectual functioning twhich would potentially compromise the participant's ability to fully comprehend and/or cooperate with the study protocol. Psychiatric disorders will be established by a review of subject's medical history. For depression, a BDI score $\geq$29 will be considered to indicate severe depression.

22. Current, active member of an organized weight loss program (e.g., Weight Watchers, TOPS)

23. Current participant in another weight loss study or other clinical trials

24. Have a friend or family member who is currently participating or is planning to participate in this clinical trial

25. Patient reported inability to walk for about 10 minutes without stopping, feeling of pain in chest when doing physical activity, or feeling of pain in chest when not doing physical activity (unless pain in chest known to be related to upper gastrointestinal disorders such as gastroesophageal reflux disease or heartburn

26. Clinically significant cardiac rhythm disorder that requires either medical and/or surgical intervention (e.g., paroxysmal or chronic atrial fibrillation).

eTable 1. Serious Adverse Events through 12 Months

Serious Adverse Event	Vagal Nerve Block (n=162)		Sham (n=77)	
	No. (%) patients	**No. events**	**No. (%) patients**	**No. events**
SAEs related to device, implant/revision, or therapy				
Neuroregulator malfunction	2 (1.2)	2	0 (0.0)	0
Atelectasis	1 (0.6)	1	0 (0.0)	0
Gallbladder disease	1 (0.6)	1	0 (0.0)	0
Emesis/vomiting	1 (0.6)	1	0 (0.0)	0
Pain, neuroregulator site	1 (0.6)	1	0 (0.0)	0
Total	6 (3.7)	6	0 (0.0)	0
SAEs related to intra-abdominal surgery				
Nausea	6 (3.7)	6	0 (0.0)	0
Cirrhosis*	1 (0.6)	1	0 (0.0)	0
Generalized ileus	1 (0.6)	1	0 (0.0)	0
Intra-operative oozing	1 (0.6)	1	0 (0.0)	0
SAEs related to pre-existing condition or not related				
Allergic reaction	1 (0.6)	1	0 (0.0)	0
Chest pain	1 (0.6)	1	0 (0.0)	0
Colitis	1 (0.6)	1	0 (0.0)	0
Gallbladder disease	1 (0.6)	1	0 (0.0)	0
Gastritis	0 (0.0)	0	1 (1.3)	1
Infection, other	1 (0.6)	1	1 (1.3)	1
Osteoarthritis	1 (0.6)	1	0 (0.0)	0
Pain, abdominal	1 (0.6)	1	0 (0.0)	0
Pain, other	2 (1.2)	2	0 (0.0)	0
Palpitations	1 (0.6)	1	0 (0.0)	0
Pericarditis	1 (0.6)	1	0 (0.0)	0
Breast cancer	0 (0.0)	0	1 (1.3)	1
Worsening back pain	0 (0.0)	0	1 (1.3)	1

*Cirrhosis was found during the implant procedure and the patient was not implanted with a Maestro System.