ReActiv8 Implantable Neurostimulation System for Chronic Low Back Pain

Published: 22-12-2016
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To evaluate the safety and efficacy of ReActiv8 for the treatment of adults with Chronic Low Back Pain and no prior spine surgery when used in conjunction with medical management.

Ethical review	Approved WMO
Status	Completed
Health condition type	Muscle disorders
Study type	Interventional

Summary

ID

NL-OMON45928

Source
ToetsingOnline

Brief title
ReActiv8-B

Condition

- Muscle disorders
- Spinal cord and nerve root disorders
- Nervous system, skull and spine therapeutic procedures

Synonym
low back pain for at least 3 months, pain at back below

Research involving
Human

Sponsors and support

Primary sponsor: MML US Inc.
Source(s) of monetary or material Support: By the sponsor: MML US Inc.

Intervention

Keyword: Chronic low Back Pain, Lumbar multifidus, Neurostimulation

Outcome measures

Primary outcome

The Primary Efficacy Endpoint is a comparison of responder rates between Treatment and Control groups, where a *responder* is a Subject with >=30% reduction from baseline in average low back pain without any increase in pain medication and/or muscle relaxants prescribed and taken in the two weeks prior to the primary outcome assessment visit.

The primary safety assessment is serious device and/or procedure related adverse events in all subjects in the Intent to Treat Cohort at the primary Endpoint Assessment visit.

Secondary outcome

The secondary efficacy objectives:

1. Comparison of change in ODI between Treatment and Control groups at the Primary End Point Assessment Visit.

2. Comparison of change in EQ-5D between Treatment and Control groups at the Primary End Point Assessment Visit

3. Comparison of Percent Pain Relief between Treatment and Control groups reported by the Subject at the Primary End Point Assessment Visit

4. Comparison of Subject Global Impression of Change at the Primary End Point Assessment Visit

5. Comparison of number of subjects with Resolution of Low Back Pain (remitters

or cure) at the Primary End Point Assessment Visit

6. Evaluation of changes in primary and secondary efficacy metrics in Crossover

Group following the Outcome Post Crossover visit.

Study description

Background summary

Chronic low back pain is a major health problem, and the World Health Organization reports that *Low back pain is the most prevalent of musculoskeletal conditions; it affects nearly everyone at some point in time and about 4-33% of the population at any given point and back pain is the number one cause of years lived with disability worldwide in 2013".
Although there has been a lot of attention and investment applied to surgical treatments for low back pain, only approximately 20% of patients are suitable surgical candidates. Exercise therapy is frequently prescribed for low back pain, but the effectiveness of exercise therapy for acute back pain is negligible. Many non-invasive conservative therapies have been tried with modest or no success.
Published studies show that subject initiated contraction of the lumbar multifidus with ultrasound guided biofeedback motor control physical therapy exercises can lead to improvements in back pain, but this approach has not been adopted due to practical challenges, economic difficulties, and patient compliance issues. The mechanism of action is believed to be restoration of motor control of the lumbar multifidus, thereby leading to rehabilitation of the muscle, improved spine stability and reduction in back pain.
The ReActiv8 has been designed to incorporate the principles of these prior approaches. Bilateral electrical stimulation of the medial branch of the dorsal ramus nerve that innervates the lumbar multifidus is delivered episodically (10 seconds *on* followed by 20 seconds *off*, for 30 minutes, during two sessions per day). Previous experience with the therapy in the European Feasibility Study showed that most subjects can perceive the muscle contractions, and report the muscle contractions as *soothing* or *pleasurable.*
In subjects with chronic low back pain and no prior surgery and with unsatisfactory pain relief despite medical management, episodic electrical stimulation of the medial branch of the dorsal ramus nerves to cause contraction of the lumbar multifidus muscles can lead to relief of low back pain and the disabling effects of back pain. ReActiv8 is an adjunct to medical management in adults with Chronic Low Back Pain for relief of pain in subjects who have failed at least medical management and physical therapy.

Study objective

To evaluate the safety and efficacy of ReActiv8 for the treatment of adults with Chronic Low Back Pain and no prior spine surgery when used in conjunction with medical management.

Study design

International, multi-center, prospective, randomized, sham controlled, blinded trial with an adaptive statistical design.
Subjects are blinded, investigators are blinded, and the assessment of primary end point data is blinded.

Intervention

All subjects who satisfy the baseline criteria are implanted with the ReActiv8, and then at the randomization visit post-implant surgery are instructed to deliver stimulation during two 30-minute sessions (morning and evening) per day. Subjects are randomized (1:1) to the treatment or control arm at the randomization visit post-implant.
Subjects randomized to the treatment arm of the study will have ReActiv8 programmed to deliver stimulation at a subject-appropriate level (the Treatment group). Determination of the subject appropriate level is described in the Implant and Programming Manual. Subjects in the Treatment group may or may not feel muscle contraction during stimulation.
Subjects randomized to the control arm will have ReActiv8 programmed to deliver minimal stimulation (the Control group). Subjects in the Control group may or may not feel muscle contraction during stimulation.

After collection of all endpoint data, all Subjects in the Control group will have the ReActiv8 IPG programmed to deliver subject appropriate stimulation to cause strong smooth contraction of the multifidus.

Surgical implantation is adapted from familiar techniques used for medial branch rhizotomy and spinal cord stimulation.
The implant procedure should take place as soon as possible following the verification of baseline criteria, at a minimum of 1 day and maximum of 45 days following Visit 1.

Study burden and risks

The purpose of electrical stimulation of the medial branch of the dorsal ramus nerve with the ReActiv8 is to help restore neural drive to the lumbar multifidus muscle (LM). There are known clinical benefits to the restoration of neural drive to and rehabilitation of the LM when delivered by guided physical therapy with image guided biofeedback including:
• Improvements in the disabling effect of low back pain
• Improvements in severity of low back pain

• Reduction in recurrence of low back pain
• Improvement in ability to handle regular daily activities, including return to work
• Improvements in Quality of Life
Based on the Feasibility Study performed with other devices, there are expected benefits from the stimulation to be delivered by the ReActiv8, including decrease in low back pain, decrease in disability, and improvements in quality of life.
There may be no benefits to the Subject as a result of participation in this trial.

All medical device treatments have the potential to cause adverse events or side effects. Adverse events are expected to be similar to other neurostimulation devices for treatment of back pain.
Risks can be minimized through the use of strict compliance with the study protocol, and adherence to the guidelines for subject selection, site training, and close monitoring of the Subject*s physiologic status at follow-up visits.

Please refer to section E9 or the study protocol for a complete overview of potential risks.

Please refer to section E4 for an overview of all required study assessments which might mean an additional burden for the study patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Age >=22 years, <=65 years
2. 7 day recall of Average Low Back Pain (VAS of >=6.0cm and <=9.0cm at baseline)
3. Oswestry Disability Index score >=21% and <=60% at the Baseline Visit.
4. Chronic Low Back Pain defined as pain and discomfort localized below the costal margin and above the inferior gluteal fold (with or without referred leg pain) that has persisted >90 days prior to the baseline visit, which has resulted in pain in at least half of the days in the 12 months prior to the baseline visit.
5. Evidence of lumbar multifidus muscle dysfunction by the Prone Instability Test (PIT).
6. Continuing low back pain despite >90 days medical management including:
a. At least one attempt of physical therapy treatment
b. For Subjects with medications prescribed and used for chronic low back pain, usage shall be at a stable dose in the 30 days prior to the baseline visit
7. Be willing and capable of giving Informed Consent
8. Ability to comply with the instructions for use and to operate ReActiv8, and to comply with this Clinical Investigation Plan.
9. Suitable for ReActiv8 surgery as determined by the implanting physician prior to inclusion.

Exclusion criteria

1. BMI > 35
2. Back Pain characteristics:
a. Any surgical correction procedure for scoliosis, or a current clinical diagnosis of moderate to severe scoliosis.
b. Lumbar spine stenosis,
c. Neurological deficit possibly associated with the back pain.
d. Back pain due to pelvic or visceral reasons or infection.
e. Back pain due to inflammation or damage to the spinal cord or adjacent structures
f. Pathology seen on MRI that is clearly identified and is likely the cause of the CLBP that is amendable to surgery.
g. Back pain due to vascular causes such as aortic aneurysm and dissection.
3. Leg pain described as being worse than back pain, or radiculopathy below the knee.

4. Source of pain is the sacroiliac joint.
5. Certain surgical or other procedures exclusions (please refer to the protocol):
6. Planned surgery:
7. Pregnant or planning to be pregnant in the next 12 months.
8. Any other active implantable device
9. Prior exposure to an implantable neurostimulator for treatment of pain

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	17-10-2017
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Mainstay ReActiv8
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	22-12-2016
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	22-03-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Not approved Date:	26-07-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-06-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT02577354
CCMO	NL55826.078.16