VNS Therapy™

VNS Therapy™ System

Glossary

October 2023

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CE 0344

The year of authorization to affix the CE mark:

Model 102	2003
Model 102R	2003
Model 103	2005
Model 104	2005
Model 105	2011
Model 106	2014
Model 1000	2017
Model 1000-D	2020
Model 8103	2019
Model 302	2003
Model 303	2006
Model 304	2009
Model 220	2002
Model 402	2005
Model 502	2003
Model 2000	2017
Model 3000	2018

A

ACLS

Advanced cardiac life support

AE

Adverse event; any symptom, sign, illness, or experience that develops or worsens in severity and/or frequency during the course of a study or procedure (i.e., any changes from baseline)

AED

Antiepileptic drug

ARR

Antidepressant resistance rating

AutoStim Mode activation

Mode of operation specific to the generator models capable of heartbeat detection. The device listens for heart beats during Normal Mode OFF-time. When an increase in heart rate is detected (indicative of some seizure types) a train of stimulation is triggered similar to that of a Magnet Mode activation.

AutoStim threshold

Configurable threshold setting for heart rate increase which triggers automatic stimulation (AutoStim)

B

baseline period (depression) — D-02 acute phase

Two pre-implantation visits (Visits B1 and B2) for both groups.

baseline period (depression) — D-02 long-term phase

For the evaluation of efficacy, the period just before initiation of VNS Therapy; during the long-term phase, the baseline period of subjects who had been assigned to the acute treatment group during the acute phase differed from that of the subjects who had been assigned to the acute sham-control group; because this baseline period is just before treatment initiation for both groups, it is more comparable for analysis purposes.

baseline period (depression) — D-04

The visit that occurs after informed consent is obtained.

baseline period (depression) — Delayed treatment group (acute sham-control group)

During the long-term phase, the baseline for the subjects who had been assigned to the acute sham-control group during the acute phase was the final two acute study visits, V8 and V9 (acute study exit)

baseline period (depression) — Treatment group

During the long-term phase, the baseline for the subjects who had been assigned to the acute treatment group during the acute phase was the pre-implantation baseline (B1 and B2).

BOL

Beginning of life

bpm

Beats per minute

C

CGI (depression)

Clinical global impressions; two 7-point scales completed by the clinical rater to assess the subject's condition regarding the severity of illness (CGI-S) and global improvement (CGI-I); severity scale range: 1 (normal, not at all ill) - 7 (among the most extremely ill patients); improvement scale range: 1 (very much improved) - 7 (very much worse). NOTE: the CGI was developed by National Institute of Mental Health (NIMH) to provide a standardized assessment with clinically relevant anchors; it is one of the most widely used brief assessment tools in psychiatry.

chronic or recurrent depression

A current major depressive episode that is of at least two years in duration or a current major depressive episode in a patient with a history of multiple prior episodes of depression

clinical benefit (depression)

Degree of improvement in depression, as measured by the HRSD24: 1) Extraordinary clinical benefit (at least a 75% reduction from baseline) 2) Highly meaningful clinical benefit (at least a 50% but less than a 75% reduction from baseline) 3) Meaningful clinical benefit (at least a 25% but less than a 50% reduction from baseline) 4) Minimal or no clinical benefit (at least no change or less than a 25% reduction from baseline) 5) Worsened (increase in HRSD24 compared with baseline) NOTE: Physician expert consultants to the sponsor developed this designation.

clinical studies (depression)

D-01, D-02, D-04; clinical trials conducted in patients with chronic or recurrent treatment-resistant depression. The D-01 study was a long-term, open-label, uncontrolled trial of adjunctive VNS Therapy. The D-02 study included acute and long-term phases. The acute phase was a double-blind, randomized, sham-controlled trial of adjunctive VNS Therapy; the long-term phase was an open-label, uncontrolled trial of adjunctive therapy. The D-04 study was a long-term, prospective, observational study of patients with chronic or recurrent treatment-resistant depression who were being treated with standard antidepressant treatments, but not VNS Therapy.

complete response (depression)

Complete responder or remitter; subjects who scored less than a pre-defined score were considered to have achieved a complete response; scores representing complete response were an HRSD24 raw score of 9 or less, a MADRS raw score of 10 or less, or an IDS-SR raw score of 14 or less; this corresponds to the concept of remission, where the illness, in this case depression, has few to no residual symptoms present

D

duty cycle

Percentage of time during which stimulation occurs; stimulation time (programmed ON time plus 2 seconds of ramp-up time and 2 seconds of ramp-down time) divided by the sum of signal ON time and OFF time

E

EAS

Electronic article surveillance

ECG

Electrocardiogram

ECT

Electroconvulsive therapy; a treatment for depression and other indications using electrodes on the surface of the head to direct electrical current into the brain to induce a generalized seizure in a patient

electrode

Mechanical and electrical interface of the system to the vagus nerve; part of the lead

electrostatic discharge

ESD; sudden and momentary electric current that flows between two objects

EMI

Electromagnetic interference

EOS

End of service

ERI

Elective replacement indicator; synonymous with NEOS

excess duty cycle

Duty cycle for which the ON time is greater than the OFF time

F

failed adequate treatment

Failure to respond to electroconvulsive therapy or an established antidepressant drug administered at an adequate dose for an adequate duration

FDA

United States Food and Drug Administration

G

generalized onset seizure (epilepsy)

Type of seizure that involves all parts of the brain and, usually, an alteration in consciousness

generator

An implantable, multi-programmable part of the system; generates electrical impulses that are delivered through the lead to the vagus nerve; housed in a hermetically sealed titanium case and powered by a single battery

H

Heartbeat Detection

A configurable threshold setting for heart beat detection

high lead impedance

Resistance to the flow of output current produced by the generator, caused by any of the following: possible fibrosis between the nerve and electrode, dry nerve (during surgery), lead fracture, lead disconnection from the generator, or high battery impedance approaching end of service

HRSD24

Hamilton Rating Scale for Depression; the HRSD is the most widely used rating scale to assess symptoms of depression; a multi-dimensional, observer-rated scale for assessing overall depression severity; the 28-item version of the scale was administered to subjects in this study; per protocol for the feasibility (D-01) study, all 28 items were used for scoring purposes; per protocol for the pivotal (D-02) study, only the first 24 items were used for scoring purposes

I

IDS-SR30

Inventory of Depressive Symptomatology Self Report; a 30-item patient self-report rating of the symptoms of mood and depression

IFI

Intensified follow-up indicator

in-session

After interrogation of the patient generator

interrogate

Software operation that gathers current settings and a data from the generator

L

lead

An implantable part of the system; delivers electrical impulses from the generator to the electrodes attached to the vagus nerve; contains flexible conductive wires within a bio-compatible insulating sheath

LIMIT output current

Output current other than that which was programmed; not a sole indicator of a device malfunction

LOCF

Last observation carried forward; this analysis technique uses the last available data point for subsequent time points where data is missing

long-term phase (depression)

The portion of the pivotal (D-02) study comprising follow-up after the acute portion of the study (after Visit 9); the long-term portion included longitudinal follow-up by a blinded rater; the analysis of the long-term data included a repeated measures within-subjects analysis of changes in depressive symptoms over 12 months of VNS Therapy

low lead impedance

Lower than expected resistance to the flow of output current produced by the generator potentially caused by a short-circuit condition that results from a break within the lead body or connector boot

M

MADRS

Montgomery-Åsberg Depression Rating Scale; a 10-item scale completed by the clinical rater for assessing overall depression severity

magnet

LivaNova-provided magnet included in patient kits

Magnet Mode activation

Brief magnet application and removal, which initiates a stimulation

microcoulomb

Unit of electrical charge; product of current and time, or output current (in mA) multiplied by the pulse width (in msec)

MOS SF-36

Medical Outcome Survey 36-Item Short Form Health Survey; a quality of life (QOL) tool that assesses overall QOL and subscales of physical functioning, role functioning-physical, bodily pain, general health perceptions, vitality, social functioning, role functioning-emotional, mental health, and overall change in health

MR

Magnetic resonance

MR Conditional

A medical device with demonstrated safety in the MR environment within defined conditions including conditions for the static magnetic field, the time-varying gradient magnetic fields, and the radiofrequency fields

MR Unsafe

A medical device which poses unacceptable risks to the patient, medical staff or other persons within the MR environment

MRI

Magnetic resonance imaging

N

NEOS

Near end of service

nominal parameters

Specific preset parameters available with the software; LivaNova suggests that the generator be set to these parameters when stimulation is first activated

Normal Mode activation

Normal Mode stimulation is the primary operating mode of therapy. This mode is always on if the output current is programmed to a value greater than 0 mA

O

out-of-session

Prior to interrogation or after ending a session with a patient generator

output current

Amount of electrical current delivered in a single pulse of a stimulation, measured in mA

P

partial onset seizure (epilepsy)

Type of seizure that begins focally with a specific sensory, motor, or psychic aberration that reflects the affected part of the cerebral hemisphere where the seizure originated

patient ID

Any three-digit combination assigned by the prescriber; generally programmed at the time of implantation

phantom

A patient-equivalent form filled with gelled saline, used for in vitro tests of MRI-related heating

Programmer

Programming computer; tablet-style touchscreen computer loaded with programming software used to program LivaNova generators

programming system

Programming wand and computer loaded with programming software

pulse width

Duration of a single pulse within a stimulation, measured in µsec

R

radio frequency (RF)

Used in MR systems during the imaging process; also responsible for heating of the patient during MRI; the lead, when exposed, can focus strong RF energy fields, such as those used during MRI, and cause excessive heating and possible injury

ramp-down

Gradual decrease over approximately 2 seconds in output current at the end of stimulation for signal frequencies of 10 Hz and greater

ramp-up

Gradual increase over approximately 2 seconds in output current at the beginning of stimulation for signal frequencies of 10 Hz and greater

receiver operating characteristic curve (ROC)

A curve that demonstrates the relationship between the sensitivity of a diagnostic and the specificity of the diagnostic.

reed switch

A mechanism that works like a gate. When the magnet closes it, the normal signal (stimulation) cannot pass; the generator is temporarily turned off

refractory

Resistant to previous treatment alternatives defined by the treating physician; generally refers to the epilepsy of patients who have tried and failed two or more antiepileptic drugs

remission (remitter) (depression)

Complete responder or remitter; subjects who scored less than a pre-defined score were considered to have achieved a complete response; scores representing complete response were an HRSD24 raw score of 9 or less, a MADRS raw score of 10 or less, or an IDS-SR raw score of 14 or less; this corresponds to the concept of remission, where the illness, in this case depression, has few to no residual symptoms present

reset parameters

Parameters to which the generator internally programs when it is reset

responder (depression)

At a given point, a subject with a greater or equal to 50% reduction in HRSD, MADRS, or IDS-SR scores from baseline or a CGI improvement rating of 1 or 2

S

SAE

Serious adverse event; any adverse event that resulted in any of the following outcomes: death, a life threatening adverse experience, in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant disability / incapacity, a congenital anomaly / birth defect, or any medical intervention that prevents one of the above Note: The sponsor also included cancer and pregnancy as SAEs

SAR

Specific absorption rate; a measure of RF power deposition in the MRI patient, usually expressed in watts per kilogram (W/kg)

sensitivity

The statistical probability that an event will be correctly identified as a positive when administering a test designed to detect a particular event

signal frequency

Repetition rate of pulses in a stimulation; measured in number of pulses per second (Hz)

signal OFF time

Interval between stimulations when there is no stimulation; measured in minutes

signal ON time

Length of time the programmed output current is delivered (does not include ramp-up and ramp-down times); measured in seconds

spatial gradient field

The change in the static magnetic field strength with respect to distance, usually expressed as Gauss/cm

specificity

The statistical probability that a non-event will be correctly identified as a negative when administering a test designed to detect a particular event

static magnetic field strength

Strength of the static magnetic field used by an MR system for MRI, usually expressed in Tesla (e.g., 1.5 T, 3 T)

statistically significant

Results are considered statistically significant if p-values for the appropriate statistical tests are less than or equal to 0.050

stimulation adjustment period (depression)

For the treatment group, a 2-week period between Visit 2 and Visit 4 during the acute portion of the study. For the delayed treatment group, a 2-week period between Visit 9 and Visit 11 at the start of the long-term study. The output current was progressively increased to a comfortably tolerable level during this period. After this period, output current was held constant for an 8-week period, unless reduction was necessary for tolerance.

stimulation parameters

Programmed output current, signal frequency, pulse width, signal ON time, and signal OFF time

stimulation time

Therapeutic output of the generator; consists of the signal ON time, plus 2 seconds of ramp-up time and 2 seconds of ramp-down time

SUDEP

Sudden unexpected death in epilepsy

T

tachycardia

Rapid, relative heart rate increase

transmit and receive RF head coil

A local imaging coil that both supplies RF energy and receives resonance signals during MRI procedure

treatment-emergent

Adverse events that occurred on or after the implant and were not present during the baseline period or events that were present during baseline that worsened in severity after the implant

treatment failures (depression)

Subjects who, after the randomization procedure, 1) exited the acute study before Visit 9 due to treatment-related adverse events, or a lack of efficacy, 2) met the suicide exclusion criteria, 3) attempted suicide resulting in hospitalization of more than 3 days, or 4) developed mania or more than three mood episodes as defined by DSM-IV Note: Subjects who were treatment failures during the acute study were also considered treatment failures for long-term analysis purposes.

U

UADE

Unanticipated adverse device effect; any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application); also, any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of patients

V

vagus nerve

Either of the pair of tenth cranial nerves that arise from the medulla and supply mainly the viscera, especially with autonomic sensory and motor fibers

vbat

Voltage of the generator battery

verify heartbeat detection

A feature that when activated by the VNS programming software, relays back heart beat detection sensed by the generator for up to 2 minutes

VNS

Vagus nerve stimulation

VNS Therapy

The registered name for vagus nerve stimulation

W

Wand

Programming wand; hand-held device used to communicate with LivaNova generators

within-group

A statistical comparison, which includes only subjects in the same group assignment

Y

YMRS (depression)

Young Mania Rating Scale; an 11-item scale completed by the clinical rater to assess the symptoms of mania

Contacts and Resources

For information and support in use of the system or any of its accessories, contact LivaNova.

Contacts

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Regulatory Authority Websites

Report all adverse events related to the device to LivaNova and to your local regulatory authority.

Australia	https://www.tga.gov.au/
Canada	https://www.canada.ca/en/health-canada.html
UK	https://www.gov.uk/government/organisations/medicines-and-healthcare-products-regulatory-agency
EU	https://ec.europa.eu/growth/sectors/medical-devices/contacts_en