

VNS Therapy™

CELEBRATING

30
years
OF STIMULATING LIFE

Vagus Nerve Stimulation Summit for Turkey and Middle East

22 - 23 November 2024
Hilton Bakirkoy, Istanbul

Endorsed by:



AGENDA

Friday, 22nd of Nov. 2024

Time	Session	Speaker	Moderator
08:30 - 09:00	Registration	ALL	
09:00 - 09:30	Welcome & Meeting Objectives	Turkish Epilepsy Society	
09:30 - 10:00	Burden of DRE Management in Turkey and the Middle East	Nerses Bebek	
10:00 - 10:30	Past, Present, and Future of Vagus Nerve Stimulation Therapy™	Jonathan Hunt	
10:30 - 11:00	Open Loop vs Closed Loop Stimulation	Ahmad Baydoun	Cigdem Ozkara
11:00 - 11:30	30 Years of Evidence Generation	Maxine Dibue	
11:30 - 12:00	Coffee Break		
12:00 - 12:30	CORE Registry	Saleh Baessa	
12:30 - 13:00	Factors Affecting QOL in DRE	Lina Nashef	
13:00 - 13:30	Panel Discussion	All	
13:30 - 14:30	Lunch & Prayer		
14:30 - 15:00	Vagus Nerve Stimulation Therapy™ in Turkey	Cigdem Ozkara	
15:00 - 15:30	Sentiva Experience in Saudi Arabia	Fawzi Babtain	
15:30 - 16:00	Road to Vagus Nerve Stimulation Therapy™ in Egypt	Nermeen Kiskh	
16:00 - 16:30	Coffee Break		Ahmad Baydoun
16:30 - 17:00	Case Presentation from Jordan	Muath Qurashi	
17:00 - 17:30	Panel Discussion	All	
17:30 - 17:40	Closing of Day 1		
19:30 - 22:00	Group Dinner	All	

AGENDA

Saturday, 23rd of Nov. 2024

Time	Session	Speaker	Moderator
09:00 - 09:30	Why a Uniform Definition of Seizure Freedom Matters?	Patrick Kwan	
09:30 - 10:00	VNS Parameters for Clinical Response in Epilepsy	Riem El Tahry	
10:00 - 10:30	VNS Therapy for Pediatrics™	David McCormick	
10:30 - 11:00	Panel Discussion	All	Hasan Hosny
11:00 - 11:30	Coffee Break		
11:30 - 12:00	Mechanism of Action	Ahmad Abbas	
12:00 - 12:30	Economical Evidence Demonstrating the Value of VNS Therapy™	Rhonda Shaw	
12:30 - 13:30	Lunch		
13:30 - 15:30	Dosing Workshop	Ahmad Abbas	
15:30	Close and Departure	Nerses Bebek	Nerses Bebek

Brief Summary¹ of Safety Information for the VNS Therapy™ System

[Epilepsy Indication] (February 2021)

1. INTENDED USE / INDICATIONS

Epilepsy (Non-US) – The VNS Therapy System is indicated for use as an adjunctive therapy in reducing the frequency of seizure in patients whose epileptic disorder is dominated by partial seizures (with or without secondary generalization) or generalized seizures that are refractory to seizure medications. AspireSR™, Sentiva™ and Sentiva DUO™ feature an Automatic Stimulation Mode which is intended for patients who experience seizures that are associated with cardiac rhythm increases known as ictal tachycardia.

2. CONTRAINDICATIONS

VagusNerve™ – The VNS Therapy System cannot be used in patients after a bilateral or left cervical vagotomy.

Diathermy – Do not use short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy on patients implanted with a VNS Therapy System. Diagnostic ultrasound is not included in this contraindication.

3. WARNINGS – GENERAL

Physicians should inform patients about all potential risks and adverse events discussed in the physician's manuals. This document is not intended to serve as a substitute for the complete physician's manuals.

The safety and efficacy of the VNS Therapy System have not been established for uses outside the "Intended Use/Indications" chapter of the physician's manuals.

The safety and effectiveness of the VNS Therapy System in patients with predisposed dysfunction of cardiac conduction systems (e-entry pathway) have not been established. Post-implant electrocardiograms and Holter monitoring are recommended if clinically indicated.

Postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. It is important to follow recommended implantation procedures and intraoperative product testing described in the Implantation Procedure chapter of the physician's manual. During the intraoperative System Diagnostics (Lead-Entry Pathway) test, bradycardia and/or asystole have occurred. If asystole/severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate is encountered during a System Diagnostics (Lead Test) or during initiation of stimulation, physicians should be prepared to follow guidelines consistent with Advanced Cardiac Life Support (ACLS). Difficulty swallowing (dysphagia) may occur with active stimulation, and aspiration may result from the increased swallowing difficulties. Patients with pre-existing swallowing difficulties are at greater risk for aspiration.

Dyspnea (shortness of breath) may occur with active VNS Therapy. Any patient with underlying pulmonary disease or insufficiency such as chronic obstructive pulmonary disease or asthma may be at increased risk for dyspnea.

Patients with obstructive sleep apnea (OSA) may have an increase in apneic events during stimulation. Lowering stimulus frequency or prolonging "OFF" time may prevent exacerbation of OSA. Vagus nerve stimulation may also cause new onset sleep apnea in patients who have not previously been diagnosed with this disorder.

Device malfunction could cause painful stimulation or direct current stimulation. Either event could cause nerve damage. Patients should be instructed to use the magnet to stop stimulation if they suspect a malfunction, and then to contact their physician immediately for further evaluation.

Patients with the VNS Therapy System or any part of the VNS Therapy System implanted should have MRI procedures performed only as described in the MRI with the VNS Therapy System instructions for use. In some cases, surgery will be required to remove the VNS Therapy System if a scan using a transmit RF body coil is needed.

Excessive stimulation at an excess duty cycle (i.e., one that occurs when "ON" time is greater than "OFF" time) and high frequency stimulation (i.e., stimulation at ≥50Hz) has resulted in degenerative nerve damage in laboratory animals.

Patients who manipulate the generator and lead through the skin (Tiddler's Syndrome) may damage or disconnect the lead from the generator and/or possibly cause damage to the vagus nerve.

The Wand, Programmer, and patient magnet are MR unsafe devices. These devices are projectile hazards and must not be brought into the MR scanner room.

Generators with AutoStim only – The AutoStim Mode feature should not be used in patients with clinically meaningful arrhythmias or who are using treatments that interfere with normal intrinsic heart rate responses (e.g., pacemaker dependence, implantable defibrillator, beta adrenergic blocker medications). Patients also should not have a history of chronotropic incompetence (commonly seen in patients with sustained bradycardia (heart rate < 50 bpm)).

4. WARNINGS – EPILEPSY

The VNS Therapy System should only be prescribed and monitored by physicians who have specific training and expertise in the management of seizures and the use of this device. It should only be implanted by physicians who are trained in surgery of the carotid sheath and have received specific training in the implantation of this device.

The VNS Therapy System is not curative. Physicians should warn patients that the VNS Therapy System is not a cure for epilepsy and that since seizures may occur unexpectedly, patients should consult with a physician before engaging in unsupervised activities, such as driving, swimming, and bathing, and in strenuous sports that could harm them or others.

Sudden unexpected death in epilepsy (SUDEP). Through August 1996, 10 sudden and unexpected deaths (definite, probable, and possible) were recorded among the 1,000 patients implanted and treated with the VNS Therapy device. During this period, these patients had accumulated 2,017 patient-years of exposure. Some of these deaths could represent seizure-related deaths in which the seizure was not observed, at night, for example. This number represents an incidence of 5.0 definite, probable, and possible SUDEP deaths per 1,000 patient-years. Although this rate exceeds that expected in a healthy (nonepileptic) population matched for age and sex, it is within the range of estimates for epilepsy patients not receiving vagus nerve stimulation, ranging from 13 SUDEP deaths for the general population of patients with epilepsy, to 3.5 (for definite and probable) to a recently studied antiepileptic drug (AED) clinical trial population similar to the VNS Therapy System clinical cohort, to 9.3 for patients with medically intractable epilepsy who were epilepsy surgery candidates.

5. PRECAUTIONS – GENERAL

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy physician's manuals.

Patients being physicians should be experienced in the diagnosis and treatment of depression or epilepsy and should be familiar with the programming and use of the VNS Therapy System.

Physicians who implant the VNS Therapy System should be experienced performing surgery in the carotid sheath and should be trained in the surgical technique related to implantation of the VNS Therapy System.

References: 1. Data on file. Survey Report. LivaNova USA, Inc. Houston, TX, October 2021. 2. Data on file. LivaNova USA, Inc. Houston, TX, November 23, 2022. 3. Mula M, Zaccara G, Galimberti CA, et al. *Epilepsia*. 2019;60(6):1111-1123. 4. Mohanji R, Brodie MJ, Eur J Neurol. 2006;13(3):277-282. 5. Luoni C, Busilfi F, Canevini MP, et al. *Epilepsia*. 2015;56(2):2181-2191. 6. Loring DW, Meador KJ, Lee GP. *Epilepsy Behav*. 2004;5(6):976-980. 7. Hamilton P, Sornay L, Dhanraj P, et al. *Epilepsy Behav*. 2018;88:120-126. 8. Elliott RE, Morsi A, Tanweer O, et al. *Epilepsy Behav*. 2012;20(3):478-483. 9. Data on file. LivaNova USA, Inc. Houston, TX, 10. Kim SJ, Kim DY, Jo HI, et al. *J Clin Neurosci*. 2017;31:385-392. 11. Ben-Menachem E. *J Clin Neurophysiol*. 2001;18(5):475-418. 12. Morris C L, Mueller WM. *Neurology*. 1999;53(8):1737-1735. 13. VNS Therapy™ System Epilepsy Physician's Manual (OUS), LivaNova USA, Inc. 2021; 14. Soleman J, Stein M, Knorr C, et al. *Epilepsy Behav*. 2018;88:139-145.

MANUFACTURER

LIVANOVA USA, INC.
100 Cyberonics Boulevard
Houston, Texas 77058, USA
Tel: +1 (281) 228-7200
+1 (800) 323-1375
Fax: +1 (281) 218-9332
www.livanova.com

EC REPRESENTATIVE

LIVANOVA BELGIUM NV
Ikaroslaan 83
B-1930 Zaventem,
BELGIUM
Tel: +32 (0)20 2099331
Fax: +32 (0)20 2066053
www.vnstherapy.co.uk

¹ The information contained in this Brief Summary of Physician's represents partial excerpts of important prescribing information taken from the physician's manuals. (Copies of VNS Therapy physician's and patient's manuals are posted at www.livanova.com) The information is not intended to serve as a substitute for a complete and thorough understanding of the material presented in all of the physician's manuals for the VNS Therapy System and its component parts nor does this information represent full disclosure of all pertinent information concerning the use of this product, potential safety complications, or efficacy outcomes. Not approved in all geographies.

All trademarks and trade names are the property of LivaNova or the property of LivaNova's consolidated subsidiaries and are protected under applicable intellectual property laws. Solely for convenience, LivaNova's trademarks and trade names may appear without the ® or TM symbols, but such references are not intended to indicate in any way that LivaNova will not assert to the fullest extent under applicable law, LivaNova's rights to these trademarks and trade names. Prior permission from LivaNova is required for use or reproduction of such intellectual property rights. EPI-2400538

The safety and effectiveness of the VNS Therapy System have not been established for use during pregnancy. VNS should be used during pregnancy only if clearly needed.

The VNS Therapy System is indicated for use only in stimulating the left vagus nerve in the neck area inside the carotid sheath. The VNS Therapy System is indicated for use only in stimulating the left vagus nerve below where the superior and inferior cervical cardiac branches separate from the vagus nerve. It is important to follow infection control procedures. Infections related to any implanted device are difficult to treat and may require that the device be explanted. The patient should be given antibiotics preoperatively. The surgeon should ensure that all instruments are sterile prior to the procedure. Children (< 12 years of age) may have a greater risk for infection when compared to adolescent and adult patients (> 12 years). Careful monitoring for site infection as well as the avoidance of manipulation of the surgical site post implant in children should be stressed.

The VNS Therapy System may affect the operation of other implanted devices, such as cardiac pacemakers and implanted defibrillators. Possible effects include sensing problems and inappropriate device responses. The patient requires concurrent implanted pacemaker, defibrillator therapy, or other types of stimulators, careful programming of each system may be necessary to optimize the patient's benefit from each device.

Reversal of lead polarity has been associated with an increased chance of bradycardia in animal studies. It is important that the electrodes are attached to the left vagus nerve in the correct orientation. It is also important to make sure that leads with dual connector pins are correctly inserted (White marker inside + connection) into the generator's lead receptacles. The patient can use a neck brace for the first week to help ensure proper lead stabilization. Do not program the VNS Therapy System to an "ON" or periodic stimulation treatment for at least 14 days after the initial or replacement implantation.

For Models 100, 101, 102 and 102R do not use frequencies of 5 Hz or below for long-term stimulation. Resetting the pulse generator turns the device OFF (output current = 0 mA). For Model 100, 101, 102 and 102R, the pulse generator will not reset in device history logs.

Patients who smoke may have an increased risk of lymphatic irritation.

Generators with AutoStim only – For devices that sense changes in heart rate, false positive detection may cause unintended stimulation. Examples of instances where heart rate may increase include exercise, physical activity, and normal autonomic changes in heart rate, both awake and asleep, etc.

Generators with AutoStim only – For the AutoStim feature, the physical location of the device critically affects its ability to properly sense heart beats. Therefore, care must be taken to follow the implant location selection process outlined in the Implantation Procedure. Note that this implant location selection procedure may be performed preoperatively as part of the patient's surgical work-up.

M1000/1000-D only – Since the Scheduled Programming feature allows the generator to apply therapy increases at scheduled intervals, it may not be appropriate for use in patients who are nonverbal or unable to use the patient magnet to stop undesired stimulation. Similarly, exercise caution for use of this feature in patients with a history of obstructive sleep apnea, shortness of breath, coughing, swallowing difficulties, or aspiration.

6. ENVIRONMENTAL AND MEDICAL THERAPY HAZARDS

Patients should exercise reasonable caution in avoiding devices that generate a strong electric or magnetic field. If a generator ceases operation while in the presence of electromagnetic interference (EMI), moving away from the source may allow the generator to return to its normal mode of operation.

VNS Therapy System operation should always be checked by performing device diagnostics after any of the procedures mentioned in the physician's manuals.

For clear imaging, patients may need to be specially positioned for mammography procedures, because of the location of the generator in the chest.

Therapeutic radiation may damage the generator's circuitry. Sources of such radiation include therapeutic radiation, cobalt machines, and linear accelerators. The total dose of radiation is cumulative, with the total dosage determining the extent of damage. The effects of exposure to such radiation can range from a temporary disturbance to permanent damage, and may not be detectable immediately.

External defibrillation may damage the generator.

Use of electrography (electrocardiography or radio frequency (RF) ablation devices) may damage the generator.

Magnetic resonance imaging (MRI) should not be performed using a transmit RF body coil for certain VNS Therapy device configurations or under certain specific conditions. In some cases, heating of the lead caused by the transmit RF body coil with MRI may result in serious injury. Static, gradient, and radio frequency (RF) electromagnetic fields associated with MRI may change the generator settings (i.e., reset parameters) or activate the VNS device if the Magnet Mode output remains "ON". Note that certain resonance (MRI) system head coils operate in receive-only mode and require use of the transmit RF body coil. Other MRI systems use a transmit/receive RF head coil. Local or surface coils may also receive-only RF coils that require the transmit RF body coil for MRI. The use of a receive RF coil does not alter hazards of the transmit RF body coil. Exposure of the VNS Therapy System to any transmit RF coil must be avoided. Do not perform MRI scans using any transmit RF coil in the defined exclusion zones. See the MRI with the VNS Therapy System instructions for use for details or further instructions for special cases such as lead breakers or partially explanted VNS Therapy systems.

Extracorporeal shockwave lithotripsy may damage the generator. If therapeutic ultrasound therapy is required, avoid positioning the area of the body where the generator is implanted in the water bath or in any other position that would expose it to ultrasound therapy. If that positioning cannot be avoided, program the generator output to 0 mA for the treatment, and then after therapy, reprogram the generator to the original parameters.

If the patient receives medical treatment for which electric current is passed through the body (such as from a TENS unit), either the generator should be set to 0 mA or function of the generator should be monitored during initial stages of treatment.

Routine therapeutic ultrasound could damage the generator and may be inadvertently consented by the device, causing the generator to cease operation.

For complete information related to home occupational environments, cellular phones, other environmental hazards, other devices, and ECG monitors, refer to the physician's manuals.

7. ADVERSE EVENTS – EPILEPSY

Adverse events reported during clinical studies as statistically significant are listed below in alphabetical order: ataxia (loss of the ability to coordinate muscular movement), dyspepsia (indigestion), dyspnea (difficulty breathing, shortness of breath), hyposthesia (impaired sense of touch), increased coughing, infection, insomnia (inability to sleep), laryngospasm (throat), laryngospasm (throat), nausea, paresthesia (prickling of the skin), pharyngitis (inflammation of the pharynx, throat), voice alteration (hoarseness), vomiting. Adverse events reported in clinical investigation of the AutoStim feature were comparable. 26-0009-0100-6 (OUS) – 1

LivaNova
Epilepsy



VNS Therapy™
STIMULATING LIFE