Protocol Registration Receipt
11/29/2008

A Safety and Tolerability Study of Intracerebroventricular Administration of sNN0029 to Patients With Amyotrophic Lateral Sclerosis

This study is not yet open for participant recruitment.
Verified by NeuroNova AB, November 2008

Sponsored by:	NeuroNova AB Medtronic ICON Clinical Research
Information provided by:	NeuroNova AB
ClinicalTrials.gov Identifier:	

Purpose

This study is conducted to evaluate the safety and tolerability of the drug product sNN0029, containing the growth factor VEGF165, when administered directly into one of the fluid filled cavities in the brain using an implanted catheter and an implanted SynchroMed® II pump. Patients with Amyotrophic Lateral Sclerosis will be enrolled.

Condition	Intervention	Phase
Amyotrophic Lateral Sclerosis	Drug: sNN0029 Drug: Placebo	Phase 1/Phase 2

Study Type: Interventional
Study Design: Treatment, Parallel Assignment, Double Blind (Subject, Caregiver, Investigator, Outcomes Assessor), Randomized, Placebo Control, Safety Study
Official Title: A Double-Blind, Randomised, Parallel Group Safety and Tolerability Study of Intracerebroventricular Administration of sNN0029 to Patients With Amyotrophic Lateral Sclerosis, Using an Implanted Catheter and SynchroMed® II Pump

Further study details as provided by NeuroNova AB:

Primary Outcome Measure:

- Safety and tolerability through assessment of adverse events, ECGs, vital signs, clinical laboratory variables, MRI of brain and spinal cord, CSF sampling, and device performance as characterized by catheter tip placement and infusion accuracy. [Time Frame: Multiple assessments over 3 months] [Designated as safety issue: No]

Secondary Outcome Measures:

- Time course of Amyotrophic Lateral Sclerosis Functional Rating Scale, Quality of life as measured by the EQ-5D rating scale [Time Frame: Multiple assessments over 3 months] [Designated as safety issue: No]

Estimated Enrollment: 28
Study Start Date: December 2008
Estimated Study Completion Date: March 2010
Estimated Primary Completion Date: March 2010

Arms	Assigned Interventions
Experimental: sNN0029	Drug: sNN0029 Continuous ICV infusion at one of three dose levels
Placebo Comparator: Placebo	Drug: Placebo Continuous ICV infusion

Vascular endothelial growth factor (VEGF) is an endogenous human protein fundamental to the development of the vascular and nervous systems in the body. A role for VEGF in ALS has been suggested from observations in animal models of the disease as well as observations of a dysregulation of VEGF production in patients with ALS.

NeuroNova intends to investigate whether intracerebroventricular administration of VEGF165 in the form of the drug product sNN029 can improve motor function and prolong survival in patients with ALS, and in this first study the safety and tolerability of treatment for 3 months will be evaluated.

Assessments will include:

- Electrocardiograms, vital signs and clinical laboratory tests
- Adverse events and withdrawals related to adverse events
- Possible pathological changes in the brain, spinal cord or retina identified through magnetic resonance imaging and funduscopy
- Possible signs of intracranial bleeding or loss of blood-brain-barrier integrity through measurements of bilirubin and albumin levels in cerebrospinal fluid collected through lumbar and cervical puncture
- Device performance as characterized by catheter tip placement (determined by imaging) and infusion accuracy (pump residual volume)

The secondary objective of this study is:

- To explore the effect of ICV administration of sNN0029 on the time course of Amyotrophic Lateral Sclerosis related parameters including:
    - Disease activity as measured by Amyotrophic Lateral Sclerosis Functional Rating Scale

- Quality of life as measured by the EQ-5D rating scale

- To explore the levels of VEGF165 in cerebrospinal fluid collected through lumbar and cervical puncture.

Eligibility

Ages Eligible for Study: 18 Years to 75 Years
Genders Eligible for Study: Both

Inclusion Criteria:

1. Clinical diagnosis of ALS classified as definite, or probable with or without additional laboratory evidence, according to the revised WFN El Escorial criteria.
2. Age 18 to 75 years inclusive.
3. If patients are being treated with riluzole, they must have been on a stable dose for at least 30 days.
4. Ophthalmological examination at screening with normal findings regarding vascular structure and function.
5. MRI/magnetic resonance angiography (MRA) examination of the brain and cervical spinal cord at screening with no findings of tumors or potential sources of pathological bleedings, or abnormality that may interfere with the assessments of safety or efficacy or that would, in the judgement of the investigator, represent a surgical risk to the subject.
6. Values of coagulation parameters including platelet count, bleeding time, normalized prothrombin complex (PK-INR), activated partial thromboplastin time (APTT) within normal ranges.
7. Patient is medically able to undergo the surgery required for stereotactic implantation of the catheter and infusion pump.
8. Patient has been given written and verbal information, has had the opportunity to ask questions about the study, and understands the time and procedural commitments.
9. Patient has given signed consent (written) to participate in the study.

Exclusion Criteria:

1. Impaired respiratory function judged to pose a risk to the patient during anaesthesia for the device implantation.
2. Hypertension defined as blood pressure >160 mmHg systolic or >90 mmHg diastolic.
3. Diagnosis of diabetes mellitus.
4. Proliferative retinopathy.
5. Non-proliferative retinopathy of moderate severity or higher.
6. Concurrent clinically significant dementia as determined by the investigator.
7. Concurrent clinically significant depression as determined by the investigator.
8. History of structural brain disease other than ALS, including tumours and hyperplasia.
9. Any disorder that precludes a surgical procedure (e.g., signs of sepsis or inadequately treated infection), alters wound healing (e.g., including bleeding disorders), or renders chronic ICV delivery or device implants medically unsuitable.
10. Presence of risk for increased or uncontrolled bleeding and/or risk of bleeding that is not managed optimally. Physicians should specifically investigate anatomical factors at or near the implant site (e.g., vascular abnormalities, neoplasms, or other abnormalities), underlying disorders of the coagulation cascade, platelet function, or platelet count (e.g., haemophilia, Von Willebrand’s disease, liver disease, or other medical conditions), and the administration of any antiplatelet or anticoagulant medication (e.g., aspirin, Plavix, NSAIDs) in the pre- or perioperative period. Any of those conditions or drugs could place a

patient at an increased risk for intraoperative or postoperative bleeding.

11. Presence of an implanted shunt for the drainage of CSF or an implanted CNS catheter.
12. Presence of cardiac pacemakers, spinal cord stimulators, implantable programmable intraspinal drug pumps, or any other device that may interfere or interact with the programmer, without prior approval by Medtronic.
13. Clinically significant abnormalities in hematology or clinical chemistry parameters as assessed by the investigator.
14. Ongoing medical condition that according to the investigator would interfere with the conduct and assessments in the study. Examples are medical disability (e.g., severe degenerative arthritis, compromised nutritional state, peripheral neuropathy) that would interfere with the assessment of safety and efficacy of investigational product or device performance, or would compromise the ability of the subject to undergo study procedures (e.g., MRI), or to give informed consent.
15. Participation in another clinical trial with an investigational drug or device within 3 months prior to Screening visit.
16. For female subjects, ongoing pregnancy or planned pregnancy during the period of treatment with study drug.
17. Breast feeding during the period of treatment with study drug.

Contacts and Locations

Locations

Belgium

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Principal Investigator: Wim Robberecht, MD PhD

Investigators

Principal Investigator:	Wim Robberecht, MD PhD	University Hospital Leuven, Department of Neurology

More Information

Responsible Party:	University Hospital Leuven (Dr Wim Robberecht)
Study ID Numbers:	sNN0029-001
Health Authority:	Belgium: FAGG