Frontier Research Study:

Brief Summary:
The purpose of this study is to determine whether NA-1 is effective in reducing global disability in patients with acute cerebral ischemia if administered early after symptom onset.

Condition or disease	Intervention/treatment	Phase
Acute Cerebral Ischemia	Drug: NA-1Drug: Placebo	Phase 3

Detailed

Description:

NA-1 is being developed as an emergency drug aimed at reducing global disability in patients with acute cerebral ischemia if administered early after symptom onset.

The primary objective is to determine the efficacy of NA-1 in reducing global disability in patients with acute stroke. The secondary objectives are to determine the efficacy of NA-1 in reducing functional dependence, improving neurological outcome, improving activities of daily living, and increasing the proportion of subjects who are candidates for endovascular recanalization therapy.

The leading safety objectives are to determine the effect of administering a target dose of 2.60 mg/kg IV infusion of NA-1 within three hours of symptom onset by paramedics in the field on serious adverse events and 90-day mortality.

This trial is a multicenter, randomized, double-blind, placebo-controlled, single dose study initiated prehospital in the ambulance. It is being conducted using Emergency Medical Services (EMS) in Canada. Subjects with suspected acute stroke will be identified in the field by trained paramedics using the approved stroke protocol in use by the local EMS system, and further screened for eligibility and approval by an on-call trial physician. The paramedics will administer the study drug. Upon arrival at the emergency department, subjects will receive standard-of-care.

An Independent Data Monitoring Committee will perform safety reviews of the clinical data.

Study Design

Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	558 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Masking:	Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Primary Purpose:	Treatment
Official Title:	A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Determine the Efficacy and Safety of Intravenous NA-1 Initiated by Paramedics in the Field for Acute Cerebral Ischemia Within Three Hours of Symptom Onset
Actual Study Start Date :	March 26, 2015
Estimated Primary Completion Date :	March 31, 2020

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Arms and Interventions

Arm	Intervention/treatment
Experimental: NA-1 2.60 mg/kg of NA-1 administered as a single 10 minute IV infusion using an ambulatory infusion pump early after stroke symptom onset.	Drug: NA-1
Placebo Comparator: Placebo Placebo administered as a single 10 minute IV infusion using an ambulatory infusion pump early after stroke symptom onset.	Drug: Placebo

Outcome Measures

Primary Outcome Measures :

1. Modified Rankin Scale (mRS) scale [Time Frame: 90 days]
   The percentage of responders, using a sliding dichotomy on the mRS

Secondary Outcome Measures :

1. mRS shift analysis [Time Frame: 90 Days or the last rating]
   Shift to reduced functional dependence analyzed across the whole distribution of scores on the mRS
2. Proportion of subjects with functional independence [Time Frame: 90 Days or the last rating]
   Proportion of subjects with functional independence, as defined by a score of a) 0-2 and b) 0-1 on the mRS
3. National Institutes of Health Stroke Scale (NIHSS) [Time Frame: 90 Days or the last rating]
   Proportion of subjects with good neurological outcome, as defined by a score of 0-1 on the NIHSS
4. Barthel Index [Time Frame: 90 Days or the last rating]
   Proportion of subjects with functional independence in activities of daily living, as defined by a score of ≥ 95 on the Barthel Index
5. Eligibility for endovascular recanalization [Time Frame: 24 hours]
   Proportion of subjects who are deemed to be candidates for endovascular recanalization therapy

Eligibility Criteria

Ages Eligible for Study: 40 Years to 95 Years (Adult, Older Adult)
Sexes Eligible for Study: All

Inclusion Criteria:

- Provisional diagnosis of acute stroke as identified by paramedics using the local stroke triage tool
- Respiratory rate 12-24 breaths per minute
- Oxygen saturation ≥ 90% on room air
- Systolic blood pressure < 90 or > 220 mmHg
- Weight 45-120 kg
- Last seen in usual state of health less than 3 hours before anticipated study drug initiation
- Independently ambulatory with or without devices prior to event
- LAMS score of 2-5 for at least 15 minutes and remains 2-5 at time of randomization
  Exclusion Criteria:
- Lack of IV access
- Canadian Triage and Acuity Scale Level 1 and/or uncorrected airway, breathing or significant circulatory problem
- Blood sugar < 3 mmol/L (< 55 mg/dL)

- Seizure at onset of symptoms or observed by paramedic
- Glasgow coma score of <10
- Major head trauma in the last three months
- Recent stroke in the last three months with or without residual deficit
- Known or presumptive signs of pregnancy or breastfeeding
- Prisoner
- Long term care facility resident
- Known advance directive to not resuscitate
- Valid Emergency Health Services Do Not Resuscitate Consent Form
- Known participation in a clinical trial with an investigational drug or device within 30 days preceding this trial
- Pre-existing neurologic, psychiatric, or advanced systemic condition that would preclude obtaining the neurological or functional outcome evaluations

Contacts

Contact: Michael Tymaisnki, M.D. (416) 603-5899 mtymianski@nonoinc.ca

Contact: Kathy Heard, M.Sc. (416) 603-5899 kheard@nonoinc.ca

Locations

Canada, British Columbia

Kelowna General Hospital **Recruiting**
Kelowna, British Columbia, Canada, V1Y 1T2
Contact: Aleksander Tkach, MD

Royal Columbian Hospital **Recruiting**
New Westminster, British Columbia, Canada, V3L 3W7
Contact: George Medvedev, MD

British Columbia Ambulance Service and British Columbia Emergency Health Services **Recruiting**
Vancouver, British Columbia, Canada, V5M 4X6
Contact: William Dick, M.D.

Vancouver General Hospital, Vancouver Coastal Health **Recruiting**
Vancouver, British Columbia, Canada, V5Z 1M9
Contact: Oscar Benavente, MD

Investigators

Principal Investigator: Jim Christenson, M.D. University of British Columbia

Principal Investigator: Richard Swartz, M.D. Sunnybrook Health Sciences Centre