A Multicentre, Randomized, Double-blinded, Placebo-controlled, Parallel Group, Single-dose Design to Determine the Efficacy and Safety of Nerinetide in Participants with Acute Ischemic Stroke Undergoing Endovascular Thrombectomy Excluding Thrombolysis

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The primary objective is to determine the efficacy of the neuroprotectant, nerinetide in:• Reducing global disability in participants with acute ischemic stroke (AIS)

Ethical review	Approved WMO
Status	Pending
Health condition type	Neurological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON54395

Source
ToetsingOnline

Brief title
ESCAPE-NEXT Trial (NA-1-009)

Condition

- Neurological disorders NEC

Synonym
Acute ischemic stroke (AIS); Stroke

Research involving
Human

Sponsors and support

Primary sponsor: NoNO Inc.
Source(s) of monetary or material Support: NoNO Inc.

Intervention

Keyword: Endovascular therapy, Nerinetide, Stroke

Outcome measures

Primary outcome

Reducing global disability in participants with acute ischemic stroke (AIS).

Secondary outcome

The secondary objectives are to determine the efficacy of nerinetide in:

• Reducing mortality rate

• Improving activities of daily living

• Improving health related quality of life

Study description

Background summary

Nerinetide (NA-1) is a first in class neuroprotectant that is designed to address the major unmet medical need for treatments that reduce the functional disability produced by acute stroke. It reduces the vulnerability of ischemic brain tissue to hypoperfusion by targeting neurotoxic pathways that lead to ischemic neuronal death. Nerinetide is intended, alone or in combination with available therapies, to treat acute stroke, a serious and life-threatening disease. For this reason, nerinetide is being developed as a drug for use in emergency situations aimed at reducing global disability in patients with acute ischemic stroke. Nerinetide may provide significant benefit for the treatment of acute cerebral ischemia if administered to stroke patients who present to medical attention before infarction is complete.

Study objective

The primary objective is to determine the efficacy of the neuroprotectant, nerinetide in:
• Reducing global disability in participants with acute ischemic stroke (AIS)

Study design

This study is a Phase 3, randomized, multicentre, blinded, placebocontrolled, parallel group, single-dose design with a single
interim analysis for safety and efficacy.

Because AIS is a medical emergency, the trial is designed to enable the administration of standard-of-care treatments without delay in order to save the life of the person concerned, restore good health or alleviate suffering. Participants harboring an acute ischemic stroke who are selected for endovascular revascularization without intravenous or intra-arterial thrombolytic therapy will be given a single, 2.6 mg/kg (up to a maximum dose of 270 mg) intravenous dose of nerinetide or placebo. Randomization will be stratified by time from stroke onset to randomization <=4.5 hours (yes/no) and done with stochastic minimization to balance baseline factors within strata. Outcomes of the main trial will be evaluated throughout a 90 day observation period.

Participants will be contacted by telemedicine or telephone at 1-Year by individuals blinded to the outcome of the main trial.
Two database locks and corresponding reports are planned for this trial. The first report will be based on the completion of Day 90 visits
for the main trial. The second report will be following the completion of the 1-Year follow up for the analytic sub-trial.

Intervention

Nerinetide 2.6 mg/kg (up to a maximum dose of 270 mg or matching placebo volume) will be administered as a single 10±1minute
intravenous infusion using an infusion pump starting after randomization.

Study burden and risks

Increase in hypotension (drop in blood pressure) within 2 hours after receiving nerinetide. The drop in blood pressure was temporary but may require treatment or monitoring.

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) Acute ischemic stroke (AIS) selected for emergency endovascular treatment.
2) Age 18 years or greater
3) Onset (last-known-well) time to randomization time within 12 hours
4) Disabling stroke defined as a baseline National Institutes of Health Stroke Score (NIHSS)
a. NIHSS > 5 for internal carotid artery (ICA) and M1-middle cerebral artery (MCA) occlusion or
b. NIHSS > 10 for M2-MCA occlusion
5) Confirmed symptomatic intracranial occlusion at one or more of the following locations: Intracranial carotid I/T/L, M1 or M2 segment MCA. Tandem extracranial carotid and intracranial occlusions are permitted
6) Pre-stroke (24 hours prior to stroke onset) independent functional

status in activities of daily living with modified Barthel Index (BI) >= 95.
Patient must be living without requiring nursing care.
7) Qualifying imaging performed less than 2 hours prior to randomization.
8) Consent process completed as per national laws and regulation and the applicable ethics committee requirements

Exclusion criteria

1) Treatment with a tissue plasminogen activator (e.g., alteplase or tenecteplase) within 24 hours before randomization
2) Determination by the treating physician, based on current treatment guidelines and medical evidence, that treatment with a plasminogen activator is indicated
3) Evidence of a large core of established infarction defined as ASPECTS 0-4
4) Evidence of absence of collateral circulation on qualifying imaging (Collateral score of 0 or 1)
5) Any evidence of intracranial hemorrhage on the qualifying imaging
6) Planned use of an endovascular device not having approval or clearance by the relevant regulatory authority
7) Endovascular thrombectomy procedure is completed as defined by the presence of TICI 2c/3 reperfusion or completion of groin / arterial closure
8) Clinical history, past imaging or clinical judgment suggesting that the intracranial occlusion is chronic or there is suspected intracranial dissection such that there is a predicted lack of success with endovascular intervention
9) Estimated or known weight > 120 kg
10) Pregnancy/Lactation; female, with positive urine or serum beta human chorionic gonadotropin (β-hCG) test, or breastfeeding
11) Known prior receipt of nerinetide for any reason, including prior enrolment in this ESCAPE-NEXT trial
12) Severe known renal impairment defined as requiring renal replacement therapy (hemo- or peritoneal dialysis)
13) Severe or fatal comorbid illness that will prevent improvement or follow-up
14) Inability to complete follow-up treatment to Day 90
15) Participation in another clinical trial investigating a drug, medical device, or a medical procedure in the 30 days preceding trial inclusion

Study design

Design

Study phase: 3

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	19-02-2022
Enrollment:	45
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Nerinetide
Generic name:	Nerinetide

Ethics review

Approved WMO Date:	14-06-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	12-10-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-12-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	08-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	04-10-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-03-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-04-2023
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
EudraCT	EUCTR2020-002360-30-NL
ClinicalTrials.gov	NCT04462536

Register	ID
CCMO	NL77356.078.21