IBIS: 2-iminobiotin for ischemic stroke

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON29036

Source
NTR

Brief title
IBIS

Health condition

Stroke, cerebral ischemia

Sponsors and support

Primary sponsor: Haaglanden Medisch Centrum
Source(s) of monetary or material Support: Jacobusstichting Haaglanden Medisch Centrum, Neurophyxia BV

Intervention

Outcome measures

Primary outcome

The main study parameters used for evaluating the short-term safety and tolerability will be vital signs (heart frequency, blood pressure and oxygen saturation) before and during 24 hours after administration of the study drug and the need for clinical intervention. Furthermore, the occurrence of adverse and serious adverse events until 7 days will be recorded on the neurology department or until discharge from the neurology department, whichever occurs earlier. For evaluation of the pharmacokinetics profile of 2-IB, 4 plasma

samples will be analysed at different intervals (4 hours, 24 hours, 25 hours, and 28 hours after study medication) Pharmacokinetic parameters to be determined will include Cmax, AUC, Tmax, T1/2, clearance (Cl), and volume of distribution (Vd).

Secondary outcome

1. Stroke Severity measured with the NIH stroke scale (NIHSS) at 24 hours and at discharge or at 7 days, whichever occurs earlier. 2. Infarct volume measured with MRI at 24-48 hours. In case of contraindication(s) for MRI, CT/CTA will be performed at day 5 or discharge.
3. Embolization in new territory on angiography during EVT or infarction in new territory on 24-48h MRI (or CT)
4. Vessel recanalization at 24 hours with MRA (or CTA in case of contraindications for MRI)
5. Any postintervention intracranial haemorrhage on neuroimaging within 48 hours.
6. Blood investigation (CBC, electrolytes, serum creatinine, serum glucose) at 24 hours
7. Blood investigation, single biomarker neurofilament light chain at 24 hours and at 7 days or discharge from hospital, whichever occurs earlier.
8. Cognitive assessment using the Cognitive Assessment scale for Stroke Patients (CASP) at 7 days or at discharge from hospital, whichever occurs earlier

Additional parameters
In addition to the primary and secondary outcome parameters, the percentage of patients with successful vessel recanalization defined as eTICI score grade 2b, 2c and 3 will be recorded. Also the percentage of patients with IVT in each group will be noted.

Study description

Background summary

This study will be a prospective, Phase 2, open label, single centre study with the primary objective to evaluate the safety and tolerability of 2-IB when administered to patients with AIS due to LVO, treated with IVT and/or EVT. The secondary objective will be to study tolerance, feasibility, pharmacokinetics and preliminary efficacy. Furthermore we will investigate the optimal timing of administration of 2-IB (as soon as possible after arrival at the emergency department or after reperfusion treatment).

Study objective

Acute Ischemic Stroke (AIS) is the second leading cause of death after coronary artery disease globally. In about 30% of cases, AIS is due to large vessel occlusion (LVO), which can be treated with intravascular therapy (IVT) with recombinant tissue plasminogen activator (rTPH) such as Alteplase® and endovascular therapy (EVT) using thrombectomy. Administration of neuroprotective drugs is a promising new therapy that could slow ischemic core growth and limit brain cell injury in AIS due to LVO after successful recanalization and reoxygenation with EVT. In preclinical experiments, 2-iminobiotin (2-IB) has been shown to

reduce brain cell injury after hypoxia-ischemia. In clinical trials in neonates after birth asphyxia and adults after cardiac arrest, 2-IB has shown no safety issues. Before embarking on a large study with efficacy as a primary endpoint, safety, tolerability and pharmacokinetics of 2-IB treatment need to be established in patients with AIS due to LVO, treated with IVT and/or EVT . Especially, the safety of the combined administration of 2-IB with Alteplase® needs to be investigated

Study design

Total follow up of 7 days (or until hospital discharge if this occurs earlier)

Intervention

Patients will be included in an alternating fashion between group 1 (treatment upon diagnosis) and group 2a/b (treatment after successful reperfusion). Patients allocated to treatment upon reperfusion will be treated in an alternating fashion with IV (n=5) or IA (n=5) administration of the initial bolus of study drug. Inclusion will continue until at least 5 patients treated with IVT are present in group 1 and 2, to test our hypothesis that no interaction exists between 2IB with Alteplase.

Contacts

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Eligibility criteria

Inclusion criteria

• Adults (age > 18 years for males and age >49 years for females)
• A clinical diagnosis of AIS
• Disabling stroke defined as a baseline NIH stroke scale score ≥5
• Alberta Stroke Program Early CT score (ASPECTS) > 4 on CT (or MRI)

• Presence of an intracranial LVO of the anterior circulation (distal ICA, M1 or proximal M2 segment of the MCA) on CTA, MRA or
DSA
• Start of EVT (arterial access puncture) possible within the first 6 hours after stroke onset or last seen well
• EVT with declared first endovascular approach as either stent retriever, aspiration device or a combined approach
• Written informed consent (after deferred consent)
• Pre-stroke independent functional status in activities of daily living (mRS≤2)

Exclusion criteria

• No informed consent
• Contraindication to EVT or EVT > 6 hours after symptom onset (or last seen well)
• Evidence of a large core of established infarction defined as ASPECTS 0-4.
• Evidence of absence/poor collateral circulation on CTA (Tan collateral score of 0 or 1)26.
• Known co-morbidity with a life expectancy of <6 months prior to acute ischemic stroke
• Women aged 49 or less or known pregnancy*
• Cognitive impairment (documented dementia) known prior to ischemic stroke
• Pre-stroke disability which interferes with the assessment of functional outcome at 90 days, i.e. mRS >2
• Intent to use any endovascular device other than a stent retriever or clot aspiration device or intra-arterial medications as the initial thrombectomy approach.
• History of life threatening allergy (more than rash) to contrast medium
• Evidence of acute hemorrhage on CT, MRI
· Significant mass effect with midline shift.
· Subjects with occlusions in multiple vascular territories (e.g., bilateral anterior circulation, or anterior/posterior circulation)
· Severe known renal impairment defined as requiring dialysis (hemo- or peritoneal) or if known a eGFR < 20 mL/min.

*As 2-IB has not been tested yet for embryonic toxicity and limited pre- and postnatal development studies have been performed, women who can be pregnant must not be included be in this study.

Study design

Design

Study type:	Interventional
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-08-2021
Enrollment:	18
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 51194
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9532
CCMO	NL77507.056.21
OMON	NL-OMON51194

Study results