EnDovascular therapy plus best medical treatment (BMT) versus BMT alone for MedIum VeSsel Occlusion sTroke - a prAgmatic, international, multicentre, randomized triaL (DISTAL)

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Central nervous system vascular disorders
Study type	Interventional

Summary

ID

NL-OMON56450

Source
ToetsingOnline

Brief title
DISTAL

Condition

- Central nervous system vascular disorders
- Embolism and thrombosis

Synonym
brain infarction, Ischemic stroke

Research involving
Human

Sponsors and support

Primary sponsor: University Hospital Basel
Source(s) of monetary or material Support: Medtronic B.V.,Penumbra Inc.,Phenox GmbH,Rapid Medical Inc.,SNF (Swiss National Fund);Bangerter-Rhyner-Stiftung; Unrestricted grants from: Stryker Neuorvascular Inc. Penumbra Inc. Rapid Medical Inc. Phenox GmbH;Medtronic..,Stryker Howmedica

Intervention

Keyword: Distal occlusion, Endovascular treatment, Medium vessel, Stroke

Outcome measures

Primary outcome

The primary outcome is the degree of dependency and disability in everyday life

(measured with the mRS) at 90 days.

Secondary outcome

Secondary efficacy outcomes include:

At 24 hours (± 6 h) post randomization:

- Normalized change in NIHSS

At 90 days (± 24 d) post randomization:

- Excellent functional outcome (mRS 0-1 versus mRS 2-6)

- Cognitive function (assessed with the Montreal Cognitive Assessment Test)

- Health-related quality of life (assessed with the Euro-Qol 5d)

At 1 year (±30 d) post randomization:

- Degree of disability and dependency (measured with the mRS)

- Health-related quality of life (assessed with the Euro-Qol 5d)

- Residential status

Safety outcomes include:

- sICH within 24 hours (defined with the modified SITS-MOST criteria)

- SAEs (neurological worsening, death, coma etc.) within 90 days

- Mortality at 90 days and 1 year.

Technical efficacy outcomes include:

- Percentage of brain tissue (penumbra) saved

- Successful reperfusion at end of EVT procedure, defined as eTICI 2b50-3

(assessed only in EVT+BMT patients)

- Recanalization of target artery at 24 hours (±6 h) post randomisation,

defined as Arterial Occlusion Lesion scale score 2-3 on CTA or MRA (assessed in

both EVT+BMT and BMT alone patients)

Study description

Background summary

Acute ischemic stroke (AIS) is one of the main causes of death and disability and thereby the third leading cause of loss of quality adjusted life years. For patients with an AIS due to an occlusion of the large vessels of the anterior circulation, endovascular therapy (EVT) has become a treatment standard after randomized trial evidence clearly showed dramatic clinical benefits with a Number Needed to Treat of 2.6 for the reduction of disability and dependency in daily activities.
However, 20-40% of all AIS patients have occlusions of smaller vessels and present with a more distal isolated Medium Vessel Occlusion (MeVO). Neurological outcome of MeVO patients is often poor, with rates of disability and death exceeding 50% for some MeVO segments.
A meta-analysis based on subgroups of AIS patients with an M2 occlusion included in seven randomized-controlled trials, indicated a positive treatment effect of EVT with a relative increase in the proportion of patients being able to continue a self-sustained life of 46.6% (58.2% intervention group vs 39.7% control group). However, these analyses include only data from 131 patients and

most had occlusions of large, proximal M2 segments, not real MeVOs. Guidelines have concluded that the data is insufficient to give a specific evidence-based recommendation for or against EVT in case of M2 occlusions. For other distal vessels, such as the M3 or M4 segment of the MCA or the ACA or the PCA no randomized-controlled data is available at all.
As of now, no RCT has investigated the effectiveness and safety of EVT in MeVOs. We hypothesize that EVT plus best medical treatment (BMT) is superior to BMT alone with regard to long-term disability and dependency in daily life (measured with the mRS at 90 days). In several retrospective and randomized studies, there were no indications that relevant harmful functional outcome effects (such as mortality or very severe disability) were associated with the procedure.

Study objective

The primary objective of this randomized trial is to determine whether patients experiencing an AIS due to an isolated medium vessel occlusion have superior functional outcome (measured with the mRS at 90 days) when treated with EVT plus BMT compared to patients treated with BMT alone.

Secondary efficacy objectives are to study: at 90 days excellent functional outcome (mRS 0-1), cognitive function and quality of life; at 24 hours after randomization change in neurologic deficit severity, vessel patency and salvaged brain tissue; and at 1 year level of dependency and disability in daily life, quality of life and residential status. Safety objectives are to study symptomatic intracranial haemorrhage within 24 hours, serious adverse events, and 90 days and 1 year mortality.

Study design

Multicentre, pragmatic, international, parallel group, randomized (ratio 1:1), open label, superiority trial with blinded endpoint assessment

Intervention

The intervention group will receive EVT + best medical treatment (including iv-thrombolysis when appropriate). For EVT the choice of device, access site and anaesthetic and antithrombotic management are per local protocol or left to the discretion of the interventionist. The control group will receive best medical treatment alone.

Study burden and risks

Burden and risk in intervention group: All patients in the intervention group will be transferred to the angiosuite. The procedure involves catheterization

of the affected intracranial vessel.
There is no established indication, that the intervention causes harm beyond local procedure related (arterial puncture site haemorrhage or (rarely) nerve injuries) complications. However, it has been hypothesized, that symptomatic intracranial haemorrhage (sICH), which is defined as a substantial haemorrhage causing clinical deterioration occurs more often in patients undergoing EVT. However, randomized-controlled data and large registries suggest, that EVT poses no greater risk for the occurrence of sICH than BMT alone.

Burden and risk for all participants: All patients will undergo follow-up CT or MRI scanning at 24h.
At 24h and at 7-10days all patients will undergo a neurological examination (which is often part of standard care). At 3 months there will be a neurological examination and short cognitive screening, which can be combined with a regular followup and often is part of standard care.
At 3 and 12 months, all patients will be interviewed by telephone (about 30 minutes) to assess neurological and functional outcome.

Benefit: Thrombectomy is of potential benefit. The ultimate benefit would be that patients maintain their life and health status as before the stroke. Survival without neurological deficits would be associated with a better quality of life in these patients.

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
2. Treatment (arterial puncture) can be initiated
2.1. Within 6 hours of last seen well (LSW)
OR
2.2. Within 6 to 24 hours of LSW AND
CT Criteria: Evidence of a hypoperfusion-hypodensity mismatch (Absence of hypodensity on the non-contrast CT within >= 90% of the area of the hypoperfused lesion on perfusion CT)
MRI Criteria: Evidence of a diffusion-hyperintensity mismatch (Absence of hyperintensity on fluid-attenuated inversion recovery (FLAIR) imaging within >= 90% of the area of the diffusion weighted imaging (DWI) lesion)
3. Isolated medium vessel occlusion (i.e. an occlusion of the co-/non-dominant M2, the M3/M4 segment of the MCA, the A1/A2/A3 segment of the ACA or the P1/P2 segment of the PCA) confirmed by CT or MRI Angiography
4. National Institute of Health Stroke Scale (NIHSS) Score of >= 4 points or symptoms deemed clearly disabling by treating physician (i.e. aphasia, hemianopia, etc.)
5. Age >=18 years
6. Deferred Written informed consent.
7. Agreement of treating physician to perform endovascular procedure

Exclusion criteria

1. Acute intracranial haemorrhage
2. Patient bedridden or presenting from a nursing home
3. In-Hospital Stroke
4. Known (serious) sensitivity to radiographic contrast agents, nickel, titanium metals or their alloys
5. Foreseeable difficulties in follow-up due to geographic reasons (e.g. patients living abroad)
6. Evidence of an ongoing pregnancy prior to randomization. A negative

pregnancy test before randomisation is required for all women with child-bearing potential.
7. Known history of arterial tortuosity, pre-existing stent, other arterial disease and/or known disease at the arterial access site that would prevent the device from reaching the target vessel and/or preclude safe recovery after EVT
8. Known, severe comorbidities, which will likely prevent improvement or follow-up (active cancer, alcohol/drug abuse or dementia)
9. Radiological confirmed evidence of mass effect or intracranial tumour (except small meningioma)
10. Radiological confirmed evidence of cerebral vasculitis
11. Evidence of vessel recanalization prior to randomisation
12. Participation in another interventional trial

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-11-2023
Enrollment:	100
Type:	Actual

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	24-10-2023

Application type:	First submission
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
ClinicalTrials.gov	NCT05029414
CCMO	NL84673.078.23