Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in The Netherlands for Late Arrivals: MR CLEAN LATE

Published: 11-09-2017
Last updated: 15-04-2024

To assess the effect of IAT compared with best medical treatment in patients with AIS caused by an intracranial large vessel occlusion of the anterior circulation, who have moderate to good collaterals and who can be treated between 6 and 24 hours...

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

Summary

ID

NL-OMON55450

Source
ToetsingOnline

Brief title
MR CLEAN LATE

Condition

- Central nervous system vascular disorders
- Embolism and thrombosis

Synonym
brain infarction, ischemic stroke

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Nederlandse Hartstichting en de Hersenstichting

Intervention

Keyword: acute treatment, endovascular treatment, ischemic stroke, Late arrival

Outcome measures

Primary outcome

The primary outcome is the score on the mRS 90 days after inclusion in the study. The primary effect parameter should take the whole range of the mRS into account and is defined as the relative risk for improvement on the mRS estimated as a common odds ratio with ordinal logistic regression. Multivariable regression analysis will be used to adjust for chance imbalances in main prognostic variables between the intervention and control group, such as age, stroke severity (NIHSS), time since onset, previous stroke, atrial fibrillation and diabetes mellitus.

Secondary outcome

Secondary outcomes include hemorrhage and stroke severity at 24 hours and 5-7 days, recanalization on CTA at 24 hours or MRA at 24-48 hours and when chosen for CTA at 24 hours; infarct size at 5-7 days on non-contrast CT will follow.

Study description

Background summary

Rationale: Intra-arterial treatment (IAT) by means of retrievable stents, in patients with acute ischemic stroke (AIS) in the anterior circulation with

confirmed proximal intracranial occlusion, in whom the procedure can be started within 6 hours from onset has been proven safe and effective. Unfortunately a large proportion of patients presents beyond the 6 hours timewindow. In the Netherlands up to 25% of acute ischemic stroke patients arrive in the hospital between 6 and 12 hours after symptom onset. Currently, only for a very select group of patients a proven effective recanalization therapy is available. DAWN and DEFUSE3 randomised patients for IAT or no-IAT in the late timewindow based on strict CT perfusion characteristics. They proved that IAT is effective for a very select group and that advanced imaging is requiered for the selection of these patients. In the ESCAPE trial, one of the recent trials which showed efficacy of IAT, patients were randomized in the 0 to 12 hours time window. Patients were selected by NCCT and CT angiography. Eligible patients needed to have a small core infarct defined as an ASPECTS score of >5, and a moderate to good collateral flow on CT angiography in addition to a proven the proximal intracranial anterior circulation occlusion. Of all recent trials, IAT was most effective in this selected population. Most patients were treated within 6 hours from symptom onset, whereasand only a small proportion was treated between 6 and 12 hours after symptom onset. The effect size in patients treated beyond 6 hours was the same as in the early treated group. However, this predefined subgroup was too small to draw firm conclusions. In pre-defined subgroup analyses of the MR CLEAN study we showed that of these two imaging parameters (ASPECTS score and collateral flow) only the degree of collateral flow showed an interaction with effect of intra-arterial treatment. We hypothesize that IAT is not only effective for patients treated within 6 hours, but also for patients selected on the presence of collateral flow treated between 6 and 24 hours after symptom onset or last seen well less than 24 hours before admission to the hospital (what also includes wake up strokes)

Study objective

To assess the effect of IAT compared with best medical treatment in patients with AIS caused by an intracranial large vessel occlusion of the anterior circulation, who have moderate to good collaterals and who can be treated between 6 and 24 hours after symptom onset or last seen well less than 24 hours before admission to the hospital (what also includes wake up strokes). We expect to demonstrate at least 10% difference in outcome in favor of endovascular treatment.

Study design

This is a multicenter clinical trial with randomized treatment allocation, open label treatment and blinded endpoint evaluation (PROBE design).
The intervention contrast is endovascular treatment versus no endovascular treatment. The treatment is provided in addition to best medical management.

Intervention

The intervention group will receive IAT with a stent retriever or other device approved by the steering committee. The control group will receive best medical treatment.

Study burden and risks

All patients in the intervention group will be transferred to the angiosuite. The procedure involves catheterization according to the Seldinger method, with a small risk of groin hematoma and dissection. Also, thrombectomy is associated with cerebral infarction at a distal side. Thrombectomy is of potential benefit. At three months, all patients will be interviewed to assess functional outcome.

Every participant will undergo 24 hours after randomization a CTA of the cerebral vessels to asses rate of recanalization and 5 - 7 days after randimization a CT brain to assess final infarct volume.Three months after inclusion all participants will be interviewed by telephone to determine final oiutcome. This call will take 15 minutes.

In the 5 IAT trials the risk for extra- and intracranieal hemmorrhage was equal in both arms. This accounted also for post-procedural complications. The overall risk for procedure-related complications was very low.

Thrombectomy might be of potential benefit outweighting this risks.

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

P Debeijelaan 25
Maastricht 6229HX
NL
Scientific
Medisch Universitair Ziekenhuis Maastricht

P Debeijelaan 25
Maastricht 6229HX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

o clinical diagnosis of acute ischemic stroke,
o caused by proximal intracranial anterior circulation occlusion (distal intracranial carotid artery or middle (M1/M2) cerebral artery confirmed by neuro-imaging (CTA),
o and presence of poor*, moderate or good collateral flow as shown by neuro-imaging (CTA)
o CT or MRI ruling out intracranial hemorrhage,
o Start of IA treatment (groin puncture) possible between 6 and 24 hours or last seen well < 24 hours including wake-up strokes,
o a score of at least 2 on the NIH Stroke Scale
o age of 18 years or older
o Written informed consent (deferred)
* Inclusion and randomization will be restricted to patients with moderate or good collaterals when 100 patients with poor collaterals have been included in the study.

Exclusion criteria

o Pre-stroke disability which interferes with the assessment of functional outcome at 90 days, i.e. mRS >2
o cerebral infarction in the previous 6 weeks with residual neurological deficit or signs of recent infarction on neuroimaging in the territory of the middle cerebral artery
o INR exceeding 3.0*
o platelet count < 40 x 109/L*
o APTT > 50 sec*
o visible infarction in > 1/3 of the territory of the middle cerebral artery
o participation in trials other than current and MR ASAP.
o ICA-T/M1 occlusion, NIHSS >=10, infarct core <=25ml and a mismatch ratio total ischemic volume/ infarct core >=2 (patient is eligible for direct EVT treatment, based on DAWN/DEFUSE 3 patient profile)

Inclusion in other intervention trials during the study period is not allowed
* In case there is no clinical indication to test for hemorrhagic diathesis, it may be assumed that the INR, APTT and platelet count are within these limits.

Study design

Design

Study phase:	3
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):	02-02-2018
Enrollment:	500
Type:	Actual

Medical products/devices used

Generic name:	retrievable stent
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	11-09-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-03-2018

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	25-05-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	05-10-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-03-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-12-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-03-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	20-04-2021
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
CCMO	NL58246.078.17