Original research

Intra-arterial tenecteplase following endovascular therapy in patients with acute posterior circulation arterial occlusion: study protocol and rationale

Chunrong Tao, Rui Li, Jun Sun, Yuyou Zhu, Li Wang, Chao Zhang, Tianlong Liu, Jianlong Song, Adnan I Qureshi, Mohamad Abdalkader, Jeffrey L Saver, Raul G Nogueira, Wei Hu

ABSTRACT

Background Recently, a randomized controlled trial showed a beneficial effect of intra-arterial thrombolysis following successful endovascular thrombectomy (EVT) in patients with acute ischemic stroke due to large vessel occlusion in the anterior circulation. Due to differences in response to thrombolitics in occlusion of the posterior circulation, the purpose of ATTENTION IA is to explore the adjunct benefit of intra-arterial thrombolysis after successful recanalization in patients presenting with large and medium vessel occlusion of the posterior circulation.

Methods ATTENTION-IA is an investigator-initiated, multicenter, prospective, randomized clinical trial with open-label treatment and blinded endpoint assessment (PROBE). After achieving successful recanalization (expanded Thrombolysis In Cerebral Infarction (eTICI) 2b-3) of an occlusion of the vertebral, basilar, or posterior cerebral artery, patients will be randomized 1:1 to receive intra-arterial tenecteplase or standard of care. The primary effect parameter is a modified Rankin Score of 0–1 at day 90.

Results The trial recently completed enrollment, and data collection/verification is ongoing. The final results will be made available on completion of enrollment and follow-up.

Conclusions ATTENTION-IA will provide definitive evidence for the efficacy and safety of adjunct intra-arterial tenecteplase after successful EVT in patients with an acute posterior circulation arterial occlusion stroke presenting within 24 hours of symptom onset.

Trial registration ClinicalTrials.gov NCT05684172.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with basilar artery occlusion undergoing endovascular therapy may face unfavorable outcomes despite successful reperfusion. Intra-arterial infusion of adjunctive thrombolytic agent after successful reperfusion with endovascular thrombectomy (EVT) has the potential to further improve outcomes.

WHAT THIS STUDY ADDS

⇒ Our trial will provide definitive evidence for the efficacy and safety of adjunct intra-arterial tenecteplase after successful EVT in patients with an acute posterior circulation arterial occlusion.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our study will provide new treatment perspectives for posterior circulation strokes, potentially leading to further improvements in patient prognosis.

INTRODUCTION

From 2015 onwards, notable advancements have occurred in endovascular thrombectomy (EVT) for acute ischemic stroke (AIS) due to large vessel occlusion (LVO). Successive waves of randomized trials demonstrated EVT benefit for: early presenting anterior circulation LVO patients; imaging-selected late presenting LVO patients; posterior circulation LVO patients; and anterior circulation, large ischemic core patients.

However, despite this benefit, patient outcomes with EVT remain far from ideal. Among early presenting, anterior circulation LVO patients treated with EVT, fewer than 30% achieve a non-disabled outcome. Persisting regions of distal hypoperfusion despite EVT revascularization of proximal target large arteries is likely an important contributor to suboptimal patient recovery. Persistent macrocirculatory and microcirculatory obstruction is common among EVT-treated patients with ‘successful reperfusion’ (expanded Thrombolysis In Cerebral Infarction (eTICI) 2b-3). Patients with an eTICI 2b-3 outcome have visible non-reperfusion in 11–50% of the initial target territory, and patients with eTICI 2c have visible non-reperfusion in 1–10%. These patients have worse functional outcomes than those with complete, eTICI 3 reperfusion. Moreover, even when tissue is visibly reperfused at the macroscopic level, microcirculatory non-reperfusion (the ‘no-reflow’ phenomenon) can prevent nutritive reperfusion.

Intra-arterial infusion of adjunctive thrombolytic agent after successful reperfusion with EVT has the potential to further improve outcome by lysing persisting visible thrombi in distal arteries
Ischemic stroke

and small thrombi within the microcirculation. This treatment approach received support for use in anterior circulation LVOs from the results of the CHOICE randomized trial. Among 121 patients who had successful reperfusion (eTICI 2b50-3), 61 were randomized to receive intra-arterial alteplase thrombolysis at procedure end, while 52 patients received a placebo. Patients who received intra-arterial alteplase thrombolysis had significantly more frequent non-disabled (mRS 0–1) outcomes at 90 days, 59.0% compared with 40.4%, with an absolute difference of 18.4% (95% CI 0.3% to 36.4%, P=0.047). Additionally, the incidence of symptomatic intracranial hemorrhage did not significantly increase and a non-significant trend toward reduced 90-day mortality was noted.

Patients with posterior circulation ischemic stroke comprise approximately 20% of all ischemic strokes, but were excluded from the CHOICE trial. AIS resulting from posterior circulation occlusion carries a poor prognosis in comparison to anterior circulation strokes, manifesting higher rates of disability and mortality. However, even with EVT therapy, nearly two-thirds of posterior circulation LVO patients have dependent or death outcome (mRS 0–2) and more than half have non-ambulatory or death outcome (mRS 0–3) at 3 months. This discrepancy between lack of good outcomes despite timely EVT may be attributed to incomplete reperfusion due to visible distal occlusions and microcirculatory no-reflow. Accordingly, it is important to assess intra-arterial thrombolysis after successful posterior circulation EVT.

Therefore, this trial aims to evaluate the efficacy and safety of intra-arterial tenecteplase bridging successful EVT in patients with acute posterior circulation large or medium vessel occlusion presenting within 24 hours from stroke onset, through a multicenter, prospective, randomized clinical trial.

METHODS

Design

The ongoing ATTENTION-IA trial (NCT05684172) is an investigator-initiated, multicenter, prospective randomized clinical trial with open label treatment and blinded endpoint assessment (PROBE). The study has a planned duration of 1 year to recruit 208 patients across 31 comprehensive stroke centers in China. The study patient flow outline is shown in figure 1. ATTENTION-IA has received approval from the ethical committee of the First Affiliated Hospital of the University of Science and Technology of China and all participating centers. Written informed consent by the patient or their legally authorized representative will be obtained for all patients.

Patient population

Adult patients (age ≥18 years old) who have had a posterior circulation LVO within 24 hours are eligible. Patients should have a National Institutes of Health Stroke Scale (NIHSS) score ≥6 at the time of neuroimaging. Patients will receive intravenous thrombolysis if eligible and are also permitted for inclusion in the study. Key exclusion criteria include pre-stroke disability >1 on the modified Rankin Scale (mRS); intracranial hemorrhage on neuroimaging; and posterior circulation Acute Stroke Prognosis Early CT Score (pc-ASPECTS) <6 on CT/CT angiography (CTA) source images/MRI-diffusion weighted imaging (DWI).

Full inclusion and exclusion criteria are listed in online supplemental material.

Randomization

After successful reperfusion (eTICI 2b50-3) of the intracranial vertebral artery, basilar artery, or the P1 segment of the posterior cerebral artery has been confirmed and written informed consent has been obtained, patients will be immediately randomly assigned to the intra-arterial tenecteplase...
group or the control group in a 1:1 ratio. The randomization procedure is web-based and runs on mobile devices or web page platforms.

**Study assessment**

The study schedule of events is shown in **Table 1**. All patients undergo assessment of the NIHSS at baseline, 24 hours, and 5–7 days. To ensure consistency in reporting of the NIHSS, these early evaluations are conducted by neurologists who are certified in NIHSS examinations and who are not necessarily blinded to the treatment assignment. At 24–72 hours after randomization, CT+CTA or MRI+MR angiography (MRA) are repeated to determine recanalization status, intracranial hemorrhage, and infarct size.

The 3-month clinical outcomes including mRS, EuroQol-5 Dimensions-5 Levels (EQ-5D-5L), and Barthel index will be assessed by an independent core laboratory blinded to the treatment allocation.

**Table 1** Schedule of assessments

<table>
<thead>
<tr>
<th>Assessment step</th>
<th>Screening</th>
<th>Enrollment period</th>
<th>Follow-up period</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–12 hours after randomization</td>
<td>24±6 hours after randomization</td>
<td>24–72 hours after randomization</td>
</tr>
<tr>
<td>Sign informed consent</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confirm inclusion/exclusion criteria</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Demographics and baseline characteristics</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medical history</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vital signs</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Laboratory data</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NIHSS</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>GCS</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>mRS, premorbid</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mRS, outcome</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barthel Index</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EQ-5D-5L scale</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imaging (CT/MRI+CTA/MRA)</td>
<td>X</td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>ECG</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Details of EVT and procedural complications</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reperfusion status (eTICI grade)</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recanalization status (mAOL grade)</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adverse events</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Symptomatic intracranial hemorrhage</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic intracranial hemorrhage</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

CTA, CT angiography; ECG, electrocardiogram; EQ-5D-5L, EuroQol-5 Dimensions-5 Levels; eTICI, extended Thrombolysis in Cerebral Infarction Scale; EVT, endovascular thrombectomy; GCS, Glasgow Coma Scale; mAOL, modified Arterial Occlusive Lesion scale; MRA, MR angiography; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale.

**Treatment or intervention**

Patients have to be randomized within 24 hours of the estimated time of intracranial vessel occlusion. Estimated arterial occlusion time is defined as the sudden onset of stroke symptoms with no consideration of any preceding minor prodromal symptoms, as adjudicated by local experienced neurologists. In patients with sleep onset or unwitnessed onset stroke, last known well time will be considered the onset time. Both treatment arms will receive EVT, including stent retrievers, thromboaspiration, balloon angioplasty, stent deployment, or various combinations of these approaches. The exact method of treatment modality for each patient is left to the discretion of the treating team. Patients randomized to the tenecteplase group will receive an intra-arterial infusion of tenecteplase (0.0625 mg/kg, maximum dose limit 6.25 mg) through a distal access catheter or microcatheter located proximal to the residual thrombus (if still present) or distal to the origin of the main pontine perforator branches over 15 s. Patients randomized to the control group will terminate the procedure without additional intra-arterial adjunctive therapy.

To minimize the occurrence of procedure-related complications, at least 100 mechanical thrombectomy procedures per year from the participating center, and 80 mechanical thrombectomy cases from the neurointerventionalist, are required.
Primary outcome
The primary outcome is defined as an mRS of 0–1 at day 90 (±14 days).

Secondary outcomes
Secondary functional outcomes are the following: (1) favorable outcome defined as an mRS of 0–2 at day 90 (±14 days); (2) ordinal shift of mRS at day 90 (±14 days); (3) score on the NIHSS at 24–72 hours and at 5–7 days or discharge; (4) score on the EQ-5D-5L and Barthel index at 90 days (±14 days).

Safety outcomes are the following: (1) symptomatic intracranial hemorrhage scored according to the modified SITS-MOST (Safe Implementation in Stroke-Monitoring Study) definition (local or remote parenchymal hemorrhage type 2, subarachnoid hemorrhage, and/or intraventricular hemorrhage on the post-treatment imaging scan, combined with a neurological deterioration of ≥4 points on the NIHSS from baseline, or from the lowest NIHSS value between baseline and 24 hours (~2/+12), or leading to death that the Clinical Events Committee and Data Safety Monitoring Board (CEC/DSMB) judges is causative of the deterioration); (2) death from all causes within 90 days (±14 days).

Radiologic outcomes are the following: (1) recanalization at 24–72 hours by CT or MRA (score of 2 or 3 modified Arterial Occlusive Lesion scale, which ranges from 0 (complete occlusion) to 3 (complete recanalization and restoration of the target artery)); (2) radiologic intracranial hemorrhage according to the Heidelberg classification.

Data Safety and Monitoring Board
An independent DSMB, consisting of non-interventional clinicians, biostatisticians, and neurointerventionalists, was established to oversee the overall conduct of the trial. The DSMB meets regularly and assesses the occurrence of adverse events. The DSMB monitors the trend of serious adverse events and submits reports to the trial steering committee.

Sample size
We based sample size on estimations of treatment effect magnitude from the results of the recent ATTENTION and CHOICE trials. Based on the findings from the ATTENTION trial, we presumed that the proportion of subjects attaining mRS outcomes of 0–1 at the 90-day follow-up visit in the control group would be 20%, and according to findings of the CHOICE trial, our estimation of the risk difference effect size indicated an 18% increase. Consequently, we anticipated the proportion of mRS 0–1 in the treatment group to reach 38%. Based on a two-sided, normal approximation test, α of 0.05, and a 1:1 randomization, 99 patients in the treatment group and 99 in the control group would provide 80% power. The sample size was adjusted to 104 patients in the treatment group and 104 patients in the control group to account for up to 5% attrition. Sample size was computed using PASS 21.0.2.

Statistical analyses
The primary effect parameter will be the risk ratio, which compares the proportion of patients with an excellent outcome (mRS 0–1) at 90 days between the two treatment groups. The estimate will be adjusted for known prognostic factors of age, pre-stroke mRS, time from onset to randomization, baseline stroke severity (NIHSS), plus any key variables with imbalances between the treatment and control group. The analyses will be based on the intention-to-treat principle.

The secondary outcomes will be analyzed using log-binomial, linear, or the ordered regression analysis method as applicable, with the same correction method as the primary outcomes.

Missing values for baseline characteristics and outcomes will be reported. Missing baseline characteristics will be imputed using regression imputation. Missing outcomes will be imputed using multiple imputation. Pre-defined subgroups by age, stroke severity (baseline NIHSS), stroke etiology (intracranial atherosclerotic disease, cardioembolic, other), early versus late time window (0 to <6 hours vs 6–24 hours), site of arterial occlusion, baseline pc-ASPECTS (6–8 vs 9–10), use of intravenous thrombolysis, first-line reperfusion device modality, and reperfusion degree before study drug (eTICI 2b/50/67 vs eTICI2c/3) will be analyzed by testing for interaction between the specific baseline characteristic and treatment. Adjusted and unadjusted estimates with corresponding 95% confidence intervals will be reported. All analyses will use 5% two-sided level of significance.

Study organization
The First Affiliated Hospital of University of Science and Technology of China is the sponsor of the trial.

DISCUSSION
The ATTENTION-IA trial aims to evaluate the safety and efficacy of intra-arterial tenecteplase administration after successful EVT in patients experiencing acute stroke caused by posterior circulation occlusion within 24 hours of stroke onset. Posterior stroke patients, especially those with basilar artery occlusions (BAO), are known to have a generally poor prognosis, making it essential to conduct a trial aimed at improving outcomes in these patients. Thus, a trial to improve the prognosis in BAO has been recognized as being among the highest priorities in the stroke field.

Our primary aim of this trial is to explore whether administering intra-arterial tenecteplase post-thrombectomy can amplify the proportion of patients with no or minor symptoms after BAO. So mRS 0–1 was chosen as the primary outcome. Another justification stems from the significant result indicating a difference in mRS 0–1 observed in the CHOICE trial.

We chose a 0–24 hour time window primarily based on the previous ATTENTION and BAOCHE trials, which demonstrated the efficacy of EVT for acute BAO within 0–12 hours and 6–24 hours, respectively. Our trial required patients to have an NIHSS score ≥6 on admission, which enhances the generalizability of our results. Unlike the previous CHOICE trial, we opted for tenecteplase rather than alteplase as the thrombolytic drug after thrombectomy. Due to its greater fibrin specificity and prolonged half-life, tenecteplase is more suitable as a single bolus after EVT compared with alteplase. The EXTEND-IA tenecteplase trial in 2018 provided support for the superiority of tenecteplase over alteplase in treating acute LVO before thrombectomy. By randomizing 202 patients, the trial showed that patients receiving intravenous tenecteplase treatment exhibited significantly improved angiographic reperfusion and functional prognosis at 90 days compared with those receiving intravenous alteplase. Furthermore, a retrospective study, comparing 33 patients who received intra-arterial tenecteplase and 48 patients treated with intra-arterial alteplase, suggested that patients treated with intra-arterial tenecteplase exhibited a trend towards a favorable clinical outcome, and there was no difference in hemorrhage rates between the two groups. Meanwhile, a series of acute stroke trials have shown that tenecteplase has non-inferior or even superior angiographic and clinical outcomes.
compared with alteplase when administered via the intravenous route.16–19

The utilization of tenecteplase in posterior circulation LVO strokes is especially intriguing due to the elevated occurrence of intracranial atherosclerosis-associated LVO strokes in the posterior circulation, particularly within Eastern populations in contrast with Western populations. Current evidence suggests that thrombolytic drugs and glycoprotein IIb/IIIa inhibitors are more effective in treating vessel stenosis and occlusion due to intracranial atherosclerosis.20 Additionally, the high proportion of acute intracranial atherosclerosis has led to a significant increase in emergency stent placement. However, it remains uncertain whether bridging intra-arterial thrombolysis after successful EVT recanalization can enhance the clinical outcomes of these patients.

We acknowledge limitations in the current trial. The treatment assignment is open-label, which may lead to bias in the interpretation of the results. To mitigate this limitation, we designed the trial to have independent and blinded adjudication of the primary outcome assessment at 90 days. Independent core lab adjudication of imaging results with readers blinded to treatment assignment will also be conducted. The sample size of our trial is based on the results of a phase IIb randomized trial of modest sample size, and hence our treatment effect calculation may have been underestimated and a larger sample size may be needed. 1 It is possible that inclusion of patients with intracranial atherosclerosis-related LVO who undergo acute balloon angioplasty or stenting and receive acute antiplatelet therapy may mitigate a treatment effect with intra-arterial tenecteplase or increase the bleeding risk to patients. These patients were included in our study to improve the generalizability of our results given the high frequency of intracranial atherosclerosis in posterior circulation occlusions in both Asian and non-Asian patients. 10 11 To study this potential differential effect further, we pre-specified subgroup analyses of patients by stroke etiology and receipt of concomitant acute antiplatelet therapy. Our trial is limited to a patient population in China, which may limit the generalizability of our results to other ethnic populations.

ATTENTION-IA enrolled its first patient on January 24, 2023, and as of August 5, 2023, has enrolled 192 subjects. Full study completion (including collection on 3-month outcomes) is expected by November 2023.

CONCLUSION

It remains uncertain whether patients with acute posterior circulation stroke benefit from intra-arterial tenecteplase treatment following successful EVT. ATTENTION-IA is a multicenter, prospective, randomized clinical trial that aims to provide evidence regarding the safety and efficacy of adjunct intra-arterial tenecteplase treatment in patients with acute LVO of the posterior circulation.

Author affiliations

1Department of Neurology, The First Affiliated Hospital of USTC, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui, China
2The Zeenat Qureshi Stroke Institute and Department of Neurology, University of Missouri, Columbia, Missouri, USA
3Department of Radiology, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts, USA
4Department of Neurology, Boston Medical Center, Boston University School of Medicine, Boston, Massachusetts, USA
5Department of Neurology and Comprehensive Stroke Center, David Geffen School of Medicine at UCLA, Los Angeles, California, USA
6the UPMC Stroke Institute, Department of Neurology and Neurosurgery, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania, USA
7Twitter Thanh N Nguyen @NguyenThanhMD
8Contributors CT, RL, AIQ, MA, TNN, JLS, RGN and WH designed and conceptualized the study. CT, RL, JS, YZ, LW, CJ, TL, JS, and WH participated in data collection. CT wrote the manuscript. All authors critically revised and approved the manuscript. Guarantor: WH.
9Competing interests RGN reports consulting fees for advisory roles with Anacodna, Biogen, Cerenovus, Genentech, Philips, Hypernia, Imperative Care, Medtronic, Phoenix, Philips, Prolong Pharmaceuticals, Stryker Neurovascular, Shanghai Wallabyy, Syntron, and stock options for advisory roles with Astrocyte, Brainomix, Cerebrotech, Ceretrieve, Corindus Vascular Robotics, Vessalo, Viz-Al, RapidPulse and Peruze. RGN is one of the Principal Investigators of the Endovascular Therapy for Low NIHSS Ischemic Strokes (ENDOLOW) trial. Funding for this project is provided by Cerenovus. RGN is the Principal Investigator of the ‘Combined Thrombectomy for Distal Medial/lVessel Occlusion StroKe (DUSK)’ trial. Funding for this project is provided by Stryker Neurovascular. RGN is an investor in Viz-Al, Peruze, Cerebrotech, RestoQ, Apel Medical, Truvic, Tulavi Therapeutics, Varstrax, Piaerus Medical, BrainCare, Quantarosis AI, and Viseon. JLS reports consulting fees for advising on rigorous and safe clinical trial design and conduct from Abbott, Acticor, Aeromincs, Amgen, Agenica, Astrocyte, Bayer, Biogen, Boehringer Ingelheim, BrainGate, BrainQ, CSL Behring, Filterlex, Genentech, Johnson & Johnson, MindRhythm, Medtronic, NeuroMerit, Neurosciences, Novo Nordisk, Occlude, Phoenix, Phillips, QuantalX, Rapid Medical, Roche, and Stream Biomedical. The other authors have no financial conflicts of interest.
10Patient consent for publication Consent obtained from next of kin.
11Ethics approval This study involves human participants and was approved by the ethical committee of the First Affiliated Hospital of the University of Science and Technology of China and all participating centers; approval ID number: 2022KF-317. Participants gave informed consent to participate in the study before taking part.
12Provenance and peer review Not commissioned; externally peer reviewed.
13Data availability statement No data are available.
14Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and/or omissions arising from translation and adaptation or otherwise.
15Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/
16ORCID IDs Chunrong Tao http://orcid.org/0000-0002-5107-657X
Rui Li http://orcid.org/0000-0002-2423-2784
Li Wang http://orcid.org/0000-0002-0528-7835
Jianlong Song http://orcid.org/0000-0002-2987-2908
Mohamad Abdalkader http://orcid.org/0000-0002-9528-301X
Thanh N Nguyen http://orcid.org/0000-0002-2810-1685
Jeffrey L Saver http://orcid.org/0000-0001-9141-2251
Raul G Nogueira http://orcid.org/0000-0003-4532-153X

REFERENCES


Supplementary Materials

Inclusion Criteria

1. Acute ischemic stroke patients with symptomatic intracranial large vessel occlusion (LVO) in the intracranial vertebral artery, basilar artery, or the P1 segment of the posterior cerebral artery.

2. Treated with endovascular thrombectomy (EVT) resulting in an eTICI score 2b-5/3 at end of the procedure.

3. Age of 18 years or older;

4. National Institutes of Health Stroke Scale (NIHSS) score on admission ≥ 6;

5. Posterior Circulation ASPECTS ≥ 6 on CT/CTA-Source Images/MRI-DWI.

6. Time from estimated time of basilar artery occlusion to randomization <24 hours;

7. Written informed consent.

Exclusion Criteria

1. Pre-existing dependency with mRS >1;

2. Contraindication to Intravenous Thrombolysis (except time to therapy);

3. Complete clinical recovery in the angiography suite by end of the EVT procedure;

4. Pregnancy; if a woman is of childbearing potential a urine or serum beta HCG test is positive;

5. Severe contrast allergy or absolute contraindication to iodinated contrast;

6. Participation in other investigational drug or device clinical trials;

7. Systolic pressure >185 mmHg or diastolic pressure >110 mmHg, and cannot be controlled by antihypertensive drugs;

8. Known genetic or acquired bleeding diathesis, lack of anticoagulant factors, or oral
anticoagulant drugs and INR > 1.7, or treated with direct oral anticoagulant agents in the prior 48 hours;

9. platelets <100 000/mm³, aPTT >40 s, or PT >15 s; Blood glucose < 2.7 or >22.2 mmol/L;

10. Severe renal Failure as defined by a serum creatinine > 3.0 mg/dl (or 265.2 μmol/l) or glomerular Filtration Rate [GFR] < 30, or patient requires hemodialysis or peritoneal dialysis;

11. Clinical presentation suggests a subarachnoid hemorrhage, even if initial CT or MRI scan is normal;

12. Suspicion of aortic dissection;

13. Presumed vasculitis or septic embolization;

14. Life expectancy < 1 year;

15. Patients that cannot complete 90-day follow-up (e.g. no fixed residence, overseas patients, etc.);

16. CT/MR shows intracranial hemorrhage;

17. Ischemic stroke within 3 months;

18. Severe head trauma within 3 months;

19. Major surgery or severe trauma within the last 2 weeks;