

Neuro/Cardio CME ISC 2024 Updates

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The academic core of  **Atrium Health**

Disclosures

- I have nothing to disclose/



Outline



- ❑ What's new from the International Stroke Conference, 2/2024
- ❑ IV Tenecteplase therapy in stroke
- ❑ Evidence for Glycoprotein IIb/IIIa inhibitor use in Acute Stroke Care
- ❑ Head Positioning in AIS patients with a LVO
- ❑ Embolization of the MMA for SDH



IV Thrombolysis

TENECTEPLASE
TNK

AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

3.6. Other IV Fibrinolytics and Sonothrombolysis	COR	LOE	New, Revised, or Unchanged
1. It may be reasonable to choose tenecteplase (single IV bolus of 0.25-mg/kg, maximum 25 mg) over IV alteplase in patients without contraindications for IV fibrinolysis who are also eligible to undergo mechanical thrombectomy.	IIb	B-R	New recommendation.
IV tenecteplase (0.25 mg/kg bolus, maximum 25 mg) was compared with IV alteplase (usual dose of 0.9 mg/kg over 60 minutes, maximum 90 mg) in the EXTEND-IA TNK trial (Tenecteplase Versus Alteplase Before Endovascular Therapy for Ischemic Stroke). ¹⁷⁸ This multicenter trial randomized 202 patients without previous severe disability and with documented occlusion of the internal carotid artery, proximal MCA (M1 or M2 segments), or basilar arteries presenting within 4.5 hours of symptom onset to receive 1 of these 2 fibrinolytic agents. Primary end point was reperfusion of >50% of the involved ischemic territory or an absence of retrievable thrombus at the time of the initial angiographic assessment. The trial was designed to test for noninferiority and, if noninferiority proven, for superiority. Secondary outcomes included the mRS score at 90 days. Median NIHSS score was 17. The primary end point was achieved by 22% of patients treated with tenecteplase versus 10% of those treated with alteplase ($P=0.002$ for noninferiority and 0.03 for superiority). In an analysis of secondary end points, tenecteplase resulted in better functional outcomes at 90 days on the basis of the ordinal shift analysis of the mRS score (common OR [cOR], 1.7 [95% CI, 1.0–2.8]; $P=0.04$) but less robustly for the proportion who achieved an mRS score of 0 to 1 ($P=0.23$) or 0 to 2 ($P=0.06$). sICH rates were 1% in both groups.			See Table XLIII in online Data Supplement 1 .

Tenecteplase vs Alteplase

- 2022 Meta-analysis
 - 14 studies with 3537 patients
 - No difference in 90 day outcomes and slightly higher rate of early neurological improvement
 - 3x higher odds of early recanalization with TNK vs alteplase in large vessel occlusions
- Advantages of TNK
 - Bolus treatment, no infusion
 - More clot specificity
 - Lower cost
- We have been using TNK since 2/2023
 - No increased bleeding
 - Much easier for our telestroke sites to use and then transfer the patient

Case

- 89 y/o woman lives at home with children. Ambulates with a walker. Is able to perform all ADLs. Known a-fib not on anticoagulation
- Presents within 90 minutes of sudden onset of right sided weakness and severe expressive aphasia. NIHSS around 15.
- BP 160/90, no tPA exclusions
- CTA shows probable acute ICA occlusion and tandem distal M1 thrombus
- CTP shows nearly entire left hemisphere is penumbra
- Treatment?
 - IV thrombolysis?
 - Direct to IR and skip thrombolysis?

Case

- We offered TNK but family declined. Patient had severe GI bleeding 20 years ago and was very afraid of bleeding which is why she wasn't on anticoagulation for a-fib
- They did agree to endovascular therapy

Case

- Patient went to IR but the ICA could not be opened.
- Stopped after 10 attempts.
- Patient ended up with huge stroke and ultimately discharged to Hospice care

EVT vs IVT + EVT

Should we skip IVT and go directly to EVT?

TNK vs alteplase before EVT

- RCT showed that
- 22% of TNK patients had successfully recanalized before EVT vs 10% of TPA patients
- TNK patients had better functional outcomes
 - mRS 2 vs 3

EVT alone is not non-inferior to IVT + EVT

- Meta-analysis of 6 trials
- Does not establish non-inferiority of EVT alone
- Median mRS was 2 for IVT + EVT and 3 for EVT alone
 - Not quite statistically significant

Campbell BCV, Mitchell PJ, Churilov L, et al. Tenecteplase versus Alteplase before Thrombectomy for Ischemic Stroke. *N Engl J Med.* 2018;378(17):1573-1582. doi:10.1056/NEJMoa1716405

Majoie CB, Cavalcante F, Gralla J, et al. Value of intravenous thrombolysis in endovascular treatment for large-vessel anterior circulation stroke: individual participant data meta-analysis of six randomised trials. *Lancet.* 2023;402(10406):965-974. doi:10.1016/S0140-6736(23)01142-X

EVT vs IVT + EVT

- At this point we still advocate for combination therapy.
- We don't think you should bypass an IVT center to go to an IR center and miss IVT window
- Clearly more studies need to happen



AHA/ASA Guideline

Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

3. IV alteplase (0.9 mg/kg, maximum dose 90 mg over 60 min with initial 10% of dose given as bolus over 1 minute) administered within 4.5 hours of stroke symptom recognition can be beneficial in patients with AIS who awake with stroke symptoms or have unclear time of onset > 4.5 hours from last known well or at baseline state and who have a DW-MRI lesion smaller than one-third of the middle cerebral artery (MCA) territory and no visible signal change on FLAIR.

IIa	B-R
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ORIGINAL ARTICLE

Tenecteplase for Stroke at 4.5 to 24 Hours with Perfusion-Imaging Selection

G.W. Albers, M. Juma, B. Purdon, S.F. Zaidi, C. Streib, A. Shuaib, N. Sangha, M. Kim, M.T. Froehler, N.E. Schwartz, W.M. Clark, C.E. Kircher, M. Yang, L. Massaro, X.-Y. Lu, G.A. Rippon, J.P. Broderick, K. Butcher, M.G. Lansberg, D.S. Liebeskind, A. Nouh, L.H. Schwamm, and B.C.V. Campbell, for the TIMELESS Investigators*

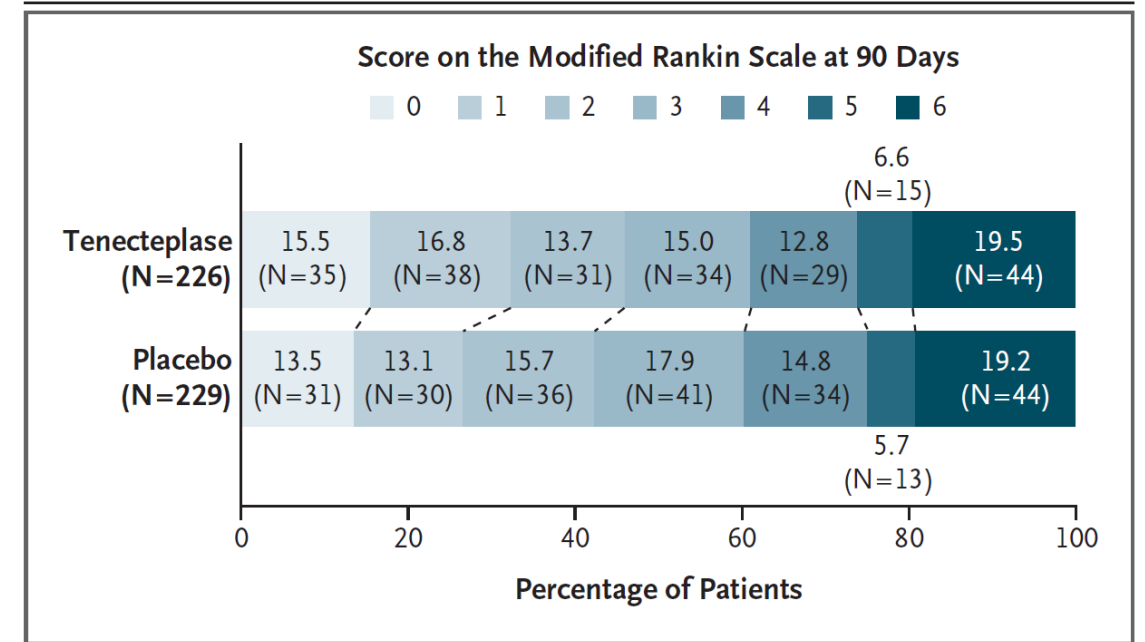
- Double-blind, randomized, placebo-controlled trial
- 108 center in US and Canada (March 2019 – Dec 2022)
- AIS in an extended time window for thrombolysis (TNK 0.25mg/kg), 4.5 to 24 hours after LKW
- Evidence of ICA, M 1/2 occlusion and had salvageable tissue as assessed on CT/MR perfusion imaging
- N 458

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Tenecteplase (N=228)	Placebo (N=230)
Median age (IQR) — yr	72 (62–79)	73 (63–82)
Female sex — no. (%)	122 (53.5)	123 (53.5)
Race or ethnic group — no. (%)†		
American Indian or Alaska Native	0	2 (0.9)
Asian	11 (4.8)	9 (3.9)
Black	31 (13.6)	32 (13.9)
Native Hawaiian or Pacific Islander	2 (0.9)	3 (1.3)
White	169 (74.1)	170 (73.9)
Unknown	15 (6.6)	14 (6.1)
Median NIHSS score (IQR)‡	12 (8–17)	12 (8–18)
Occlusion site — no. (%)§		
Internal carotid artery	20 (8.8)	17 (7.4)
M1 segment	110 (48.2)	117 (50.9)
M2 segment	89 (39.0)	84 (36.5)
Other	9 (3.9)	12 (5.2)
Median duration (IQR)		
From time that the patient was last known to be well to randomization — hr	12.3 (9.2–15.6)	12.7 (8.7–16.5)
From randomization to administration of tenecteplase or placebo — min¶	13 (7–20)	14 (7–20)
From administration of tenecteplase or placebo to arterial puncture — min	15 (3–25)	17 (3–27)
Endovascular thrombectomy performed — no. (%)	176 (77.2)	178 (77.4)

Table 2. Clinical, Imaging, and Safety Outcomes.*

Outcome	Tenecteplase (N=228)	Placebo (N=230)	Adjusted Odds Ratio (95% CI)	P Value
Primary efficacy outcome				
Median score on the modified Rankin scale at 90 days (IQR)†	3 (1–5)	3 (1–4)	1.13 (0.82–1.57)	0.45
Secondary efficacy outcomes				
Functional independence at 90 days — no./total no. (%)‡	104/226 (46.0)	97/229 (42.4)	1.18 (0.80–1.74)	
Recanalization at 24 hr — no./total no. (%)§	148/193 (76.7)	124/194 (63.9)	1.89 (1.21–2.95)	
Reperfusion at 24 hr — no./total no. (%)¶	99/174 (56.9)	105/182 (57.7)	1.04 (0.69–1.57)	
Reperfusion at the conclusion of endovascular thrombectomy — no./total no. (%)	156/175 (89.1)	152/178 (85.4)	1.42 (0.75–2.67)	
Safety outcomes**				
Death — no./total no. (%)				
Within 30 days	32/218 (14.7)	32/214 (15.0)	—	—
Within 90 days	43/218 (19.7)	39/214 (18.2)††	—	—
Symptomatic intracranial hemorrhage within 36 hr — no./total no. (%)‡‡				
	7/218 (3.2)	5/214 (2.3)	—	—
Parenchymal hematoma within 72 hr — no./total no. (%)				
Type 1	2/218 (0.9)	1/214 (0.5)	—	—
Type 2	8/218 (3.7)	6/214 (2.8)	—	—



No benefit in functional outcome with TNK as compared with placebo administered 4.5 to 24 hours after symptom onset in patients with AIS who had been selected on the basis of a favorable perfusion-imaging profile.

Case

- 49 year old man with HTN, HLD admitted after awakening with left sided weakness and slurred speech and sensory loss. He had trouble walking but did not come to the ED until around noon.
- In the ED, BP was 195/110, HR 88, afebrile.
- On neuro exam he is dysarthric, has a left facial droop, left hemiparesis with some movement in the left arm and drift in the leg, fairly significant sensory loss on the left side but no neglect. NIHSS = 8.
- Head CT scan is negative. CTA does not show an LVO.
- Localization is right subcortical, maybe thalamus.
- Admitted for stroke workup and treated with aspirin.

Case

- That evening, the nurses call you that he has had a change in exam. With worsening of his left sided weakness. His arm is now plegic and he is no longer antigravity in his leg and his stroke scale has worsened from 8 to 11?
- His BP is stable at 180/98 and has not had a significant drop.
- STAT head CT shows no hemorrhage
- How would you treat him?
 - Well, we're doing all we can
 - Heparin gtt?
 - Additional antiplatelet therapy?

Case

- I would treat with aggressive antiplatelet therapy with clopidogrel load of 300 or 600 mg in addition to the aspirin he is already on.
- There is no role for heparin in this situation.
 - Remember heparin is not lytic and is likely just predisposing patient to bleed
- Aggressive antiplatelet therapy can have acute fibrinolytic effect on fresh thrombus.
 - This was shown many years ago with abciximab when it was being trialed as an acute stroke therapy. Abciximab is a Glycoprotein IIb-IIIa inhibitor

A photograph of a modern, multi-story building with a grid of windows. The building is white with dark window frames. In the foreground, there is a courtyard with various plants, including a large tree with red leaves and a smaller tree with green leaves. The sky is blue with some light clouds. A semi-transparent yellow banner is overlaid on the right side of the image, containing the title and subtitle.

Glycoprotein IIb/IIIa Inhibitor Use

ACUTE ISCHEMIC STROKE



AHA/ASA Guideline

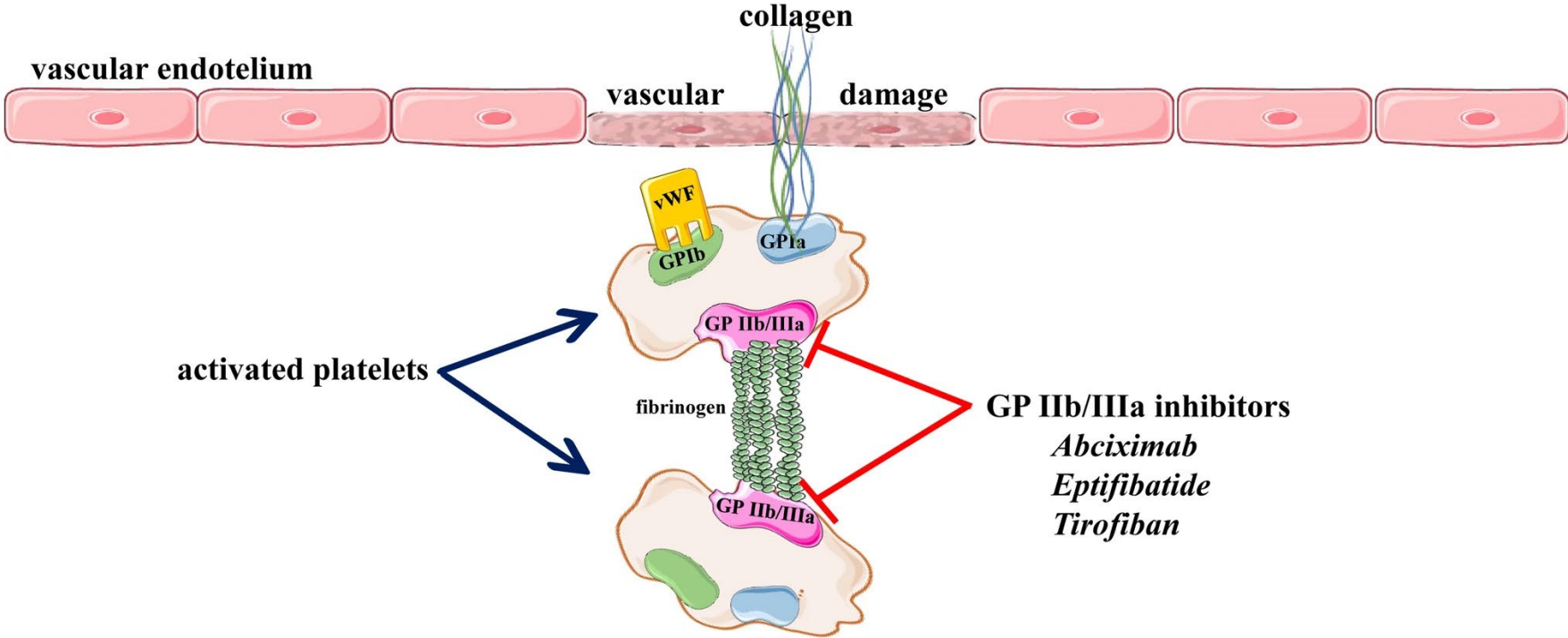
Guidelines for the Early Management of Patients With Acute Ischemic Stroke: 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

4. <u>The efficacy of the IV glycoprotein IIb/IIIa inhibitors tirofiban and eptifibatide co-administered with IV alteplase is not well established.</u>	IIb	B-R
3. <u>The efficacy of the IV glycoprotein IIb/IIIa inhibitors tirofiban and eptifibatide in the treatment of AIS is not well established.</u>	IIb	B-R
5. The administration of the IV glycoprotein IIb/IIIa <u>inhibitor abciximab</u> as medical treatment for AIS is potentially harmful and should not be performed.	III: Harm	B-R
3. At present, the <u>usefulness of argatroban, dabigatran, or other thrombin inhibitors for the treatment of patients with AIS is not well established.</u>	IIb	B-R
4. The safety and usefulness of oral factor Xa inhibitors in the treatment of AIS are not well established.	IIb	C-LD

***Not GP2b/3a Inhibitors**

Glycoprotein IIb/IIIa Inhibitors



RESCUE BT2 Trial

Tirofiban for Stroke without Large or Medium Sized Vessel Occlusion

- Multicenter trial in China, enrolled patients with IS without LVO or meVO and with a NIHSS of 5 or more and at least one moderately to severely weak limb.

- Ineligible for thrombolysis or thrombectomy & within 24 hours of LKW
- Progression of stroke symptoms 24 to 96 hours after onset (>2 points)
- Early neurologic deterioration after thrombolysis (increase of ≥ 4 points)
- Thrombolysis with no improvement at 4 to 24 hours (<2 points)



- Assigned to receive IV tirofiban (plus oral placebo) or oral aspirin (100 mg per day, plus IV placebo) for 2 days; all patients then received oral aspirin until day 90.

Table 1. Demographic and Clinical Characteristics of the Patients at Baseline.*

Characteristic	Tirofiban Group (N=606)	Aspirin Group (N=571)
Median age (IQR) — yr	68.0 (58.0–75.0)	68.0 (59.0–76.0)
Male sex — no. (%)	379 (62.5)	373 (65.3)
Han Chinese ethnic group — no. (%)†	576 (95.0)	546 (95.6)
Clinical history — no. (%)		
Hypertension	375 (61.9)	381 (66.7)
Hyperlipidemia	189 (31.2)	193 (33.8)
Coronary heart disease	50 (8.3)	54 (9.5)
Diabetes mellitus	162 (26.7)	167 (29.2)
Cerebral infarction	96 (15.8)	83 (14.5)
Smoking	213 (35.1)	188 (32.9)
History of antiplatelet use	20 (3.3)	21 (3.7)
History of anticoagulation	1 (0.2)	0
NIHSS score‡		
Median (IQR)	9.0 (7.0–10.0)	9.0 (7.0–10.0)
Distribution — no. (%)		
5–9	394 (65.0)	359 (62.9)
≥10	212 (35.0)	212 (37.1)
Median ASPECTS (IQR)§	9.0 (9.0–10.0)	9.0 (9.0–10.0)
Median systolic blood pressure at hospital arrival (IQR) — mm Hg	155 (142–166)	156 (144–167)
Median glucose level at hospital arrival (IQR) — mmol/liter¶	6.6 (5.6–8.5)	6.4 (5.4–8.7)

Presentation type — no. (%)

Ineligible for reperfusion treatment and within 24 hr after stroke onset	332 (54.8)	318 (55.7)
Ineligible for reperfusion treatment and progression 24–96 hr after stroke onset	199 (32.8)	180 (31.5)
IVT followed by early neurologic deterioration	45 (7.4)	45 (7.9)
IVT followed by no neurologic improvement	30 (5.0)	28 (4.9)

Localization of presenting deficit — no. (%)

Anterior circulation	489 (80.7)	456 (79.9)
Posterior circulation	92 (15.2)	94 (16.5)
Anterior circulation plus posterior circulation	5 (0.8)	7 (1.2)
Unknown	20 (3.3)	4 (2.5)

Presumed mechanism of ischemic cerebral event — no./total no. (%)**

Artery-to-artery embolism	56/601 (9.3)	50/566 (8.8)
Hypoperfusion or impaired emboli clearance beyond a stenosis	25/601 (4.2)	30/566 (5.3)
Penetrating artery disease	438/601 (72.9)	417/566 (73.7)
In situ thrombo-occlusion distal to a stenosed artery	8/601 (1.3)	8/566 (1.4)
Mixture of the above	48/601 (8.0)	42/566 (7.4)
Unknown	26/601 (4.3)	19/566 (3.4)
Median time from stroke onset or progression of stroke symptoms to randomization (IQR) — hr	10.9 (7.2–16.1)	11.2 (7.4–16.8)

Table 2. Primary and Secondary Efficacy End Points (Intention-to-Treat Population).*

End Point	Tirofiban Group (N=606)	Aspirin Group (N=571)	Effect Measure†	Effect Value (95% CI)‡	P Value
Primary efficacy end point					
Score of 0 or 1 on the modified Rankin scale at 90 days — no./total no. (%)‡	176/604 (29.1)	126/567 (22.2)	Risk ratio	1.26 (1.04–1.53)	0.02
Secondary efficacy end points					
Global outcome at 90 days§	—	—	Common odds ratio	1.38 (1.07–1.78)	0.01
Median score on the modified Rankin scale at 90 days (IQR)¶	2 (1–3)	2 (2–3)	Common odds ratio	1.23 (1.00–1.51)	0.06
Score of 0, 1, or 2 on the modified Rankin scale at 90 days — no./total no. (%)	375/604 (62.1)	320/567 (56.4)	Risk ratio	1.07 (0.98–1.16)	—
Median EQ-5D-5L score at 90 days (IQR)**	0.83 (0.64–0.93)	0.78 (0.56–0.84)	Win ratio	1.40 (1.23–1.62)	—
Score of 0 or 1 on the modified Rankin scale at 30 days — no./total no. (%)	139/605 (23.0)	96/568 (16.9)	Risk ratio	1.29 (1.03–1.62)	—
Score of 0, 1, or 2 on the modified Rankin scale at 30 days — no./total no. (%)	307/605 (50.7)	263/568 (46.3)	Risk ratio	1.06 (0.95–1.18)	—

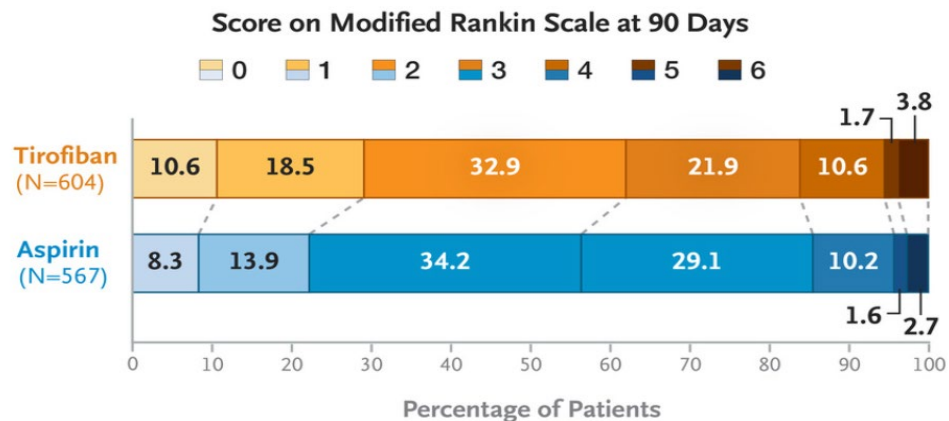
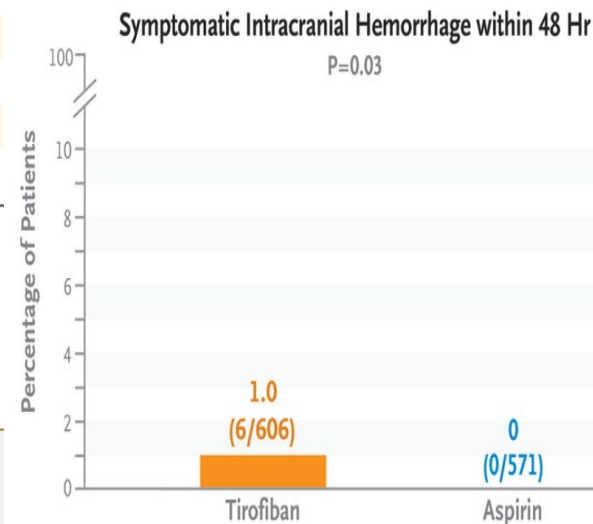


Table 3. Safety End Points.

End Point	Tirofiban Group (N=606)	Aspirin Group (N=571)	P Value
Primary end points			
Death — no. of patients/total no. (%)	23/604 (3.8)*	15/567 (2.6)*	0.12
Symptomatic intracranial hemorrhage — no. of patients (%)†			
As defined in HBC criteria‡	6 (1.0)	0	0.03
Hemorrhage infarction type 1	1 (0.2)	—	—
Hemorrhage infarction type 2	1 (0.2)	—	—
Parenchymal hematoma type 1	1 (0.2)	—	—
Parenchymal hematoma type 2§	3 (0.5)	—	—
As defined by NINDS criteria¶	6 (1.0)	0	0.03
As defined by ECASS II criteria	5 (0.8)	0	0.06
As defined by ECASS III criteria**	5 (0.8)	0	0.06
As defined by SITS-MOST criteria††	4 (0.7)	0	0.13
Secondary end points — no. of patients (%)			
Intracranial hemorrhage on any imaging	6 (1.0)	0	0.03
Serious adverse event‡‡	97 (16.0)	74 (13.0)	0.14
Any adverse event§§	—	9 (61.1)	0.58
Bleeding event¶¶			
Severe	1 (0.2)	—	—
Moderate	0	—	—
Mild	2 (5.6)	—	—





American Stroke Association
A division of the American Heart Association.

International Stroke Conference 2024
February 7-9, 2024 | Phoenix, AZ
Phoenix Convention Center

TREND Trial

IV Tirofiban Reduces Early Neurological Deterioration in AIS

- PROBE design, N 426 patients in China (July 2020 – March 2023)
- AIS patients who did not receive intravenous thrombolysis or endovascular treatment within 24 h of ictus in 10 centers.
- Randomized in a 1:1 ratio to receive either intravenous tirofiban for 72 h, followed by oral antiplatelet therapy, or oral antiplatelet therapy directly.
- Presumed non-cardioembolic IS
- NIHSS score 4-20 within 24 hours of LKW or symptom onset



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- The primary efficacy outcome was Neurological Deterioration within 72 h after randomization, defined as an increase of NIHSS ≥ 4 points.
 - 9 patients (4.2%) in the tirofiban group vs 28 (13.2%) in the control group (RR, 0.32; 95% CI, 0.15 to 0.66; **P = 0.001**)
- In the tirofiban group, 161 patients (75.2%) achieved non-disability at 90-day vs 145 (68.4%) in the control group (RR, 1.10, 95% CI, 0.98 to 1.24, **P = 0.117**).
- The incidence of systemic bleeding did not differ significantly between the groups.



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Glycoprotein IIb/IIIa Inhibitors

- So, acute treatment for progressing strokes with these agents is not yet ready for prime time, but makes sense
- Are the results in China generalizable to other patient populations?
- Provides extrapolating data to use aggressive DAPT in these progressing small artery strokes.
- It also provides some indirect safety data about use of IIb-IIIa inhibitors in the acute setting of thrombectomy after IVT or EVT or both when rescue stenting is needed and these drugs are used in the acute setting to prevent acute stent thrombosis



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MOST Trial

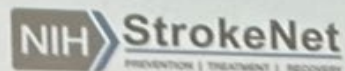
Multi-Arm Optimization of Stroke Thrombolysis

- Three-arm RCT trial
- 57 sites in
- Randomize eptifibatide
- IV thrombo
- NIHSS ≥ 6
- Primary effi
- 90-day mRS
- Primary saf
- 36 hours fro
- Trial halted

Primary Efficacy Outcome

	Placebo	Argatroban		Eptifibatide	
		Mean (95% CI)	Mean (95% CI)	Posterior Mean Difference (SD)	Mean (95% CI)
90-day uw-mRS (Range 0-10, higher score = better outcomes)	6.8 (6.4, 7.2)	5.2 (4.2, 6.2)	-1.5 (0.5)	6.3 (5.9, 6.8)	-0.5 (0.3)

- Probability of argatroban being better than placebo was 0.002 or 0.2%
- Probability of eptifibatide being better than placebo was 0.009 or 0.9%
- Futility threshold was probability less than 0.20 or 20%



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MOST: Multi-arm Optimization of Stroke Thrombolysis

RESULTS: In participants with acute ischemic stroke (AIS), the use of argatroban or eptifibatide and thrombolysis did not improve functional outcomes at 90 days but did not significantly increase symptomatic intracerebral hemorrhage compared to participants who received placebo and thrombolysis within three hours of symptom onset.

PURPOSE: To determine the safety and efficacy of argatroban (100µg/kg bolus followed by 3µg/kg/min infusion for 12 hrs) or eptifibatide (135µg/kg bolus followed by 0.75µg/kg/min infusion for 2 hrs) as compared with placebo in participants with AIS treated with standard of care IV thrombolysis within three hours of symptom onset.

TRIAL DESIGN: Phase 3 randomized controlled clinical trial, singled-blind three arm design at 57 sites in the U.S.; trial closed with n=514 following recommendations from the Data Safety and Monitoring Board.

	Argatroban		Eptifibatide		Placebo
Primary Endpoint	Mean (95% CI)	Posterior Mean Difference (SD)	Mean (95% CI)	Posterior Mean Difference (SD)	Mean (95% CI)
90-day uw-mRS	5.2 (4.2, 6.2)	-1.5 (0.5)	6.3 (5.9, 6.8)	-0.5 (0.3)	6.8 (6.4, 7.2)
Secondary Endpoint	N (%)	N=54 P value	N (%)	N=212 P value	N=217 N (%)
Symptomatic ICH within 36 hours	2 (3.7%)	0.343	7 (3.3%)	0.377	4 (1.8%)

Key Takeaways: The addition of argatroban or eptifibatide to thrombolysis in participants with AIS was determined to be safe but did not improve clinical outcomes compared to participants who received placebo and thrombolysis.

A photograph of a modern, multi-story building with a grid of windows. The building is white with dark window frames. In the foreground, there is a courtyard with various plants, including a tree with bright red leaves and a bush with yellow flowers. The sky is blue with some light clouds. A semi-transparent yellow banner is overlaid on the right side of the image, containing the text.

Head Positioning

ACUTE ISCHEMIC STROKE WITH LVO



ZODIAC: Zero Degree Head Positioning in Acute Large Vessel Ischemic Stroke

RESULTS: In participants with hyperacute large vessel occlusion (LVO) ischemic stroke awaiting thrombectomy, 0-degree head of bed (HOB) positioning resulted in better neurological outcomes compared to participants with 30-degree HOB positioning.

PURPOSE: To determine if the use of 0-degree HOB positioning prior to thrombectomy in patients with LVO results in greater clinical stability and/or improvement compared to an elevated HOB (30 degrees).

TRIAL DESIGN: Prospective randomized outcome blinded evaluation clinical trial from 12 U.S. hospitals; trial closed with n=92 following recommendations from the Data and Safety Monitoring Board for overwhelming efficacy.

	0-degree HOB	30-degree HOB	HR (95%CI)	Difference (P value)
Primary Endpoints				
NIHSS worsening ≥ 2	1/45 (2.22%)	26/47 (55.32%)	50.5 (6.83-373)	<0.001; Z=5.59 53.1% absolute difference
NIHSS worsening ≥ 4	1/45 (2.22%)	20/47 (42.55%)	32.6 (4.36-243)	<0.001; Z=4.61 40.3% absolute difference

Key Takeaways: Prior to thrombectomy, 0-degree head positioning resulted in better neurological outcomes in participants with LVO suggesting it may be one of the critical first steps in management of patients with LVO during the pre-thrombectomy period.

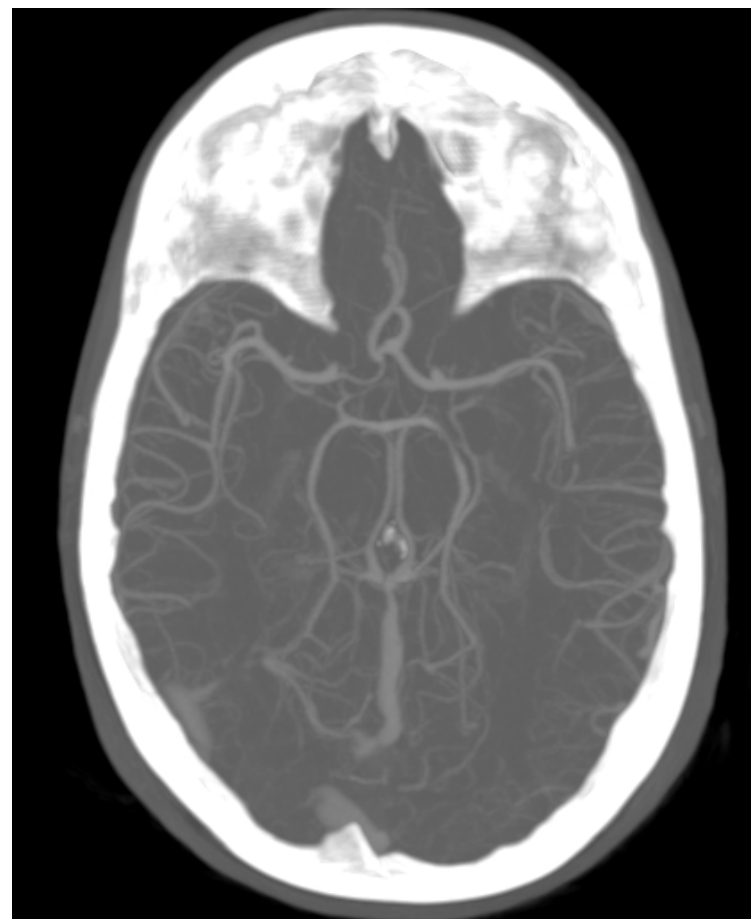


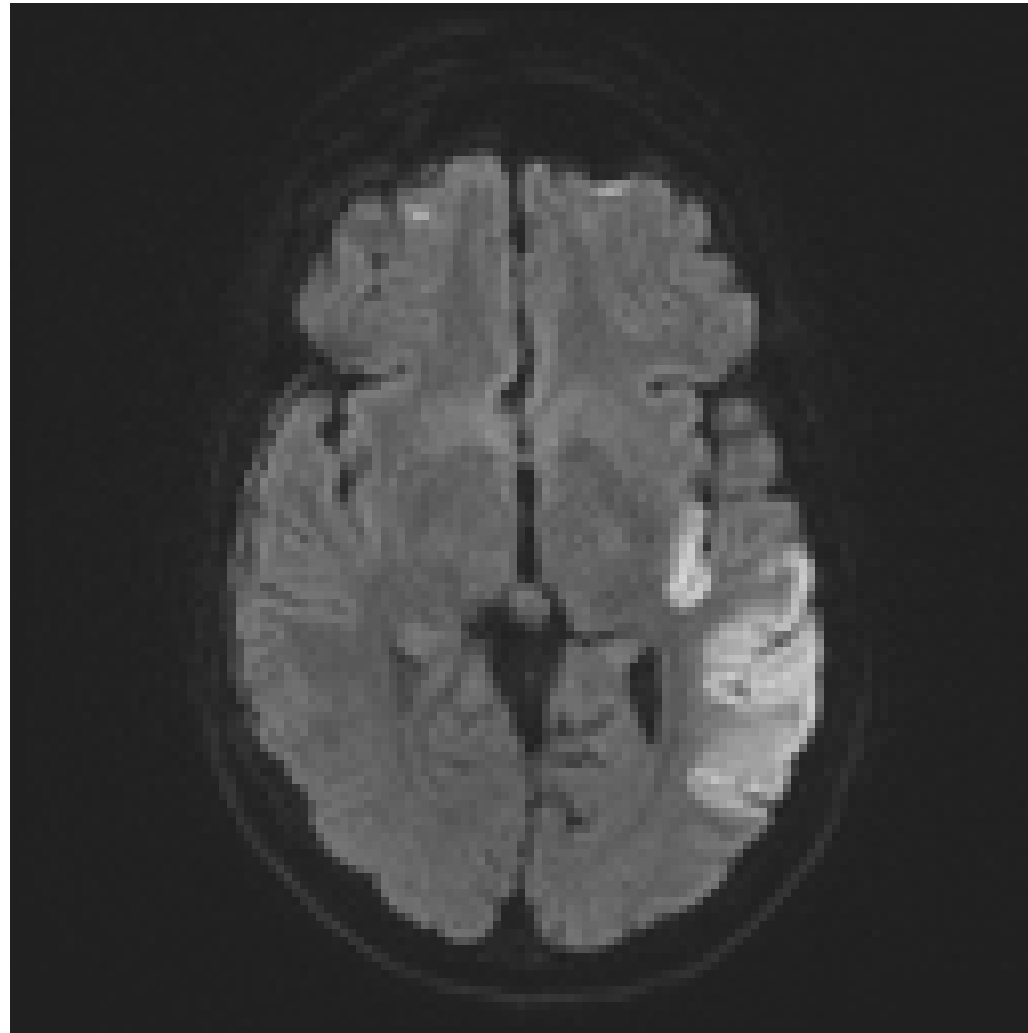
Presented by: Anne W. Alexandrov, PhD, ANVP-BC, University of Tennessee, USA. International Stroke Conference 2024. © 2024, American Heart Association. All rights reserved. Results reflect the data available at the time of presentation.

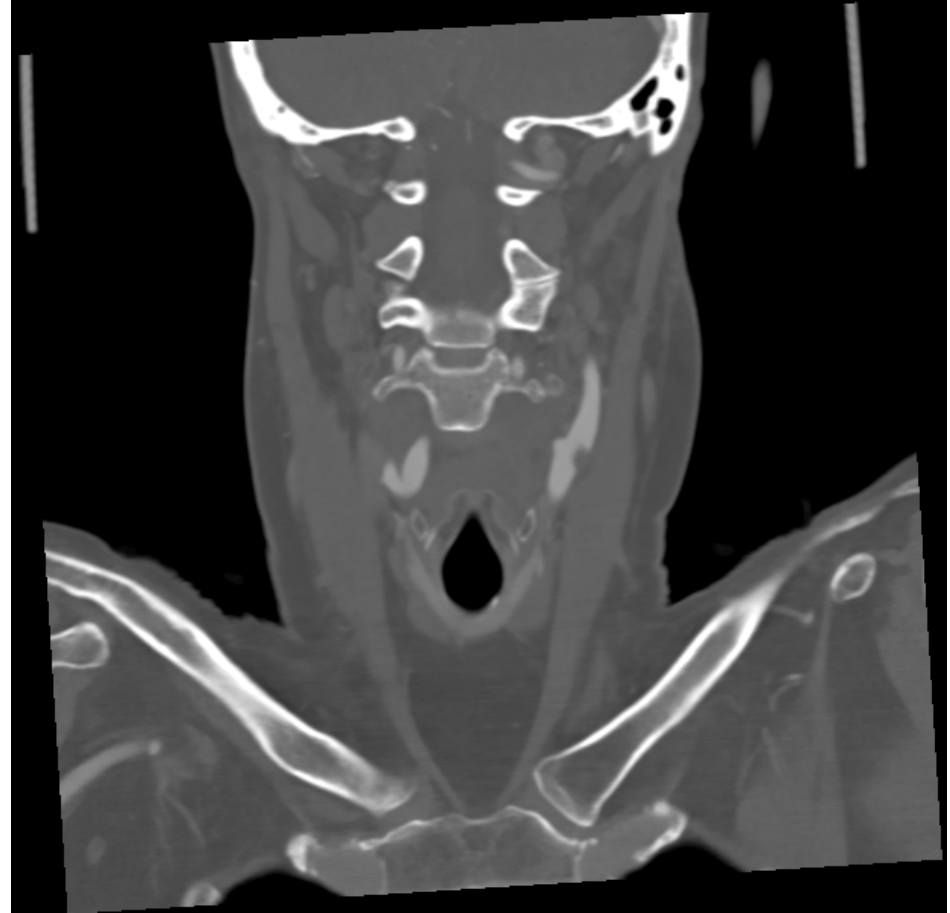
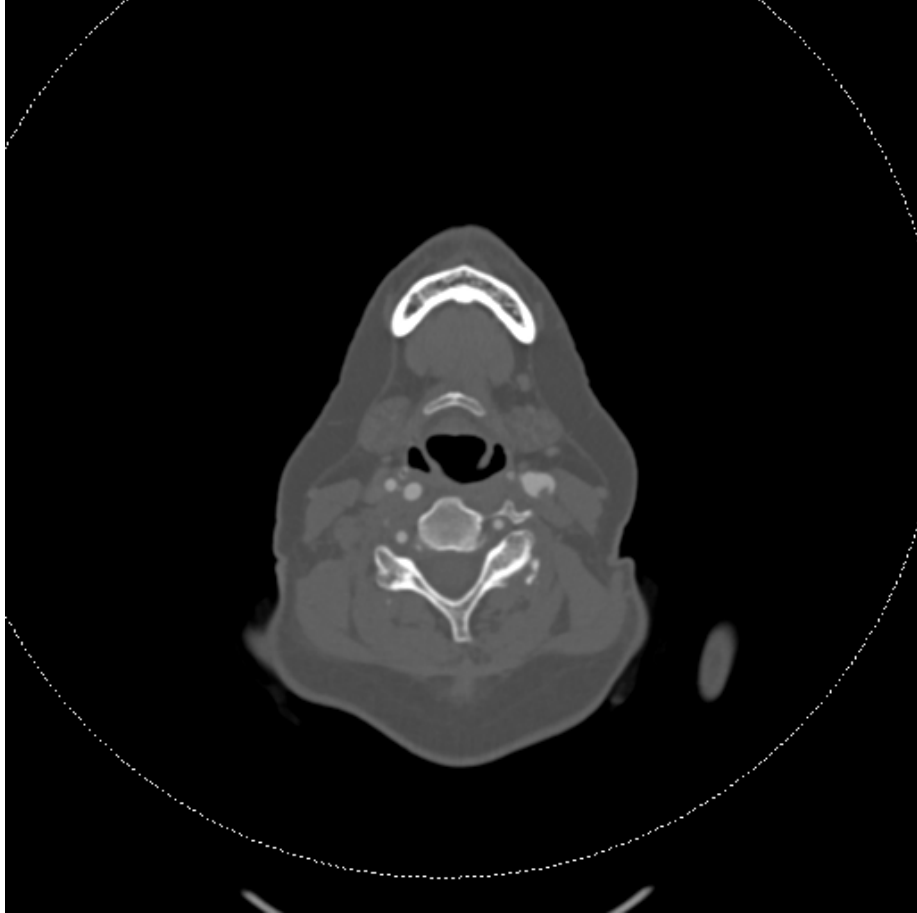
#ISC24

Case

- 59 y/o with HTN and HLD suffered a fall and hit her head. She was noted to have some alteration of her speech but refused to go to the ED and instead just went to bed.
- The next morning she was still having speech trouble and went to the ED where head CT scan showed a right sided subdural and she was transferred to our ED where she was noted to have an expressive aphasia but no motor weakness. NIHSS was 4.
- CTA showed left distal M2 thrombus/high-grade stenosis with 18cc penumbra on perfusion imaging. There was noted to be a possible left ICA carotid web with possible associated thrombus.









Case

- So, I think that she probably had the stroke which caused her to fall and get the SDH.
- Her aphasia improved in the hospital fairly quickly

How do you treat her?

- Likely carotid web with associated thrombus.
- You could anticoagulate her for 3 months
 - What about the SDH?
- Could stent the carotid and tack down that web and thrombus.
 - What about the SDH?
 - Have to give Aspirin/Clopidogrel or Aspirin/Ticagrelor after the stent

What did we do?

- So, she was taken to angio and her right MMA was embolized and then her carotid was stented.
- She did great, and her aphasia improved and last time I saw her she was just making occasional paraphasic errors.
- Her SDH resolved.
- Her stent has remain patent and she is now just on aspirin.
- In f/u in clinic she was neurologically normal with no aphasia. Back to work as an accountant.
- SDH gradually resolved.

A photograph of a modern, multi-story building with a grid of windows. The building is white with dark window frames. In the foreground, there is a courtyard with various plants, including a tree with bright red leaves and a bush of yellow flowers. The sky is blue with some light clouds. A semi-transparent yellow banner is overlaid on the right side of the image, containing the title and subtitle.

Embolization of MMA

SUBDURAL HEMATOMA

MAGIC-MT: Managing Non-Acute Subdural Hematoma Using Liquid Materials: A Chinese Randomized Trial of MMA Treatment

RESULTS: In participants with symptomatic non-acute subdural hematoma (SDH), the use of middle meningeal artery (MMA) embolization resulted in less hematoma recurrence and progression compared to standard care alone.

PURPOSE: To demonstrate that performing additional MMA embolization using Onyx in patients with non-acute symptomatic SDH leads to a reduction in hematoma recurrence for those undergoing surgical treatment and a decrease in hematoma progression for those managed conservatively.

TRIAL DESIGN: multi-center, prospective, randomized (1:1) controlled trial (n=727)

	Embolization (n=360)	Usual Care (n=362)	Odds Ratio (95%CI)	P value
Primary Endpoint- no. (%)	26 (7.2)	44 (12.2)	-4.93 (-9.37 to 0.63)	0.02
<ul style="list-style-type: none"> Any death Symptomatic SDH recurrence Symptomatic SDH progression 	2 (0.6) 17 (4.7) 7 (1.9)	8 (2.2) 19 (5.2) 17 (4.7)		
Safety Outcome				
Serious adverse events within 90 days	24 (6.7)	42 (11.6)	0.54 (0.32 to 0.92)	0.02

Key Takeaways: Incorporating middle meningeal artery embolization in patients with symptomatic non-acute subdural hematoma could lead to better treatment outcomes and potentially improved prognosis.



STEM: SQUID Trial for the Embolization of the Middle Meningeal Artery for Treatment of Chronic Subdural Hematoma

RESULTS: In participants with symptomatic chronic subdural hematoma (CSDH), the addition of middle meningeal artery embolization (MMAE) with SQUID™ resulted in reduced treatment failure rate compared to standard management alone.

PURPOSE: To investigate the safety and effectiveness of MMAE with SQUID™ non-adhesive liquid embolic agent for the management of CSDH compared to standard management (surgical or non-surgical).

TRIAL DESIGN: pivotal, international, multi-center, prospective, randomized (1:1) controlled trial (n=310).

	Standard Management	Standard Management + MMAE with SQUID™	OR (95%CI)	P value
Primary Effectiveness Endpoint				
Residual/re-accumulation of the SDH (≥10 mm) on 180-day scan from intervention, re-operation/surgical rescue or any new, major disabling stroke, MI or death from any (neurological) cause within 180-days of randomization.	39.2% Failure Rate	15.2% Failure Rate	3.60 (1.91-6.78)	0.0001
Primary Safety Endpoint				
All cause death	5 (3.1%)	4 (2.7%)		

Key Takeaways: Incorporating MMAE with SQUID™ into both surgical and non-surgical management of CSDH could potentially enhance treatment outcomes.

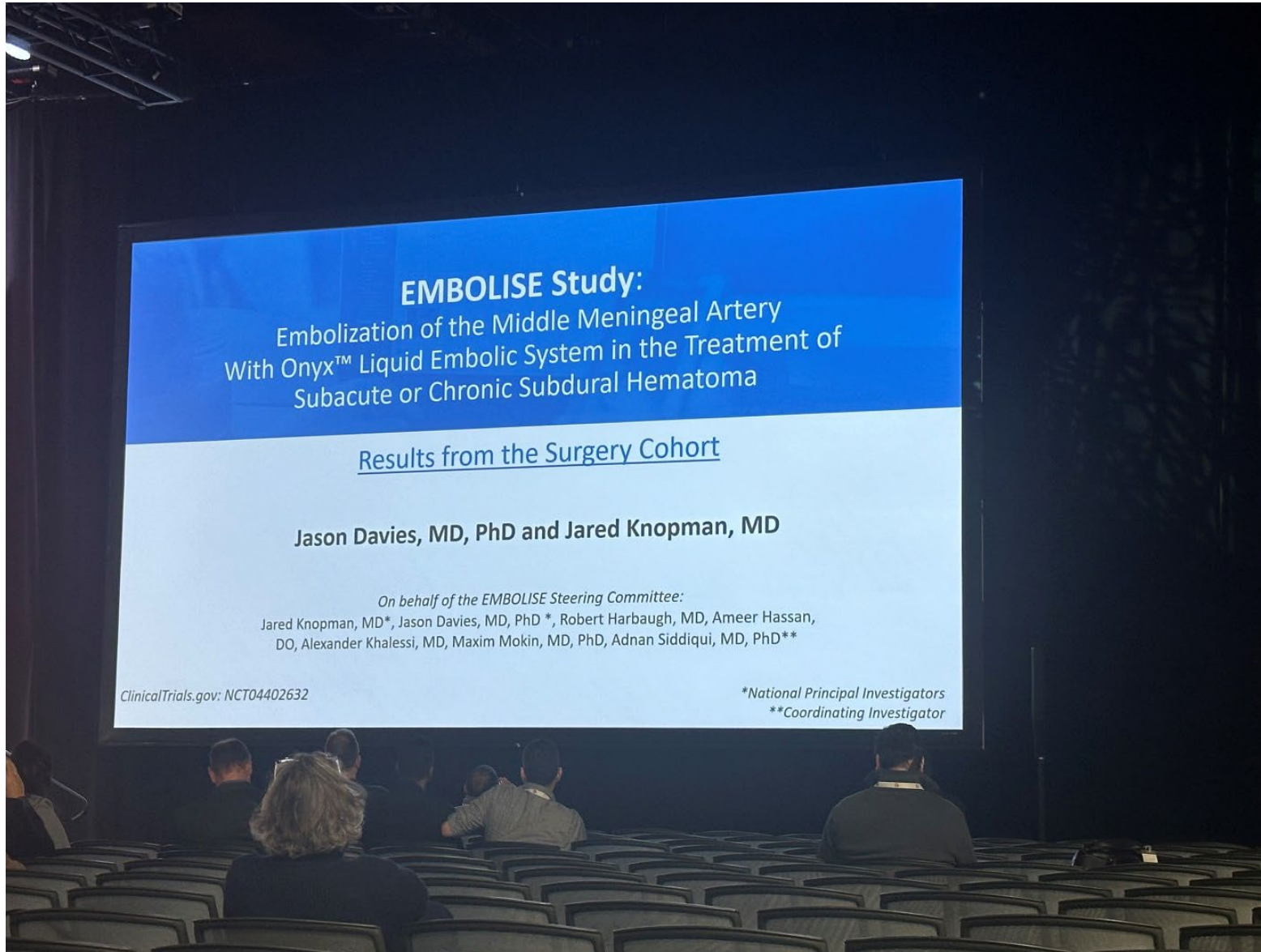


Presented by: Adam S Arthur, Semmes-Murphey Neurological Clinic, TN. International Stroke Conference 2024. © 2024, American Heart Association. All rights reserved. Results reflect the data available at the time of presentation.

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Key Endpoints

PRIMARY ENDPOINT*

Rate of hematoma recurrence/progression requiring surgical drainage within 90 days post-treatment, per CEC adjudication

SECONDARY CLINICAL ENDPOINTS

Non-inferiority assessment of Onyx™ LES embolization treatment compared to Standard of Care based on deterioration in neurologic function at 90 days.
Deterioration defined as follows:
For mRS < 3 at baseline: mRS ≥ 3 at 90 days
For mRS ≥ 3 at baseline: having an increase of ≥ 1 mRS unit at 90 days.

SAFETY ENDPOINTS

- Incidence of device-related serious Adverse Events (AEs) up to 30 days
- Incidence of procedure-related serious AEs up to 30 days
- Incidence of neurological death up to 90 days and 180 days**
- Incidence of device-related AEs up to 90 days and 180 days**

SECONDARY EFFECTIVENESS ENDPOINTS

- Hospital readmissions up to 90 days
- Change in hematoma volume at 90 days compared to baseline, per core lab ***
- Change in midline shift at 90 days compared to baseline, per core lab ***
- % change in hematoma thickness at 90 days compared to baseline, per core lab ***

*Per protocol Rev E. Additional updates may be required for regulatory submissions.

**Presented within 90 days

***Data pending. Core lab adjudication in progress.





Primary Endpoint Results

SDH Recurrence/Progression Requiring Surgical Drainage Through 90 Days Per CEC Adjudication – With Multiple Imputation – ITT Population

Outcome	Onyx Embo + Surgery (Treatment) (N=197)	Surgery Only (Control) (N=203)	Relative Risk [95% CI]	P-Value
SDH Recurrence/ Progression Requiring Surgical Drainage Through 90 Days	4.1% [1.8%, 7.8%] ¹	11.3% [7.3%, 16.5%] ²	0.36 [0.11, 0.80]	0.0081

Outcome is imputed for subjects who failed to attend the 90-day evaluation visit (based on completion of the 90-day subject visit or the 90-day imaging requirement) and who did not have CEC-adjudicated hematoma recurrence/progression requiring surgical drainage within 90 days post-treatment.

¹Note: 2 patients in the ITT population who exhibited recurrence/progression requiring surgical drainage had not been embolized with Onyx due to presence of dangerous anatomical variants.

²Does not include an additional 3 patients who experienced hematoma recurrence/progression and were retreated outside protocol (with Onyx Embo only). As these 3 patients were not retreated surgically, they did not contribute to the primary endpoint. However, they met clinical criteria to warrant retreatment.



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Summary – EMBOLISE IDE Surgical Cohort Outcomes

Reoperation

- MMA embolization with Onyx led to a **~3-fold reduction** in recurrences requiring surgical drainage compared to Surgery Alone – per CEC adjudication (4.1% vs 11.3%, $p=0.0081$).

Clinical Deterioration

- The Onyx Embo + Surgery group was **non-inferior** to the Surgery Alone group for the incidence deterioration in neurologic function (11.9% vs 9.8%, non-inferiority $p=0.0022$, NI margin of 12%).

Safety

- Zero (0%) AEs related to the Onyx device within 90 days.
- Low rate of serious AEs related to the MMAe procedure alone, within 30 days (2.0%, 4/197).
- No difference in rates of stroke (2.0% vs 1.5%, $p=0.72$) or neurological death (4.6% vs 2.0%, $p=0.17$) within 90 days
- No (0%) neurological deaths or serious ICH related to the Onyx device or the MMAe procedure through 90 days.

Conclusion

Adjunctive MMAe with Onyx was associated with significantly reduced rates of reoperation without compromising neurologic function or safety. **MMAe should be considered** for patients presenting with symptomatic subacute/chronic SDH requiring surgery.



Wake Forest University
School of Medicine

The academic core
of Atrium Health

Conclusions

- TNK is probably superior to alteplase and should be offered to patients if eligible
- Extended time window IVT is probably not efficacious
- Glycoprotein IIb-IIIa inhibitors are showing promise as a potential treatment to prevent worsening in non-large vessel occlusion strokes
- Embolization of MMA seems very promising for SDH treatment
- Head positioning could become an important adjunct to pre-EVT patient care

Questions?

How things started. December 2005
Children's Home #2 Dnipro, Ukraine



How its going. High School Graduation, May 2023

