ARGATROBAN – ARTSS-2

INCLUSION CRITERIA

1. Disabling Ischemic stroke symptoms with onset ≤ 3 hours treated with IV tPA by local standards*.
   * or ≤ 4.5 hours according to local standard of care.
2. Age ≥18.
3. NIHSS ≥ 10* or any NIHSS with an intracranial clot demonstrated on TCD or CTA in any one of the following areas: distal ICA, MCA (M1 or M2), PCA (P1 or P2), distal vertebral or basilar artery.

TCD: TIBI 0, 1, 2 or 3	CTA: TIMI 0 or 1

-TCD or CTA can be performed before or **immediately** after tPA bolus (only if study can be performed and interpreted in time to start Argatroban within the 60min window)

*** NIHSS ≥ 10, demonstration of clot on neuroimaging is not necessary (i.e., enrollment can proceed with non-contrast head CT alone), but if performed, a clot must be demonstrated.**

4. GFR must be ≥ 60 (if enrolled with CTA).
5. Negative serum pregnancy test - Females of childbearing potential
6. Signed informed consent

EXCLUSION CRITERIA

1. Plan to treat with IA therapy other endovascular procedures
2. Evidence of intracranial hemorrhage (ICH) on baseline CT scan or diagnosis of a non-vascular cause of neurologic deficit.
3. NIHSS Level of Consciousness score (1a) ≥ 2.
4. Pre- mRS ≥ 2.
5. CT scan findings of hypoattenuation of the x-ray signal (hypodensity) involving ≥ 1/3 of the MCA territory.
6. Any evidence of clinically significant bleeding, or known coagulopathy.
7. INR >1.5.
8. Patients with an elevated aPTT greater than the upper limit of normal (test can be repeated if investigator suspects a falsely elevated value such as when the collection tube is not completely filled).
9. Patients currently, or within the previous 24 hours, on an oral direct thrombin inhibitor (i.e., dabigatran).
10. Heparin flush required for an IV line. Line flushes with saline only.
11. Any history of ICH, known ateriovenous-malformation or unsecured cerebral aneurysms.
12. Significant bleeding episode [e.g. gastrointestinal (GI) or urinary tract] within the 3 weeks before study enrollment.
13. Major surgery or serious trauma in last 2 weeks.
14. Patients who have had an arterial puncture at a non-compressible site, biopsy of parenchymal organ, or lumbar puncture within the last 2 weeks.
15. Previous stroke, myocardial infarction, post myocardial infarction pericarditis, intracranial surgery, or significant head trauma within 3 months.

EXCLUSIONS (CON'T)

16. Uncontrolled hypertension (SBP > 185 mmHg or DBP >110 mmHg) that does not respond to intravenous anti-hypertensive agents.
17. Surgical intervention (any reason) anticipated within the next 48 hours.
18. Known history of clinically significant hepatic dysfunction or liver disease – including a current history of alcohol abuse.
19. Blood glucose <50 mg/dL (2.7 mmol/L).
20. History of primary or metastatic brain tumor.
21. Current platelet count < 100,000/mm^3.
22. Life expectancy < 3 months.
23. Patients who, in the judgment of the investigator, needs to be on concomitant (i.e., during the Argatroban infusion) anticoagulants other than Argatroban, including any form of heparin, UFH, LMWH, defibrinogenating agent, dextran, other direct thrombin inhibitors or thrombolytic agents, GPIIb/IIIa inhibitor or warfarin.
    [*Caveat: However, if in the judgment of the investigator a patient needs to be anticoagulated, **but** this can be deferred for 48 hours, then they could be included.]
24. Participation in any investigational study in past 30 days.
25. Known hypersensitivity to Argatroban or its agents.

Additional exclusion criteria if patient presents between 3-4.5 hours:

a) Age >80
b) Currently taking oral anticoagulants (regardless of INR)
c) A history of stroke and diabetes.
d) NIHSS > 25.

Randomization Website:
https://cru.ccts.uth.tmc.edu/stroke

Username: _____ Password: _____

***Argatroban bolus must be initiated within 1 hour BEFORE THE TPA INFUSION IS COMPLETED.**

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