Inclusion/Exclusion Criteria

Inclusion Criteria:

1. Acute ischemic stroke patients
2. Treated with 0.9mg/kg IV rt-PA or 0.25mg/kg IV TNK within 3 hours of stroke onset or time last known well
3. Age 2: 18
4. NIHSS score ≥ 6 prior to IV thrombolysis
5. Able to receive assigned study drug within 60 minutes but no later than 75 minutes of initiation of IV thrombolysis

Exclusion Criteria:

1. Known allergy or hypersensitivity to argatroban or eptifibatide
2. Previous stroke in the past 90 days
3. Previous intracranial hemorrhage, neoplasm, subarachnoid hemorrhage, or arterial venous malformation
4. Clinical presentation suggested a subarachnoid hemorrhage, even if initial CT scan was normal
5. Any surgery, or a biopsy of parenchymal organ in the past 30 days
6. Trauma with internal injuries or ulcerative wounds in the past 30 days
7. Severe head trauma in the past 90 days
8. Systolic blood pressure persistently >180mmHg post-IV thrombolysis despite antihypertensive intervention
9. Diastolic blood pressure persistently >105mmHg post-IV thrombolysis despite antihypertensive intervention
10. Serious systemic hemorrhage in the past 30 days
11. Known hereditary or acquired hemorrhagic diathesis, coagulation factor deficiency, or oral anticoagulant therapy with INR >1.5
12. Positive urine or serum pregnancy test for women of child bearing potential
13. Glucose <50 or >400 mg/dl
14. Platelets <100,000/mm3
15. Hematocrit <25 %
16. Elevated pre-thrombolysis PTT above laboratory upper limit of normal
17. Creatinine > 4 mg/dl
18. Received Low Molecular Weight heparins (such as Dalteparin, Enoxaparin, Tinzaparin) in full dose within the previous 24 hours
19. Ongoing renal dialysis, regardless of creatinine
20. Abnormal PTT within 48 hours prior to randomization after receiving heparin or a direct thrombin inhibitor (such as bivalirudin, argatroban, dabigatran or lepirudin)
21. Received Factor Xa inhibitors (such as Fondaparinaux, apixaban or rivaroxaban) within the past 48 hours
22. Received glycoprotein IIb/IIIa inhibitors within the past 14 days
23. Pre-existing neurological or psychiatric disease which confounded the neurological or functional evaluations e.g., baseline modified Rankin score >3
24. Other serious, advanced, or terminal illness or any other condition that the investigator felt would pose a significant hazard to the patient if rt-PA, TNK, eptifibatide or argatroban therapy was initiated
    a. Example: known cirrhosis or clinically significant hepatic disease
17. Current participation in another research drug treatment or interventional device trial
    - Subjects could not start another experimental agent until after 90 days
18. Informed consent from the patient or the legally authorized representative was not or could not be obtained
19. High density lesion consistent with hemorrhage of any degree
20. Large (more than 1/3 of the middle cerebral artery) regions of clear hypodensity on the baseline CT Scan. Sulcal effacement and/or loss of grey-white differentiation alone are not contraindications for treatment

Important Enrollment Reminders

- Study drug bolus should be administered within 60 minutes but **no later than 75 minutes** from initial IV thrombolysis bolus administration
- Dosing Information is populated on **Randomization Verification Form** after entering subject weight on Randomization CRF
- Orders for bolus volume and infusion rates should follow exactly what is generated on this form and confirmed by study and clinical personnel
- **Dosing is WEIGHT-BASED – there will be leftover drug**
- Promptly at 12 hours after study drug bolus administration, discontinue the study drug infusion for all study arms

WebDCU™ Website:

https://webdcu.musc.edu/login.asp

WebDCU™ Emergency Randomization Hotline:

1-866-450-2016

Experiencing problems with randomization

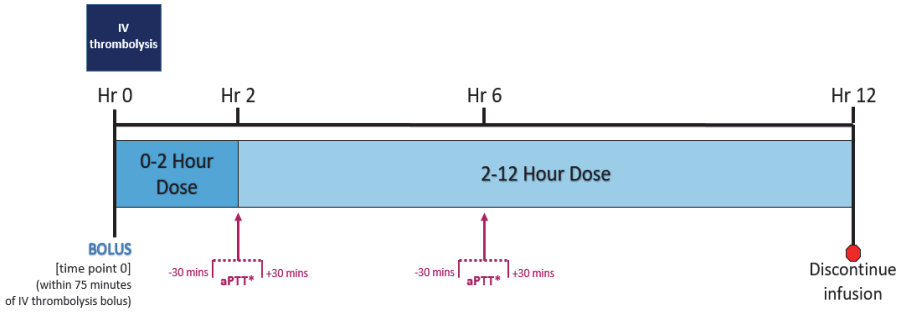
MOST Clinical (PI) Hotline:

1-833-229-MOST (6678)

Urgent safety and protocol related issues

v3.0

Study Drug Administration Timeline



ARGATROBAN ONLY* 2-12 hour infusion dose titration instructions:

1. Enter the baseline aPTT value in WebDCU™ under **Form 501 aPTT** and print the MOST Titration Table that is generated
2. Collect aPTT specimen as early in 2 and 6 hour windows as possible to allow time for processing and for the value to result
3. Based on the result of the aPTT increase, decrease, or make no change to the rate of the argatroban 2-12 hour infusion dose according to the Titration Table

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