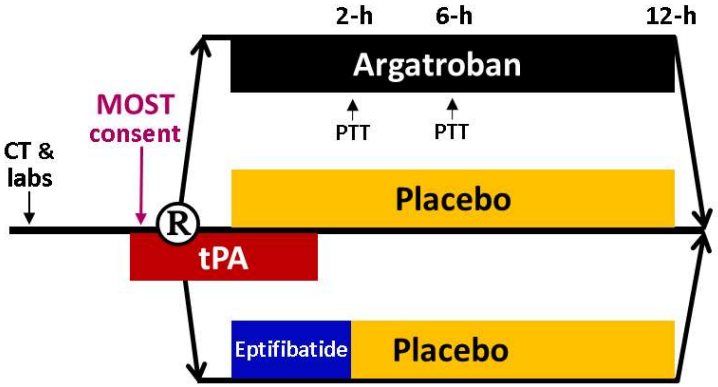
MOST Phase-3 Randomized NIH Stroke Trial

Trial Aim

In <3-hour tPA-treated strokes, does addition of **Argatroban** or **Eptifibatide**, compared to **Placebo**, reduce 90-day stroke disability?



Argatroban Half-life: 50 min

Eptifibatide Half-life: 2.5 hrs

Drug Name	MOST Study Drug Line Compatibility
Alteplase	Incompatible
Dexmedetomidine	Incompatible
Etomidate	Incompatible
Hydralazine hydrochloride	Incompatible
Ketamine hydrochloride	Incompatible
Propofol	Incompatible
Fentanyl citrate	Compatible via Y-Site
Labetolol hydrochloride	Compatible via Y-Site
Midazolam hydrochloride	Compatible via Y-Site
Nicardipine hydrochloride	Compatible via Y-Site
Rocuronium	Compatible via Y-Site
Succinylcholine chloride	Compatible via Y-Site
Vecuronium bromide	Compatible via Y-Site

Endovascular Key points

- **Cannot delay endovascular therapy for trial procedures.**
- ***MAXIMIZE*** *tPA-study drug overlap* - **Study drug bolus should be started within 60min from tPA bolus** but can be started **up to 75min** from tPA bolus.
- Study drug administration may occur before or during the endovascular procedure.
- Stenting for extracranial carotid stenosis or occlusion **should be avoided**. Intracranial stenting is a **protocol violation**.
- Additional IV antithrombotics or thrombolytics during the procedure, other than heparinized saline flush, are **protocol violations** (heparin bolus, tPA, 2b/3a inhibitors).

Reversal Protocol

If ICH is suspected:

- Stop tPA and/or study drug infusion until ICH is ruled out
- Immediately perform CT scan
- Draw coagulation tests that may include INR, PT, aPTT, platelet count, fibrinogen, thromboelastography (TEG) and type and screen
- If ICH is not present, re-start the tPA and/or study drug infusion at the discretion of the investigator

If ICH confirmed:

- Administer tPA reversal agents per local protocol

For patients who receive eptifibatide:

- Consider DDAVP infusion (0.3mcg/kg IV x 1 at the discretion of investigator); and/or
- Consider a transfusion of platelet concentrates (based on absolute low platelet count <100k or reduced MA value on TEG) per local protocol or Cryoprecipitate (if prolonged K-value on TEG) in case of major or life-threatening bleeding or urgent need for normalization of platelet function in case of surgery

Acute Carotid Disease

1. **Attempt angioplasty**
2. **Recommendations if stent is deemed absolutely necessary:**

A) No oral antiplatelets until 24hrs after tPA and a follow-up CT or MRI

****OR****

B) Start 325mg Aspirin per NG or 300mg PR at:

i. Placebo arm - End of procedure
ii. Eptifibatide arm - End of epitifibatide infusion or EVT procedure (whichever is later)
iii. Argatroban arm - End of Argatroban infusion at 12-hrs

A second oral antiplatelet can be started at 24hrs after a CT or MRI at the discretion of the investigator.

****OR****

C) Similar Aspirin approach as **B**, but starting second oral antiplatelet sooner (within 24hrs). In these cases, we recommend a CT or MRI before starting the second agent to exclude hemorrhage.