Multi-arm Optimization of Stroke Thrombolysis (MOST) Trial

Phase 3 Blinded Placebo Controlled Randomized Trial

- rt-PA + Placebo
- rt-PA + Argatroban
- rt-PA + Eptifibatide

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Team

- **Principal Investigators**
  - Opeolu Adeoye, University of Cincinnati
  - Andrew Barreto, University of Texas-Houston
  - Jim Grotta, Memorial Hermann Hospital, Houston
  - Joe Broderick, University of Cincinnati
  - Colin Derdeyn, University of Iowa
- **Primary Statisticians**
  - Berry Consultants
- **Data Management/Unblinded Statisticians**
  - MUSC – Jordan Elm
- **Enrollment**
  - 80 StrokeNet, 30 non-StrokeNet US sites

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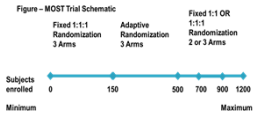
Multi-arm Optimization of Stroke Thrombolysis (MOST) Trial

- Study Arms:
  - rt-PA 0.9mg/kg (control arm)
  - rt-PA 0.9mg/kg plus argatroban 100µg/kg bolus and a 12-hour infusion at 3µg/kg/min
  - rt-PA 0.9mg/kg plus eptifibatide 135µg/kg bolus and a 2-hour infusion at 0.75µg/kg/min



110 sites across the US (80 StrokeNet, 30 non-StrokeNet)

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Primary Endpoints

- **Efficacy** - 90-day functional outcomes as measured by the mRS
- **Safety** - sICH rates (ET only and overall)

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MOST Interventions

- All patients will receive standard of care 0.9mg/kg IV rt-PA within three hours of symptom onset. The study arms are:
  - 1. rt-PA 0.9mg/kg (control arm)
  - 2. rt-PA 0.9mg/kg plus argatroban 100µg/kg bolus and a 12-hour infusion at 3µg/kg/min
  - 3. rt-PA 0.9mg/kg plus eptifibatide 135µg/kg bolus and a 2-hour infusion at 0.75µg/kg/min

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Inclusion Criteria

- Acute ischemic stroke patients aged ≥18 years and treated with IV rt-PA within 3 hours of stroke onset or last known well time
- Pre IV rt-PA NIHSS score of ≥6
- Endovascular therapy is allowed in eligible patients

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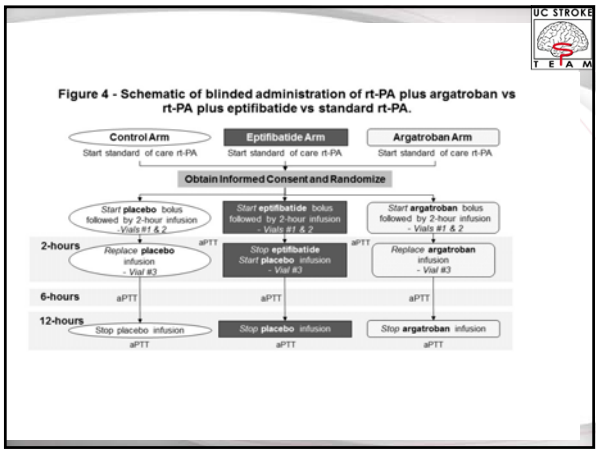

Primary Endpoints

- **Efficacy** - 90-day functional outcomes as measured by the mRS
- **Safety** - sICH rates
  - SITS-MOST definition – parenchymal hemorrhage type 2 associated with a 4 point worsening on the NIH stroke scale

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Moving Parts

- Protocol and Drugs
  - UC Davis
  - Eagle/Auromedics
    - Indemnification/insurance
    - Impact on budget
  - ARL
  - FDA
- Contracts (timing)
- Site selection
- Imaging
- Central outcomes assessment (Glasgow)

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Substudies

- Substudies – opportunities for collaboration and getting involved
- Please email opeolu.adeoye@uc.edu

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Continuing Resolution

March?

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Current Status

- Protocol Finalized
- Blinding/reconstitution of drugs
  - UC Davis, FDA requirements – stability testing
- Anticipated timelines
  - Submit to FDA by mid-February – seek conditional (on completion of stability testing) approval
  - Submit to IRB by end of March
  - Complete drug stability testing by May/June
  - Resubmit to FDA beginning of June
  - Plan first patient in by early Fall

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