Stroke Hyperglycemia Insulin Network Effort Trial
NIH-NINDS Sponsored Trial
In collaboration with the Neurological Emergencies Treatment Trials network (NETT)

Comments from the SHINE trial on MR CLEAN, ESCAPE and EXTEND Results

February 2015

All,

While the new data on acute stroke intervention do not directly affect the SHINE trial, please consider the following as your site reviews the new data.

The recently published MR CLEAN trial (Berkhemer, OA, N Engl J Med 2015; 372:11-20), ESCAPE trial (Goyal, M, N Engl J Med 2015; DOI: 10.1056/NEJMoa1414905) and EXTEND trial (Campbell, BCV, N Engl J Med 2015; DOI: 10.1056/NEJMoa1414792) require that all of our sites reconsider standard care for acute ischemic stroke patients. The SHINE trial team would like our enrolling sites to be aware that **these new data do not substantially change how patients will be enrolled in SHINE** and that the SHINE trial will continue as planned. Our design and plans for statistical analysis have incorporated the possibility that cerebral endovascular treatments might be efficacious or harmful and therefore patients receiving these treatments are still potentially eligible for SHINE. Please consider the following when re-evaluating acute ischemic stroke patient flow at your site:

MR CLEAN, ESCAPE, EXTEND

1. Data support endovascular treatment of imaged proximal occlusion in the anterior circulation (ICA, MCA) (note – only 3 subjects were treated with ACA occlusion in 1 trial)
2. Data support IV tPA prior to endovascular treatment as standard care
3. Endovascular treatment must be provided very early with 2 trials having median time to reperfusion of just over 4 hours and the 3rd requiring completion of procedure by 6 hours
   - MR CLEAN required treatment completion by 6 hours (median stroke onset to groin puncture – 4 hrs 20 min)
   - EXTEND required groin puncture within 6 hours (median time from stroke onset to reperfusion 4 hrs 8 mins)
   - ESCAPE required randomization within a 12 hour window (the median time from symptom onset to reperfusion was 4 hrs 1 min)
4. Data support imaging suggesting modest core and adequate collaterals

SHINE

1. SHINE requires that devices used for endovascular treatment are FDA cleared.
2. SHINE eligible patients may be randomized before or after endovascular treatment. If randomized prior to endovascular treatment, study treatment may be paused until it is possible to resume the treatment protocol (For detailed pause procedures, see MOP – Section 5).
3. SHINE requires an NIHSS score within 30 minutes prior to randomization into the trial. Intubated patients are not eligible if no NIHSS score has been completed within 30 minutes prior to randomization before intubation occurred (full NIHSS score cannot be completed for patients that are intubated as dysarthria is untestable when intubated).
4. Your research team may want to prospectively consider how research options will be incorporated into the patient care flow.

We are happy to work with your team if you feel these trial results will affect your acute stroke flow in a way that you think will impact your SHINE recruitment. We anticipate that the SWIFT PRIME results will not

substantially change these considerations but will summarize those results when published if they require additional comment.

Thank you for your continued efforts.

The SHINE leadership team