StrokeNet Thrombectomy Endovascular Platform Domain A Training (V3.0)

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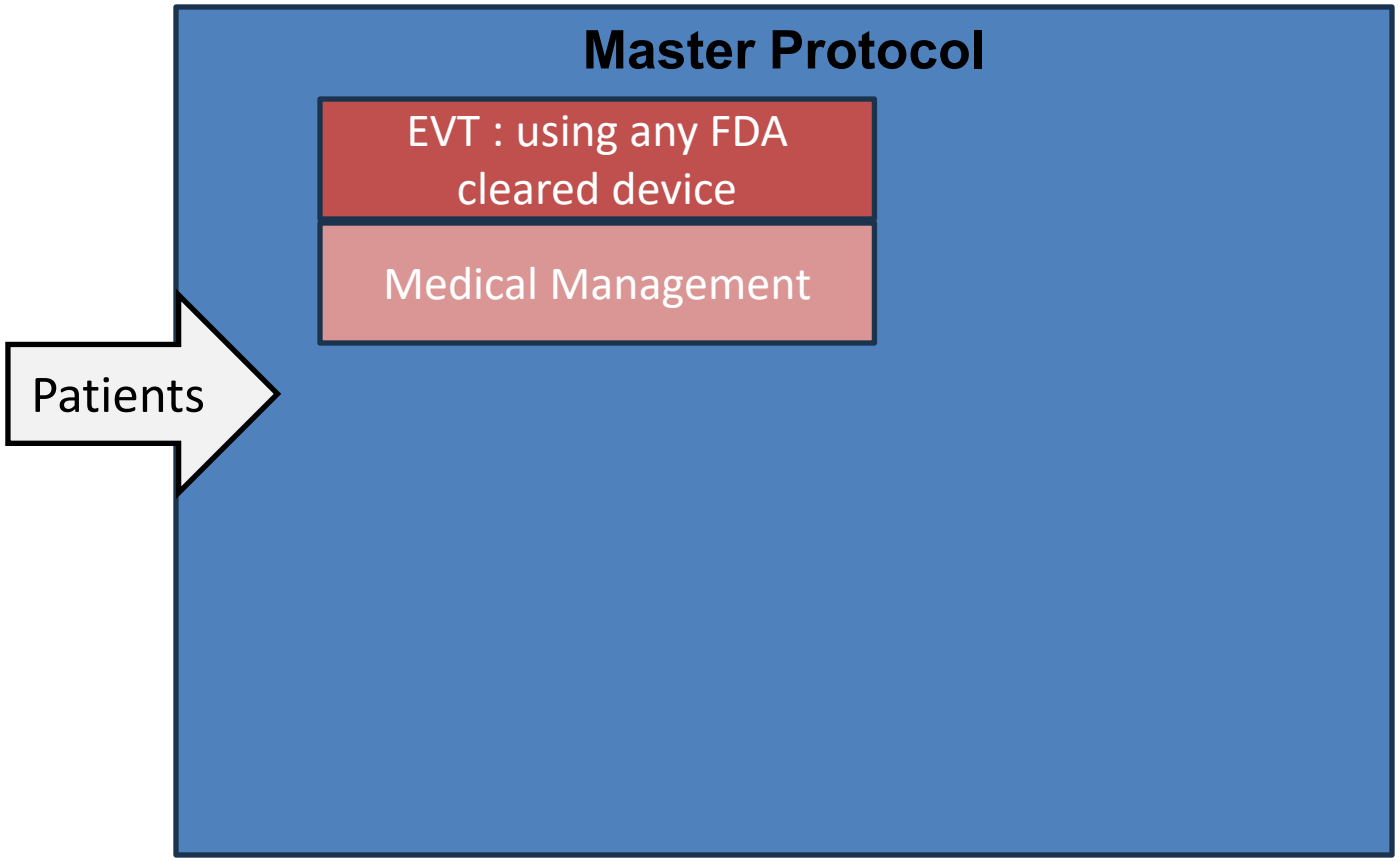
on behalf of the STEP Executive Committee

Domain A- EVT Indication Expansion



- Inclusion:
  1. Age 18 years or older
  2. Pre-stroke modified Rankin Scale score 0-2
  3. Presentation to enrolling hospital within 24 hours of last known well/stroke onset

Inclusion criteria- continued…

4. Has any one or more of the following presentations:

1. LVO patients with mild deficits/low NIHSS (must have both):
   - Mild presenting neurologic deficits - NIHSS 0-5
   - Occlusion of the intracranial ICA or M1 MCA

2. Medium/Distal Vessel Occlusion (must have all 4):
   - **Visualized occlusion or perfusion deficit supportive of a cortical branch occlusion** (10 cc volume of Tmax >4s) in one of the following vessels:
     - ✓ Non-dominant/Co-dominant M2 (defined as serving ≤ 50% of entire overall MCA territory); M3; M4; A1; A2; A3; P1; P2; P3 (dcu.musc.edu/Campus/ProjectTraining/STEPBaselineImagingAssessment9_27_24.mp4
   - **Less than 50% core in the territory supplied by the occluded vessel** as evident by hypodensity and loss of grey-white border on NCCT or ADC <620 mm^2/s on diffusion MRI or rCBF<30% on CTP after 6h of symptom onset.
   - **NIHSS ≥ 4 or NIHSS 2-3 with clearly disabling deficits** at presentation to enrolling hospital
   - **Able to initiate arterial puncture within 2 hours** from qualifying CTA/MRA or CTP/MRP imaging.

*CT/MR and qualifying CTA/MRA or CTP/MRP should be repeated if more than 120 minutes have elapsed since the imaging and randomization has not been performed.

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

STEP Platform

Exclusion criteria

1. Presumed septic embolus; suspicion of bacterial endocarditis
2. Seizure at stroke onset or between onset and enrollment
3. Known anaphylactic reaction to contrast material that precludes endovascular reperfusion therapy
4. Intracranial occlusion suspected to be chronic, based on history and/or imaging
5. Intracranial dissection, based on history and/or imaging
6. Cerebral Vasculitis, based on history and/or imaging
7. Known pregnancy
8. Known pre-existing medical, neurological or psychiatric disease that would confound the neurological or functional evaluations
9. Known serious, advanced, or terminal illness or life expectancy less thqan 6 months in the investigator judgement
10. Known platelet count < 100,000

Exclusion criteria continued

11. CT ASPECT score <6 (MRI ASPECT score <7)

dcu.musc.edu/Campus/ProjectTraining/STEPBaselineImagingAssessment9_27_24.mp4

12. Unfavorable vascular anatomy that limits access to the occluded artery precluding endovascular reperfusion therapy.

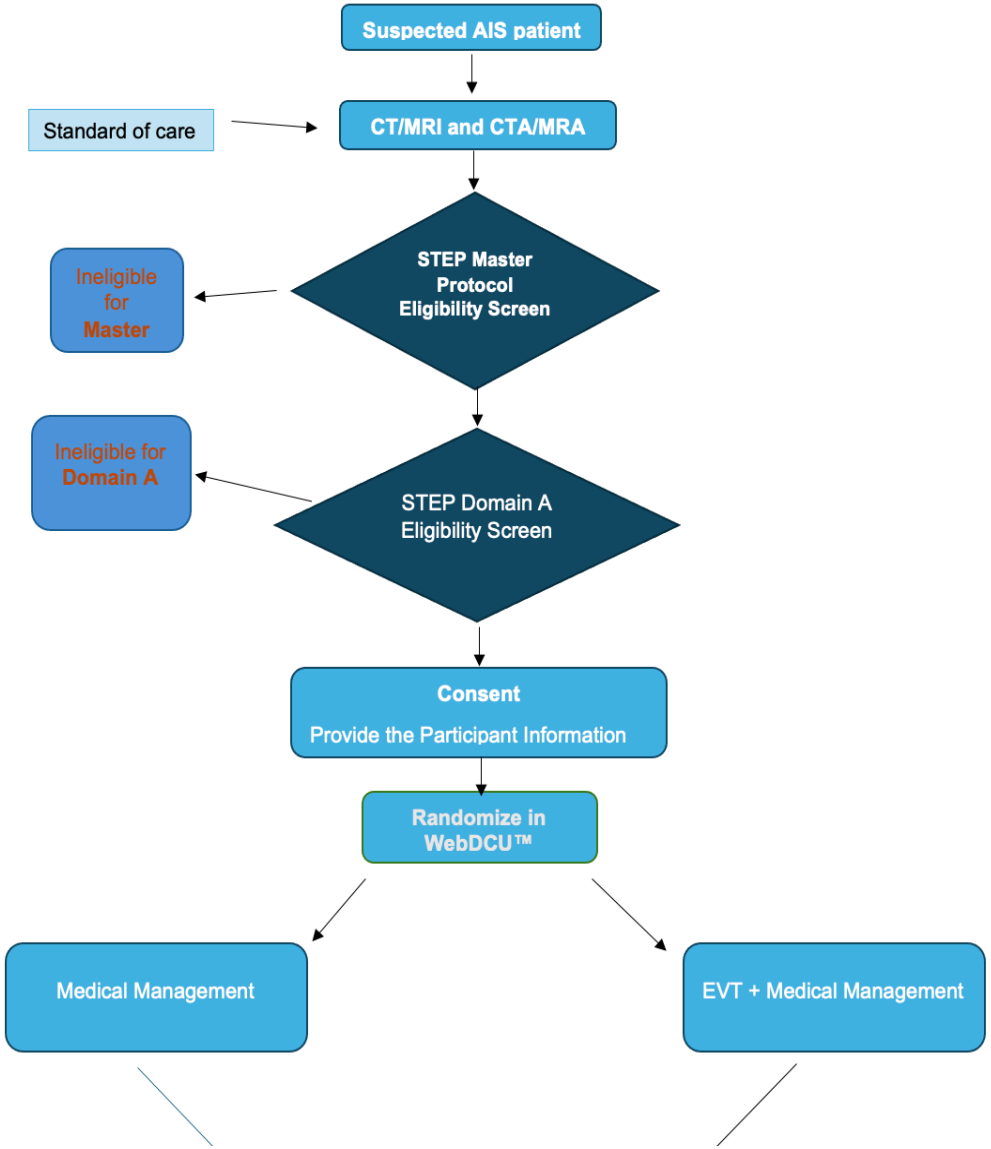
13. Acute occlusions in multiple vascular territories (e.g., bilateral anterior circulation, or anterior/posterior circulation)

14. Significant mass effect with midline shift (>5mm)

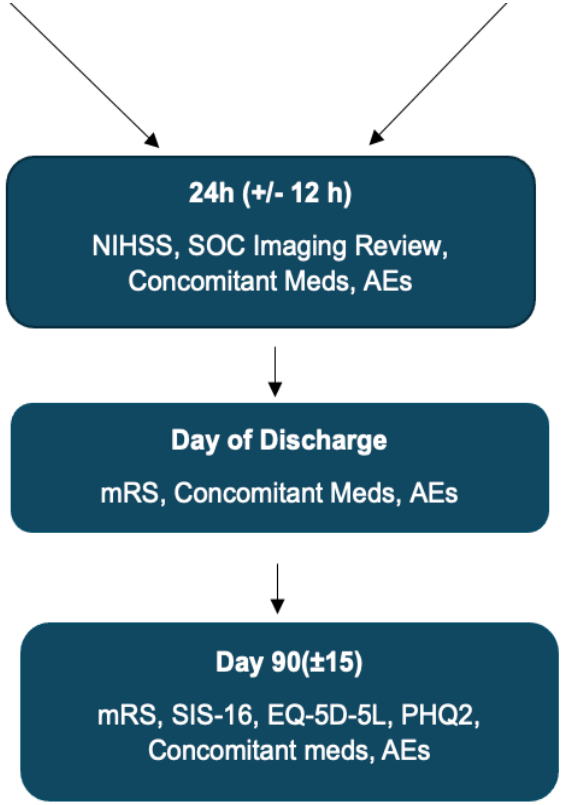
15. Evidence of intra-axial tumor (except small meningioma)

16. Evidence of acute intracranial hemorrhage

Workflow for Domain A



Workflow for Domain A



Domain A Interventions

1. EVT:
   - Using legally marketed devices.
   - Choice of device(s) deployed will be at the discretion of the expert neurointerventionalist performing the procedure.
   - Endovascular procedure conduct training:
     https://dcu.musc.edu/Campus/ProjectTraining/STEPThrombectomyBest%20Practices9_27_24.mp4

2. Medical Management:
   - As per the national American Heart Association/American Stroke Association clinical practice guidelines
   - Administer thrombolysis and antithrombotic (including DAPT) as indicated. Use of DAPT will be tracked.

Domain A Rescue Therapy

- For participants in the mild neurological deficit strata (NIHSS 0-5) and randomized to MM, rescue **EVT is allowed if there is sustained neurological worsening to a total NIHSS score of ≥ 6 points and the participant is still within 24 hours of stroke onset or last known well.**

- For the DMVO strata, **rescue therapy is not allowed**.

EVT performed outside of these protocol-allowed recue treatment will be considered protocol violation and a crossover.

Domain A Definition of symptomatic ICH

Symptomatic intracranial hemorrhage (sICH) within (≤) 36 hours after randomization, defined as presence of both 1) and 2):

1) Brain image finding of major parenchymal hematoma (PH2), remote intraparenchymal hemorrhage, subarachnoid hemorrhage, or intraventricular hemorrhage, and

2) Clinical Deterioration, evidenced by:

   i) In all patients: ≥ 4-point increase on NIHSS, OR

   ii) In patients with mild NIHSS 0-5 deficits at entry: ≥ 2-point increase on any single NIHSS subitem

dcu.musc.edu/campus/ProjectTraining/STEPHeidelbergBleedingClassificationTraining.mp4

Domain A Sample size and Statistical Analysis
EVT Indications Expansion

- **The maximum sample size for this domain :**
  - 1,000 patients with LVO mild deficits/low NIHSS (over 4 years)
  - 1,000 patients with MVO/DMVO (over 2.5 years)

- We will analyze the effects of EVT vs MM using a **change-point model** over baseline NIHSS.
- Domain-specific model designed to be flexible enough to derive separate conclusions about the cut point of NIHSS for benefit amongst vessel occlusion subgroups.

Domain A and ENDOLOW

- ENDOLOW is an ongoing, investigator-initiated, industry-funded RCT of EVT vs Medical Management for LVO patients with low NIHSS. Patients enrolled in ENDOLOW will be considered towards STEP's final sample size.
  - ENDOLOW will close participant enrollment on December 2024 – Jan 2025
- ENDOLOW CCC and DCC will handover the contracting and trial data to the NIH StrokeNet NCC and NDMC respectively
- Existing ENDOLOW sites that are selected as STEP sites (8 in US, 4 in Canada) will continue enrollment under the STEP protocol.
  - ENDOLOW sites not selected for participation in STEP will close enrollment with the ENDOLOW trial closure