

Concentric Retriever 510(k) Application

Questions for panel discussion

- 1) The results of the MERCI trial reported the rates of serious adverse events in the treated population. These were defined in the IDE as: symptomatic intracranial hemorrhage, vessel dissection or perforation, and embolization of clot into a previously uninvolved territory. The rates of these serious adverse events were compared to the rates seen in the placebo group in the PROACT II study, where appropriate.
 - a. The overall rate of serious adverse events was 13% with serious device- or procedure-related adverse events at 7%. Does this data support the safe use of the device in the removal of clots from the neurovasculature?
 - b. The overall rate of symptomatic intracranial hemorrhage at 24 hours in the MERCI trial was 8%, higher than the 2% rate seen in the placebo group in the PROACT II trial. Please discuss whether this raises safety concern regarding the use of this device in the proposed patient population.
 - c. The mortality rate in the MERCI trial was 38%, with a 32% rate seen in patients with MCA occlusions. This shows a trend toward a higher rate than that seen in placebo group in the PROACT II trial (27%). Please discuss whether this raises a safety concern regarding the use of this device in the proposed patient population.
- 2) The efficacy endpoint in this trial was successful revascularization, defined as achieving TIMI II or III flow. The trial results demonstrate a 52% revascularization rate (intent-to-treat) and a 47% serious adverse event-free revascularization rate. This was statistically significant compared to the spontaneous revascularization rate of 18% seen in placebo group in PROACT II and the goal of > 30% set forth in the IDE. Is this adequate to demonstrate efficacy of the device in restoring flow in occluded vessels within the neurovasculature?
- 3) The MERCI trial was designed using successful revascularization as a surrogate endpoint for improved clinical outcomes. Although not the primary endpoint, the sponsor collected 30 and 90 day clinical outcomes (NIHSS and modified Rankin Score) for patients enrolled in the study. Please comment on whether you believe that the results observed, i.e., the trend toward improved clinical outcome in patients where revascularization was successful, supports this surrogate outcome measure.

- 4) One aspect of the Agency's review of a new product is to assess the adequacy of the product's labeling. The labeling must give appropriate instructions for use to the treating physician.
 - a. Given the results of the MERCI trial, does the indication for use adequately define the patient population that should be treated with the Concentric Retriever? Specifically, should the population be limited in terms of: the time between onset of symptoms to initiation of treatment; location of occlusions that can be treated; the severity of strokes at baseline; or treatment with the Retriever only when a patient is not a candidate for other approved treatment (IV tPA)?
 - b. Are there any additional warnings or contraindications that should be added to the labeling specifically with reference to adverse events seen in the MERCI trial?