

Panel Questions - Evaluation of Risk and Benefits of Endovascular Medical Devices Intended to Treat Intracranial Aneurysms

MARCH 1, 2018 NEUROLOGICAL DEVICES PANEL MEETING

PRESENTED BY:

CHRISTOPHER M. LOFTUS MD, FAANS

NEUROSURGEON AND CHIEF MEDICAL OFFICER

DIVISION OF NEUROLOGICAL AND PHYSICAL MEDICINE DEVICES

OFFICE OF DEVICE EVALUATION (ODE)

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH (CDRH)

U.S. FOOD AND DRUG ADMINISTRATION

Question #1 - Safety - Adverse Events & Endpoints



Typically, aneurysm device trial primary safety endpoints have focused on death and major ipsilateral stroke (defined as an increase in the National Institutes of Health Stroke Scale (NIHSS) by 4 points at the time of stroke event within 1 year after treatment). Additional safety events (adverse events or AEs) that are considered in our safety assessment of new devices include:

Adverse Events
Access Site Issues (e.g., Dissections, Hematomas)
Aneurysm Leak, Rupture, or Contrast Extravasation
Distal Embolic Phenomena
Dual Antiplatelet Therapy (DAPT) Related AEs
Mechanical Device Failures and/or Acute or Delayed Device Migration or Embolization
Minor Strokes (NIHSS Change < 4)
Transient Ischemic Attacks (TIAs)

Please address the following:

- a. Is the AE list above complete? If not, what AE(s) should be added?**
- b. Are there specific rates of AEs that would raise serious concerns about the safety of any specific device?**

Question #2 - Safety - Adverse Events & Endpoints



The modified Rankin Scale (mRS) has often been incorporated as a secondary safety endpoint. Can the mRS at 1 year also be a potential primary safety outcome measure for all endovascular aneurysm device trials? If yes, what magnitude of decline in the mRS and for what percentage of treated subjects with a decline in the mRS at 1 year follow-up would raise serious concerns about the safety of the device? If no, what alternative primary safety outcomes are possible and for what duration of time?

Question #3 - Safety & Patient Demographics



Considering the AE list above and any additional AEs specified in response to question #1.a., what patient characteristics (e.g., malignancy, advanced age, aneurysm size) justify foregoing treatment for an aneurysm that would otherwise be considered for treatment?

Question #4 - Effectiveness Measures

Typically, intracranial aneurysm device trial primary effectiveness endpoints have focused on the percentage of subjects who achieve a Raymond Classification I (complete 100% occlusion) without significant parent artery stenosis ($\geq 50\%$) or re-treatment at 1 year post-procedure. Please address the following:

- a. Do you consider the Raymond classification scale to be the standard to assess effectiveness for ALL endovascular intracranial aneurysm treatment devices? If you do not consider the Raymond classification scale to be standard, please identify an alternative well accepted assessment(s) to adequately assess effectiveness for ALL endovascular intracranial treatment devices.
- b. Many studies have used the Raymond classification scale. If the Raymond classification scale is used, is Raymond II (or higher) classification a satisfactory outcome for aneurysm patients with *unruptured* aneurysms? And is Raymond II (or higher) classification a satisfactory outcome for aneurysm patients with *ruptured* aneurysms?

Question #5 - Aneurysm Occlusion (Effectiveness)



For device effectiveness, what percent of morphological occlusion is acceptable and in what percent of patients should this result be achieved?

Question #6 – Aneurysm Occlusion (Effectiveness)



Do your aneurysm occlusion assessment recommendations using Raymond (or another system if identified in question #4.a.) differ for endosaccular devices (e.g., neurovascular embolization coils, balloon assisted coiling (BAC), stent-assisted coiling (SAC), saccular obturation devices)? Intraluminal flow diversion devices? If so, how?



Question #7 - Follow Up

What length of follow-up is recommended to assess effectiveness for endovascular aneurysm treatment devices? Please discuss how your recommendation is impacted if the aneurysm status of the patient at 1 year is a Raymond II or III classification.

Question #8 - Retreatment



Some initial interventions result in a clinically unacceptable outcome and retreatment is considered. Does a worsening in the Raymond scale at follow-up imaging warrant re-treatment and should FDA consider a worsening of the Raymond scale during 1 year follow-up to represent a failure of treatment?



Question #9 - Alternative Imaging Assessments

We consider digital subtraction angiography (DSA) to be the gold standard to assess aneurysm occlusion at follow-up. Can magnetic resonance angiography (MRA) or computed tomography angiography (CTA) serve as a surrogate follow-up examination and when should this take place?

Question #10 - Post Approval Studies



In some cases, a post-approval study may be warranted, for example when limited follow up exists for patients. What is a sufficient long term follow-up period for a post-approval study where the majority of patients have the following outcomes for *ruptured or unruptured* aneurysms?

- a. Raymond I**
- b. Raymond II**
- c. Raymond III**



Question #11 - Labeling

What patient characteristics should be specified in the Indications for Use (IFU) (i.e., age, aneurysm morphology, location, size, Type 1 or Type 2 status, ruptured vs. unruptured)? For intraluminal flow diverters? And for endosaccular devices?

Thank You