Review of Potential RAPID Use Cases From April 2016

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RAPID Phase III Goal

- Phase III: Use a coordinated registries network (CRN) for studies supporting a regulatory decision.
  - Projects would extract minimal core data from different registries or other data sources, such as centers using the same EHR system
  - Individual projects might need supplementary data
  - Prospective clinical trial, pre-market study
  - Post-market study, surveillance
  - Objective performance criteria creation

- Goal: Total Product Life Cycle evaluation of devices in real world practice.

First Proposal – Multiple Options from Abbott

- Performance goal (PG) refinement or development with larger, more robust, real-world data

Option 1 - Superficial femoral /popliteal artery PG refinement

- Is the current PG reflective of real SFA/popliteal stenting outcomes? Should it be updated?
  - VIVA PG for safety and effectiveness developed by Rocha-Singh, et al. in 2007 based on 116 PTA pts from FDA studies and 191 pts from literature
  - Goal for effectiveness for metallic self-expanding stents set at 2x PTA patency (66%)
  - Does this reflect real outcomes? Should it be modified?

First Proposal – Multiple Options from Abbott (cont.)

- Performance goal (PG) refinement or development with larger, more robust, real-world data

Option 2 - Infrapopliteal arteries

  - Do the suggested PG's developed by Conte et al. for catheter based treatment of CLI patients work in the current regulatory environment?
  - Do follow-up angiograms that evaluate patency in CLI patients add unnecessary risk?
    - Development of a PG for tibial artery lesion patency based on RB Class or WIfI classification using non-invasive (eg. duplex) methods
    - Development of a PG related to wound healing in CLI patients or develop standardized method to assess wound healing

First Proposal – Multiple Options from Abbott (cont.)

Option 3 - Comparison of two existing PAD treatment modalities for SFA

- Utilization of concurrent control rather than RCT or historical treatment

Option 4 - Comparison of a new device type for PAD treatment of the SFA, popliteal, or Infrapopliteal arteries

- Utilization of concurrent control rather than RCT or historical treatment
- Combined approach – use of registry data, supplemented as needed, with collection of additional data elements related to new device

First Proposal – Multiple Options from Abbott (cont.)

Option 5 - Randomized Controlled Trial

- What will be needed to demonstrate cost effectiveness?
- Comparison of two existing PAD treatment modalities for patients with claudication and SFA/popliteal disease to evaluate clinical outcomes, cost effectiveness, and QoL in real-world patients

  - Revascularization with different devices or surgery
  - Revascularization with different devices plus optimal medical therapy and exercise, versus optimal medical therapy and exercise alone

Second Proposal – Multiple Options From Bard

Option 1 - Traditional (Original) PMA's Require Traditional Methods (i.e., pivotal study data)

- However, PMA Supplements provide opportunities for alternative strategies.. Why not use a RAPID study to gain approval for;
  - Design Modifications
  - Indication Expansions

Second Proposal – Multiple Options From Bard (cont.)

Option 2 – Investigator Sponsored Study (ISS)

- Current ISS Proposal
  - Multicenter, Randomized, Controlled Study for Indication Expansion of Vascular Stent
  - Advantage of ISS: Non-biased, clinical need/question drove interest, 2 year follow-up
  - Challenge: Less Oversight & Compliance (i.e., X-ray)
- Status Pending
  - Perhaps use of registry core data elements would be a more streamline path for indication expansion
  - Challenge: collection of non-SoC imaging
    - Risk Assessment – Increased Radiation Exposure vs. Device Attribute Assessments

Second Proposal – Multiple Options From Bard (cont.)

Option 3 - Post-Market Surveillance Plan to Address 522 Requirements

- Used the example of the Vena Cava Filter 522 Order from FDA.
- Could a RAPID trial provide a more cost effective, real world data set to address concerns FDA or health care providers might have?

Third Proposal – From Cook

- Utilizing the RAPID Core Data Set
  Case Study: Zilver® PTX® Drug-Eluting Peripheral Stent
- Near-Label Use and Expanded Indication
  - Industry has responsibility to understand device performance in near-label use
- Traditional PAS costly:
  - Little value with strict indication
  - Considerable overhead under IDE for near-label use
- Can RAPID Core Data Set be used to collect data on actual post-market usage patterns and inform:
  - The need for pursuing additional indications
  - Development of future products to fill unmet needs

Third Proposal – From Cook (cont.)

- How can the RAPID CDS assist near-label use?
  - Identify actual usage rate for treating in-stent restenosis and other near-label uses in clinical practice
- How can the RAPID CDS assist expanded indication?
  - Provide a pathway for collecting clinical data to support an expanded indication

Utilization of RAPID CDS

- Post-approval Safety & Performance Monitoring
  - Possible ways RAPID can help:
    - Shift some of pre-market burden into post-market space
    - Decreased timeline for physician and patient access to new and improved technologies
    - Eventual replacement of traditional post-approval studies
    - Data on more patients, broader (i.e., near-label) population, more quickly
    - More accurate evaluation of post-market performance
    - Earlier notification/availability of emerging safety signals

Fourth Proposal – From CSI

RAPID Use Case – CLI Study

- Objectives
  - Determine consistent guidelines/treatment algorithm(s) for the treatment of CLI
  - Reduce the number of amputations
- Potential Study Design
  - Large, prospective, multicenter study
  - All endovascular devices eligible • Surgical revascularization?
  - QoL, 6MWT, MAEs, TLR/TVR, patency
  - Acute & long-term follow-up
  - Economic data capture
    • Link to CMS/private payor databases

Fourth Proposal – From CSI (cont.)

Does this Use Case Pass the Litmus Test?

- Practice Guidelines Updated to Reflect Real World Data
- Addresses FDA's Focus Areas
  - Safe, effective and patient-centric outcomes
- Cost of Healthcare Driven Down
  - Benefits CMS, private payers and taxpayers
- Potential for Indications for Use Expansion

Real World Examples, Not Theory

Stakeholder Discussion Questions

- How can the RAPID Core Data Set and upcoming Clinical Trial(s) benefit stakeholders?
- What questions or concerns do you (or your organization) have regarding the use of the RAPID Core Data Set to support trials?
- What are your organizations' basic requirements to participate in a RAPID related trial?
- Will multi-stakeholder format leverage your Clinical investments?

Potential Areas of Discussion

- Data & work flows
- IRB approvals/exemptions
- Use of patient-identifiers (or not) (de-identified, limited or full)
- Informed consent
- Data quality (& Integrity)
- Data governance: Access for Stakeholders
- Data provenance: Verifiable & reproducible; every manipulation or edit can be audited
- Leverage of Costs – Stakeholder payments / support, directly or indirectly
- IDE Waivers or Acceleration for RAPID trials
- Requirement for FDA trial acceptance & future approvals, clearances, indication changes, etc.
- Linking RAPID trials to CMS cost data & future payment decisions
- RAPID trials addressing CMS / MEDCAC PAD concerns