Nesting Clinical Trials /

Studies for Labeling Changes

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National Coordinated Registry Network (CRN) Think-Tank
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Center for Devices and Radiological Health
CDRH

Potential CRN Uses for Cardiovascular Devices

- Meeting post-approval requirements for new devices
- Leveraging the CRN infrastructure to nest IDE studies
- More broadly contribute to a learning health model

Basic Principles for Success

- Developing uniform definitions and CRFs for a particular area
- Defining relevant questions
- Establishing quality by design principles to ensure data quality and ability of registry to withstand audit
- Successfully addressing any relevant informed consent issues
- Developing incentives for sustainability of the registry

Peripheral Arterial Disease

- **R**egistry **A**ssessment of **P**eripheral **I**nterventional **D**evices (**RAPID**)
  - Launched June 5, 2015
- Goal
  - Standardize core data elements that could serve as a **global case report form** for both pre- and post-market assessment of peripheral arterial interventional devices

Co-Chairs

- **Jack Cronenwett**
  - Society for Vascular Surgery (SVS) Vascular Quality Initiative (VQI)
- **Robert Thatcher**
  - Cardiovascular Systems, Inc. (CSI)
- **Pablo Morales**
  - Food and Drug Administration (FDA)

Project Manager

- **Rebecca Wilgus**
  - Clinical Informatics, Duke Clinical Research Institute (DCRI)

RAPID Partners

- Societies / Registries
  - American College of Cardiology (**ACC**)
    - National Cardiovascular Disease Registry (**NCDR**)
  - Society of Interventional Radiology (**SIR**)
    - National Interventional Radiology Quality Registry (**NIRQR**)
  - Society for Vascular Surgery (**SVS**)
    - Vascular Quality Initiative (**VQI**)
- Agencies
  - FDA (**CDRH** pre- and post-market, and **CDER**)
  - Japan's Pharmaceuticals and Medical Devices Agency (**PMDA**)
  - Centers for Medicare and Medicaid Services (**CMS**)
- MDEpiNet Coordinating Center
  - Duke Clinical Research Institute (**DCRI**)

RAPID Partners

- Device Manufacturers
  - Abbott
  - Avinger
  - Boston Scientific
  - Cardiovascular Systems Inc
  - Cook Medical
  - CR Bard
  - Medtronic
  - Spectranetics Corp
  - Terumo
  - Volcano Corp/Phillips Health Technology
  - WL Gore

Why RAPID?

- Current Challenge = Heterogeneity

Devices Heterogeneity

- Multiple devices used at a given intervention
- Different technologies
  - Angioplasty Balloons
    - Plain, drug coated, cutting, cryoplasty
  - Atherectomy devices
    - Laser, mechanical
  - Total occlusion crossing devices
  - Stents
    - Bare metal
      - » Self-expanding, balloon expandable
    - Covered
    - Drug-eluting

Patient and Disease Heterogeneity

- Age, gender, diabetes influence outcomes
- Disease Severity
  - Claudication (life style) vs. Critical Ischemia (limb threat)
  - Differing lesion length, occlusion vs. narrowing, calcification
- Disease Location
  - Large (iliac),
  - Medium (SFA, popliteal),
  - Small (tibial) Arteries

Provider Heterogeneity

- Variable Physician Specialty, Training, Experience
  - Cardiologists, radiologists, surgeons
- Variable Treatment Options
  - Numerous device types, on- and off-label use in practice

RAPID Project Plan

- **Phase I: Identify minimal set of core data elements for registry assessment of lower extremity arterial devices**
  - Select data elements from existing registries and industry case report forms used for pivotal device approvals
  - Develop structured comparison report of data elements using DCRI methodology
  - Define core data elements and definitions, including patient and pathology data, device characteristics, endpoints for safety and effectiveness, and patient reported outcomes
    - Clinical and Informatics Panels representing all RAPID partners
    - Plan: HL7 balloting, linkage with ONC standards, sharing with EHR manufacturers to allow extraction from multiple sources

RAPID Project Plan

- **Phase 1a: Develop a method for registries to extract UDI data for relevant lower extremity arterial devices**
  - Work with FDA Global Unique Device Identification Database (GUDID) and National Library of Medicine to develop an automated method to periodically extract specific device data from Access GUDID to populate relevant registries
  - Work with FDA and NLM to assess usefulness of current lower extremity arterial device categorization and suggest improvements as appropriate

RAPID Project Plan

- **Phase II: Develop data extraction interoperability** across peripheral registries and hospital EHRs that provide patient-level data for core data elements
  - The ACC, SIR and SVS peripheral intervention registries would incorporate the core data elements
  - EHR manufacturers would be encouraged to develop smart data elements for the core data elements
  - Core data elements would be provided to other national registries participating in the International Consortium of Vascular Registries (ICVR)

RAPID Project Plan

- **Phase III: Apply a coordinated registries network to studies supporting a regulatory decision.**
  - Post-market study, surveillance
  - Prospective IDE clinical study, pre-market study
  - Objective performance criteria creation
  - Goal: Total Product Life Cycle evaluation in real world practice

RAPID Targets

- Phase I = December 2015
- Phase II = December 2016
- Phase III = December 2017

RAPID Progress

- Infrastructure Established
  - DCRI Informatics Team, Project Manager
  - Clinical Experts, Informatics and GUDID groups selected
    - Multiple stakeholders represented in each group
- Registry and CRF forms, definitions submitted
  - ACC NCDR, SIR, SVS VQI registries
  - Nine manufacturers in process of submitting
- Office National Coordinator (ONC) interest and involvement
  - integration of data model and facilitate interoperability
- Global medical device nomenclature (GMDN)

RAPID Progress

- Full day planning meeting at FDA on June 5, 2015
- Weekly/Bi-weekly teleconferences of leadership group
- Full day working meeting at Heart House on Nov 6, 2015
- Full day workshop scheduled for April 13, 2016
  - Finalize Phase I
  - Plan and start execution for Phase II and III

Informatics Group Update

- The informatics group has combined the case report forms from the **SIR**, **SVS VQI**, **ACC NCDR** peripheral intervention modules, plus **seven** CFR provided by manufacturers
- From these case report forms over 3904 variables were identified
  - **2021** were considered 'peripheral arterial disease (PAD)-Specific' (meaning they are important to PAD and not routinely collected for other purposes e.g., demographics) and the group is narrowing them down to the 100 "must have data elements"
- From the PAD-Specific pool, 100-125 have been selected for the initial RAPID core data set.

Clinical Experts Group Update

- The clinical working group is working on:
  - Standardizing definitions for the RAPID core data set
  - Designing potential clinical studies scenarios to test the global case report form

GUDID Group Update

- The GUDID working group is testing the capabilities to interconnect the two biggest peripheral vascular registries using as a bridge the unique device identification (UDI) numbers

Nesting Clinical Trials?

- Once the RAPID core data set are selected, defined and finalized, we plan to blend them into the existing registries with peripheral intervention modules
- Since by then the these registries will be capable to collect and pull data side-to-side, a testing exercise collecting data from real devices will be performed
- If we succeed, the next step will be to conduct a clinical study using the platform designed and hopefully such study will allow us to make some source of regulatory decision

Potential Scenarios of Clinical Studies to be Nested

- Randomized Clinical Trial – (e.g., Does direct thrombin inhibitor improve patency of SFA interventions)
- Expansion of approved device indications
- Comparison of two existing treatment modalities (e.g. atherectomy vs angioplasty in popliteal or any comparison of new device type with historical treatment.)
- Developing objective performance goals (e.g. for tibial artery treatment in diabetic patients based on current real world practice)

To be decided - RAPID workshop on Wednesday, April 13, 2016

Deliverables

- RAPID should allow for Standardization and Homogeneity
- Global CRF with respective definitions should lower the reviewer regulatory burden as well as decrease cost to sponsors
- GUDID / NLM should allow:
  - for device specific outcomes searches
  - lessen the cost for device data entry
  - optimize accuracy of device data

Take home message

- Registries are here to stay and if we develop them together they can work on our behalf

Contact Information

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