Registry Assessment of Peripheral Interventional Devices (RAPID)

Pre-Market Registry-based Trial Use Case Synopsis

Background and Rationale for Use Cases:

1) The use cases were developed by the RAPID working groups (clinical, informatics, and GUDID) to help guide each group and ensure that the core data elements contained information that will be pertinent for common and/or specific PAD issues that will potentially be tested in the future using this approach.
2) The use cases do not represent concrete plans to study the items described below; they were developed as an exercise to think broadly about the PAD population being studied so that the data set is useful and applicable
3) Many aspects of the use cases are not factual (rather designed to be hypothetical) and the data elements that have been created will be useful for studying questions like this (not necessarily this exact question with the specific details described).
4) RAPID data elements will be used to populate a registry and/or clinical trial database.
5) Informatics terminology – there is a lot of terminology used by informatics experts involved in RAPID. We will attempt to provide explanations for this. As a start, the clinical and informatics working groups divided the clinical data elements into PAD-specific data elements and non-PAD-specific data elements. After this, the focus remained on PAD-specific data elements (as we will use previously established and validated non-PAD or general data elements from other projects like PCORnet and NIH Collaboratory). In terms of PAD-specific data elements, we tried to group them into 5 large domains to begin with – Condition, Test, Treatment, Device, and Outcome.

Business and operational success factors include:

1) The results of the study are acceptable to the FDA to modify the label of the device
2) The operations and process of the study are acceptable to the industry sponsor paying for the study.
3) The evaluation and inclusion of UDI and linkages to GUDID.

1. The Missing Link in Vascular Device Trials Michael R. Jaff, DO Jan 23, 2015
2. Outcomes for Clinical Studies Assessing Drug and Revascularization Therapies for Claudication and Critical Limb Ischemia in Peripheral Artery Disease Scott Kinlay, MBBS, PhD

Project Summary

This registry-based trial will assess the safety and effectiveness of Device X (new technology) vs. Device Y (currently approved technology) or OPC (objective performance criteria) in patients between the ages of 40 and 85 years old with femoropopliteal (FP) stenosis experiencing any symptoms of PAD (including intermittent claudication or critical limb ischemia).

Rationale & Background Information

"Atherosclerotic peripheral artery disease (PAD), venous thromboembolic disease and aortic diseases represent one of the largest composite of diseases facing the world today"[1]. "The objective of device clearance by regulatory bodies such as the Food and Drug Administration by meeting minimum performance criteria is different from evaluating whether a strategy offers clinical benefit beyond usual care or other devices. Although the Food and Drug Administration permits device evaluation by single-arm comparisons with historical controls in specified situations (e.g., prosthetic heart valves), this is an unsatisfactory solution to PAD therapies in which lack of standardization across trials is the rule, particularly for percutaneous treatments".[2] Coupled with the lack of consistent definitions and nomenclature across the trial domain, this poses as a significant barrier to gathering and comparing knowledge across PAD therapies and technologies. The FDA Regulatory Science in FDA's Center for Devices and Radiological Health: A Vital Framework for Protecting and Promoting Public Health emphasizes seven priority areas of focus in regulatory science on 1) advancing medical device innovation, 2) improving device quality and manufacturing, 3) analyzing medical device performance, 4) improving medical device safety, 5) developing novel ways to use clinical data in evaluating medical devices, 6) protecting against emerging infectious diseases, and 7) improving health of pediatric and other special populations.

Randomized clinical trials can more quickly identify successful treatment options for PAD as well as point out those that offer no benefit therefore more efficiently recognizing the cost benefit to the patient population which targets many of the seven priority areas outlined by the FDA.

Study Design

The proposed research design will be a single-blind, registry-based, 1:1 randomized controlled clinical trial of 500 male and female participants between the ages of 18 and 65, meeting the inclusion/exclusion criteria, seeking to compare device performance and acute/intermediate/long-term clinical outcomes (cardiovascular endpoints, limb endpoints, functional measures, and quality of life measures) for the treatment of PAD.

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Participants will be recruited during routine standard of care visits by using EHR data. All participants meeting the basic inclusion criteria of a PAD diagnosis with Rutherford scores within specified range, being within the specified age-range, willing to be randomized to a treatment plan and sign the informed consent will be eligible for screening and enrollment.

Patient Flow

Baseline/Screening

Participants will present to the clinic for a routine care visit. Upon identification by study staff/coordinator as a potential participant for the RAPID Registry use case, they will be informed about the study and asked to consent to participate. Upon consent, participants will go through a screening process including collection of:

- demographic characteristics (e.g. age, DOB, race, ethnicity, gender)
- vital signs
- medical history
- assessment for other cardiac disease, history of cardiac procedures, and risk factors (e.g. smoking, diabetes, hypertension)
- physical examination findings
- PAD-specific assessments
    - diagnosis
    - duration
    - severity as measured by the Rutherford score
    - ABI
    - six-minute walk test
    - quality of life measures (PAQ or EQ5D)
- laboratory values (hemoglobin (complete blood count), creatinine (basic metabolic panel), PT, PTT)
- Current cardiac medications.
- Other implanted medical devices

The participant will then be randomized to one of the procedures and a procedure date will be set. If a participant is ineligible for the registry, they will be flagged as a screen failure and alternative/most appropriate care will be provided.

Relevant data elements from this baseline/screening clinic visit will be pushed directly into the Registry system via the EHR.

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Procedure

Participants will present to the catheterization lab, radiology suite, office-based clinic, or ambulatory surgical center on the scheduled day of the procedure. Pre- during- and post-procedure assessments will be taken by medical staff including vitals, ABI, labs, Rutherford scores, angiographic/procedure details, lesion details, devices used and implanted, device ids, safety and success of the procedure.

Relevant data elements from this baseline/screening clinic visit will be pushed directly into the Registry system via the EHR.

Follow-Up

Participants will present to the clinic for a routine care/follow up visits at six weeks, 3 months, 6 months and 1 year post procedure. During these follow-up visits, participants will be assessed by the medical staff to determine the success of the procedure by measuring physical exam, vitals, quality of life and six minute walk test, post procedure complications, repeat procedures and adverse events, medical history, labs, lesion details, etc.

Relevant data elements from this baseline/screening clinic visit will be pushed directly into the Registry system via the EHR.

Methodology

The RAPID Registry will be mined for participants who have the XXXX procedure and meet the following inclusion/exclusion criteria. To be included in this study, a registry participant must have symptomatic peripheral artery disease (PAD) with moderate to severe claudication (Rutherford score 2-3), chronic critical limb ischemia with pain while at rest (Rutherford 4), or with ischemic ulcers (Rutherford 5-6), >=50% stenosis of affected artery, (insert additional project-specific inclusion criteria here). Participants are excluded from this study if any of the following are applicable: a major bleeding event in the past two months, no informed consent…, (insert additional project-specific exclusion criteria here).

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Assessments

	Time and Events Schedule						
Assessment	**Screening Baseline**	**Pre-Procedure**	**Procedure**	**4-6 Weeks**	**3 Month**	**6 Month**	**1 Year End of Study**
Consent	X						
Inclusion/Exclusion	X		X				
Randomization			X				
Demographics	X						
Medical History	X	X					
Physical Exam	X		X			X	X
Vitals	X	X	X	X	X	X	X
Labs	X	X	X		X	X	X
Medications	X	X	X	X	X	X	X
Equipment Use			X				
Lesion Details (lesion length, lesion location, degree of calcification, and degree of stenosis - use of angio core lab and duplex core lab)	X		X				X
Safety Endpoints (Surgical & Procedural Complications, Acute Procedural Success	x	x	X	X	X	X	x

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Rutherford Class	X	X		X	X	X	X
Restenosis/Patency				X	X	X	X
ABI Measures	X			X	X	X	X
Quality of Life Measures/Questionnaires	X			X	X	X	X
6-Minute Walking Test	X			X	X	X	X
Ascertainment of Endpoints	x	x	x	x	x	x	x
Repeat Revascularization				X	X	X	X
Adverse Events			X	X	X	X	X
Implanted Devices (UDI)			X				

Duration of the Project

Overall this study is expected to be completed within 3 years.

Planning & Startup: 6 months.

Enrollment period: 12 months.

Follow-up period: 12 months post procedure.

Closeout & Analysis: 6 months.

1. The Missing Link in Vascular Device Trials Michael R. Jaff, DO Jan 23, 2015
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Registry Assessment of Peripheral Interventional Devices (RAPID)

Post-Market Surveillance Study Use Case Synopsis

Background and Rationale for Use Cases:

1) The use cases were developed by the RAPID working groups (clinical, informatics, and GUDID) to help guide each group and ensure that the core data elements contained information that will be pertinent for common and/or specific PAD issues that will potentially be tested in the future using this approach.
2) The use cases do not represent concrete plans to study the items described below; they were developed as an exercise to think broadly about the PAD population being studied so that the data set is useful and applicable
3) Many aspects of the use cases are not factual (rather designed to be hypothetical) and the data elements that have been created will be useful for studying questions like this (not necessarily this exact question with the specific details described).
4) RAPID data elements will be used to populate a registry and/or clinical trial database.
5) Informatics terminology – there is a lot of terminology used by informatics experts involved in RAPID. We will attempt to provide explanations for this. As a start, the clinical and informatics working groups divided the clinical data elements into PAD-specific data elements and non-PAD-specific data elements. After this, the focus remained on PAD-specific data elements (as we will use previously established and validated non-PAD or general data elements from other projects like PCORnet and NIH Collaboratory). In terms of PAD-specific data elements, we tried to group them into 5 large domains to begin with – Condition, Test, Treatment, Device, and Outcome.

Business and operational success factors include:

1) The study design, data collection methods and quality, and results are acceptable to the FDA for additional clinical data to evaluate the long-term safety and efficacy and satisfy the post-approval clinical requirements.
2) The operations and process of the study are acceptable to the industry sponsor paying for the study.
3) The evaluation and inclusion of UDI and linkages to GUDID.

Project Summary

This proposal entails a registry-based trial that will look at post-market surveillance of all FDA-approved (device XXXX) Drug-Coated Balloons (DCB) to evaluate the incidence of rare events (e.g. acute limb ischemia) in patients with atherosclerotic PAD who get treated for their symptoms with a DCB.

Rationale & Background Information

The purpose of the RAPID registry study is to collect additional safety and efficacy information on the XXXX Drug Coated Balloon used in PAD patients who have received this intervention for treatment of stenosis or occlusion of the XXXX arteries in a larger patient population. The ability to track adverse events along with lesion location (SFA, PA, etc.), CTO, calcification, inflow and outflow status, pre-dilation balloon use, post-dilation balloon use, provisional stent use, dissection, and procedural success over an extended period of time post procedure will assist in providing data to detect rare (occurring at 1-2%) adverse events in this patient population.

Methodology

The proposed research design is a prospective, open-label, multicenter, observational, single-arm study designed to further inform the safety evaluation of XXX Drug-Coated Balloon during commercial use in real-world settings. The registry will contain 5000 male and female participants with atherosclerotic PAD who get treated for their symptoms with a DCB from 20 sites across the United States who have undergone percutaneous cardiovascular intervention using the XXXXX Drug-Coated Balloon only. There are no exclusion criteria for this surveillance study.

Patient Flow

Baseline

Participants will present to the cardiac/vascular clinical care unit for routine follow up. Upon identification by study staff/coordinator as a potential participant for the RAPID Registry use case, they will be informed about the study and asked to consent to participate. Upon consent, participants will undergo a screening process to collect information about the balloon procedure, vitals, labs, demographics – age, DOB, race, ethnicity, gender; medical history, physical exam, quality of life measures, labs, previous PAD treatment history, and current cardiac medications. The participant will then be enrolled in the registry.

Relevant data elements from this baseline/screening clinic visit will be pushed directly into the Registry system via the EHR.

Follow-Up

Participants will present to the clinic for study follow-up visits and will be followed for the registry either in person or via telephone at 6, 12, 18, 24, 36, 48 and 60 months. During these follow-up visits, participants will be

assessed by the medical staff to determine safety and efficacy of balloon procedure by measuring vitals, quality of life measures, post procedural complications, clinical outcomes, safety and adverse events, etc.

Relevant data elements from this baseline/screening clinic visit will be pushed directly into the Registry system via the EHR.

Assessments

Time and Events Schedule

Assessment	Baseline	6 Months Telephone	12 Months	18 Months Telephone	24 Months	30 Months Telephone	36 Month	48 Month	60 Month End of Study Withdrawal
Consent	X								
Demographics	X								
Medical History	X								
Physical Exam	X		X		X		X	X	X
Vitals	X		X		X		X	X	X
Labs	X		X		X		X	X	X
Medications	X	X	X	X	X	X	X	X	X
Lesion Details (lesion length, lesion location, degree of calcification, and degree of stenosis)	X								
Safety Measures (Surgical & Procedural Complications, Success, Repeat procedures)		X	X	X	X	X	X	X	X
Quality of Life Measures/Questionnaires	X	X	X	X	X	X	X	X	X
Adverse Events		X	X	X	X	X	X	X	X

Data Management & Statistical Analysis

Baseline and procedure data will be collected via the Registry following their standard operating procedures. EHR, administrative claims (e.g. Medicare and private insurance), and PAD registry (e.g. SVS-VQI and ACC-PVI) data will be obtained by the data coordinating center (e.g. call center). Data received from those sources will be integrated in a study database where operational reporting will be performed and all data will be assessed for

quality as determined by the requirements of the intended analysis. Data will be extracted from the study database and transferred to the statistician for interim and/or final analysis. Analyses will be performed using statistical methods described in the study protocol.

Duration of the Project

Overall this study is expected to be completed within 5 years.

Planning & Startup: 6 months.

Enrollment period: 12 months.

Follow-up period: 36 months post procedure.

Closeout & Analysis: 6 months.

Registry Assessment of Peripheral Interventional Devices (RAPID)

Randomized controlled trial of Adjunctive Pharmacologic Treatment Use Case Synopsis

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Background and Rationale for Use Cases:

1) The use cases were developed by the RAPID working groups (clinical, informatics, and GUDID) to help guide each group and ensure that the core data elements contained information that will be pertinent for common and/or specific PAD issues that will potentially be tested in the future using this approach.
2) The use cases do not represent concrete plans to study the items described below; they were developed as an exercise to think broadly about the PAD population being studied so that the data set is useful and applicable
3) Many aspects of the use cases are not factual (rather designed to be hypothetical) and the data elements that have been created will be useful for studying questions like this (not necessarily this exact question with the specific details described).
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Business and operational success factors include:

1. Rationale and design of the dual antiplatelet therapy study, a prospective, multicenter, randomized, double-blind trial to assess the effectiveness and safety of 12 versus 30 months of dual antiplatelet therapy in subjects undergoing percutaneous coronary intervention with either drug-eluting stent or bare metal stent placement for the treatment of coronary artery lesions. Mauri, Laura et al. American Heart Journal, Volume 160, Issue 6, 1035 - 1041.e1

1) Determining the optimal duration of Dual-Antiplatelet Therapy (DAPT) post revascularization for all patients undergoing endovascular revascularization for LE PAD.
2) The operations and process of the study are acceptable to the industry sponsor paying for the study.
3) The evaluation and inclusion of UDI and linkages to GUDID.

Project Summary

The project is a Randomized Clinical Trial (RCT) of one month of DAPT versus six months of DAPT following infrainguinal revascularization to evaluate the comparative effectiveness and safety of one approach versus another for target vessel revascularization in patients with lower extremity PAD. The RCT will be broad enough to provide the ability to do subgroup analyses of different device technologies, anatomic segments, and Rutherford classification (2-6).

Rationale & Background Information

Revascularization is a common treatment for patients with PAD. DAPT is often prescribed after revascularization procedures in patients with PAD for its potential ability to prevent thrombosis and new/future cardiovascular events. There is uncertainty about the optimal duration of DAPT and physicians mostly rely on clinical judgment to determine duration which can be anywhere between zero and 12 months of therapy. "The incremental risk of late stent thrombosis (ST) in Drug-Eluding Stents (DES) versus Bare Metal Stents (BMS) is not known with certainty as randomized trials to date have been limited in their power to detect rare and late events, and observational studies are limited by selection and ascertainment bias."[1] A randomized controlled clinical trial comparing DAPT duration of one month to DAPT duration of six months will provide much needed clinical evidence/support in determining the optimal duration for DAPT maximum effectiveness.

Study Design

The proposed research design will be a registry-based multi-center randomized double-blind clinical trial enrolling XXXX male and female PAD patients who are scheduled to have endovascular revascularization for PAD.

Participants will be recruited from the pool of patients presenting for revascularization for IC or CLI. All participants meeting the basic inclusion criteria of a PAD diagnosis (based on the results of a CTA, MRA, or angiography) with Rutherford scores within specified range, being within the specified age-range, willing to be randomized to a treatment plan post-revascularization procedure and sign the informed consent will be eligible to participate in this trial.

1. Rationale and design of the dual antiplatelet therapy study, a prospective, multicenter, randomized, double-blind trial to assess the effectiveness and safety of 12 versus 30 months of dual antiplatelet therapy in subjects undergoing percutaneous coronary intervention with either drug-eluting stent or bare metal stent placement for the treatment of coronary artery lesions. Mauri, Laura et al. American Heart Journal, Volume 160, Issue 6, 1035 - 1041.e1

Patient Flow

Pre-Procedure/Baseline

Participants will be scheduled to undergo revascularization for IC or Critical Limb Ischemia (CLI). Upon identification by study staff/coordinator as a potential participant for the RAPID Registry use case, they will be informed about the study and asked to consent to participate. Upon consent, participants will provide baseline information including collection of vitals, labs, demographics – age, DOB, race, ethnicity, gender; medical history, physical exam, PAD-specific assessments – diagnosis, duration, severity as measured by the Rutherford score, ABI, six-minute walk tests, quality of life measures other cardiac disease and procedures, and current cardiac medications. The participant will then be enrolled and randomized to a treatment arm in the registry. If a participant is ineligible for the registry, they will be flagged as a screen failure and alternative/most appropriate care will be provided.

Relevant data elements from this pre-procedure/baseline data will be pushed directly into the Registry system via the EHR.

Procedure

Participants will present to the radiology suite, catheterization laboratory, and/or surgical center as scheduled for revascularization for IC or CLI. Pre- during- and post-procedure assessments will be taken by medical staff including vitals, Rutherford scores, lesion details, details about revascularization process, safety and success of the procedure, ABI and labs.

Relevant data elements from this baseline/screening clinic visit will be pushed directly into the Registry system via the EHR.

Follow-Up

Participants will present to the clinic for a routine care/follow up visits at 30 days, 3, 6, 9 and 12months post procedure. During these follow-up visits, participants will be assessed by the medical staff to determine safety and efficacy by measuring physical exam, vitals, quality of life and six minute walk test, post procedure complications, repeat procedures and patency, other tests and adverse events, medical history, labs, lesion details, etc.

Relevant data elements from this baseline/screening clinic visit will be pushed directly into the Registry system via the EHR.

Methodology

The RAPID Registry will be mined for participants who meet the following inclusion/exclusion criteria. To be included in this study a participant must be scheduled for revascularization for Critical Limb Ischemia,

1. Rationale and design of the dual antiplatelet therapy study, a prospective, multicenter, randomized, double-blind trial to assess the effectiveness and safety of 12 versus 30 months of dual antiplatelet therapy in subjects undergoing percutaneous coronary intervention with either drug-eluting stent or bare metal stent placement for the treatment of coronary artery lesions. Mauri, Laura et al. American Heart Journal, Volume 160, Issue 6, 1035 - 1041.e1

geographically stable and willing to sign the informed consent. Participants are excluded from this study if any of the following are applicable: a major bleeding event in the past two months, no informed consent, geographically unstable …XXXXX

Assessments

Time and Events Schedule

Assessment	Pre-Procedure Baseline	Procedure	30 Days	3 Month	6 Month	9 Month	12 Month
Consent	X						
Inclusion/Exclusion	X						
Randomization		X					
Demographics	X						
Medical History	X						
Physical Exam	X				X	X	X
Vitals	X	X	X	X	X	X	X
Labs	X	X		X	X	X	X
Medications	X		X	X	X	X	X
Revascularization Procedure & Details		X					
Drug Dispense		X	X	X	X	X	X
Duplex Ultrasound		X	X	X	X	X	X
Questionnaires	X	X	X	X	X	X	X
Safety Measures (Bleeding)			X	X	X	X	X
ABI/TBI Measures	X		X	X	X	X	X
Quality of Life Measures/Questionnaires	X		X	X	X	X	X

1. Rationale and design of the dual antiplatelet therapy study, a prospective, multicenter, randomized, double-blind trial to assess the effectiveness and safety of 12 versus 30 months of dual antiplatelet therapy in subjects undergoing percutaneous coronary intervention with either drug-eluting stent or bare metal stent placement for the treatment of coronary artery lesions. Mauri, Laura et al. American Heart Journal, Volume 160, Issue 6, 1035 - 1041.e1

6-Minute Walking Test	X		X	X	X	X	X
Outcomes			X	X	X	X	X
(Serious) Adverse Events			X	X	X	X	X

Data Management & Statistical Analysis

Baseline and procedure data will be collected via contributing registries following their standard operating procedures. Processes for obtaining other data will be managed by the project teams according to the study protocol. Data received from all sources will be integrated in a study database where operational reporting will be performed and all data will be assessed for quality as determined by the requirements of the intended analysis. Data will be extracted from the study database and transferred to the statistician for interim and/or final analysis. These analyses will be performed using statistical methods described in the study protocol.

Duration of the Project

Overall this study is expected to be completed within 2.5 years.

Planning & Startup: 6 months.

Enrollment period: 12 months.

Follow-up period: 12 months post procedure.

Closeout & Analysis: 6 months.

1. Rationale and design of the dual antiplatelet therapy study, a prospective, multicenter, randomized, double-blind trial to assess the effectiveness and safety of 12 versus 30 months of dual antiplatelet therapy in subjects undergoing percutaneous coronary intervention with either drug-eluting stent or bare metal stent placement for the treatment of coronary artery lesions. Mauri, Laura et al. American Heart Journal, Volume 160, Issue 6, 1035 - 1041.e1