Safety & Performance Study of the FANTOM Sirolimus-Eluting Bioresorbable Coronary Scaffold

Published: 10-04-2015
Last updated: 15-04-2024

To evaluate the safety of a new scaffold platform in native coronary arteries that includes incorporation of a deformable expansion technology and an enhanced scaffold material that is a polycarbonate co-polymer of tyrosine analogs. This will be...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON55419

Source
ToetsingOnline

Brief title
FANTOM II Trial

Condition

- Coronary artery disorders

Synonym
Insufficient blood flow, tissue of the heart muscle

Research involving
Human

Sponsors and support

Primary sponsor: REVA Medical, Inc.
Source(s) of monetary or material Support: REVA Medical;Inc.

Intervention

Keyword: Coronary Artery Disease, Drug-Eluting Stents, Performance, Safety

Outcome measures

Primary outcome

Major Adverse Cardiac Events (MACE) and Late Lumen Loss at 6 months.

Secondary outcome

All Cohort A Patients

- QCA derived parameters at 6 -0/+ 1 month (e.g. Late Loss, Restenosis Rate,

%DS & MLD)

- IVUS & OCT imaging on a subset of patients at 6 -0/+ 1 month

Up to 25 Cohort A Patients

- QCA derived parameters at 24 -0/+ 1 month (e.g. Late Loss, Restenosis Rate,

%DS & MLD)

- IVUS & OCT imaging on a subset of patients at 24 -0/+ 1 month

- Dual Source CT Scan

All Cohort B Patients

- QCA derived parameters at 9 -0/+ 1 month (e.g. Late Loss, Restenosis Rate,

%DS & MLD)

- IVUS & OCT imaging on a subset of patients at 9 -0/+ 1 month

Up to 25 Cohort B Patients

- QCA derived parameters at 48 -0/+ 1 month (e.g. Late Loss, Restenosis Rate,

%DS & MLD)

- IVUS & OCT imaging on a subset of patients at 48 -0/+ 1 month

- Dual Source CT Scan

All Patients

- MACE through 60 months

- TLR, TVR and TVF through 60 months post procedure

- Procedural success * percentage of patients with angiographic success (final

diameter stenosis <50% without occurrence of MACE)

- Technical success * successful delivery and deployment of a Fantom scaffold

Study description

Background summary

Coronary arteries, which supply blood to the heart muscle, are particularly susceptible to the buildup of plaque, which can block or inhibit blood flow. The process of arterial narrowing is referred to as atherosclerosis, or coronary artery disease. If the coronary arteries become too narrow, cardiac tissue may become starved of nutrients and oxygen, especially during exercise when myocardial oxygen consumption increases, and pain (angina) may occur. As vessel narrowing becomes more severe, death of myocardial muscle cells downstream from the occlusion can occur due to the lack of oxygen. The sudden death of these myocardial cells can result in a life threatening heart attack (myocardial infarction).

Coronary artery disease accounts for the greatest mortality among all forms of heart disease. Given the staggering morbidity and mortality associated with coronary artery disease, any effort to return these patients to a productive, pain-free existence is undeniably worthwhile and valuable to the individual and society.

Coronary balloon angioplasty is a minimally invasive method of opening blocked arteries. The procedure is more formally known as *PTCA* (percutaneous transluminal coronary angioplasty). While angioplasty is successful in

restoring blood flow initially, restenosis or renarrowing of the treated vessel occurs within six months in about 40% of cases.

To address this problem a device called a coronary stent was developed to improve the clinical outcome after PTCA. The introduction of stents in the early 1990s was a major breakthrough in the treatment of restenosis. A stent is a flexible metal wire mesh tube, typically made from stainless steel alloys. Coronary stents are typically mounted on a balloon and expanded during implantation to the desired diameter. It was found that the implantation of a stent reduces the incidence of restenosis to roughly 20% to 30%.

Currently stents are used in approximately 90% of all interventional procedures worldwide.

The next major development in this endeavor came in the form of a combination drug-device known as a Drug-Eluting Stent (DES). These metal stents commonly combine a thin polymer coating and therapeutic drug that inhibits the build-up of tissue during wound healing after stent delivery.
The most recent DES clinical trials demonstrated a restenosis rate of less than 10%.

In spite of these significant advancements, the use of metal-based drug-eluting stents that remain permanently embedded within the arterial wall still has a number of potential drawbacks. These drawbacks include:

* predisposition to late-stage stent thrombosis
* prevention of late vessel adaptive or expansive remodeling
* prevention of normal vasomotion and compliance
* hindrance to and sometimes a barrier for surgical revascularization
* Impairment of imaging with multi-slice CT

Additionally, as general coronary intervention procedures move towards treating more diffuse disease, more stents are used in a single vessel. The use of multiple stents within a single vessel often results in a vessel that has been *paved* with stents. The paving of a vessel results in a situation by where it is often difficult to perform future surgical bypass when prescribed; in some cases, it is prohibited.

In an effort to continually improve outcomes in interventional cardiology patient care, researchers are pursuing novel approaches to solve the drawbacks described above while preserving the advances offered by current metallic stents and DES. One such effort involves stenting coronary vessels with fully bioresorbable scaffolds that act as *temporary* stents to support the vessel during the initial critical months of healing and remodelling after dilation.
Such an approach can provide the benefits of metal stents * prevention of acute vessel recoil and abrupt closure, and avoid the late negative consequences of pathological remodelling of the vessel that may lead to late restenosis since

the bioresorbable stent is not permanent. In addition, if the bioresorbable scaffold were drug-eluting, it could offer the additional benefit of a traditional metallic DES by inhibiting neointimal hyperplasia.

Early efforts demonstrated:

* The use of polymer resorbable scaffolds is feasible * resorbable polymer scaffolds have been successfully deployed in human patients.
* In most cases, deployment of the scaffold was accomplished using a non-commercially viable, heated balloon catheter to expand the polymer scaffold without stressing the bioresorbable material
* The use of *off-the-shelf* polymers may not be sufficient to address the design requirements of a coronary scaffold. Optimization of polymer-based coronary scaffolds may require a scaffold design and polymer materials specifically engineered for vascular scaffold applications.
* Novel solutions are required to address the lack of visibility by X-ray with these early materials, which is a standard clinical requirement for accurate scaffold placement.

From the beginning, REVA Medical took a unique approach to fully integrate both a novel material and a novel design in developing a REVA Sirolimus-Eluting Bioresorbable Coronary Scaffold that provides the benefits of metal without the permanency. The desired performance benefits include adequate strength, both at the time of implantation and during the critical initial three month period of vessel remodelling, scaffold expansion over the traditional (and expected) expansion range of metal stents and x-ray visibility of the device.

A major drawback of contemporary polymers is that they lack intrinsic radiopacity. An important advancement in the development of this polymer has been the enhancement of x-ray visibility. Incorporation of iodine into the polymer backbone allows the scaffold to be visualized using the angiographic techniques that are currently used by physicians today.

The REVA Scaffold has been developed with two unique expansion designs. The first design included a Slide and Lock expansion mechanism. Unlike traditional deformable metal stent designs, the Slide & Lock design deploys by sliding open and locking the scaffold into place. This novel scaffold design eliminates the need to significantly deform the device during deployment. More recently, the REVA scaffold has also been designed with a traditional deformable configuration for expansion.

The purpose of the FANTOM II study is to evaluate a scaffold with a traditional method of stent expansion of the REVA FANTOM Scaffold in a similar clinical setting.

Study objective

To evaluate the safety of a new scaffold platform in native coronary arteries that includes incorporation of a deformable expansion technology and an enhanced scaffold material that is a polycarbonate co-polymer of tyrosine analogs. This will be accomplished through the implantation and evaluation of the REVA FANTOM Sirolimus-Eluting Bioresorbable Coronary scaffold comprised of Poly(I2DAT -co-lactic acid)

Study design

Prospective, multi-center, safety & performance study

Intervention

Implantation of the REVA Sirolimus-Eluting Bioresorbable Coronary Scaffold.

Study burden and risks

Risks: possible side effects of the study procedure (see also question E9).

Burden: the scheduled visits at the study doctor (see also questions E3 and E3a).

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* The patient is * 18 years of age
* The subject must have evidence of myocardial ischemia (e.g. stable, unstable angina, post-infarct angina or silent ischemia) suitable for elective PCI. Subjects with stable angina or silent ischemia and < 70% diameter stenosis must have objective signs of ischemia as determined by one of the following: echocardiogram, nuclear scans, ambulatory ECG or stress ECG. In the absence of noninvasive ischemia, FFR must be done and must be indicative of ischemia
* The patient is an acceptable candidate for PTCA, stenting and emergent CABG
* The patient is willing and able to comply with the specified follow-up evaluations
* The patient*s written informed consent has been obtained prior to the procedure
* Each lesion must meet all the following baseline criteria (prior to pre-dilation):
- De novo lesion in a native coronary artery
- Visually estimated stenosis of * 50% and <100%
- Visually estimated RVD * 2.5 mm and * 3.5 mm
- Lesion length * 20 mm by visual estimate
- Baseline TIMI flow * 2 per visual estimate
* During pre-dilatation the pre-dilatation balloon is uniformly expanded to the full intended diameter
* Immediately after the pre-dilatation process the patient does not experience chest pain or ECG changes lasting longer than 10 minutes
* Each lesion must meet all the following criteria after pre-dilatation:
- Visually estimated stenosis of * 40%
- Target vessel reference diameter * 2.5 mm and * 3.5 mm by QCA, IVUS or OCT
- Lesion length * 20 mm by visual estimate
- Post pre-dilatation TIMI flow * 3 per visual estimate
- No dissections * type C

Exclusion criteria

* The patient has a known allergy, intolerance, or is contraindicated to aspirin, both heparin and bivalirudin, clopidogrel and/or contrast media, and cannot be adequately pre-medicated
* The patient has experienced an acute myocardial infarction (AMI: STEMI or NSTEMI) within 72 hours of the procedure and either CK-MB or Troponin has not returned to within 2X ULN. Note: In the event that CK-MB is not measured prior to treatment, the patient will be considered to have met this enrollment criteria provided that the Troponin assessment is within 2X ULN and a blood sample is drawn prior to the procedure; the CK-MB analysis must then be performed post-procedure
* The patient is currently experiencing clinical symptoms consistent with AMI
* The patient has a left ventricular ejection fraction of <40%
* The patient requires or has had an additional intervention of a coronary lesion in the target vessel within 1 year of the index procedure
* The patient requires additional intervention of another coronary lesion in the target epicardial vessel (LAD, LCX or RCA) or branch of the target epicardial vessel during the index procedure
Note: Staged procedures to treat lesions in non-target epicardial vessels are allowed during the index procedure or > 30 days after REVA scaffold implantation. If a non-target lesion requires treatment during the index procedure, the non-target lesion should be treated first
* The patient has unprotected left main coronary disease with * 50% stenosis
* The patient has a significant (* 50%) untreated stenosis proximal or distal to the target lesion
* The patient has a scaffold(s) or stent located within 3 mm of the target lesion borders
* The target vessel is totally occluded (TIMI Flow 0 to 1)
* Excessive proximal tortuosity, vessel hinging at the lesion location or lesion angulation, such that in the operator*s judgment it is unlikely that the REVA Bioresorbable Coronary Scaffold or a standard scaffold could be delivered and/or expanded
* The patient is currently participating in another investigational drug or device trial that has not completed the entire follow-up period
* The patient has a co-morbidity, which reduces life expectancy to * 24 months, or factors making clinical follow-up difficult
* The patient has:
- Known hepatic impairment (Liver function tests (SGOT, SGPT, and ALT) >3 times normal)
- Known impaired renal function (serum creatinine * 2.5 mg/dL)
- A platelet count <100,000 cells/mm3 (thrombocytopenia); and/or >700,000 cells/mm3
* The patient has a history of stroke (CVA) or TIA within the prior 6 months
* The patient has an active peptic ulcer or upper GI bleeding within the prior 6 months

* The patient has a history of bleeding diathesis or coagulopathy or will refuse blood transfusions
* The patient is a woman that is pregnant or lactating
* Target lesion ostial (within 3mm of vessel origin)
* Target lesion has moderate to severe calcification
* Target segment has side branches or a bifurcation > 1.5 mm in diameter
* Target lesion is located within an arterial bypass graft conduit or saphenous vein graft
* Target lesion is located within a previously stented region
* Target lesion is located within a segment supplied by distal graft
* Target lesion has possible or definite thrombus
* The patient is currently receiving or will require chronic anticoagulation therapy (e.g. coumadin, dabigatran, apixaban, rivaroxaban or any other agent for any reason)
* The patient is known to need or has a planned surgical procedure or any other reason is present which might require discontinuing aspirin and/or clopidogrel within 1 year of the FANTOM scaffold implantation
* Patient has a known allergy to tyrosine derived polycarbonate or Sirolimus and its structurally related compounds

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-07-2015
Enrollment:	19
Type:	Actual

Medical products/devices used

Generic name:	REVA FANTOM Sirolimus-Eluting Bioresorbable Coronary Scaffold

Registration:	No

Ethics review

Approved WMO Date:	10-04-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-10-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT02539966
CCMO	NL51852.018.15