Sirolimus Eluting Angioplasty Balloon for In-Stent REstenosis (SABRE) Trial

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Evaluate the safety and performance of the Virtue* Sirolimus Eluting Balloon for the treatment of in-stent restenosis (ISR) in native coronary arteries.

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

Summary

ID

NL-OMON41496

Source
ToetsingOnline

Brief title
SABRE

Condition

- Coronary artery disorders

Synonym
coronary heartdisease, In-stent restenosis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Coronary, DEB, ISR, Sirolimus

Outcome measures

Primary outcome

Primary Endpoints

Primary Safety * Target Lesion Failure (TLF) * composite of cardiac death, target vessel Myocardial infarction (MI) and clinically driven target lesion revascularization (TLR) up to 30 days post index procedure.
* A revascularization (TLR or TVR) is considered clinically indicated if angiography at follow-up shows a percent diameter stenosis *50% (core lab QCA assessment) and abnormal results from a fractional flow reserve (FFR) test.
* MI is indicated when in patients with normal baseline CK-MB, the peak CK-MB measured within > 48 hours of the procedure rises to > 10x the local laboratory ULN, or to > 5x ULN with new pathologic Q-waves in 2 contiguous leads or new persistent LBBB.

Primary Late Lumen Loss (LLL) at 6 months follow-up assessed by Quantitative Coronary Angiography (QCA) and adjudicated by an independent Angiographic Core Lab. (Clinical work-up must be completed prior to any catheterization procedure.)

LLL = MLDp * MLD6 months,

where MLD is minimal lumen diameter

Secondary outcome

Secondary Endpoints

* Percent in-treatment volume obstruction at 6 months follow-up as measured by IVUS core lab.

* Device Success: The Investigational Device was delivered, dilated, delivered the Sirolimus therapeutic dose and was retrieved from the target lesion.

* Procedural Success: Defined as *Device Success* without the occurrence of Major adverse cardiac events [MACE] per CEC adjudication (death, recurrent non-fatal myocardial infarction, emergent CABG and/or clinically indicated target vessel revascularization (TVR), clinically driven target lesion revascularization (TLR), and target vessel failure (TVF)) during the index hospitalization.

* MACE rates at the following time periods: in hospital, 30 days, 6-months, 1, 2, and3 year follow-up.

* Binary in-stent restenosis rate at 6 months follow-up:

o Binary restenosis via QCA;

o Follow up % diameter stenosis via QCA;

Study description

Background summary

Since about 2006, a new class of angioplasty balloons has been under development: drug eluting balloons (DEB), consisting of typical angioplasty balloons that have been coated with an anti-restenotic drug. DEBs thus reduce the high restenosis rate associated with angioplasty, without the use of a permanent metal stent. Several DEB products are currently sold, mainly in the EU, for both coronary and peripheral use, all of which employ the same anti-restenotic drug, paclitaxel. However, another anti-restenotic drug, sirolimus (aka rapamycin), is preferred over paclitaxel (nearly 100% in the

U.S.) for use with drug eluting stents due to its superior safety profile. Because sirolimus does not function well as a balloon coating , a liquid nanoparticle formulation has been developed that enables sirolimus to be delivered via a porous angioplasty balloon, and to persist in the target vessel long enough to effectively block restenosis. A detailed discussion on the treatments for coronary artery disease and mechanism of action for the Virtue*Sirolimus Eluting Balloon is contained in the Investigator Brochure.

Study objective

Evaluate the safety and performance of the Virtue* Sirolimus Eluting Balloon for the treatment of in-stent restenosis (ISR) in native coronary arteries.

Study design

Prospective multicentre study evaluating a Drug Eluting Balloon in patients undergoing percutaneous revascularization of coronary in-stent restenosis.

Intervention

Percutaneous access must comply with existing hospital standard procedures. Once access is obtained, heparin, or other antiplatelet therapy, should be administered to keep ACT > 250 seconds (see Concomitant Therapies). If other antiplatelet therapy is used (Angiomax, clexane, etc.) then dose and timing along with standard hospital lab and monitoring procedures must be documented. ACT may not be appropriate when heparin is not used.
Baseline angiography should be obtained after intracoronary injection of nitroglycerin.

It is recommended to cross the lesion with a 0.014* (0.355 mm) exchange-length guide wire. The involved lesion should be pre-dilated with appropriately sized balloon (POBA, cutting or scoring) using standard techniques prior to Virtue Device procedure. It is recommended that the pre-dilatation balloon diameter be chosen to achieve * 40% stenosis.
- Angiography and IVUS will be obtained immediately after the pre-dilatation.
- Eligibility determined <= 40% stenosis

It is strongly encouraged that the investigators use similar materials and techniques throughout the study to maintain consistency and standardization of care. Stenotic, stented regions that are 9 to 21 mm in length, with reference vessel diameters * 2.5 mm and * 3.5 mm are eligible. The Virtue balloon length should be 4-8 mm longer than the target lesion. The Virtue balloon should extend no more than 2 mm beyond edge of a stent. Lesions located at the edge of a stent requiring dilation > 2mm beyond stent are not permitted.

The Therapeutic Formulation will be re-constituted, filtered and delivered to

the device according to IFU. The investigational device will be assembled, delivered and deployed according to the IFU by the investigator or appropriately trained personnel.

Angiography, ECG and IVUS will be obtained immediately after the deployment. Within 4 to 6 hours after the index procedure a Cardiac Enzyme CK-MB analysis will be run. MI is indicated when patients with normal baseline CK-MB show a peak CK-MB level measured within 48 hours of the procedure at * 10x the local laboratory ULN, or to * 5x ULN with new pathologic Q-waves in * 2 contiguous leads or new persistent LBBB.
- concomitant medication
- angina status and vital signs
- adverse events will be assessed throughout the entire procedure

Study burden and risks

Potential risks
The following risks are potential complications associated with use of the Virtue Device:
* Death
* Myocardial infarction
* Acute vessel closure
* Total occlusion of the coronary artery or bypass graft
* Coronary vessel dissection, perforation, rupture or injury
* Restenosis of the dilated vessel
* Hemorrhage or hematoma
* Angina or unstable angina
* Arrhythmias, including ventricular fibrillation
* Drug reactions, allergic reaction to contrast medium
* Hypotension or hypertension
* Infection
* Coronary artery spasm
* Arteriovenous fistula
* Thrombosis and or air embolism
* Stroke or TIA
* Cardiovascular accident
* Pseudoanyreusm
* Cardiac tamponade
* Renal failure
* Coronary aneurysm
* Drug interactions causing a change in metabolism of sirolimus

Potential Benefits
For the subjects involved in this study, the potential advantages of the Virtue treatment include the following:
* Widen the narrowed blood vessels, increasing the flow of blood to the heart.

This decreases the risk of a heart attack, reduces the symptoms of angina, and slows the progress of coronary artery disease.
* Provide timed release therapeutic treatment of the target site tissue in addition to the angioplasty to slow or prevent restenosis.
* Use of safer drug for coronary vessel treatment, sirolimus VS paclitaxel
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*Widen the narrowed blood vessels, increasing the flow of blood to the heart. This decreases the risk of a heart attack, reduces the symptoms of angina, and slows the progress of coronary artery disease.
*Provide timed release therapeutic treatment of the target site tissue in addition to the angioplasty to slow or prevent restenosis.
*Use of safer drug for coronary vessel treatment, sirolimus VS paclitaxel.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Inclusion Criteria
1.Age > 18 years
2.Patient is willing to provide informed written consent and comply with follow-up visits and testing schedule.
3.Patients eligible and indicated for in-stent PCI with documented evidence of ischemia by invasive or non-invasive diagnostic method.
4.Patients who are eligible for coronary revascularization (angioplasty and/or CABG)
5.Female patients of child bearing potential must have a negative pregnancy test within one week before treatment and must use adequate contraception.
6.Previous history of native coronary bare metal stenting * 1 month or drug eluting stenting * 3 months.;Angiographic Inclusion Criteria
7.Target vessel with Reference Vessel Diameter (RVD) from 2.5 to 3.5 mm by coronary angiography.
8.Target lesion is in a native coronary artery with previous bare metal stent or drug eluting stent. Target lesion with overlapping stents is acceptable if lesion is within stent. (Balloon should be sized so that it does not extend more than 2 mm from the edge of the stent.)
9.Inclusion permitted following successful pre-dilatation of target ISR lesion with remaining residual stenosis of * 40%.
o No SAEs
o No flow limiting dissection requiring additional procedures or implantation of a stent
o Lesion continues to meet inclusion criteria of length and diameter
o No uncontrollable spasm
10.Target lesion length < 21mm by coronary angiograph (note: Virtue should extend at least 2mm beyond pre-dilatation balloon length to avoid geographical miss).
11.Guide wire is able to cross lesion and be placed in distal vessel prior to enrollment.
12.Inclusion permitted after successful treatment of 1 non-study, low risk lesion in a single non-study vessel.

Exclusion criteria

Exclusion Criteria
1.Patient enrolled in another study with any investigational drug or device, who have not reached primary endpoint.
2.Patients scheduled for a major surgical intervention within 7 months of enrollment of the study.
3.Patients with recent (* 72 hours) unstable coronary syndromes (e.g. ACS or STEMI * ST elevated myocardial infarction (MI)). If patient has had NSTEMI prior to 72 hrs. and enzyme level is decreasing within 72 hrs. (at least 2 measurements showing decreasing trend) and patient meets AHA risk guidelines for PCI procedure (low risk) then patient is eligible.
4.Patients with a contraindication to an emergency coronary bypass surgery.
5.Any individual who refuses a blood transfusion if needed.
6.Patients with serum creatinine > 2.0 mg/dL or > 177umol/L.

7.Patients with platelet count < 50,000 cells/mm³.
8.Patients who had a cerebral stroke < 6 months prior to the index procedure.
9.Documented LVEF (Ejection Fraction) < 30% tested within 4 weeks prior to index procedure.
10.Patients with any known allergy, hypersensitivity or intolerance to anti-platelet therapy (for example ASA, clopidogrel or ticlopidine) and sirolimus.
11.Any known allergy to contrast medium that cannot be pre-treated.
12.Women who are pregnant or breastfeeding.;Angiographic Exclusion Criteria
13.More than 1 target lesion within the target vessel.
14.Presence of any non-target lesion within the target vessel.
15.Failure to successfully treat the non-target vessel (non-target vessel must be treated prior to the target vessel)
16.Aorto-ostial lesion (Left Main or Ostial Right Coronary Artery).
17.Target lesion distance from the ostium of LAD/LCX is < 5 mm.
18.Target lesion is located in either a venous or arterial graft.
19.Lesions at edge of stent requiring dilatation > 2 mm beyond stent.
20.Angiographic evidence of thrombus at the target site.
21.Acute total occlusions of non-target lesion or > 40% stenosis of target lesion following pre-dilatation.
22.Lesion requiring additional implant or results in flow limiting dissection following pre-dilatation.
23.Bifurcation lesions (lesions < 5 mm from a side branch vessel with > 2 mm diameter.)

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):	04-02-2014
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	Drug eluting balloon
Registration:	No

Ethics review

Approved WMO Date:	24-09-2013
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-11-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-12-2015
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
CCMO	NL44884.100.13