Italian National Registry on Bioresorbable Vascular Scaffold (ABSORB) for diffuse coronary disease

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Trial Type:

Multicenter prospective registry

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Compliance Statement

This registry will be conducted in accordance with this Clinical Investigational Plan, the Declaration of Helsinki, applicable sections in ISO 14155:2011 and the appropriate local legislation(s). The most stringent requirements, guidelines or regulations applicable to registries must always be followed. The conduct of the registry will be approved by the appropriate Medical Ethics Committee (MEC) of the respective clinical site and as specified by local regulations.

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PROTOCOL SYNOPSIS

PROTOCOL TITLE: Italian National Registry on Bioresorbable Vascular Scaffold (ABSORB) for diffuse coronary disease

CLINICAL PHASE: IV

AIM OF THE STUDY: to investigate the procedural as well as the long-term clinical performance of the ABSORB technology in patients with an indication to percutaneous coronary intervention for: 1) multivessel disease (at least two significant stenosis in 2 different coronary arteries), or 2) long (>24 mm) single vessel disease.

PRIMARY ENDPOINT: the cumulative hierarchical incidence of major adverse cardiac events (MACE) defined as: cardiac death, non-fatal target vessel myocardial infarction (MI), or clinically driven target lesion revascularization (TLR).

SECONDARY ENDPOINTS: All causes mortality, clinically driven TLR, clinically driven target vessel revascularization (TVR), any revascularisation (non TLR, non TVR) and ARC-defined stent thrombosis, at any time point, any type of angina.

STUDY DESIGN: multicenter (50 to 80 centers across the Italian territory), prospective observational registry aiming to enroll a population of 1000 patients.

STUDY DURATION: We project 12 months for recruitment, 5 year follow-up duration after last patient in the registry.

CLINICAL FOLLOW-UP PLAN: 30 days, 6 months, 1 year, and then yearly up to 5 years after the index procedure.

PATIENTS SELECTION CRITERIA:

- Indication to percutaneous coronary intervention for multivessel disease or long (≥24 mm) single vessel disease following:
  - § Stable angina or evidence of myocardial ischemia with stress echocardiography/ myocardial SPECT/exercise test, or
  - § Unstable angina / non ST-elevation myocardial infarction
  - § ST-elevation myocardial infarction with de novo culprit lesion.

EXCLUSION CRITERIA:

- Known intolerance to any of the device components
- Contraindication to dual antiplatelet therapy (DAPT)
- Lesion in a saphenous vein graft
- Lesion to left internal mammary artery
- Unprotected left main stenosis
- Woman with childbearing potential
- Age < 18y/o
- Concomitant indication to open heart surgery
- Inability to provide written informed consent

EFFICACY PARAMETERS: TLR and TVR up to 5-year follow-up.

SAFETY "PATIENT ORIENTED" PARAMETERS: all cause mortality, any myocardial infarction, Stent thrombosis based on the ARC classification, up to 5-year follow-up. Data on dual antiplatelet therapy use will also be collected and analyzed.

Sample size justification: Being this an observational registry aiming at quantifying effect estimates without direct comparisons to literature benchmarks, we relied on confidence interval profiling for sample size justification, without proceeding with formal power analysis. As the main analysis is a pooled analysis of patients with multivessel disease and/or long lesions, an overall and comprehensive analysis is planned as the primary analytical approach. Accordingly, we computed that a target

sample of 1000 patients will enable the computation of reasonably precise 95% confidence intervals. Specifically, assuming a 4.2% MACE rate at 1 year (in keeping with ABSORBD EXTEND data), confidence intervals computed with the adjusted Wald method would be 3.1% to 5.6% for a 1000-patient sample (point estimate 42/1000 [4.2%]).

Given that the registry aims to reflect real-world patients and practice, no provision to limit or restrict patient enrolment depending on the presence of multivessel disease vs long lesions is envisioned.

Analytical plan: Continuous variables will be reported as mean (standard deviation) and categorical variables as n (%). Survival analysis will be performed with the Kaplan-Meier method. Statistical inference will be based on the computation of overall 95% confidence intervals using the adjusted Wald method. Additional analyses will involve key subgroups defined according to baseline, lesion, and procedural features, with statistical significance set at the 5% 2-tailed level. Specifically, Student t, Fisher exact, and log-rank tests will be used for such bivariate analyses, whereas multivariable linear regression, logistic regression, and Cox proportional hazard analyses will be used to adjust for confounders. In addition, separate analyses for patients with only multivessel disease, patients with only long lesions, and patients with both conditions will be performed.

1. INTRODUCTION

The Italian National Registry on Bioresorbable Vascular Scaffold (ABSORB) for diffuse coronary disease is a investigator-initiated, single arm, prospective, multicenter post-market registry of patients with an indication to percutaneous coronary intervention for: 1) multivessel disease (at least two significant stenosis in 2 different coronary arteries), or 2) long (>38 mm) single vessel disease to de novo lesions treated with the Absorb Bioresorbable Vascular Scaffold (Absorb BVS, manufactured by Abbott Vascular) per IFU (on-label use). This Registry will enroll a minimum of 500 patients in approximately 50 sites throughout the Italian territory where Absorb BVS has regulatory approval and is commercially available.

2. BACKGROUND INFORMATION

2.1 Coronary device evolution

In 1977 Andreas Grüntzig performed the first balloon coronary angioplasty a revolutionary treatment that lead to the birth of a new specialty, “interventional cardiology”.

Since that pioneering procedure, extensive developments and advances culminated in percutaneous coronary intervention (PCI) being 1 of the most frequently performed invasive medical procedures in clinical practice today.

Coronary stents, which were first developed in the mid- 1980s (1), have ultimately replaced “plain old balloon angioplasty” (POBA) as the preferred method of performing PCI, after the observed improvements in angiographic and clinical outcomes seen with their use (2,3).

Coronary stenting became widely implemented after the publication of the landmark BENESTENT trial (4) and the STRESS (5), together with evidence indicating that stenting was safe in the absence of anticoagulation therapy with the use of dual antiplatelet therapy (DAPT) (6-8) and/or adequate stent deployment (9).

By 1999, coronary stenting was performed in 84.2% of PCI procedures (10); however, despite their obvious advantages, there were associated problems and concerns. Most notably, and in addition to the risk of subacute thrombosis, an iatrogenic problem emerged in the form of in-stent neointimal hyperplasia (11-13). This intrastent growth of scar tissue, which was the result of proliferation and migration of vascular smooth muscle cells, and directly linked to stent implantation, resulted in restenosis rates of 20% to 30% (14). It was the attempts to minimize this in-stent neointimal hyperplasia, and thereby reduce rates of repeat revascularization, that ultimately lead to another revolution: the DES. The dramatic reduction in restenosis rates seen with the use of these DES compared with BMS (15-19) has been the major driving force behind the exponential growth of PCI as a treatment for patients with coronary artery disease (CAD). This increased confidence lead to a rapid and unprecedented uptake in their use, so that by 2005, 80% to 90% of all revascularization procedures in the U.S. were performed using a DES (20).

Even drug-eluting permanent metallic stents, however, have some short and long-term limitations: a still unclear duration of dual antiplatelet therapy which is strongly linked to the risk of stent thrombosis that, although infrequent, is a ominous event with poor prognosis; the preclusion of surgical revascularization; the jailing of side branches; the impairment of non-invasive imaging of coronary arteries with multi-slice computed tomography and magnetic resonance; the limitation of the ability of a treated segment to completely regain the functionality observed after balloon angioplasty.

2.2 Absorb BVS technology

The Absorb BVS System is a bioresorbable poly(L-lactide) (PLLA) scaffold with a drug and bioresorbable polymer coating [formulation of everolimus in a bioresorbable poly(D,L-lactide) (PDLLA) coating]. The transient nature of the Absorb BVS reduces the potential for late inflammation and thrombosis, which may subsequently reduce the need for long-term dual antiplatelet therapy (DAPT), permit late expansive remodeling of tissue and the return of natural vasomotion, as well as provides compatibility with a broader range of diagnostic imaging technologies.

The Absorb BVS System was granted Conformité Européenne (CE) Mark approval on December 14, 2010. The Abbott Vascular ABSORB Clinical Program currently has one completed clinical trial (ABSORB Cohort A), three on clinical follow-up (ABSORB Cohort B, ABSORB EXTEND, and ABSORB II RCT) and two that are actively enrolling (ABSORB FIRST and ABSORB III). To date, the ABSORB Cohort A, ABSORB Cohort B and ABSORB EXTEND clinical trials have provided acute and preliminary long-term data on the safety and performance of Absorb. ABSORB Cohort A and B also revealed preliminary evidence of vasomotion suggests natural vessel function.

ABSORB Cohort A/B .

The First in Man clinical investigation is a prospective, open-labeled, non-randomized, multi-center trial that was divided into ABSORB Cohort A Trial (n=30) and ABSORB Cohort B Trial (n=101). In the ABSORB Cohort A trial, among 29 patients, the 5-year MACE rate was 3.4%, due to only one ischemic MACE event (non-Q wave MI.) Additionally, there were no incidences of scaffold thrombosis or cardiac death out to 5 years. On Cohort B. design modifications to the device were made to improve the performance of Absorb. The materials are the same, and the drug (everolimus) release rate profiles are similar in both devices. The currently commercial Absorb BVS device is the same design as the Cohort B device. The ABSORB Cohort B trial had two subgroups (B1 and B2). 3-year follow-up data is available for Group B1 (n=45) and was recently reported at the ACC 2013 meeting. In the ABSORB Cohort B trial, among 100 patients f, the 3-year ischemic driven MACE rate was 10.0%- There has been no reported scaffold thrombosis .

ABSORB EXTEND

ABSORB EXTEND is a prospective, single-arm, open-label clinical study that is planned to enroll up to 1,000 subjects at up to 100 global sites. Clinical follow-up is being planned on all subjects enrolled in the trial for up to 3 years. Based on an interim data snapshot presented during PCR Rotterdam 2013 the first 450 patients have completed the 12-month follow-up. At 12-months, ischemic driven MACE rate was 4.20%. Scaffold thrombosis rate was 0.9%.

ABSORB II

ABSORB II is a pivotal ABSORB trial designed to demonstrate superiority Absorb compared to a commercially approved, active control stent, XIENCE PRIME. ABSORB II is a randomized, active-controlled, single-blinded, multicenter clinical trial and will enroll approximately 501 subjects in approximately 40 investigational sites in Europe. This trial will evaluate the following novel primary endpoints of vasomotion and change in lumen diameter. Enrollment has been completed on June 2013.

ABSORB III

The ABSORB Randomized Controlled Trial (RCT) is designed to evaluate the clinical safety and efficacy of Absorb for US approval. Absorb will be compared to the commercially approved, active control stent in the XIENCE family. The ABSORB III

is a prospective, randomized, active-control, single-blind, multi-center clinical trial that will register approximately 2,250 subjects in up to 220 sites in the US and outside the US. ABSORB III started at December 2012

ABSORB FIRST
The ABSORB FIRST Registry is a single arm, prospective, international post-market registry of patients with de novo lesions in previously untreated vessels
The ABSORB FIRST Registry will enroll a minimum of 10,000 patients in approximately 300 sites throughout multiple countries. ABSORB FIRST started at January 2013

While these results available were obtained in patients with relatively simple lesion complexity, the **Italian National Registry** is intended to provide an **independent assessment** of the safety and clinical outcomes of the Absorb BVS device in patients with multivessel/diffuse disease. Clinical effectiveness in smaller vessels, longer lesions and more complex type of lesions in patients with MDV and diffuse disease, with more frequent use of planned overlapping devices and at higher risk of coronary and cardiovascular events has not been demonstrated. Although implantation of DES in patients with MVD has become common practice, data about efficacy and safety of DES in this specific setting are scarce. Question regarding use of PCI vs CABG is this population is still opened. The availability of potential more effective devices as ABSORB could hypothetically improve the efficacy of PCI

2.2 Registry Device

The device to be used in this registry is the Absorb Bioresorbable Vascular Scaffold (Absorb BVS) System manufactured by Abbott Vascular. The Absorb BVS system refers to a system that consists of the Absorb BVS and a delivery system. Absorb BVS refers to the product in general (see the IFU for details concerning indications for use, contraindications, system preparation, precautions, and warnings).

3 REGISTRY OBJECTIVE

To investigate the procedural as well as the long-term clinical performance of the ABSORB technology in patients with an indication to percutaneous coronary intervention for:

1) multivessel disease (at least two significant stenosis in 2 different coronary arteries), or

2) long (≥24 mm) single vessel disease.

4 REGISTRY FLOW AND CLINICAL FOLLOW-UP SCHEDULE

The Italian National Registry is a prospective multi-center nation-wide registry evaluating the safety and clinical outcomes of the Absorb BVS in daily use in patients with de novo lesions in previously untreated vessels with indication to PCI for multivessel or long single coronary artery disease.
Indications, however, are per the most recent Absorb IFU.

4.1 Number of Patients to be Registered and Patient Follow-up

The Italian National Registry will enroll a of 1000 patients in approximately 50 sites throughout the Italian territory where Absorb BVS has regulatory approval and is commercially available.

Patients will have clinical follow-up by telephone contact or office visits.

4.2 Measures Taken to Avoid and Minimize Bias

In order to minimize bias in assessing MACE outcomes, these events will be adjudicated by an independent committee.

4.3 Clinical follow-up plan: 30 days, 6 months, 1 year, and then yearly up to 5 years after the index procedure.

5. OUTCOMES/ENDPOINTS

Outcomes are as specified below:

5.1 Primary: the cumulative hierarchical incidence of major adverse cardiac events (MACE) defined as: cardiac death, non-fatal target vessel myocardial infarction (MI), or clinically driven target lesion revascularization (TLR);

5.2 Secondary endpoints: All causes mortality, clinically driven TLR, clinically driven target vessel revascularization (TVR), any revascularisation (non TLR, non TVR) and ARC-defined stent thrombosis, at any time point. Any type of angina post procedure measured by means of the Cardio Test, proposed by the ANMCO (Associazione Nazionale Medici Cardiologic Ospedalieri) [21]

5.3 Efficacy parameters: TLR and TVR up to 5-year follow-up.

5.4 Safety "patient oriented" parameters: all cause mortality, any myocardial infarction, Stent thrombosis based on the ARC classification, up to 5-year follow-up. Data on dual antiplatelet therapy use will also be collected and analyzed.

6. PATIENTS

6.1 Patient Population

Patients enrolled into this registry will be male and female patients derived from the general interventional cardiology population who satisfy the inclusion and exclusion criteria. The Italian National Registry will enroll 1000 patients in approximately 50 sites throughout the national terrritory (see section 4.1).

6.2 Patient Screening and Informed Consent

6.2.1 Patient Screening

All patients admitted for PCI should be evaluated for participation in the registry.

6.2.2 Informed Consent

The Investigator or designee, who has been trained on the protocol, will explain the nature and scope of the registry and inform the patient of the potential risks and benefits of participation, and document consent to treatment with an Absorb BVS device according to standard hospital practice. For this registry the patient must consent to data collection and follow-up visits. All patients (or legally authorized patients' representatives if applicable) must sign, date and time Medical Ethics Committee (MEC) approved informed consent prior to data collection for this registry. Obtaining the consent, provision of a copy to the patient, along with the date and time must be documented in the patient's medical records. The informed consent form must be signed by the investigator. In addition, the signed informed consent must be kept in the patient's medical records.

6.3 Eligibility Criteria

6.3.1 General Eligibility Criteria

Assessment for general eligibility criteria is based on medical records of the site and interview with a candidate patient. Patients must meet at least one of the angiographic inclusion criteria to be considered for the registry. If ANY of the exclusion criteria is met, the patient is excluded from the clinical evaluation and cannot be registered.

6.3.2 Inclusion Criteria

The inclusion criteria must follow the most recent IFU which may include but are not limited to the following:

- Patient must be at least 18 years of age at the time of signing the Informed Consent Form
- Patient is to be treated for de novo lesions located in previously untreated vessels.
- Patient must agree to undergo all required follow-up visits and data collection.
- Patient must have indication to percutaneous coronary intervention for multivessel disease (at least two significant stenoses in two different segments NOT as a bifurcation lesion) or long (≥24 mm) single vessel disease following:
    - Stable angina or evidence of myocardial ischemia with stress echocardiography/ myocardial SPECT/exercise test, or
    - Unstable angina / non ST-elevation myocardial infarction
    - ST-elevation myocardial infarction with de novo culprit lesion.

6.3.3 Exclusion Criteria

The exclusion criteria must follow the most recent IFU which may include but are not limited to the following:

- Known intolerance to any of the device components
- Contraindication to dual antiplatelet therapy (DAPT)
- Lesion in a saphenous vein graft
- Lesion to left internal mammary artery
- Unprotected left main stenosis
- Woman with childbearing potential
- Age < 18y/o
- Concomitant indication to open heart surgery

- Inability to provide written informed consent

6.4 Patient Discontinuation

Once registered, each patient shall remain in the registry until completion of the required follow-up period; however, a patient's participation is voluntary and the patient has the right to withdraw at any time without penalty or loss of benefit. Conceivable reasons for discontinuation may include but not be limited to the following:

- Patient voluntary withdrawal
- Patient withdrawal by physician as clinically-indicated
- Patient lost-to-follow-up: If the patient misses two consecutive scheduled follow up time points, and attempts at contacting the patient are unsuccessful, then the patient is considered lost to follow-up.

No additional data is needed and will be recorded from patients once withdrawn from the registry. Patients will not be replaced.

6.5 Registry Completion

An eCRF registry completion form must be completed when:

- the patient is considered lost-to-follow-up per the above definition or
- the patient withdraws from the registry or
- the investigator withdraws the patient from the registry or
- the patient's follow-up is terminated upon registry follow-up completed (see Section 4.3 for details)

7. TREATMENT AND SCHEDULE OF EVENTS

The treatment strategy will be determined by the investigator. It is required that each enrolling investigator review the most recent Absorb BVS IFU and assess the contraindications, warnings and precaution sections with respect to the risks and benefits for treating potential patients.

7.1 Baseline

Patient preparation will be in accordance with standard hospital policy for the care of interventional cardiology patients.

Baseline data will be collected as per eCRF. The Syntax score will be calculated in all patients.

7.2 Procedure

During the procedure, patients will receive appropriate anticoagulation and other therapies according to standard hospital practice. The Absorb BVS will be inspected, prepared, and implanted according to the IFU.

QCA analysis is recommended pre implantation of the ABSORB, for correct sizing. IVUS, VH-IVUS and OCT techniques are encouraged: these imaging tools will be subject of subgroup analysis.

7.3 Post–procedure (In-hospital)

Post procedure data will be collected as per eCRF

7.3.1 Follow-up Antiplatelet Medications

A minimum of 6 months duration of DAPT is recommended. Specific type of DAPT

will be recorded as per eCRF.

7.4 Clinical Follow-up

Clinical follow-up visits by telephone contact or office visits per the following schedule.

- **30 days**: office visit is encouraged
- **6 months**: office visit is encouraged
- **1 year**, and then yearly **up to 5 years** after the index procedure: office visit is encouraged.

7.5 Angiographic follow up

The angiographic follow up will be clinically driven. However, patients undergoing angio follow up and IVUS or OCT follow up will be included in subgroup analysis.

8. ADJUDICATION OF EVENTS

In order to minimize bias in assessing MACE outcomes, these events will be adjudicated by an independent Clinical Event Committee, which will also act as Data Safety and Monitoring Board for the study.

9. STATISTICAL ANALYSIS

9.1 Statistical Overview

The data will be reviewed by a Data Safety and Monitoring Board.
The Data Safety and Monitoring Board will be also responsible for:

- Determining whether information collected are sufficient to address the

objectives

- Recommending modifications to the statistical analysis plan to address additional research questions based on review of the data

9.2 Analysis Population

All patients who are successfully registered will be included in the analysis. A limit of one third of the entire population will be set for the group of Multivessel Disease patients treated with ABSORB and a conventional stent (“hybrid group”).

9.3 Sample Size Calculations and Assumptions

Being this an observational registry aiming at quantifying effect estimates without direct comparisons to literature benchmarks, we relied on confidence interval profiling for sample size justification, without proceeding with formal power analysis. As the main analysis is a pooled analysis of patients with multivessel disease and/or long lesions, an overall and comprehensive analysis is planned as the primary analytical approach. Accordingly, we computed that a target sample of 1000 patients will enable the computation of reasonably precise 95% confidence intervals. Specifically, assuming a 4.2% MACE rate at 1 year (in keeping with ABSORBD EXTEND data), confidence intervals computed with the adjusted Wald method would be 3.1% to 5.6% for a 1000-patient sample (point estimate 42/1000 [4.2%]).

Given that the registry aims to reflect real-world patients and practice, no provision to limit or restrict patient enrolment depending on the presence of multivessel disease vs long lesions is envisioned.

9.4 Statistical Analyses

Continuous endpoints will be summarized by presenting the total number of patients, mean, standard deviation, median, minimum, and maximum. Tabulation of

categorical parameters will include counts and percentages. The outcomes will be summarized as both a discrete and a continuous variable using the method described above. Survival analysis will be performed with the Kaplan-Meier method. Statistical inference will be based on the computation of 95% confidence intervals using the adjusted Wald method. Additional analyses will involve key subgroups defined according to baseline, lesion, and procedural features, with statistical significance set at the 5% 2-tailed level. Specifically, Student t, Fisher exact, and log-rank tests will be used for such bivariate analyses, whereas multivariable linear regression, logistic regression, and Cox proportional hazard analyses will be used to adjust for confounders. In addition, separate analyses for patients with only multivessel disease, patients with only long lesions, and patients with hybrid revascularization will be performed.

10. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The investigator/institution will permit direct access to source data/documents in order for registry-related monitoring, audits, MEC review, and regulatory inspections to be performed.

As part of the informed consent, the investigator or designee will obtain permission for registry monitors or regulatory authorities to review, in confidence, any records identifying the patients in this registry.

11. QUALITY CONTROL AND QUALITY ASSURANCE

11.1 Protocol and Informed Consent Approval

The Principal Investigator at each site must confirm and agree with the content of the protocol prior to participation in this registry. Also, the Principal Investigator will obtain written approval of the protocol, informed consent form, and other registry related documents from the MEC. In addition, the investigator will take actions

necessary for ongoing registry approval at their site per established procedures of the MEC.

The investigator will advise the MEC of the progress of this registry on a regular basis until registry completion as required by the MEC.

The investigator will submit any amendments to the protocol as well as associated informed consent form changes and obtain written MEC approval prior to implementation as required by the MEC.

11.2 Monitoring

A monitoring plan will be established. Remote monitoring by the CRO and source documents analysis for events throughout the study period by an independent Event Committee, will be conducted to ensure compliance with the protocol and applicable regulatory requirements.

12. DATA HANDLING AND RECORD KEEPING

For the registry duration, the investigator will maintain complete and accurate documentation including but not limited to the following: medical records, registry progress records, laboratory reports, electronic case report forms, signed informed consent forms, device serial numbers for monitoring malfunctions, correspondence with the MEC and registry monitor/Sponsor, SAE reports, and information regarding patient discontinuation or registry completion.

12.1 Source Documentation

- Medical history/physical condition of the patient before involvement in the registry sufficient to verify protocol entry criteria

- Dated and signed notes on the day of entry into the registry referencing the sponsor, protocol number, patient ID number and a statement that informed consent was obtained
- Dated and signed notes from each patient visit
- Adverse events reported and their resolution including supporting documents such as discharge summaries, catheterization laboratory reports, ECGs, and lab results including documentation of site awareness of SAEs and of investigator device relationship assessment of AEs.
- Notes regarding Dual Anti Platelet Therapy medications taken during the registry
- (including start and stop dates)
- Patient's condition upon completion of or withdrawal from the registry
- Any other data required to substantiate data entered into the CRF

12.2 Electronic Case Report Form Completion

Primary data collection based on source-documented hospital and /or clinic chart reviews will be performed clearly and accurately by site personnel trained on the protocol and eCRF completion. eCRF data will be collected for all patients that are registered.

13. ETHICAL CONSIDERATION

13.1 Medical Ethics Committee Review

Medical Ethics Committee (MEC) approval for the protocol and informed consent form /other written information provided to the patient will be obtained by the Principal Investigator at each investigational site prior to participation in this registry. No changes will be made to the protocol or informed consent form or other written information provided to the patient without appropriate approvals by the MEC.

Until the registry is completed, the Investigator will advise his/her MEC of the progress of this registry, per MEC requirements.

Further, any amendments to the protocol as well as associated informed consent form changes will be submitted to the MEC and written approval obtained prior to implementation, according to each institution's MEC requirements.

APPENDIX I: ABBREVIATIONS AND ACRONYMS

%DS: percent diameter stenosis

AE: adverse event

BVS: Bioresorbable Vascular Scaffold

CABG: coronary artery bypass graft

CE: Conformité Européene (EU)

DAPT: Dual Anti Platelet Therapy

DES: drug eluting stent

eCRF: electronic Case Report Form

GCP: Good Clinical Practice

IFU: Instructions for Use

MACE: major adverse cardiac event

MEC: medical ethics committee

MI: myocardial infarction

PCI: percutaneous coronary intervention

PDLLA: Poly-D,L-lactide

PLLA: Poly-L-lactide

SAE: serious adverse event

TLR: target lesion revascularization

TVR: target vessel revascularization

APPENDIX II: REFERENCES

1) Sigwart U, Puel J, Mirkovitch V, Joffre F, Kappenberger L. Intravascular stents to prevent occlusion and restenosis after transluminal angioplasty. N Engl J Med 1987;316:701– 6.
2) Gruntzig AR, Senning A, Siegenthaler WE. Nonoperative dilatation of coronary-artery stenosis: percutaneous transluminal coronary angioplasty. N Engl J Med 1979;301:61– 8.
3) de Feyter PJ, de Jaegere PP, Serruys PW. Incidence, predictors, and management of acute coronary occlusion after coronary angioplasty. Am Heart J 1994;127:643–51.
4) Serruys PW, de Jaegere P, Kiemeneij F, et al., for the Benestent Study Group. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. N Engl J Med 1994;331:489 –95.
5) Fischman DL, Leon MB, Baim DS, et al., for the Stent Restenosis Study Investigators. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. N Engl J Med 1994;331:496 –501.
6) Barragan P, Sainsous J, Silvestri M, et al. Ticlopidine and subcutaneous heparin as an alternative regimen following coronary stenting. Catheter Cardiovasc Diagn 1994;32:133– 8.
7) Schomig A, Neumann FJ, Kastrati A, et al. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. N Engl J Med 1996;334:1084 –9.
8) Cutlip DE, Leon MB, Ho KK, et al. Acute and nine-month clinical outcomes after “suboptimal” coronary stenting: results from the STent Anti-thrombotic Regimen Study (STARS) registry. J Am Coll Cardiol 1999;34:698 –706.
9) Colombo A, Hall P, Nakamura S, et al. Intracoronary stenting without anticoagulation accomplished with intravascular ultrasound guidance. Circulation 1995;91:1676–88.
10) Serruys PW, Kutryk MJ, Ong AT. Coronary-artery stents. N Engl J Med 2006;354:483–95.
11) Karas SP, Gravanis MB, Santoian EC, Robinson KA, Anderberg KA, King SB III. Coronary intimal proliferation after balloon injury and stenting in swine: an animal model of restenosis. J Am Coll Cardiol 1992;20:467–74.
12) Gordon PC, Gibson CM, Cohen DJ, Carrozza JP, Kuntz RE, Baim DS. Mechanisms of restenosis and redilation within coronary stents— quantitative angiographic assessment. J Am Coll Cardiol 1993;21:1166 –74.
13) Hoffmann R, Mintz GS, Dussaillant GR, et al. Patterns and mechanisms of in-stent restenosis. A serial intravascular ultrasound study. Circulation 1996;94:1247–54.
14) Moliterno DJ. Healing Achilles—sirolimus versus paclitaxel. N Engl J Med 2005;353:724 –7.

15) Stettler C, Wandel S, Allemann S, et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network metaanalysis. Lancet 2007;370:937– 48.
16) Spaulding C, Daemen J, Boersma E, Cutlip DE, Serruys PW. A pooled analysis of data comparing sirolimus-eluting stents with bare-metal stents. N Engl J Med 2007;356:989 –97.
17) Stone GW, Moses JW, Ellis SG, et al. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. N Engl J Med 2007;356:998 –1008.
18) Mauri L, Hsieh WH, Massaro JM, Ho KK, D'Agostino R, Cutlip DE. Stent thrombosis in randomized clinical trials of drug-eluting stents. N Engl J Med 2007;356:1020 –9.
19) Kastrati A, Mehilli J, Pache J, et al. Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents. N Engl J Med 2007;356:1030 –9.
20) Jeremias A, Kirtane A. Balancing efficacy and safety of drug-eluting stents in patients undergoing percutaneous coronary intervention. Ann Intern Med 2008;148:234–8.
21) Bolognese B et al. La cardiopatia ischemica cronica: il problema della valuatazione dei sintomi. Una proposta dell'Associazione Nazionale Medici Cardiologi Ospedalieri (ANMCO). G Ital Cardiol 14(3): 155-161