Cardiovascular Revascularization Medicine 17 (2016) 34–37

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Evaluation of the short- and long-term safety and therapy outcomes of the everolimus-eluting bioresorbable vascular scaffold system in patients with coronary artery stenosis: Rationale and design of the German–Austrian ABSORB RegIstRy (GABI-R)☆,☆☆

Holger Nef [a,*], Jens Wiebe [a], Stefan Achenbach [b], Thomas Münzel [c], Christoph Naber [d], Gert Richardt [e], Julinda Mehilli [f], Jochen Wöhrle [g], Till Neumann [h], Janine Biermann [h], Ralf Zahn [i], Johannes Kastner [j], Axel Schmermund [k], Thomas Pfannebecker [l], Steffen Schneider [m], Tobias Limbourg [m], Christian W. Hamm [a,n]

[a] University of Giessen, Medizinische Klinik I, Department of Cardiology, Giessen, Germany
[b] University of Erlangen, Medizinische Klinik II, Department of Cardiology, Erlangen, Germany
[c] Department of Medicine II, University Medical Center, Johannes Gutenberg University Mainz, Mainz, Germany
[d] Klinik für Kardiologie und Angiologie, Elisabeth-Krankenhaus, Essen, Germany
[e] Herzzentrum, Segeberger Kliniken GmbH, Bad Segeberg, Germany
[f] Department of Cardiology, Klinikum Großhadern, Ludwig- Maximilian Universität, Munich, Germany
[g] Department of Internal Medicine II, University of Ulm, Ulm, Germany
[h] University of Essen, Department of Cardiology, Essen, Germany
[i] Abteilung für Kardiologie, Herzzentrum Ludwigshafen, Ludwigshafen, Germany
[j] Department of Cardiology, University of Vienna Medical School, Vienna, Austria
[k] CCB, Cardioangiologisches Centrum Bethanien, Frankfurt, Germany
[l] Abbott Vascular Deutschland GmbH, Wetzlar, Germany
[m] Institut für Herzinfarktforschung, Ludwigshafen, Germany
[n] Kerckhoff Heart and Thorax Center, Department of Cardiology, Bad Nauheim, Germany

ARTICLE INFO

Article history:
Received 28 June 2015
Received in revised form 31 August 2015
Accepted 8 September 2015

Keywords:
Coronary artery disease
Bioresorbable scaffolds
BVS
Stenosis

ABSTRACT

Background: Third-generation drug-eluting metal stents are the gold standard for treatment of coronary artery disease. The permanent metallic caging of the vessel, however, can result in limited vasomotion, chronic inflammation, and late expansive remodeling, conditions that can lead to late and very late stent thrombosis. The development of bioresorbable scaffolds (BRSs) promises advantages over metal stents due to complete biodegradation within 2–4 years. Theoretically, since vessel scaffolding is temporary and no permanent implant remains in the vessel, BRSs, as opposed to metal stents, once degraded would no longer be potential triggers for stent-related adverse events or side effects.

Methods/design: The short- and long-term outcome after implantation of an everolimus-eluting, poly-L-lactic acid-based bioresorbable scaffold system (ABSORB, Abbott Vascular, Santa Clara, CA, USA) in the world-wide greatest all-comers cohort will be evaluated in the prospective, non-interventional, multicenter German–Austrian ABSORB RegIstRy (GABI-R). GABI-R will include over 5000 patients from about 100 study sites in Austria and Germany. Safety endpoints such as cardiac death, myocardial infarction, and clinically driven percutaneous or surgical target lesion and vessel revascularization will be evaluated during hospitalization and in the follow-up period (minimum of 5 years).

Conclusion: Although two randomized controlled trials and several registries have documented safety and efficacy as well as non-inferiority of this everolimus-eluting ABSORB device compared with drug-eluting metal stents, the current knowledge regarding clinical application, treatment success, and long-term safety of using this BRS in daily routine is limited. Thus, the goal of GABI-R is to address this lack of information.

Abbreviations: ARC, Academic Research Consortium; BRS, bioresorbable scaffold; CABG, coronary artery bypass graft surgery; DES, metallic drug-eluting stent; GABI-R, German–Austrian ABSORB Registry; MACE, major adverse cardiac event; PCI, percutaneous coronary intervention; PLLA, poly-L-lactic acid; PDLLA, poly-D,L-lactic acid; QoL, quality of life; TLF, target lesion failure; TVF, target vessel failure; TVR, clinically driven percutaneous or surgical target vessel revascularization.

☆ Funding: The GABI Registry is supported by ABBOTT Vascular, Santa Clara, California, USA.

☆☆ Conflict of interest: Holger Nef: research grants (institutional) and speaker honoraria — Abbott Vascular, Gert Richart: advisory board — Abbott Vascular, Stephan Achenbach: research grants (institutional) — Abbott Vascular and Siemens Healthcare, Julinda Melihi: lecture fees and advisory board — Abbott Vascular and Terumo, lecture fees Lilly/Daiichi Sankyo and Boston Scientific, Axel Schmermund: speaker honorarium — Abbott Vascular, Christian Hamm: speaker honorarium — Abbott Vascular. None of the other authors report any potential conflict of interest.

* Corresponding author at: Medizinische Klinik I, Department of Cardiology, University of Giessen, Klinikstrasse 33, 35392 Giessen, Germany. Tel.: +49 641 985 42101; fax: +49 641 985 42109.
E-mail address: holger.nef@innere.med.uni-giessen.de (H. Nef).

http://dx.doi.org/10.1016/j.carrev.2015.09.002
1553-8389/

1. Introduction

The objective of percutaneous coronary intervention (PCI) is to improve the blood flow in the presence of coronary artery stenosis. Established methods include balloon angioplasty and stent implantation. Restenosis rates with the use of a stent are considerably lower than with balloon angioplasty alone, with anti-inflammatory drug-eluting stents being superior to bare metal stents [1–3]. Consequently, metallic drug-eluting stents (DESs) are the current gold standard for PCI according to existing guidelines [4].

The implantation of bioresorbable scaffolds (BRSs) is a new, promising technique for the treatment of coronary artery disease that was developed in order to reduce the potential risk of late and very late stent thrombosis, which is associated with a permanent metallic implant. Currently, the most-investigated BRS is an everolimus-eluting, poly-L-lactic acid (PLLA)-based device (ABSORB BVS, Abbott Vascular, Santa Clara, California, USA) [5]. Two recent randomized controlled trials have demonstrated mid-term clinical and angiographic results that are comparable to those obtained with DESs [6,7]. Furthermore, limited all-comers data show reasonable results in a broad spectrum of clinical settings and lesion types [8–11]. Nevertheless, there is still a considerable lack of information about procedural and clinical outcome derived during daily clinical practice, since present evaluations either had too small a sample size or were retrospective in design. The prospective German–Austrian ABSORB Registry (GABI-R) has been conceived to provide an analysis of acute and long-term safety as well as therapy outcomes of the largest cohort to date of patients with coronary artery disease treated with the ABSORB BVS.

2. Methods/design

2.1. Registry objective

The registry collects prospective data regarding the quality of care with the use of the ABSORB BVS for coronary revascularization, including the following specific objectives:

- Documentation of all consecutive patients having been treated with the ABSORB BVS system under clinical real-world conditions
- Documentation of indications, procedural results, and short- and long-term outcomes
- Documentation of the technical performance of ABSORB implantation procedures
- Collection of safety data, in particular documentation of in-hospital mortality, major non-fatal complications (especially myocardial infarction, re-PCI or coronary artery bypass graft surgery (CABG), and scaffold thrombosis)
- Documentation of long-term patient safety characterized by mortality and major non-fatal complications (especially myocardial infarction, re-PCI or CABG, and thrombosis) at discharge from hospital and at 30 days, 6 months, 2 years, and 5 years after the procedure
- Gathering of data on the quality of life (QoL) pre- and post-ABSORB implantation to document individual QoL dimensions as well as individual symptoms
- Gathering of health economics data (capture of direct costs, especially with respect to change of medication and outpatient/inpatient hospital services, and indirect costs) pre- and post-ABSORB™ implantation

2.2. Registry design

The German–Austrian ABSORB Registry (ClinicalTrials.gov: NCT02066623) is a prospective, non-interventional, multicenter, clinical follow-up study of consecutive patients with significant coronary artery stenosis who have been treated with the everolimus-eluting ABSORB BVS. The registry is an observational study, and a patient's participation in this trial has no impact on his or her indication for diagnostics, coronary angiography, or therapy. Patients are treated in compliance with currently valid instructions for use as well as medical society guidelines and the hospital's internal directives. Drug therapy is designed to meet medical society guidelines or the clinic's internal directives.

2.3. The ABSORB BVS system

The circumferential and cross-linked struts of the ABSORB BVS are made of poly-,L-lactic acid (PLLA) with a thickness of 150 μm. The ABSORB BVS elutes a 1:1 mixture of poly-D,L-lactic acid and the antiproliferative drug everolimus. To provide visualization, radiopaque markers are located at a distance of 0.3 mm to 1.1 mm from either end. Complete resorption of the current generation of ABSORB BVS was observed after approximately 3 years in animal models [12,13]. Systematic information of the time to complete dissolution in humans is sparse and can only be assumed to be comparable to that in animals.

Implantation of the ABSORB BVS is followed by a series of restructuring processes that finally lead to the scaffold being completely resorbed. In the early phase, the polymers absorb fluids from the luminal blood and the surrounding tissue. Long-chain polymers are hydrolyzed to short-chain polymers, resulting in fragmentation of the scaffold struts and loss of radial strength. Finally, the polymer microparticles are restructured and resorbed, resulting in L-lactate being degraded via pyruvate and citric acid cycle to CO_2 and H_2O. The degradation process of the polymer scaffold depends on the length of the polymer chains (molecular weight) and the hydrophilic characteristics of the polymers.

2.4. Number of patients and duration of the registry

All patients at the participating centers in Germany and Austria who have been implanted with the ABSORB BVS are to be included in the registry. Starting in November 2013, a minimum of 5000 patients from about 100 study sites in Austria and Germany will have been enrolled. Participation in the registry is offered to all study sites in Germany and Austria implanting the ABSORB BVS. Participating sites have committed to consecutively enroll in the registry all patients meeting the inclusion criteria. The one and only inclusion criterion for admission of a patient to GABI-R is his or her individual clinical indication for at least one ABSORB™ BVS implant. The only exclusion criterion is a patient's refusal to sign the informed consent form, i.e. his or her explicit wish not to participate in this registry.

Since it is known that a positive correlation between strut thickness and flow disturbances exists and that this relationship carries negative clinical consequences such as higher restenosis and target vessel revascularization rates after implantation of ABSORB™ BVS, dual anti-platelet therapy is recommended for 12 months.

Clinical events are recorded during hospitalization and in the follow-up period (minimum of 5 years) in terms of the number and time of occurrence of serious adverse cardiac events. Follow-up is to be conducted centrally for all sites by the "Institut für Herzinfarktforschung GmbH" (IHF, Ludwigshafen, Germany), which will analyze all data sets in a manner that is independent of any sponsor. At 30 days, 6 months, 2 years, and 5 years, patients will be notified in writing via mail and asked to fill out "Follow-Up" and the "Quality of Life" questionnaires and to return them to the IHF. If there is no reply, standardized interviews with the patients will be conducted over the phone. If it is not possible to reach a patient, the local residents' registration office will be contacted. Participating study sites are free to document any additional patient visits within 5 years from the index hospital stay (e.g. in case of repeat hospitalization).

2.5. Target parameters

Major adverse cardiac events (MACEs) comprise cardiac death, any myocardial infarction, and clinically driven percutaneous or surgical target lesion revascularization. Target vessel failure (TVF) includes cardiac