JACC: CARDIOVASCULAR INTERVENTIONS VOL. 6, NO. 5, 2013

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC. http://dx.doi.org/10.1016/j.jcin.2012.12.131

Intracoronary Optical Coherence Tomography and Histology of Overlapping Everolimus-Eluting Bioresorbable Vascular Scaffolds in a Porcine Coronary Artery Model

The Potential Implications for Clinical Practice

Vasim Farooq, MB ChB,* Patrick W. Serruys, MD, PhD,* Jung Ho Heo, MD,* Bill D. Gogas, MD,* Yoshinobu Onuma, MD,* Laura E. Perkins, DVM, DACVP,† Roberto Diletti, MD,* Maria D. Radu, MD,* Lorenz Räber, MD,* Christos V. Bourantas, MD, PhD,* Yaojun Zhang, MD,* Eric van Remortel, BSc,‡ Ravindra Pawar, BSc,‡ Richard J. Rapoza, PhD,† Jennifer C. Powers, BS,† Heleen M. M. van Beusekom, PhD,* Hector M. Garcìa-Garcìa, MD, MSc, PhD,* Renu Virmani, MD, PhD§

Rotterdam, the Netherlands; Santa Clara, California; and Gaithersburg, Maryland

Objectives This study sought to assess the vascular response of overlapping Absorb stents compared with overlapping newer-generation everolimus-eluting metallic platform stents (Xience V [XV]) in a porcine coronary artery model.

Background The everolimus-eluting bioresorbable vascular scaffold (Absorb) is a novel approach to treating coronary lesions. A persistent inflammatory response, fibrin deposition, and delayed endothelialization have been reported with overlapping first-generation drug-eluting stents.

Methods Forty-one overlapping Absorb and overlapping Xience V (XV) devices (3.0 × 12 mm) were implanted in the main coronary arteries of 17 nonatherosclerotic pigs with 10% overstretch. Implanted coronary arteries were evaluated by optical coherence tomography (OCT) at 28 days (Absorb n = 11, XV n = 7) and 90 days (Absorb n = 11, XV n = 8), with immediate histological evaluation following euthanasia at the same time points. One animal from each time point was evaluated with scanning electron microscopy alone. A total of 1,407 cross sections were analyzed by OCT and 148 cross sections analyzed histologically.

Results At 28 days in the overlap, OCT analyses indicated 80.1% of Absorb struts and 99.4% of XV struts to be covered ($p < 0.0001$), corresponding to histological observations of struts with cellular coverage of 75.4% and 99.6%, respectively ($p < 0.001$). Uncovered struts were almost exclusively related to the presence of "stacked" Absorb struts, that is, with a direct overlay configuration. At 90 days, overlapping Absorb and overlapping XV struts demonstrated >99% strut coverage by OCT and histology, with no evidence of a significant inflammatory process, and comparable % volume obstructions.

Conclusions In porcine coronary arteries implanted with overlapping Absorb or overlapping XV struts, strut coverage is delayed at 28 days in overlapping Absorb, dependent on the overlay configuration of the thicker Absorb struts. At 90 days, both overlapping Absorb and overlapping XV have comparable strut coverage. The implications of increased strut thickness may have important clinical and design considerations for bioresorbable platforms. (J Am Coll Cardiol Intv 2013;6:523–32) © 2013 by the American College of Cardiology Foundation

From the *Erasmus University Medical Centre, Rotterdam, the Netherlands; †Abbott Vascular, Santa Clara, California; ‡Cardialysis BV, Rotterdam, the Netherlands; and the §CVPath Institute, Gaithersburg, Maryland. The porcine study was supported by Abbott Vascular (Santa Clara, California). Drs. Perkins, Rapoza, and Powers are employees of Abbott Vascular. Dr. Virmani has received research support from Medtronic AVE, Abbott Vascular, Atrium Medical, OrbusNeich Medical, Terumo

JACC: CARDIOVASCULAR INTERVENTIONS, VOL. 6, NO. 5, 2013
MAY 2013:523–32

Everolimus-eluting bioresorbable vascular scaffolds (Absorb, Abbott Vascular, Santa Clara, California) are a novel approach to treating coronary lesions, in that they provide transient vessel support and drug delivery to the vessel wall, without the long-term limitations of standard metallic drug-eluting stents (DES), such as metallic caging. Unlike with permanent metallic stenting, the Absorb will potentially allow for future surgical revascularization, expansive remodeling, restoration of reactive vasomotion, and reliable noninvasive imaging of coronary arteries with multislice computed tomography (1–4). Given the temporary presence of the Absorb, the small, but potentially fatal, risk of late or very late stent thrombosis associated with conventional metallic platform DES, may be reduced or even eliminated (5,6).

First-generation DES, namely overlapping sirolimus-eluting and paclitaxel-eluting stents, have previously been demonstrated in pre-clinical models to show evidence of a persistent inflammatory response, fibrin deposition, and delayed endothelialization (7,8). The purpose of this study is to assess the vascular response of overlapping Absorb compared to the overlapping newer generation everolimus-eluting metallic platform stents (Xience V [XV], Abbott Vascular) in a porcine coronary artery model.

Abbreviations and Acronyms

DES = drug-eluting stent(s)
EEL = external elastic lamina
IQR = interquartile range
OCT = optical coherence tomography
SA ratio = scaffold/stent to artery ratio
SEM = scanning electron microscopy
XV = Xience V stent(s)

Methods

Experimental studies received protocol approval from the institutional animal care and use committee and were conducted in accordance with American Heart Association guidelines for pre-clinical research and the *Guide for the Care and Use of Laboratory Animals* (National Institutes of Health, 2010). Seventeen healthy, nonatherosclerotic Yorkshire-Landrace swine were implanted via femoral access according to standard procedures (9). Each animal was implanted with overlapping 3.0 × 12.0-mm Absorb or XV stents in up to 3 of the main coronary vessels according to a predetermined matrix of randomization. A maximum of 2 overlapping Absorb and 1 overlapping XV were permitted per animal. The Absorb and XV sizes were matched to the vessel size at a target balloon-to-artery ratio of 1.1 to 1.0 (10% overstretch). In total, 17 animals (41 vessels) were implanted with overlapping Absorb or overlapping XV. Eight and 9 pigs underwent follow-up at 28 days (Absorb n = 12, XV n = 8), and 90 days (Absorb n = 12, XV n = 9), respectively (Online Appendix). These time points have been reported to be representative of peak neointimal growth in humans at 6 months (28 days) and 18 months (90 days) (10). Coronary angiography and OCT analyses were performed at baseline and at both time points. One animal from each of the 28 and 90 day time points was excluded from OCT and histological analyses, and implanted arteries evaluated with scanning electron microscopy (SEM) alone. All pigs were humanely euthanized at follow-up immediately after angiography (SEM) or OCT (all others).

OCT analyses. OCT evaluation of the Absorb and XV overlap were performed at a pullback speed of 1.0 mm/s at baseline and at follow-up, utilizing a commercially available time-domain OCT system (M3 System, LightLab Imaging, Westford, Massachusetts). The image wire was passed distal to the treated vessel without the conventional support of the balloon occlusion catheter to minimize the risk of disrupting the endothelial coverage in the treated vessel. Bolus doses of Ringer's lactate were used to clear blood distal to the inflated occlusion balloon in the proximal vessel, and OCT pullbacks were initiated. Quantitative and qualitative analyses were performed with proprietary software for off-line analysis (LightLab Imaging). With adjustment for pullback speed, analyses of continuous cross sections were performed at 1-mm longitudinal intervals consistent with previously validated methodologies (Online Appendix) (1,11,12). OCT analyses were performed by a team of physicians and analysts of an independent core laboratory (Cardialysis BV, the Netherlands). Specifically for the overlapping Absorb, struts were defined by their overlay configuration, namely "stacked inner," "stacked outer," and "other" (i.e., without a clear direct overlay configuration) (Fig. 1) (13). The threshold for coverage of the Absorb strut is 30 μm, corresponding to the average interobserver measurement (difference in 300 struts analyzed 2 times, 35 ± 6 μm) of the endoluminal light backscattering strut boundary (14). To allow full visualization of the spatial distribution of strut coverage struts in the overlapping devices, "spread-out-vessel graphs"—a visual representation of the vessel as if it had been cut along the reference angle (0°) and spread out on a flat surface—were created based upon previously described methodologies (11).

Histological analyses and SEM. Histological analyses are described in the Online Appendix. SEM was performed with a Hitachi Model 3600N scanning electron microscope (Hitachi, Tokyo, Japan). Sections were stained with hematoxylin and eosin and elastic van Gieson or Movat pentachrome.

Statistical analyses. Continuous variables are reported as mean ± SD, categorical variables as counts (%). Comparisons were made with the Student *t* test/Mann-Whitney *U* test and chi-square/Fisher exact test as appropriate. Tissue

Corporation, Cordis Corporation, and BioSensors International; and is a consultant for Medtronic AVE, Abbott Vascular, W.L. Gore, Atrium Medical, Arsenal Medical, and Lutonix. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received November 14, 2012; revised manuscript received December 3, 2012, accepted December 21, 2012.