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ORIGINAL ARTICLE

Bioresorbable Vascular Scaffold (ABSORB BVS); first report in Egyptian patients with 6 month angiographic/IVUS follow up

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KEYWORDS

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Abstract Objective: To evaluate the feasibility, efficacy, and safety of the ABSORB BVS (Bioresorbable Vascular Scaffold) for the treatment of de novo native coronary artery stenosis.

Methods: Thirty patients with ischemic heart disease were selected between September 2012 and December 2012 and received ABSORB BVS for the treatment of de novo native significant coronary artery stenosis. Patients were followed up for six months after the procedure. In each patient, the treated segment and the periscaffold segments (5 mm proximal and distal to the scaffold edge) were analyzed by Quantitative coronary angiography (QCA) and phased-array intravascular ultrasound (IVUS) catheters in paired matched angiographic views after the procedure and at follow-up. The major clinical end point was ischemia-driven major adverse cardiac events (ID-MACE) defined as a composite of cardiac death, myocardial infarction or ischemia-driven target lesion revascularization.

Results: Overall the scaffold area remained unchanged. The angiographic late lumen loss amounted to 0.27 ± 0.32 mm with an IVUS relative decrease in minimal lumen area of 1.94% ($p = 0.12$), without significant changes in the mean lumen area. After 2 weeks, 1 patient presented with STEMI, control coronary angiography revealed a patent stent with thrombus distal to it that was treated with a metallic drug-eluting stent (Xience V). There were no cardiac deaths or ischemia-

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driven target lesion revascularizations. At six months the hierarchical ID-MACE was 3.3%.

Conclusions: ABSORB BVS seems an attractive option for the treatment of significant de novo native coronary artery stenosis with low risk of serious adverse events.

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1. Introduction

Drug-eluting stents (DES) were conceived as the next evolutionary step in improving the limitations of bare metal stents (BMS). Initial studies were highly promising, with large-scale reductions in restenosis rates that were reported at 0% in highly selective lesions 4% and up to 16% in a broader range of patients and lesions.¹

A potential complication subsequently became evident with first-generation DES, namely that of subacute and late stent thrombosis as a consequence of delayed healing of the permanent metallic struts. Furthermore, late acquired malapposition of the struts implanted in a thrombotic rich milieu was also demonstrated to be a potential issue.²

The prospect of a temporary vascular stent, termed “scaffold” due to its being based on a temporary bioresorbable platform, has been always a goal of the interventional community. Such a device could offer transient radial strength to resist acute vessel recoil, and at a later stage would be fully resorbed, leading to restoration of the vessel’s biological properties.³

The polymeric material as an implantation medium potentially has numerous advantages compared to metal. The main challenges faced by the ABSORB (BVS) are its limited distensibility, and therefore its suitability for implantation in appropriately sized vessels. Consequently, at present Quantitative coronary angiography (QCA) guidance is mandatory for implantation of the device. Although the radial strength of the ABSORB (BVS) has been reported to be comparable to metallic stents, this is provided the BVS is deployed within the limits of its size. If the BVS is over-stretched beyond its designed limits, it has been shown to lose some of its radial strength and may possibly fracture. Much effort has been invested in improving its supportive properties, with the introduction of a new strut design in order to enhance the distensibility of the device while maintaining its radial strength, features which are expected in the next generation BVS.³

Bioabsorbable drug-eluting vascular scaffolds (BVS; Abbott Vascular, Santa Clara, Calif) are novel approach that provides transient vessel support with drug delivery capability without the long-term limitations of metallic drug-eluting stents such as permanent caging with or without malapposition.⁴

Permanent metallic stenting also may preclude surgical revascularization, prevent late lumen enlargement, result in jailing of side branches, and hamper noninvasive imaging of coronary arteries with multislice computed tomography and MRI.⁵

Bioresorbable technology is an alternative and challenging therapeutic approach for the treatment of coronary artery disease. Although the scenario of a dynamic device that “does the job and disappears”, leading to the restoration of vascular physiology, is here (“vascular reparative therapy”), this innovative and rapidly progressing technology is still in its infancy.³

2. Aim of the work

The aim of this study was assessment of the safety and efficacy of the BVS (Bioresorbable Vascular Scaffold) for the treatment of de novo native coronary artery stenosis.

3. Methods

3.1. Study design and patients

The study included 30 cases admitted to the catheterization laboratory in Wadi El-Neel hospital diagnosed as having ischemic heart disease with significant coronary artery stenosis necessitating PCI. We included full history, clinical evaluation, Standard 12 leads surface ECG, Echocardiography, Ischemic driven non-invasive test for controversy patient with chest pain.

3.2. Inclusion criteria

- Patients who were able to verbally confirm understanding of risks, benefits and treatment alternatives of receiving the Everolimus Eluting BVS and he/she or his/her legally authorized representative provided written informed consent prior to any clinical investigation related procedure.
- Patients must have evidence of myocardial ischemia.
- Patients must agree to undergo all clinical investigation plan required.
- Target lesion(s) were:
 - De novo located in a native coronary artery.
 - Measure ≤ 24 mm in length by visual estimation.
 - In a major artery or branch with a visually estimated stenosis of $\geq 50\%$ and $< 100\%$ with a TIMI flow of ≥ 1 .

3.3. Exclusion criteria

- Patients with LV systolic dysfunction (EF $< 30\%$), cardiogenic shock.
- Patients who received a heart transplant.
- Patients who received or scheduled to receive chemotherapy for malignancy within 30 days prior to or after the procedure.
- Patients receiving immunosuppressive therapy.
- Patients with known hypersensitivity or contraindication to aspirin, heparin, clopidogrel, everolimus, poly L-lactide (PLLA), poly DL-lactide (PDLLA) or contrast sensitivity that cannot be adequately pre-medicated.
- Patients with end stage liver or renal disease.

- Patients with recent bleeding or cerebrovascular accident (CVA) or transient ischemic neurological attack (TIA) within the past six months.
- Pregnant or nursing patients and those who plan pregnancy during the clinical investigation.
- Patients who received brachytherapy in any epicardial vessel.
- Target lesion(s) meet any of the following criteria:
 - o Any vessel having any previous metallic stent.
 - o Any arterial or venous grafts.
 - o Excessive tortuosity proximal to or within the lesion (extreme angulation ($\geq 90^\circ$) proximal to or within the lesion), heavy calcification or in-stent restenosis.

3.4. Study device

BVS balloon-expandable device consists of a polymer backbone of poly L-lactide (PLLA) coated with a thin layer of a 1:1 mixture of poly DL-lactide (PDLLA) polymer and the anti-proliferative drug everolimus to form an amorphous drug-eluting coating matrix containing 100 μg everolimus/ cm^2 scaffolds. The implant is radiolucent but has 2 platinum markers at each end that allow easy visualization on angiography and other imaging modalities. PDLLA allows controlled release of the everolimus so that 80% is eluted in 30 days; the elution rate, tissue concentration, and dose density of everolimus for the BVS device are similar to the XIENCE Everolimus-eluting stent.

Both PLLA and PDLLA are fully resorbable. The polymer degrades via a bulk erosion process through hydrolysis of the ester bonds in the backbone. The resulting lactic acid monomer and oligomers eventually leave the polymer matrix once they reach high enough diffusivity and water solubility. They are rapidly metabolized in surrounding tissues and blood by entering the pyruvate and Krebs energy cycles. In this second iteration of the scaffold device, the hydrolysis of the polymer has been slowed through a proprietary manufacturing process. According to preclinical studies, the time for complete absorption of the polymer backbone is assumed to be 2 years, whereas the polymer coating is absorbed faster.⁶

3.5. Study procedure

Target lesions were treated using standard interventional techniques with mandatory pre-dilatation. Post-dilatation with a balloon shorter than the implanted stent was allowed at the operator's discretion (if an optimal angiographic result was not obtained immediately after scaffold deployment). Bailout stenting with Xience-V for edge dissection and insufficient coverage of the lesion was recommended if needed. Treatment with aspirin was started at least 24 h before the procedure and continued throughout the length of the clinical investigation, followed by lifelong aspirin treatment. A loading dose of 300 mg clopidogrel was administered before the procedure, followed by 75 mg daily for a minimum of 6 months.

3.6. Definitions

Clinical device success was defined as successful delivery and deployment of the clinical investigation scaffold at the in-

tended target lesion with attainment of a final residual stenosis of $< 20\%$ of the target lesion by QCA (by visual estimation if QCA unavailable). Bailout stenting was not considered a device failure. Clinical procedure success was defined as above using any adjunctive device without the occurrence of ischemia-driven major adverse cardiac events up to 7 days after the index procedure.

The composite end point was cardiac death, any myocardial infarction, or ischemia-driven target lesion revascularization for a QCA DS (diameter stenosis) of $\geq 50\%$ either with symptoms or ischemia or with DS $\geq 70\%$ at the time of scheduled (180 ± 14 days) or unscheduled angiography. For non-Q-wave myocardial infarction, elevation of creatine kinase (CK) levels > 2 times the upper limit of normal with elevated CK-MB was required.⁷

3.7. Angiographic assessment

In all patients, the treated segment and the peri-scaffold segments (defined by a length of 5 mm proximal and distal to the scaffold edge) were analyzed by QCA in paired matched angiographic views after the procedure and at follow-up. The following QCA parameters were computed: minimal luminal diameter (MLD), reference vessel diameter obtained by an interpolated method, late loss, and binary restenosis, ascertained in scaffold, in periscaffold segment, and in segment (scaffold plus peri-scaffold segments).

Information on the type of the largest balloon used during procedure was also collected. The predicted balloon diameter was obtained from the chart of Post-dilatation balloon provided by the manufacturer using the balloon diameter and the pressure during the procedure. In addition, the Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery (SYNTAX) score was calculated to quantify the complexity of coronary anatomy using dedicated software available at the website (www.syntax-score.com) that integrates the number of lesions with their specific weighting factors based on the amount of myocardium distal to the lesion and the morphological features of each single lesion.⁸

3.8. IVUS gray-scale analysis

Treated vessels after the procedure and at follow-up were examined with phased-array IVUS catheters (Eagle Eye, Volcano Corp, Rancho Cordova, Calif) using an automated pullback at 0.5 mm/s. The region of interest beginning 5 mm distal to and extending 5 mm proximal to the treated segment was examined. The vessel area, scaffold area, lumen area, intrascaffold neointimal area, and luminal area stenosis were measured with a computer-based contour detection program.

The percentage of lumen area stenosis was calculated as 100 times the mean lumen cross-sectional area within the scaffold minus the minimal lumen area within scaffold divided by mean lumen cross sectional area. Incomplete apposition was defined as 1 or more scaffold struts separated from the vessel wall; acquired late incomplete apposition was defined as incomplete apposition at follow-up that was not present after the procedure.⁹

3.9. Statistical analysis

This was a feasibility study designed to provide preliminary information on the performance of the BVS. The sample size was not defined on the basis of an end-point hypothesis but rather to provide information on device performance. For binary variables, percentages were calculated. When provided, the 95% confidence intervals were computed with the gaussian approximation, taking into account the paired analysis. Paired comparisons between post procedural and follow-up results were done by a Wilcoxon signed-rank test.

Because no formal hypothesis testing was planned for assessing the success of the study, no statistical adjustment was applied. *P* values presented here are exploratory analyses only and should therefore be interpreted cautiously.

4. Results

Thirty patients were enrolled, and the investigational device was successfully implanted in all patients (Table 1). No bailout stents were implanted. There were no deaths, either peri-procedurally or at 6 months. At 2 weeks, 1 patient presented with STEMI, control coronary angiography revealed a patent stent with thrombus distal to stent that was treated with a metallic drug-eluting stent (Xience V), ID-MACE 3.3%.

4.1. Angiographic results

Table 2 summarizes the results of QCA data at baseline and at follow-up. At follow-up, the intrascaffold MLD decreased from 2.32 ± 0.28 to 2.13 ± 0.29 mm ($P < 0.001$). There were no significant changes in MLD at the proximal and distal edges of the scaffold. The angiographic late loss was 0.27 ± 0.32 mm. In-scaffold binary restenosis was 0%, whereas 1 proximal edge restenosis was documented by angi-

ography in a symptomatic patient (1 of 30; 3.3% in-segment binary restenosis).

4.2. Gray-scale IVUS

The results of gray-scale IVUS are presented in Table 3. At follow-up, there was no significant change in vessel area, but decreases in mean scaffold area, minimal scaffold area, mean lumen area, and minimum lumen area attained significance, although the relative decreases at follow-up of these parameters were small, 2.0%, 4.6%, 3.1%, and 5.4%, respectively.

On baseline IVUS, 4 patients showed incomplete scaffold apposition (ISA) with respective volumes of 27.7, 2.6, 5.7, and 1.1 mm³. One ISA persisted at follow-up, and 3 ISAs resolved. At follow-up, 3 patients developed a late acquired ISA with respective volumes of 3.0, 1.7, and 1.5 mm³.

5. Discussion

In this study, we reported that the late luminal loss was 0.19 mm documented at 6 months which was in the range observed with current metallic drug-eluting stents. Besides, absence of stent area shrinkage, in conjunction with the growth of a small amount of neointima resulted in a very modest reduction in lumen area over 6-month period.

5.1. IVUS analysis of late recoil

Grayscale IVUS and IVUS-based imaging modalities during the last years have become useful in the assessment not only of drug eluting stent, but also of new Bioresorbable Vascular Scaffolds. Although IVUS resolution is not sufficient for determining stent coverage (optical coherence tomography is the gold standard), serial IVUS can measure intimal hyperplasia, assess acute and late incomplete stent apposition, detect the

Table 1 Baseline characteristics.

Characteristic	Intention to treat, <i>n</i> = 30
Age, mean \pm SD (y)	62 \pm 8
Male gender, <i>n</i> (%)	22 (73)
Current smoker, <i>n</i> (%)	7 (23.3)
Diabetes mellitus, <i>n</i> (%)	11 (36.6)
Hypertension requiring medication, <i>n</i> (%)	18 (60)
Hyperlipidemia requiring medication, <i>n</i> (%)	18 (60)
Prior myocardial infarction, <i>n</i> (%)	13 (43.3)
SYNTAX score (mean \pm SD)	7.98 \pm 2.27
Target vessel, <i>n</i> (%)	
Left anterior descending artery	12 (40)
Left circumflex	8 (27)
Right coronary artery	10 (33)
AHA/ACC lesion classification, <i>n</i> (%)	
A	1 (3.3)
B1	15 (50)
B2	13 (43.3)
Mean reference vessel diameter, mean \pm SD (mm)	2.62 \pm 0.37
MLD (Minimum Luminal Diameter), mean \pm SD (mm)	1.26 \pm 0.23
DS (Diameter Stenosis), mean \pm SD (%)	64 \pm 13
Lesion length, mean \pm SD (mm)	12.2 \pm 3.4

Table 2 Paired QCA analysis ($n = 30$).

	Intention-to-treat population (30 pairs)			
	Proximal	In-scaffold	Distal	In-segment
<i>Reference vessel diameter, mean \pm SD (mm)</i>				
After the procedure	2.67 \pm 0.40	2.76 \pm 0.38	2.64 \pm 0.36	2.72 \pm 0.40
At 6 month follow-up	2.72 \pm 0.36	2.65 \pm 0.37	2.53 \pm 0.38	2.60 \pm 0.40
<i>P</i> between after the procedure and follow-up	<0.0001	<0.0001	<0.0001	0.0014
<i>MLD, mean \pm SD (mm)</i>				
After the procedure	2.46 \pm 0.52	2.32 \pm 0.28	2.24 \pm 0.45	2.09 \pm 0.37
At 6 month follow-up	2.38 \pm 0.49	2.13 \pm 0.29	2.15 \pm 0.38	1.97 \pm 0.35
<i>P</i> between after the procedure and follow-up	0.1	<0.0001	0.1	0.02
<i>Immediate gain, mean \pm SD (mm)</i>				
Late loss, mean \pm SD (mm)	0.07 \pm 0.27	0.27 \pm 0.32	0.07 \pm 0.30	0.11 \pm 0.28
<i>DS, mean \pm SD (%)</i>				
After the procedure	14.5 \pm 10.8	15.5 \pm 6.1	15.3 \pm 9.8	22.9 \pm 8.1
At 6 month follow-up	12.7 \pm 11.5	19.2 \pm 7.6	14.8 \pm 9.40	24.0 \pm 9.6
<i>P</i> between after the procedure and follow-up	0.086	0.0005	0.36	0.74

Table 3 IVUS results: paired gray-scale IVUS measurements per lesion, intention to treat ($n = 30$).

	Post PCI (Mean \pm SD)	At 180 days (Mean \pm SD)	Difference (95% CI) Based on individual data (%)	<i>P</i>
Vessel area (mm ²)	14.22 \pm 3.75	14.49 \pm 3.67	2.4 \pm 7.4 (-0.08-4.87)	0.06
Scaffold area (mm ²)	6.58 \pm 1.17	6.44 \pm 1.11	-2.0 \pm 4.8 (-3.56-0.34)	0.015
Minimum scaffold area (mm ²)	5.51 \pm 1.02	5.24 \pm 0.93	-4.6 \pm 7.4 (-7.05-2.12)	<0.001
Neointimal hyperplasia area (mm ²)	-	0.08 \pm 0.13	-	-
Mean lumen area (mm ²)	6.60 \pm 1.22	6.37 \pm 1.12	-3.1 \pm 7.0 (-5.45-0.75)	<0.005
Minimum lumen area (mm ²)	5.49 \pm 1.03	5.17 \pm 0.97	-5.4 \pm 8.7 (-8.29-2.47)	<0.001
Lumen area stenosis (%)	16.8 \pm 4.8	18.7 \pm 7.5	14.6 \pm 40.4 (1.09-28.04)	0.24

presence and persistence of edge dissections, study edge effects and look for causes of restenosis and thrombosis. In addition other IVUS-based imaging modalities, such as IVUS-VH, iMAP or palpography, can be used to study the serial compositional and mechanical changes of the plaque behind stent struts and also to follow the bioresorption of the new bioresorbable scaffolds, analyzing the backscattering signal coming from the polymeric struts.

The 20-MHz IVUS catheter is not a sheath-based pullback system, and the mechanical pullback of the IVUS catheter itself (0.5 mm/s) can be impeded by calcium or tortuosity, so the measurement of the scaffold length is not always reliable. Therefore, we reported our IVUS measurements in area units and not in volume (area time length) units. Although the term late recoil has been used frequently in interventional cardiology to describe the constrictive remodeling of the external elastic membrane area, in the present case, it relates more specifically to the area reduction of the treated segment, a phenomenon not previously observed in metallic stents which was attributed to early alteration of the mechanical integrity of the scaffold.

Late loss measurements by QCA, scaffold area assessment by gray-scale IVUS all confirm the almost complete disappearance of this phenomenon. On gray-scale IVUS, the intrascaffold neo-intima is conventionally measured from endoluminal leading edges of echogenic struts and is minimal (0.07 mm²) in the present analysis.

6. Limitations

A relatively small number of patients with a short duration of follow-up.

7. Conclusions

The promising results at 6 months of bioresorbable drug-eluting scaffold constitute proof of concept that this device can adequately revascularize coronary vessels and prevent restenosis. Considering the favorable outcomes of BVS, it is deemed appropriate and timely to initiate a randomized pivotal trial comparing a metallic drug-eluting stent with this drug-eluting Bioresorbable Vascular Scaffold.

Conflict of interest

None declared.

References

- Garg S, Serruys PW. Coronary stents: looking forward. *J Am Coll Cardiol* 2010;**56**:S43-78.
- Räber L, Wohlwend L, Wigger M, et al. Five-year clinical and angiographic outcomes of a randomized comparison of sirolimus-eluting and paclitaxel-eluting stents: results of the Sirolimus-Eluting

- Versus Paclitaxel-Eluting Stents for Coronary Revascularization LATE trial. *Circulation* 2011;**123**:2819–28.
3. Gogas Bill D, Farooq Vasim, Onuma Yoshinobu, Serruys Patrick W. The ABSORB Bioresorbable Vascular Scaffold: an evolution or revolution in interventional cardiology? *Hellenic J Cardiol* 2012;**2012**(53):301–9.
 4. Ormiston JA, Serruys PWS. Bioabsorbable coronary stents. *Circ Cardiovasc Interv* 2009;**2**:255–60.
 5. Okamura T, Onuma Y, García-García HM, Regar E, Wykrzykowska JJ, Koolen J, et al. 3-Dimensional optical coherence tomography assessment of jailed side branches by bioresorbable vascular scaffolds aproposal for classification. *J Am Coll Cardiol Cardiovasc Interv* 2010;**3**:836–44.
 6. Onuma Y, Serruys PW, Perkins LEL, Okamura T, Gonzalo N, García- García HM, et al. Intracoronary optical coherence tomography and histology at 1 month and at 2, 3 and 4 years after implantation of everolimus-eluting bioresorbable vascular scaffolds in aporcine coronary artery model: an attempt to decipher the human optical coherence tomography images in the ABSORB trial. *Circulation* 2010;**2010**(122):2288–300.
 7. Tunstall-Pedoe H, Kuulasmaa K, Amouyel P, Arveiler D, Rajakangas AM, Pajak A. Myocardial infarction and coronary deaths in the World Health Organization MONICA Project. Registration procedures, event rates, and case-fatality rates in 38 populations from 21 countries in four continents. *Circulation* 1994;**90**:583–612.
 8. Serruys PW, Onuma Y, Garg S, Sarno G, van den Brand M, Kappetein AP, et al. Assessment of the syntax score in the SYNTAX study. *Euro Interv* 2009;**5**:50–6.
 9. Mintz GS, Nissen SE, Anderson WD, Bailey SR, Erbel R, Fitzgerald PJ, et al. American College of Cardiology clinical expert consensus document on standards for acquisition, measurement and reporting of intravascular ultrasound studies (IVUS): a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2001;**37**:1478–92.