Perspective

Bioresorbable vascular scaffolds—what does the future bring?

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Abstract: Bioresorbable vascular scaffolds (BVS) have emerged as an interesting alternative since the presence of the prosthesis in the coronary artery is transient. This technology enables to restore the normal vasomotor tone and allows positive remodeling, simultaneously reducing the trigger for persistent inflammation and facilitating further interventions by percutaneous or surgical means. Absorb BVS® is the first generation everolimus-eluting poly-L-lactide (PLLA) bioresorbable scaffold. In recent meta-analyses Absorb BVS® was definitely proved to be safe and effective device in the treatment of symptomatic coronary artery disease. This was recently confirmed by FDA advisory panel of experts who recommended approval of the device based on an analysis of its risks and rewards. Nevertheless, still there are some concerns regarding stent thrombosis, and the real vessel functionality restoration at long-term observation. Worth mentioning is the fact that apart from stable coronary disease Absorb BVS® is used successfully in a series of off-label clinical settings such as acute coronary syndromes including STEMI, in-stent restenosis, coronary bifurcations, left main stenting or chronic total occlusions. Moreover, new bioresorbable scaffolds are under development with DEsolve® and DREAM 2G®, which are the most advanced.

Keywords: Absorb; DEsolve; DREAM 2G; hybrid approach

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Introduction

Drug-eluting stents (DES) have significantly improved long-term outcomes of percutaneous coronary interventions (PCI) by decreasing the excessive growth of neointima. However, the permanent presence of the metallic platform and the durable polymer might impair the natural healing process of the coronary vessel wall, leading to the prolonged inflammatory response and untoward clinical outcomes (1,2).

Recently, PCI with bioresorbable vascular scaffolds (BVS) have emerged as an interesting alternative since the presence of the prosthesis in the coronary artery is transient. This technology enables to restore the normal vasomotor tone and allows positive remodeling, simultaneously reducing the trigger for persistent inflammation and facilitating further interventions by percutaneous or surgical means. Also, in theory it should offer reduced or even abolished late/very late stent thrombosis risk (3).

The balloon-expandable Absorb BVS® (Abbott Vascular) consists of a poly-L-lactide (PLLA) backbone (strut thickness 150 μm), the anti-proliferative drug everolimus at the concentration of 100 μg/cm^2 (Novartis Pharmaceuticals Corporation) and poly-D, L-lactide polymer in a 1:1 ratio (PDLLA). Both PLLA and PDLLA are fully bioresorbable. PDLLA is thought to be totally resorbed in nine months and PLLA in approximately 24–36 months. A lactic acid is the final product of both PLLA and PDLLA degradation (4).

Absorb BVS as good as Xience?

Recently, in the *Lancet* journal, Stone *et al.* published a paper comparing Abosrb BVS® and Xience® (cobalt-chromium everolimus-eluting stent) (5). It was a meta-analysis of four randomized trials (ABSORB II, ABSORB

Japan, ABSORB China, and ABSORB III) in which patients with stable coronary artery disease or a stabilized acute coronary syndrome were enrolled. This meta-analysis of 3,389 randomly assigned patients provided greater power to analyze effectiveness and safety profile of Absorb BVS® versus Xience® than each individual study alone. The analysis yielded similar results for Absorb BVS® and for Xience® regarding the patient-oriented composite endpoint (all-cause mortality, all myocardial infarction, or all revascularization) as well as the device-oriented composite endpoint (cardiac mortality, target vessel-related myocardial infarction, or ischemia-driven target lesion revascularization) at 1 year. Although Absorb BVS® is the first-generation BVS technology and despite the fact that in these trials Absorb BVS® was compared with one of the lowest rate of stent thrombosis devices, the accumulation of available data supported the safety and effectiveness of Absorb BVS® at 12 months in the treatment of patients with stable coronary artery disease or stabilized acute coronary syndromes.

However, one should also mention some limitations of this paper. In three from four analyzed studies (Absorb Japan, Absorb China, Abosrb III) the device overlap was forbidden unless bailout stenting was required. Moreover, the treated lesion length was rather short (mean value: 13 mm). Also in the group of Absorb BVS® significantly more frequently more potent new generation P2Y12 inhibitors (ticagrelor, prasugrel) were used (24% *vs.* 21%, P=0.047). And finally, the routine angiography was performed very diversely (not at all in Absorb III or after 3 years in Absorb II) what also might influence on the target lesion revascularization/target vessel revascularization rates.

On the top of it, the procedure success rate was worse in the Absorb BVS® comparing with Xience® (95.6% *vs.* 99.4%, P<0.0001). And despite more aggressive optimization in the Absorb BVS® group or maybe because of it (post-dilatation 66.2% *vs.* 55.3%, P<0.0001), target lesion failure tended to be higher with Absorb BVS® comparing with Xience® within 30 days (target vessel related myocardial infarction 5.1% *vs.* 3.3%, P=0.04). Also, worth pointing out is the fact that authors stress many times in the paper very late thrombosis issue, but they presented only one year results. Moreover, in the presented data there was a trend for higher thrombosis rates in the Absorb BVS® group (definite/probable stent thrombosis 1.3% *vs.* 0.6%, P=0.08). Also, other recently published meta-analyses confirm similar target revascularization rates between Absorb BVS® and Xience®, but simultaneously they stress the increased risk of stent thrombosis as well (6-8).

And finally, the aim of developing BVS was to ensure vascular restoration therapy at long-term observation. However, although Absorb BVS® is available on the market for several years up to now there are published clinical trials showing only the vessel status after complete Absorb BVS® decomposition, and no vessel reactivity assessment (e.g., vessel lumen response to acetylcholine infusion) (4). However, there are two *in vivo* studies showing promising results in mid- and long-term follow-up (9,10). But today it already looks that stent struts should be thinner and probably the most advanced coronary lesions (calcified, severely fibrotic) do not prognosticate for regain of vessel function.

Hybrid approach—does it make sense?

Absorb BVS® deployment might facilitate to avoid performing the so-called "full metal jacket". As such, the hybrid use of BVS and classical DES might be an interesting approach. This strategy can be applied to reduce the costs of the PCI procedure as well as the length of a metallic scaffold. Moreover, BVS use only in long lesions with significantly calcified segments may not be reasonable if lesion preparation is inadequate or significant residual stenosis remains after balloon pre-dilatation. One should be aware that there are crucial differences in the sequence of stent (DES)—scaffold (BVS) deployment (11). In the hybrid DES-BVS technique, BVS lays on top of the metallic scaffold at the overlapped segment. If the BVS was positioned first proximally and then overlapped distally with a DES, the thinner metallic struts lay on top of the thicker BVS scaffold at the overlapped segment. Once the BVS scaffold under the metallic strut resorbs, it leaves an overhanging metallic strut segment that is not apposed to the vessel wall. The longer the overlapped segment, the longer the potentially malapposed stent segment is. Also, the expansive remodelling property of the BVS may contribute to the malapposition at the DES-BVS overlap junction. Therefore overlapping DES-BVS during PCI must be done adequately to minimize the potential risk of in-stent thrombosis (12). This approach was recently proved safe and effective (13).

Absorb BVS in various clinical settings

Apart from stable coronary disease Absorb BVS® is used successfully in a series of off-label clinical settings such as

acute coronary syndromes including STEMI (14-16), in-stent restenosis (17), coronary bifurcations (18), left main stenting (19) or chronic total occlusions (20). However, larger studies with long-term follow-up are needed to adequately address the safety and efficacy of Absorb BVS® use in such settings.

Future directions

Absorb BVS® is not the only biodegradable scaffold under development. As always with new technologies there are many issues in the prototype device introduced into the market that can be improved. The Absorb BVS® strut thickness is deemed to be potentially accountable for the increased adverse event rate. The new scaffolds being under development, as the DEsolve®, the MeRes100® or the Biolute® have strut thickness of 100, 100 and 108 μm, respectively (21). This improvement if successful allow for obtaining the proper radial strength with simultaneous decrease in the crossing profile. Additionally, thinner struts might minimize coronary blood flow perturbations and strut protrusion into the vessel lumen when overlapping as well as this can lead to the decreased thrombogenicity of such devices. Analogous technical improvement can be observed in the Mirage BVS® (a microfiber scaffold with streamlined strut geometry—round struts) that is supposed to decrease blood flow separation and ensure high shear stress with subsequent reduced platelet activation (21).

The another key issue is to establish the ideal right time for resorption bearing in mind that radial strength reduction cannot be too rapid. Shortening the resorption process might reduce the risk of stent thrombosis but also might account for the increased risk of vessel/plaque recoil. In this respect, promising results were reported with the DEsolve scaffold. Its biodegradation and bioresorption take place in one and two years, respectively (22).

Also, the possibility to post-dilatate the scaffold (preferably overexpand) without fracture poses another important issue. In this regard, the Fantom® (a desaminotyrosine-derived polycarbonate scaffold), the DEsolve® and the Amaranth Fortitude® (both PLLA-based polymer scaffolds) showed greater resistance to overexpansion. Moreover, magnesium-based metallic bioresorbable scaffolds were developed in order to ensure mechanical characteristics of a classic DES. After the initial discouraging results, the DREAMS 1G® (paclitaxel-eluting) and the DREAMS 2G® (sirolimus-eluting) scaffolds yielded promising results, as in BIOSOLVE II study (23,24).

Conclusions

Absorb BVS® was definitely proved to be safe and effective device in the treatment of symptomatic coronary artery disease. This was recently confirmed by FDA advisory panel of experts who recommended approval of the device based on the analysis of its risks and rewards. Also, Abbott Vascular Company said that 5-year superiority data will be presented in 2020, from its 5-year Absorb IV trial. Nevertheless, still there are some concerns regarding stent thrombosis, and the real vessel functionality restoration at long-term observation.

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Footnote

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References

1. Stettler C, Wandel S, Allemann S, et al. Outcomes associated with drug-eluting and bare-metal stents: a collaborative network meta-analysis. Lancet 2007;370:937-48.
2. Kandzari DE, Leon MB, Meredith I, et al. Final 5-year outcomes from the Endeavor zotarolimus-eluting stent clinical trial program: comparison of safety and efficacy with first-generation drug-eluting and bare-metal stents. JACC Cardiovasc Interv 2013;6:504-12.
3. Rzeszutko L, Depukat R, Dudek D. Biodegradable vascular scaffold ABSORB BVS™ - scientific evidence and

methods of implantation. Postepy Kardiol Interwencyjnej 2013;9:22-30.
4. Bil J, Pawlowski T, Gil RJ. Coronary spasm revascularized with a bioresorbable vascular scaffold. Coron Artery Dis 2015;26:634-6.
5. Stone GW, Gao R, Kimura T, et al. 1-year outcomes with the Absorb bioresorbable scaffold in patients with coronary artery disease: a patient-level, pooled meta-analysis. Lancet 2016;387:1277-89.
6. Cassese S, Byrne RA, Ndrepepa G, et al. Everolimus-eluting bioresorbable vascular scaffolds versus everolimus-eluting metallic stents: a meta-analysis of randomised controlled trials. Lancet 2016;387:537-44.
7. Zhang XL, Zhu L, Wei ZH, et al. Comparative Efficacy and Safety of Everolimus-Eluting Bioresorbable Scaffold Versus Everolimus-Eluting Metallic Stents: A Systematic Review and Meta-analysis. Ann Intern Med 2016;164:752-63.
8. Lipinski MJ, Escarcega RO, Baker NC, et al. Scaffold Thrombosis After Percutaneous Coronary Intervention With ABSORB Bioresorbable Vascular Scaffold: A Systematic Review and Meta-Analysis. JACC Cardiovasc Interv 2016;9:12-24.
9. Gogas BD, Benham JJ, Hsu S, et al. Vasomotor Function Comparative Assessment at 1 and 2 Years Following Implantation of the Absorb Everolimus-Eluting Bioresorbable Vascular Scaffold and the Xience V Everolimus-Eluting Metallic Stent in Porcine Coronary Arteries: Insights From In Vivo Angiography, Ex Vivo Assessment, and Gene Analysis at the Stented/Scaffolded Segments and the Proximal and Distal Edges. JACC Cardiovasc Interv 2016;9:728-41.
10. Lane JP, Perkins LE, Sheehy AJ, et al. Lumen gain and restoration of pulsatility after implantation of a bioresorbable vascular scaffold in porcine coronary arteries. JACC Cardiovasc Interv 2014;7:688-95.
11. Yew KL. Overlapping technique for hybrid percutaneous coronary intervention strategy utilising drug eluting stent and ABSORB bioresorbable vascular scaffold. Int J Cardiol 2015;178:e8-e10.
12. Capodanno D, Gori T, Nef H, et al. Percutaneous coronary intervention with everolimus-eluting bioresorbable vascular scaffolds in routine clinical practice: early and midterm outcomes from the European multicentre GHOST-EU registry. EuroIntervention 2015;10:1144-53.
13. Gil RJ, Bil J, Pawłowski T, et al. The use of bioresorbable vascular scaffold Absorb BVS® in patients with stable coronary artery disease: one-year results with special focus on the hybrid BVS and DES treatment. Kardiol Pol 2016;74:627-33.
14. Kraak RP, Hassell ME, Grundeken MJ, et al. Initial experience and clinical evaluation of the Absorb bioresorbable vascular scaffold (BVS) in real-world practice: the AMC Single Centre Real World PCI Registry. EuroIntervention 2015;10:1160-8.
15. Dudek D, Rzeszutko Ł, Zasada W, et al. Bioresorbable vascular scaffolds in patients with acute coronary syndromes: the POLAR ACS study. Pol Arch Med Wewn 2014;124:669-77.
16. Chakraborty R, Patra S, Banerjee S, et al. Outcome of everolimus eluting bioabsorbable vascular scaffold (BVS) compared to non BVS drug eluting stent in the management of ST-segment elevation myocardial infarction (STEMI) - A comparative study. Cardiovasc Revasc Med 2016;17:151-4.
17. Jamshidi P, Nyffenegger T, Sabti Z, et al. A novel approach to treat in-stent restenosis: 6- and 12-month results using the everolimus-eluting bioresorbable vascular scaffold. EuroIntervention 2016;11:1479-86.
18. Capranzano P, Gargiulo G, Capodanno D, et al. Treatment of coronary bifurcation lesions with bioresorbable vascular scaffolds. Minerva Cardioangiol 2014;62:229-34.
19. Cortese B, Orrego PS, Sebik R, et al. Biovascular scaffolding of distal left main trunk: experience and follow up from the multicenter prospective RAI registry (Registro Italiano Absorb). Int J Cardiol 2014;177:497-9.
20. Vaquerizo B, Barros A, Pujadas S, et al. Bioresorbable everolimus-eluting vascular scaffold for the treatment of chronic total occlusions: CTO-ABSORB pilot study. EuroIntervention 2015;11:555-63.
21. Caiazzo G, Kilic ID, Fabris E, et al. Absorb bioresorbable vascular scaffold: What have we learned after 5 years of clinical experience? Int J Cardiol 2015;201:129-36.
22. Abizaid A, Costa RA, Schofer J, et al. Serial Multimodality Imaging and 2-Year Clinical Outcomes of the Novel DESolve Novolimus-Eluting Bioresorbable Coronary Scaffold System for the Treatment of Single De Novo Coronary Lesions. JACC Cardiovasc Interv 2016;9:565-74.
23. Haude M, Ince H, Abizaid A, et al. Safety and performance of the second-generation drug-eluting absorbable metal

scaffold in patients with de-novo coronary artery lesions (BIOSOLVE-II): 6 month results of a prospective, multicentre, non-randomised, first-in-man trial. Lancet 2016;387:31-9.
24. Haude M, Erbel R, Erne P, et al. Safety and performance of the drug-eluting absorbable metal scaffold (DREAMS) in patients with de-novo coronary lesions: 12 month results of the prospective, multicentre, first-in-man BIOSOLVE-I trial. Lancet 2013;381:836-44.

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