Use of bioresorbable scaffolds in cardiology practice today, where do we stand?

Use of bioresorbable technology is long dated in medicine dating back to resorbable sutures to closure devices used after femoral access. Use of bioresorbable scaffolds in interventional cardiology heralded a major breakthrough in terms of its ability to dissolve after a specified period allowing the vessel to reassume its vascular responsiveness (auto-regulation) and patency. Since its introduction in humans in 2006, BVS has shown excellent safety and feasibility at implantation. Initial one year results from major trials and registries shows comparable results to benchmark Drug Eluting Stents Longer term follow up showed higher target vessel revascularization due to higher periprocedural MI and emergence of late scaffold thrombosis risk that is higher than for metallic drug eluting stents. Furthermore vessel autoregulation remained deficient after 2 years in some trials. Abbott decided to halt production as of September 2017 citing low market penetration. Further use in the setting of registries and studies continues. Many of results are yet awaited.

Keywords: bioresorbable scaffolds, percutaneous intervention, scaffold thrombosis, periprocedural MI

Introduction

In 1977, Andreas Gruntzig performed the first human balloon angioplasty and ushered in the era of percutaneous treatment for coronary artery disease. Initial enthusiasm was tampered down by reports of acute vessel occlusion due to dissections and late constrictive remodeling. Next large leap was the introduction of bare metal stents. The BENESTENT trial reported reduced vessel restenosis (22% vs. 32%, P=0.02), and the need for repeat coronary angioplasty (RR, 0.58; P=0.005) in BMS treated patients [1,2]. The rate of sub-acute vessel occlusion decreased to 1.5%; reducing the need for emergency bypass surgery.

In 1996, researchers introduced dual antiplatelet instead of anticoagulant therapy, resulting in 82% lower risk of MI and 78% reduction in need for repeat interventions (RR 0.25(0.06-0.77) [3].

In 2001, Surreys first reported on Drug Eluting Stents in 45 patients treated with Sirolimus eluting Bx VELOCITY stents with negligible neo-intimal hyperplasia at one year follow-up [4]. The RAVEL trial reported lower mean late luminal loss (-0.01 mm vs. 0.80 mm, P<0.001) and no recurrent revascularization attempts (vs. 26% in control). Reports about late stent thrombosis surfaced, which increased to 3.5% at 4 years [5-7].

The promise of bioresorbable scaffolds

Initially, Tamai examined the feasibility of a bio-absorbable poly-L-lactic acid (PLLA) Igaki-Tamai stents (Igakl Medical, Kyoto, Japan), with a thickness of 0.17 mm, a zigzag helical coil pattern (not drug eluted) [8,9]. They reported 18% repeat revascularization at 4 years, and 28% target vessel revascularization at 10 years [10]. One case of definite stent thrombosis was reported [10-14]. Di Mario et al used magnesium stents in denovo coronary lesions, with modest results (1 year Target Lesion Revascularization rate 45%) [11].

The Bioresorbable Vascular Scaffold (BVS) (Abbott Vascular, California) consists of processed Poly-L-Lactic acid (PLLA) backbone covered with amorphous Everolimus/PLA matrix coating for controlled drug release [12,13]. The use of polylactic acid is widespread in clinical practice, ranging from absorbable sutures to orthopedic screws and dermatology fillers. Safety of PLLA is supported by the benign vascular response to its use in Angioseal

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*Author for correspondence: welabbassi@yahoo.com closure devices. PDLLA (poly (D,L-lactide), the polymer used for controlled release of Everolimus, has been used previously [14]. Everolimus (Novartis, Switzerland) is a semisynthetic macrolide immunosuppressant which blocks cell proliferation by arresting cell division in G1-S phase. BVS contains 8.2 mcg/mm of Everolimus, 80% of which is released within 30 days; similar to Xience V stent. Safety and efficacy of Everolimus eluting stents were attested in SPIRIT and FUTURE trials [14-16].

The BVS stent strives to perform comparably to others: its crossing profile is comparable to that of BX Velocity stent (1.4 mm). At room temperature, its radial strength is similar to MULTILINK stent [12]. Its balloon delivery system is the same as for MULTI LINK, VISION and XIENCE V stents. BVS shows higher conformability to vessel structure [17-22].

Its initial version (Revision 1.0) had to be stored at low temperatures to avoid device instability and cracks upon deployment. The second generation (Revision 1.1) can be stored at room temperature [20,23,24]. Its previous polymer treatment and scaffold design were replaced with in-phase zigzag hoops linked by bridges, allowing for more uniform strut distribution, higher radial support, less vessel recoil and uniform drug distribution [25-31].

The BVS is composed of repeating units of PLLA/PDLLA. After implantation, bonds between repeating units get hydrolyzed producing lactic acid, which is metabolized via Krebs cycle [21]. Residual small particles (<2 micrometers) are phagocytized by macrophages.

Chemically, scaffold resorption takes place in three phases; initially water starts hydrolysis of ester bonds, resulting in decline in stent's molecular weight. In the second stage there is scission of chains linking regions, causing decline in radial strength. At third stage, remaining short polymer chains diffuse out of the device to get reabsorbed into blood.

Degradation of scaffold governs mechanical performance, which divides into three phases: during initial "revascularization phase" it acts like mainstream drug eluting stents (comparable deliverability, minimal acute recoil and high radial strength). At the restoration phase there is hydrolysis at amorphous regions and connecting points, causing a decline in radial strength. In studied cases it took three months after implantation to start. During the last "resorption phase" the BVS becomes discontinuous and ceases to act as a scaffold while it continues its hydrolysis to generate Land D-lactate into the body [22], while stent strut sites become occupied by proteoglycan material and strut outline becomes surrounded by calcification [23]. In most cases this may take up to 24 months. In animal studies there was complete luminal endothelialization and minimal Inflammatory response, comparable to earlier reports with Cypher stents (J&J, Miami,Fl) [12]. At 6 months these arteries were still splinted; and at 12 months the vessel became capable of auto-vasomotion [12,24].

In 2006, Ormiston J reported on the first in man implantation at mid LAD [13]. In 2008 the ABBSORB FIRST reported on 30 patients with single denovo coronary lesions with 94% device success [17]. At one year one patient had target vessel revascularization. IVUS showed post-procedural incomplete strut apposition in 6 patients. No late stent thrombosis recorded. At 6 months, the OCT sub-study showed 99% of struts where tissue covered. At 2 years there was 34.5% decrease in strut thickness [24]. These patients showed higher acute stent recoil than EES stents (percent recoil 6.9% vs. 4.3% historical data from SPIRIT FIRST and SPIRIT II; P=0.25) [18], IVUS data also noted significant late stent recoil (7.6% vs. 0.03% Xience V [15,17,19]. This translated into 0.44 mm late lumen loss at six months. Partly, this is due to neointimal hyperplasia; rest is due to reduction inside stent area. Hyperplasia was comparable to that observed in SPIRIT FIRST with Xience and better than with BMS [25]. Reduction in inside stent area was due to acute stent recoil, non-uniform vessel wall support and loss of radial strength through scaffold resorption. Instent restenosis rate was 11.5%, which did not necessitate re-intervention [28,29].

From 6 months to 2 years there was a reduction in plaque area [20-24], while the vessel size remained same, leading to gain in lumen area, with no scaffold mal-apposition noted [26]. At 3 and 5 years [27,31-33], the ischemia-driven major adverse cardiac event rate was 3.4%. Scaffold thrombosis was not observed.

The ABSORB II trial enrolled 501 patients with one or two de-novo native vessel disease to receive BRS or Xience (Abbott Vascular, Santa Clara, CA, USA) [34-38]. Although acute recoil was similar, acute lumen gain was less for BVS (IVUS: 2.85 mm² vs. 3.60 mm², p<0.0001) [39-44]. Composite device orientated endpoint at 1-year was similar (5% vs. 3%, p=0.35, MI (4% vs. 1%), TLR 1% vs. 2%) [45,46-49]. Three BVS patients had definite or probable scaffold thrombosis. At three years BVS showed no difference in vasomotor reactivity (BVS 0.047 mm vs. Xience 0.056 mm; $p_{superiority}$ 0.49) [50-55,58]. Late luminal loss was larger for BVS (0.37 mm vs. 0.25 mm; $p_{\text{non-inferiority}}$ 0.78). This was confirmed by IVUS (BVS MLA 4.32 mm² vs. 5.38 mm² Xience; p<0.0001). There was a higher rate of device-oriented composite endpoint due to more target vessel MI (10% vs. 5%, HR 2.17; 1.01-4.70; p=0.0425; target vessel MI: 6% vs. 1%; p=0.0108) [53-56].

The ABSORB III is a multicenter trial where 2008 patients undergoing PCI for one or two new native coronary lesions, randomly assigned to BRS or Xience [51]. High-pressure post-dilatation was enforced to achieve <10% residual stenosis. Acute segmental gain was less for BVS, as was MLA. At 1 year target-lesion failure occurred in 7.8% of BVS and 6.1% in Xience $(p_{non-inferiority} = 0.007, p_{superiority} = 0.15)$. Sub-acute thrombosis up to 30 days was more common with BVS, similar to findings noted from GHOST EU (1.4% 30 days, 1.9% 180 days, 2.0% 360 days). The primary end point remained similar between years 1 and 2 [57-59]. At the end of year 2, BVS arm had a higher risk of target lesion failure (10.9% vs.7.8% for DES; p<0.05). This is driven by target vessel MI (7.3% vs. 4.9% for DES; p<0.05).

The ABSORB IV trial avoided small vessels, while aggressive pre-dilatation and routine high-pressure post-dilatation were encouraged [60]. 3000 patients were randomized 1:1 to Absorb BVS or XIENCE). Post-dilatation was at pressures 16-18 atmospheres, and with a balloon-to-scaffold ratio of 1.1-1. At 30 days, TVF occurred in 5.1% of BVS patients and 3.7% of EES patients (p=0.07). The composite of death, MI, and revascularization occurred in 5.2% of BVS and 4.1% of EES patients (p=0.17). Device thrombosis occurred in 0.6%

of BVS vs. 0.2% of EES patients (p=0.06) [61].

The EVERBIO II randomly assigned 240 patients to EES, Biolimus Eluting Stents (BES), or BVS [50]. Nine months in-stent lumen loss was similar (BVS: 0.28 mm vs. EES/BES: 0.25 mm; p=0.30). Patient-oriented MACE was similar (27% in BVS; 26% in EES/BES group; p=0.83) as was device-oriented MACE rate (12% in BVS; 9% in the EES/BES group; p=0.6).

In the largest metanalysis of BVS trials (3389 patients with stable CAD or stabilized ACS assigned to BVS: n=2164) or Xience: n=1225) [52]. BVS implantation took longer (43.7 vs. 39.7, p<0.05), attained a smaller reference vessel diameter (2.37 vs. 2.58; p<0.05), despite a higher post-dilatation rate (66% vs. 55%; p<0.05); and required a higher IVUS/OCT use (23.9 vs. 20; p=0.02). At 1 year, rates of patient-oriented and device-oriented composite endpoints were similar (RR] 1.09 (0.89-1.34), p=0.38 for earlier and 1.22;0.91-1.64, p=0.17 for latter), the rate of Target vessel MI was increased with BVS due to increased periprocedural myocardial infarction and device thrombosis with BVS (TVMI RR 1.45; 1.02-2.07, p=0.04; BVS thrombosis 1.3% vs. 0.6%; RR 2.09:0.92-4.75, p=0.08), highlighting the issue of BVS thrombosis and shedding light on the need for attention to details required when implanting BVS.

Evidence from real life registries

The large GHOST-EU registry in 11 European centers looked at target lesion failure among 1549 lesion in 1,304 real life patients [35]. It was an "all-comer" registry, including patients with ostial lesions, in-stent restenosis (ISR), bifurcations, chronic total occlusions and left main disease. 53% of patients were treated for stable angina, while rest presented with an acute coronary syndrome. Acute technical success was 99.7%. Target Lesion Failure was 2.2% at 30 days; 4.4% at six months. At six months cardiac death was 1.0%, target vessel infarction was 2.0%, and Target Lesion Revascularization was 2.5%. Procedural-related myocardial injury was higher in the BVS group (25% vs. 12%, p=0.001). Diabetes mellitus was an independent predictor of TLF (HR 2.41; 1.28-4.53; p<0.05). The incidence of definite/probable scaffold thrombosis was 1.5% at 30 days and 2.1% at six months. Diabetes mellitus and the treatment of ostial lesions were independent risk factors [36]. Patients with ostial lesions had higher incidence of prior revascularization and less post-dilation (43% vs. 58% in non-ostial group, p=0.008) and higher residual stenosis (30% vs. 26%, p=0.035). 12-month rates of scaffold thrombosis were 4.9% vs. 2.0% (ostial vs. non-ostial lesion, p=0.005; HR 2.65; 1.41-4.97; p=0.0025) [37]. Sizing was another important issue. Quantitative coronary angiography (OCA) showed that BVS patients with under-sizing had more MACE (7.9% vs. 4.6%; p=0.015; HR 2.65; 95% CI: 1.27-5.53, p=0.009). This was true for the number of implanted scaffolds too (HR 1.33; 1.04-1.70, p=0.024). BVS overlap did not increase MACE (HR 1.05, 0.48-2.20; P = 0.904) [46], as confirmed by another group [47].

Another analysis looked at BVS use in diffusely diseased vessels [39]. Patients were divided into 3 groups [short: <30mm), intermediate: 30-60mm), and long scaffold length: \geq 60mm). Patients with longer BRS were mostly diabetics (24% vs. 30.8% vs. 34.6%, p=0.01) with higher SYNTAX scores (10.4 ± 7.2 vs. 14.6 ± 8.6 vs. 16.4 ± 7.8, p<0.001). Despite higher use of Intravascular ultrasound and postdilatation, there was higher incidence of periprocedural myocardial infarction (MI) in longer BVS group (6.5% vs. 7.5% vs. 11.3%, p=0.45). Target lesion failure was higher at 1-year (14.3% long vs. 4.8% in short and 4.5% in intermediate group; p=0.001). This lead to a higher rate of repeat revascularization (HR=1.962; 95% CI: 1.25-3.08; p=0.0034) [39]. Incidence of scaffold thrombosis was higher in the long stent group (3.8% vs. 2.1% in short, 1.1% in intermediate group; p=0.29) [38]. Mode of presentation was significant determinant too (one year MACE 3.7% in stable vs. 6.9% in ACS patients; p<0.05). BVS restenosis was observed in 15.6% among diffusely diseased lesions (median follow-up 192 days), compared to 3.4% ISR in the whole GHOST EU registry [42]. Overall, restenosis patients had a higher prevalence of diabetes (20% vs. 7%, p=0.03), longer implanted BVS $(33.4 \pm 26 \text{ mm vs. } 28.0 \pm 18 \text{ mm, } p=0.33)$, more residual stenosis >20% (56% vs. 9%, p<0.001) despite higher post-dilation rate (55% vs. 30%, p=0.02). BVS restenosis was mostly focal (body in 47%, margin in 35%) and rarely diffuse (3% of lesions). Total occlusion was observed in 6% of lesions and aneurysm formation was

seen in 6% of lesions. Percent residual stenosis post implantation was the only independent predictor for restenosis [40,42].

In another registry, 302 bifurcation lesions were treated using BVS (provisional singlestenting 86%; elective double-stenting 14%). True bifurcation (Medina 1,1,1/1,0,1/0,1,1) were observed in 45%. Pre-dilation and postdilation of the main branch were performed in 96% and 61%. Final kissing inflation with small protrusion of a side branch balloon into main branch was performed in 19%. At 356 days follow up rates of target lesion failure and scaffold thrombosis were high at 6.4% and 2.5%. Independent predictors for TLF were ACS presentation and diabetes (HR 4.67; 1.78-12.3; P=0.002 and HR 3.37; 95%:1.38-8.26; P=0.008, respectively). Majority of patients with scaffold thrombosis occurred within 35 days from index PCI (75%) and lacked use of intravascular imaging [41,44].

Presenting with ACS once more showed poorer outcomes (MACE 9.3% vs. 4.7%, p<0.001; TLR 6.1% vs. 1.9%, p<0.001), with stent thrombosis also increased (BVS 2.8% vs. 0.9% EES group, p=0.01) [46]. Here postdilatation resulted in lower MACE (BVS with post-dilatation 6.0% vs. 12.6% BVS without post-dilatation vs. 4.7% EES group, p<0.001). Post dilatation did not alter the rate of Stent thrombosis (post-dilatation: 2.6% vs. no post-dilatation: 3.2% vs. 0.9%: EES patients, p=0.045) [46].

Review of real world registries shows an increasing trend for post-dilation. We note a change from 52.3% rate in GHOST EU, to 68% in GABI-R, 72% in FRANCE ABSORB, to 96.8% in IT-DISAPPEAR; which also enrolled the most complicated patients (59%, diabetics 23.7%, bifurcation lesions 22.3%) [37,53-56]. This is accompanied by a concomitant decline in BVS thrombosis, initially observed at 3.4% in GHOST EU (least post-dilatation rate) to 0.6% in IT-DISAPPEAR.

Recent emphasis on implantation technique formulated the nomenclature of four PS': Prepare the lesion with non-compliant balloon, Proper sizing with use of intracoronary nitroglycerin and imaging as necessary; Pay attention to expansion limits; staying within nominal limits of 0.5 mm and expanding the scaffold at 2 mm every five seconds while implanting, then staying 30 seconds when fully expanded before deflating. Finally Post-dilating with a noncompliant balloon at high pressure aiming at <10% residual stenosis after implantation. By using this protocol and avoiding small vessels with lumen diameters <2.5; BVS thrombosis rates can be reduced by 70% [57].

In order to clarify the issues concerning BVS use for clinicians, the FDA issued a "Dear Doctor" letter noting it that the higher risk of stent-related thrombosis and other major cardiac events among patients who got Absorb GT1 BVS is under investigation. It reminds operators using BVS to follow instructions in FDA labeling, avoiding its use in small vessels and to adhere to the label's recommended implantation technique.

In 14th September 2017, Abbott decided to voluntarily withdraw its product from market except for patients in the setting of a registry or study, citing low market penetration. Abbott promised to come back with a new improved scaffold of 92 micrometer thickness.

To summarize, despite having only a fraction of the tensile strength of metallic stents (30-45 compared to 820 to 1200 MPA); the

BVS showed favorable 1 year results in large studies despite a possible small but statistically significant increased risk of peri-procedural MI. Longer term follow up showed higher BVS late thrombosis rates and higher target lesion failure. This may be due to numerous factors. For example, 19% of patients in ABSORB III were treated for vessels which were smaller than the size advised by the FDA [58-61]. Clinicians tend to use visual assessment to in estimating vessel size rather than quantitative analysis. This may result in underestimating vessel size. Moreover, techniques of implantation have been largely suboptimal (only 63% of BVS recipients had post-dilatation in ABSORB III). Diligent attention to choosing vessels of appropriate diameter and paying attention to technique of implantation, more frequent use of imaging for vessel sizing should result in improved outcomes. This needs to be shown in long-term follow up of Absorb III and IV studies which could then open the door for introduction of newer generation of scaffolds. Other scaffolds are also already in clinical use [62,63], though to a lesser extent and their long term clinical efficacy remains to be shown too.

REFERENCES

Meier B, Rutishauser W. Transluminal Coronary Angioplasty-state of the art 1984. *Acta. Med. Scand. Suppl.* 701, 142-147 (1985).

Surreys PW, De jeaggere P, Keimeneij F, et al. A comparison of Balloon expandable stent implantation with balloon angioplasty in patients with coronary artery disease. Benestent Group. *N. Engl. J. Med.* 331(8), 489-495 (1994).

Schömig 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.* 334(17), 1084-1089 (1996).

Sousa JE1, Costa MA, Abizaid AC, et al. Sustained suppression of neointimal proliferation by sirolimus-eluting stents: one-year angiographic and intravascular ultrasound follow-up. *Circulation*. 104(17), 2007-2011 (2001).

Morice MC1, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N. Engl. J. Med.* 346(23), 1773-1780 (2002).

Daemen J1, Wenaweser P, Tsuchida K, et al. Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. *Lancet.* 369(9562), 667-678 (2007).

Serruys PW, Onuma Y, Garg S, et al. 5-Year Clinical Outcomes of the ARTS II (Arterial Revascularization Therapies Study II) of the Sirolimus-Eluting Stent in the Treatment of Patients With Multivessel De Novo Coronary Artery Lesions. *J. Am. Coll. Cardiol.* 55(11), 1093-1101 (2010).

Ormiston JA1, Serruys PW, Regar E, et al. A bioabsorbable everolimus-eluting coronary stent system for patients with single de-novo coronary artery lesions (ABSORB): a prospective open-label trial. *Lancet.* 371(9616), 899-907 (2008).

Tamai H, Igaki K, Kyo E, et al. Initial

and 6-month results of biodegradable poly-l-lactic acid coronary stents in humans. *Circulation*. 102(4), 399-404 (2000).

Tamai H. Biodegradable stents. Four year follow up. TCT 2004. Washington DC (2004).

Erbel R, Di Mario C, Bartunek J, et al; PROGRESS-AMS (Clinical Performance and Angiographic Results of Coronary Stenting with Absorbable Metal Stents) Investigators. Temporary scaffolding of coronary arteries with bioabsorbable magnesium stents: a prospective, nonrandomised multicentre trial. *Lancet*. 369(9576), 1869-1875 (2007).

Absorb Trial Investigator Brochure. Abbott Vascular, Santa Clara, Ca.

Ormiston JA, Webster MW, Armstrong G. First-in-human implantation of a fully bioabsorbable drug-eluting stent: the BVS poly-L-lactic acid everolimus-eluting coronary stent. *Catheter Cardiovasc. Interv.* 69(1), 128-131 (2007).

Grube E, Sonoda S, Ikeno F, et al. Six- and twelve-month results from first human experience using everolimuseluting stents with bioabsorbable polymer. *Circulation*. 109(18), 2168-2171 (2004).

Serruys PW, Ong AT, Piek JJ, et al. A randomized comparison of a durable polymer Everolimus-eluting stent with a bare metal coronary stent: The SPIRIT first trial. *EuroIntervention* 1(1), 58-65 (2005).

Tsuchida K, Piek JJ, Neumann FJ, et al. One-year results of a durable polymer everolimus-eluting stent in de novo coronary narrowings (The SPIRIT FIRST Trial). *EuroIntervention*. 1(3), 266-272 (2005).

Ormiston JA, Serruys PW, Regar E, et al. A bioabsorbable everolimus-eluting coronary stent system for patients with single de-novo coronary artery lesions (ABSORB): a prospective open-label trial. *Lancet.* 371(9616), 899-907 (2008).

Tanimoto S, Serruys PW, Thuesen L, et al. Comparison of in vivo acute stent recoil between the bioabsorbable everolimuseluting coronary stent and the everolimuseluting cobalt chromium coronary stent: insights from the ABSORB and SPIRIT trials. *Catheter Cardiovasc Interv.* 70(4), 515-523 (2007).

Tanimoto S, Bruining N, Radeva P et al. Late stent recoil of the bioabsorbable everolimus-eluting coronary stent and its relationship with plaque morphology. *J. Am. Coll. Cardiol.* 52(20), 1616-1620 (2008).

García-García HM, Gonzalo N, Thuesen L, Ormiston JA, Serruys PW. Assessment of the absorption process following bioabsorbable everolimuseluting stent implantation: temporal changes in strain values and tissue composition using intravascular ultrasound radiofrequency data analysis. A sub study of the ABSORB clinical trial.

EuroIntervention. 4(4), 443-448 (2009).

García-García HM, Schultz C, Duckers E, Ligthart J, van Geuns RJ. Five-year follow-up of the ABSORB bioresorbable everolimus-eluting vascular scaffold system: multimodality imaging assessment.

EuroIntervention. 8(10), 1126-1127 (2013).

Oberhauser JP, Hossainy S, Rapoza RJ. Design principles and performance of bioresorbable polymeric vascular scaffolds. *EuroIntervention.* 5 Suppl F, F15-22 (2009).

Vorpahl M, Finn AV, Nakano M, Virmani R. The bioabsorption process: tissue and cellular mechanisms and outcomes. *EuroIntervention*. 5 Suppl F, F28-35 (2009).

Garg S, Serruys P. Biodegradable stents and non-biodegradable stents. *Minerva Cardioangiol.* 57(5), 537-565 (2009).

Serruys PW, Ong AT, Piek JJ, et al. A randomized comparison of a durable polymer Everolimus-eluting stent with a bare metal coronary stent: The SPIRIT first trial. *EuroIntervention*. 1(1), 58-65 (2005).

Serruys PW, Ormiston JA, Onuma Y, et al. A bioabsorbable everolimuseluting coronary stent system (ABSORB): 2-year outcomes and results from multiple imaging methods. *Lancet*. 373(9667), 897-910 (2009).

Onuma Y, Thuesen L, Webster M, Nieman K, Serruys PW. Fiveyear clinical and functional multislice computed tomography angiographic results after coronary implantation of the fully resorbable polymeric everolimuseluting scaffold in patients with de novo coronary artery disease: the ABSORB cohort A trial. *JACC Cardiovasc Interv.* 6(10), 999-1009 (2013).

Nishio S, Kosuga K, Igaki K, et al. Long-Term (>10 Years) clinical outcomes of first-in-human biodegradable poly-llactic acid coronary stents: Igaki-Tamai stents. *Circulation*. 125(19), 2343-2353 (2012).

Okamura T, Onuma Y, García-García HM, et al. 3-Dimensional Optical Coherence Tomography Assessment of Jailed Side Branches by Bioresorbable Vascular Scaffolds: A Proposal for Classification. J. Am. Coll. Cardiol. Intv. 3(8), 836-844 (2010).

Kimura T, Abe K, Shizuta S, et al. Long-term clinical and angiographic follow-up after coronary stent placement in native coronary arteries. *Circulation*. 105(25), 2986-2991 (2002).

Werner M, Micari A, Cioppa A, et al. Evaluation of the biodegradable peripheral Igaki-Tamai stent in the treatment of de novo lesions in the superficial femoral artery: the GAIA study. *JACC Cardiovasc. Interv.* 7(3), 305-312 (2014). 31. Okamura T, Garg S, Gutiérrez-Chico JL, et al. In vivo evaluation of stent strut distribution patterns in the bioabsorbable everolimuselutingdevice: an OCT ad hoc analysis of the revision 1.0 and revision1.1 stent design in the ABSORB clinical trial. *EuroIntervention.* 5(8), 932-938 (2010).

Gomez LJ, Garcia HM, Onuma Y, Ormiston JA, Serruys PW. A comparison of the conformability of everolimuseluting bioresorbable vascular scaffolds to metal platform coronary stents. *JACC Cardiovasc. Interv.* 3(11), 1190-1198 (2010).

Onuma Y, Serruys PW, Ormiston JA, et al. Three-year results of clinical follow-up after a bioresorbable everolimus-eluting scaffold in patients with de novo coronary artery disease: the ABSORB trial. *EuroIntervention*. 6(4), 447-453 (2010).

Serruys PW, Onuma Y, Garcia HM, et al. Dynamics of vessel wall changes following the implantation of the absorb everolimus-eluting bioresorbable vascular scaffold: a multi-imaging modality study at 6, 12, 24 and 36 months. *EuroIntervention*. 9(11), 1271-1284 (2014).

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*. 10(10), 1144-1153 (2015).

Ruparelia N, Kawamoto H, Capodanno D, et al. BRS and thrombosis: insights from the GHOST-EU registry. EuroPCR, (2016).

Gori T, Wiebe J, Capodanno D, et al. Early and midterm outcomes of bioresorbable vascular scaffolds for ostial coronary lesions: insights from the GHOST-EU registry. *EuroIntervention* 12(5), e550-556 (2016).

Kawamoto H, Latib A, Geraci S, et al. One-year clinical outcomes following BRS implantation for diffuse coronary lesions: a sub-study from the GHOST-EU registry. EuroPCR, (2016).

Schnorbus B, Capodanno D, Nef H, et al. Comparison of the outcomes of patients undergoing percutaneous coronary intervention with Bioresorbable Vascular Scaffolds (BVS) with acute coronary syndrome and stable coronary artery disease (S-CAD). 6 months data from the European multicentre GHOST-EU registry. EuroPCR (2015).

Baquet M, Nef H, Grujic K, et al. Pattern of restenosis after bioresorbable vascular scaffold implantation: angiographic substudy of the European multicentre GHOST-EU Registry. EuroPCR (2015).

Latib A, Naganuma T, Capodanno D, et al. Expansion of bioresorbable vascular scaffold use to coronary bifurcation lesions: a substudy of the European multicentre GHOST-EU registry. EuroPCR (2015).

Wiebe J, Capodanno D, Gori T, et al. Everolimus-eluting bioresorbable scaffold as a treatment option for patients with in-stent restenosis: insights from the multicentre GHOST-EU registry. EuroPCR (2015).

Pyxaras S, Capodanno D, Gori T, et al. Impact of device sizing on outcome in patients undergoing percutaneous coronary intervention with bioresorbable scaffolds: insights from the GHOST-EU registry. EuroPCR (2015).

Naganuma T, Colombo A, Lesiak M, et al. Bioresorbable vascular scaffold use for coronary bifurcation lesions: A substudy from GHOST EU registry. *Catheter Cardiovasc. Interv.* 89(1), 47-56 (2017).

Ortega-Paz L, Capodanno D, Giacchi G, et al. Impact of overlapping on 1-year clinical outcomes in patients undergoing everolimus-eluting bioresorbable scaffolds implantation in routine clinical practice: Insights from the European multicenter GHOST-EU registry. *Catheter Cardiovasc. Interv.* 89(5), 812-818 (2016)

Imori Y, D'Ascenzo F, Gori T, et al. Impact of postdilatation on performance of bioresorbable vascular scaffolds in patients with acute coronary syndrome compared with everolimus-eluting stents: A propensity score-matched analysis from a multicenter "real-world" registry. *Cardiol. J.* 23(4), 374-383 (2016).

Biscaglia S, Ugo F, Ielasi A, et al.

Bioresorbable Scaffold vs. Second Generation Drug Eluting Stent in Long Coronary Lesions requiring Overlap: A Propensity-Matched Comparison (the UNDERDOGS study). *Int. J. Cardiol.* 208, 40-45 (2016).

Serruys PW, Chevalier B, Dudek D, Cequier A, Carrié D. A bioresorbable everolimus-eluting scaffold versus a metallic everolimus-eluting stent for ischemic heart disease caused by denovo native coronary artery lesions (ABSORB II): an interim 1-year analysis of clinical and procedural secondary outcomes from a randomized controlled trial. *Lancet.* 385(9962), 43-54 (2015).

Puricel S, Arroyo D, Corpataux N, et al. Comparison of everolimusand biolimus-eluting coronary stents with everolimus-eluting bioresorbable vascular scaffolds. *J. Am. Coll. Cardiol.* 65(8), 791-801 (2015).

Stephen GE, Dean JK, Christopher M, et al. Everolimus-Eluting Bioresorbable Scaffolds for Coronary Artery Disease. *N. Engl. J. Med.* 373(20), 1905-1915 (2015).

Stone GW, Gao R, Kimura T, Onuma Y, Serruys PW. 1-year outcomes with the Absorb bioresorbable scaffold in patients with coronary artery disease: a patient-level, pooled meta-analysis. Lancet. 387(10025), 1277-1289 (2016).

Nef H, Wiebe J, Achenbach S, et al. Evaluation of the short- and longterm 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). *Cardiovasc. Revasc. Med.* 17(1), 34-37 (2016).

France ABSORB registry - Inhospital and one-month results in 2,000 patients, presentation in Congress: EuroPCR (2016).

Testa L, Biondi ZG, Tomai F, Bedogni F, De Carlo M. Italian Diffuse/Multivessel Disease ABSORB Prospective Registry (IT-DISAPPEARS). Study design and rationale. *J. Cardiovasc. Med.* 16(3), 253-258 (2015).

Italian Diffuse/Multivessel Disease ABSORB Prospective Registry (IT-DISAPPEARS); Lecture in Theatre Boardeu; EuroPCR (2016).

Puricel S, Cuculi F, Weissner M, et al. Bioresorbable Coronary Scaffold Thrombosis Multicenter Comprehensive Analysis of Clinical Presentation, Mechanisms, and Predictors. *J. Am.* Coll. Cardiol. 67(8), 921-931 (2016).

Rapoza R, Wang Y, Oberhauser JP, et al. Bioabsorbable stent that modulates plaque geometric morphology and chemical composition. US Patent Application No. 12/510076.

Tamai H, Igaki K, Tsuji T, et al. A Biodegradable poly(lactic acid) coronary stent in the porcine coronary artery. *J. Interven. Cardiol.* 12(6), 443-450 (1999).

Personal communication Tamborino C, et al. EuroPCR (2015).

http://www.acc.org/latest-incardiology/articles/2017/10/26/12/56/ tues-2pm-absorbii-tct-2017.

Haude M, Ince H, Abizaid A, et al. Safety and performance of the secondgeneration drug-eluting absorbable metal scaffold in patients with de-novo coronary artery lesions (BIOSOLVE-II): 6 month results of a prospective, multi centre, non-randomized, first-in-man trial. *Lancet.* 387(10013), 31-39 (2016).

Wijns W, Vrolix M, Verheye S, et al. Randomised study of a bioabsorbable polymer-coated sirolimus-eluting stent: results of the DESSOLVE II trial. *EuroIntervention*. 10(12), 1383-1390 (2015).

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