Bioresorbable vascular scaffolds technology: current use and future developments

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Abstract: Coronary bioresorbable vascular scaffolds are a new appealing therapeutic option in interventional cardiology. The most used and studied is currently the Absorb BVSTM. Its backbone is made of poly-L-lactide and coated by a thin layer of poly-D,L-lactide, it releases everolimus and is fully degraded to H2O and CO2 in 2–3 years. Absorb BVSTM seems to offer several theoretical advantages over metallic stent, as it gives temporary mechanical support to vessel wall without permanently caging it. Therefore, long-term endothelial function and structure are not affected. A possible future surgical revascularization is not compromised. Natural vasomotion in response to external stimuli is also recovered. Several observational and randomized trials have been published about BVS clinical outcomes. The main aim of this review is to carry out a systematic analysis about Absorb BVSTM studies, evaluating also the technical improvements of the Absorb GT1 BVSTM.

Keywords: Absorb GT1, Absorb BVSTM, bioresorbable vascular scaffold, BRS, coronary scaffold

Introduction

Percutaneous coronary intervention (PCI) is commonly performed by implantation of metallic stents.1 However, stent implantation is affected by a substantial burden of complications as, for example, in-stent restenosis and stent thrombosis.2–5

In this scenario, a new valuable therapeutic option may be represented by bioresorbable vascular scaffolds, which give temporary post-PCI support to the vessel wall and then are biodegraded. Several scaffolds are currently under development, but currently only two have the certificate Conformité Européenne mark approval for coronary angioplasty: the Absorb BVSTM (Abbott Laboratories, Abbott Park, IL, USA) and the DESolve™ (Elixir Medical Corporation, Sunnyvale, CA, USA). The best studied and the most used is the former, with several registries/trials published and >100,000 patients treated.6,7

This review aims to perform a systematic literature analysis about clinical outcomes of Absorb BVSTM in coronary artery disease (CAD), evaluating also technical improvements of the Absorb GT1 BVSTM.

Absorb BVSTM design and technology

The Absorb BVSTM has a bioresorbable polymeric structure made of poly-L-lactide, coated by a thin polymer of poly-D,L-lactide, which controls the release of the antiproliferative drug everolimus. Poly-L-lactide and poly-D,L-lactide are hydrolyzed
and fully metabolized to lactic acid. It is degraded via the Krebs cycle to $\text{H}_2\text{O}$ and $\text{CO}_2$. The Absorb BVSTM has two platinum radio-opaque markers at each edge that allow angiographic visualization. Average strut thickness is 150 $\mu$m and crossing profile ~1.2 mm. First-generation backbone (version 1.0) presented circumferential out-of-phase zigzag circles linked together by longitudinal struts. Conversely, the second-generation (Absorb BVSTM 1.1) has in-phase zigzag rings linked by bridges, with better mechanical integrity and higher support to vessel wall.$^{9,10}$ Absorb BVSTM 1.0 clinical performance was evaluated in the ABSORB A study.$^{11}$ This is a prospective, multicenter, single-arm study. It enrolled 30 patients suffering from stable/unstable angina or silent ischemia and de novo coronary lesions treated by BVS 1.0 delivery. Five-year clinical outcome was satisfactory, with an ischemia-driven major adverse cardiac event (MACE) rate of 3.4%. No scaffold thrombosis (ST) was reported.

After coronary delivery, the Absorb lifecycle has three phases: revascularization, restoration, and reabsorption. In the first phase (lasting ~3 months), the scaffold performs similarly to a drug-eluting stent (DES) in terms of deliverability, radial strength, acute recoil, and neointimal thickening. In the restoration phase, the BVS is degraded and starts losing its radial strength. Natural vasomotion is theoretically restored at the end of the second phase. Finally, in the last phase, the polymeric backbone is totally degraded into lactic acid monomers and oligomers, rapidly metabolized by the body.$^{12}$

The Absorb scaffold offers several theoretical advantages over permanent metallic caging of the vessels.$^{13,14}$ Tempor ary scaffolding allows long-term restoration of endothelial structure and function. It does not affect a possible future surgical coronary revascularization. Scaffolded vessels show late lumen gain, as well as recovery of natural vasomotion, in response to external stimuli.

**Absorb BVSTM in literature: state of the art**

A lot of original articles, case reports/case series, abstracts, reviews, and editorials have been published about Absorb scaffold, accounting for >400 records.$^{15,16}$

We herein considered all published studies reporting clinical outcomes of subjects treated with second-generation BVS, excluding case reports/series (accounting for less than ten patients), studies assessing only angiographic outcomes, preclinical studies, reviews, and articles evaluating BVS performance in non-CAD (Table 1).

Studies are classified into three arms, according to study design: registries and single-arm studies, propensity-score matching comparison, and randomized trials. Registries account both for single- and multicenter registries.

**Meta-analyses are also reported (Table 2).**

**Registries and single-arm studies**

Several single- and multicenter registries on the Absorb BVSTM have been published. We herein divided them and single-arm studies into four groups, according to clinical follow-up: short-term follow-up, mid-term follow-up (also accounting for registries focusing on specific lesions subsets), 1-year follow-up, and long-term follow-up.

**Short-term follow-up**

The BVS ST-segment elevation myocardial infarction (STEMI) first study and Kajiya et al registry reported good early outcomes of BVS in STEMI. The former reported a 1-month MACE rate of 2.6% and the latter 9.1%.$^{17,18}$

The Polish National Registry reported good acute clinical outcomes of BVS delivery in an all-comers population, with no peri-procedural deaths.$^{19}$

The ABSORB FIRST is a prospective, all-comers registry, currently ongoing but not recruiting (NCT01759290)$^{20}$

Target lesion failure (TLF), defined as the composite of cardiac death, target vessel myocardial infarction (MI), and target lesion revascularization (TLR), will be evaluated at 1 year. ST, device success (successful BVS delivery with residual stenosis of <50%), and procedure success (device delivery with no TLF within 3 days of the index procedure) will also be investigated. This registry is intended to provide ongoing postmarketing surveillance on safety and performance of the Absorb BVSTM. It will enroll a minimum of 1,800 patients with de novo coronary lesions treated with at least one scaffold Absorb. An interim analysis about a 30-day outcome of the first 1,200 patients has been reported, with good device and procedure success rate (98.4% and 97.9%, respectively).$^{21}$

**Mid-term follow-up and specific lesion subsets**

Six-month BVS performance in acute coronary syndrome (ACS) has been evaluated in several registries.$^{22–24}$ MACE rate was satisfactory, ranging between 4.9% and 10.7%. In BVS-RAI registry, Prague 19, and Gori et al series, BVS patients were also compared with a control group of subjects treated with metallic stent, with no difference in clinical endpoint.$^{22–24}$

BVS 6-month outcome has also been investigated in specific lesions subsets.

Capranzano et al evaluated BVS performance in bifurcation lesion subset, with good results (one TLR at day 227).$^{26}$
<table>
<thead>
<tr>
<th>Study/reference</th>
<th>Study type</th>
<th>Follow-up</th>
<th>BVS patients (n)</th>
<th>STEMI (%)</th>
<th>Clinical outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABSORB B52</td>
<td>Prospective, single-arm trial that enrolled patients with one or two de novo coronary artery lesions and with stable/unstable angina or silent ischemia</td>
<td>5 years</td>
<td>101</td>
<td>0</td>
<td>MACE (cardiac death, MI, and ischemia-driven TLR) =11.0%</td>
</tr>
<tr>
<td>ABSORB II60</td>
<td>Single-blind, multicenter, randomized trial (BVS vs DES Xience in a 2:1 ratio) enrolling subjects with one or two de novo coronary artery lesions and with stable/unstable angina or silent ischemia</td>
<td>1 year</td>
<td>501</td>
<td>0</td>
<td>DOCE (cardiac death, TV-MI, and clinically indicated TLR) BVS 5% vs DES 3%; P=0.35</td>
</tr>
<tr>
<td>ABSORB III62</td>
<td>Single-blind, multicenter, randomized trial (BVS vs DES Xience in a 2:1 ratio) enrolling subjects suffering from stable/unstable angina or silent ischemia</td>
<td>1 year</td>
<td>1,322</td>
<td>0</td>
<td>TLF (cardiac death, TV-MI, and ischemia-driven TLR) BVS 7.8% DES 6.1%; P=0.007 for noninferiority, P=0.16 for superiority</td>
</tr>
<tr>
<td>ABSORB CHINA63</td>
<td>Single-blind, multicenter, randomized trial (BVS vs DES Xience in a 1:1 ratio) enrolling subjects with one or two de novo coronary artery lesions and with stable/unstable angina or silent ischemia</td>
<td>1 year</td>
<td>241</td>
<td>0</td>
<td>POCE (death, MI, any revascularization) BVS 8.0% DES 9.7%; P=0.51 DOCE (cardiac death, TV-MI, and ischemia-driven TLR) BVS 3.4% DES 4.2%; P=0.62 MACE (cardiac death, MI, and ischemia-driven TLR) =9.3%</td>
</tr>
<tr>
<td>ABSORB EXTEND51</td>
<td>Prospective, multicenter registry that enrolled patients with one or two de novo coronary artery lesions (&lt;28 mm in length and with reference vessel diameter of 2.0–3.8 mm) and with stable/unstable angina or silent ischemia</td>
<td>3 years</td>
<td>250</td>
<td>0</td>
<td>Device success (successful BVS delivery with residual stenosis of &lt;50%) =98.4% Procedure success (device delivery with no TLF within 3 days of the index procedure) =97.9%</td>
</tr>
<tr>
<td>ABSORB FIRST21</td>
<td>Prospective, observational registry, open-label patients to assess BVS performance in daily PCI practice</td>
<td>30 days</td>
<td>1,200</td>
<td>NR</td>
<td></td>
</tr>
<tr>
<td>ABSORB JAPAN41</td>
<td>Single-blind, multicenter, randomized trial (BVS vs DES Xience in a 2:1 ratio) enrolling subjects with one or two de novo coronary artery lesions and with stable/unstable angina or silent ischemia</td>
<td>1 year</td>
<td>266</td>
<td>0</td>
<td>TLF (cardiac death, TV-MI, and ischemia-driven TLR) BVS 4.2% DES 3.8%; P=0.0001 for noninferiority</td>
</tr>
<tr>
<td>ABSORB-STEMI TROFI II59</td>
<td>Single-blind, multicenter, noninferiority, randomized trial (BVS vs DES Xience in a 1:1 ratio) enrolling STEMI subjects</td>
<td>6 months</td>
<td>95</td>
<td>100</td>
<td>DOCE (cardiac death, TV-MI, and clinically driven TLR) BVS 1.1% vs DES 0.0%; P=0.05 TVF (all-cause mortality, MI, and TVR) =8.5%</td>
</tr>
<tr>
<td>AMC PCI Registry36</td>
<td>Prospective, observational registry open-label patients who were enrolled according to operator’s discretion</td>
<td>6 months</td>
<td>135</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>ASSURE registry40</td>
<td>Prospective, multicenter registry that enrolled consecutive patients with lesion length &lt;28 mm, vessel diameter between 2.0 and 3.3 mm</td>
<td>1 year</td>
<td>183</td>
<td>27</td>
<td>MACE (cardiovascular death, MI, and ischemia-driven TLR) =5%</td>
</tr>
<tr>
<td>BVS-EXAMINATION Study57</td>
<td>Retrospective, multicenter trial comparing a cluster of STEMI-BVS consecutive patients with other two of STEMI-Xience/BMS patients (EXAMINATION population), matched by propensity score</td>
<td>1 year</td>
<td>290</td>
<td>100</td>
<td>DOCE (cardiac death, TVre-MI, and TLR) BVS 4.1% vs DES 4.1%; P=0.994 BVS 4.1% vs BMS 5.9%; P=0.306</td>
</tr>
<tr>
<td>BVS EXPAND48</td>
<td>Prospective, single-center registry that enrolled patients with silent ischemia, stable/unstable angina, NSTEMI, and de novo coronary stenosis treated by BVS delivery</td>
<td>559 (371–733) days</td>
<td>250</td>
<td>0</td>
<td>MACE (cardiac death, MI, and TLR) at 1 year =5.5%</td>
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</table>

(Continued)
<table>
<thead>
<tr>
<th>Study/reference</th>
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</tr>
</thead>
<tbody>
<tr>
<td>BVS-RAI registry22</td>
<td>Prospective, two-arm registry, comparing STEMI patients treated with BVS with another one of STEMI-Xience patients</td>
<td>220 (178–369) days</td>
<td>563</td>
<td>100</td>
<td>POCE (cardiac death, MI, and TLR) at follow-up BVS 4.9% vs DES 7.0%; P = 0.4</td>
</tr>
<tr>
<td>BVS STEMI first study23</td>
<td>Prospective, single-arm registry</td>
<td>30 days</td>
<td>49</td>
<td>100</td>
<td>MACE (cardiac death, any re-MI, emergent CABG, or clinically driven TLR) = 2.6% TVF (cardiac death, target-vessel MI, and clinically driven TVR) = 0% Clinical adverse events at follow-up: 1 TLR at day 227</td>
</tr>
<tr>
<td>Capranzano et al24</td>
<td>Prospective, single-center registry, evaluating BVS performance in bifurcation lesions</td>
<td>6 months</td>
<td>46</td>
<td>0</td>
<td>MACE (death, MI, and TVR) BVS 3.3% vs DES 7.6%; P = 0.19</td>
</tr>
<tr>
<td>Costopoulos et al25</td>
<td>Prospective, two centers, open-label registry, comparing a cluster of BVS consecutive patients with another one of Xience/Promus patients (matched by propensity score)</td>
<td>6 months</td>
<td>92</td>
<td>NR; ACS = 10.9</td>
<td>Focus on clinical outcomes. This table includes various studies evaluating the performance of bioresorbable vascular scaffolds (BVS) compared to drug-eluting stents (DES). The studies vary in their design, including prospective and retrospective registries, and evaluate outcomes such as procedural success, clinical adverse events, and composite endpoints like death, myocardial infarction (MI), target lesion revascularization (TLR), and target vessel failure (TVF). The outcomes are compared between BVS and DES, with some studies showing non-inferiority or superior efficacy of BVS. The table highlights the importance of clinical follow-up in assessing long-term safety and efficacy of these devices.</td>
</tr>
</tbody>
</table>
### Study/reference | Study type | Follow-up* | BVS patients (n) | STEMI (%) | Clinical outcomes
--- | --- | --- | --- | --- | ---
Jaguszewski et al. | Prospective, two-center registry, open-label patients with complex anatomical and/or clinical conditions, enrolled according to operator’s discretion | 147±119 days | 106 | 17.0 | POCE (death, MI, and any revascularization) =6.1% (P = 0.05) DOCE (cardiac death, TV-MI, and ischemia-driven TLR) =2.0% (P = 0.12) MACE (death, MI, and TVR) =12% (P = 0.674)
Kawamoto et al. | Retrospective, two-center registry, comparing outcomes between FPJ (BVS total length ≥60 mm) and non-FPJ BVS implantation | 1 year | 142 (FPJ) 23 | 0 | MACE (death, TV-MI, and TVR) =9.1% (P = 0.14)
Kochman et al. | Single-arm registry, open-label patients with STEMI | 1 year | 19 | 100 | Clinical adverse events at follow-up: non-TVR 5.3% (P = 0.05)
Kajiya et al. | Registry, single group, STEMI patients who underwent PCI with intent of BVS | 1 month | 11 | 100 | MACE (cardiac death, MI, and TVR) =9.1% (P = 0.05) BVS 5.7% vs DES 5.3%; P = 0.05
Matesini et al. | Prospective, two-center registry, enrolling consecutive complex coronary lesions treated by OCT-guidance and BVS or DES (control group) implantation | 8.5±2.8 months | 35 | 0 | MACE (cardiac death, MI, and TVR) =4.8% (P = 0.674)
Moscarella et al. | Prospective, multicenter registry, assessing clinical outcomes of BVS in in-stent restenosis | 7 (3–18) months | 83 | 6 | MACCE (cardiac death, Q-wave MI, stroke, and TLR) =12% (P = 0.05)
Muramatsu et al. | Retrospective, multicenter registry, comparing BVS diabetic patients vs BVS no-diabetic ones. Diabetic BVS subjects were also compared with another group of Xience DES diabetic patients (matched by propensity score) | 1 year | 551 (diabetic 136) | 0 | DOCE (cardiac death, TV-MI, and TLR) =2% (P = 0.05)
Diabetic BVS 3.7% vs no-diabetic BVS 5.1%; P = 0.64
Diabetic BVS 3.9% vs diabetic DES 6.4%; P = 0.38
Ojeda et al. | Prospective, single-center registry, enrolling CTO treated by BVS delivery | 13±5 months | 42 | 0 | MACE (cardiac death, MI, and TVR) =4.8% (P = 0.05)
Sato et al. | Prospective, single group registry with consecutive patients presenting ACS | 1 year | 100 | 16 | MACE (cardiac death, MI, and TVR) =4.8% (P = 0.05)
Polar ACS Study | 1 year | 100 | 16 | MACE (cardiac death, MI, and TVR) =4.8% (P = 0.05)
Prague 19 | Prospective registry, consecutive STEMI patients with lesion length <24 mm, culprit vessel caliber between 2.3 and 3.7 mm, compared with a control group of subjects treated with a metallic stent | 6 months | 41 | 100 | MACE (cardiac death, MI, and TVR) =4.8% (P = 0.05)
Polish National Registry | Retrospective, single group, open-label patients who had a previous PCI with BVS | In-hospital | 591 | 11 | No peri-procedural deaths
Sato et al. | Retrospective, two centers, open-label registry, comparing a cluster of BVS consecutive patients with another one of Xience/Promus DES patients (matched by propensity score) | 1 year | 96 | NR | MACE (cardiac death, MI, and TVR) =4.8% (P = 0.05)
BVS 10.2% vs DES 10.5%; P = 0.82
Tamurino et al. | Retrospective, all-comers patients, multicenter trial comparing a cluster of BVS patients (HOST-EU registry population) with another of Xience DES subjects (XIENCE V USA registry population), matched by propensity score | 1 year | 905 | 10.7 | TLF (cardiac death, TV-MI, and ischemia-driven TLR) =4.8% (P = 0.05) BVS 5.8% vs DES 7.6%; P = 0.12
Wiebe et al. | Prospective registry, assessing BVS outcome in CTO lesions | 108 (79.5–214.5) days | 23 | 0 | MACE (cardiac death, MI, and TVR) =4.8% (P = 0.05)
Wiebe et al. | Registry, single group, STEMI patients who underwent PCI with intent of BVS | 132.7±68.7 days | 25 | 100 | MACE (cardiac death, MI, and TVR) =4.8% (P = 0.05)

Note: *Follow-up data shown as number, mean ± SD, or median (interquartile range).

Abbreviations: ACS, acute coronary syndrome; BMS, bare metal stent; BVS, Absorb bioresorbable vascular scaffold; CAGB, coronary artery bypass graft; CTO, chronic total occlusion; DES, drug-eluting stent; DOCE, device-oriented composite endpoint; FPJ, full-plastic jacket; MACCE, major adverse cardiac or cerebrovascular events; MACE, major adverse cardiac event; MI, myocardial infarction; NR, not reported; NSTEMI, non-ST-segment elevation myocardial infarction; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; POCE, patient-oriented composite endpoint; STEMI, ST-segment elevation myocardial infarction; TIMI, thrombolysis in myocardial infarction; TLF, target lesion failure; TVL, target lesion revascularization; TVF, target vessel failure; TV-MI, target vessel myocardial infarction; TVR, target vessel revascularization; TVx-MI, target vessel re-myocardial infarction.
Grundeken et al also investigated BVS outcome in bifurcations.27 Indeed, they studied 6-month outcomes in bifurcation lesions treated by combined Tryton dedicated coronary bifurcation stent and Absorb scaffold delivery. Results were satisfactory with a TLR rate of 20% (n=2) and no deaths, MIs, or stent thrombosis.

Some series investigated BVS outcomes in coronary chronic total occlusions.28–31 Results were good, with a MACE rate at short–mid-term ranging between 0 and 4.8%. Besides, in GHOST-CTO registry, BVS subjects were also compared with a historical group of DES treated patients. Although there was no in-hospital clinical event in the BVS arm, the DES group had a higher rate of technical success (successful scaffold/stent delivery and implantation, postprocedural residual diameter stenosis <30% within the treated segment, and restoration of thrombolysis in MI grade 3 flow: BVS 78.1% vs DES 96.3%; P=0.012) and procedural success (technical success with no in-hospital MACE: BVS 78.1% vs DES 94.4%; P=0.035).

Ielasi et al and Moscarella et al in their multicenter registries investigated the outcomes with BVS implantation in in-stent restenosis.32,33 In both series, 7-month results were satisfactory: Ielasi et al reported a MACE incidence of 8.0%; meanwhile, Moscarella et al reported a major adverse cardiac or cerebrovascular event rate of 12%.

BVS performance in complex anatomical and/or clinical conditions was investigated by Jaguszewski et al.34 They assessed a patient-oriented composite endpoint (POCE) (defined as a composite of death, MI, and any revascularization) and a device-oriented composite endpoint (DOCE) (composite of cardiac death, target vessel MI, and ischemia-driven TLR) at mid-term. Results were satisfactory, with POCE and DOCE rates of 6.1% and 2.0%, respectively.

Mattesini et al studied MACE rate with BVS delivery in complex coronary lesions.35 BVS was compared with a DES control group. In both registry arms, device implantation was guided by optical coherence tomography. There was no difference in the primary outcome measure between the BVS and DES groups (BVS 5.7% vs DES 5.3%, P=0.05).

The AMC PCI registry and the GHOST-EU registry investigated mid-term BVS outcomes in an all-comers population.36,37 At 6-month follow-up, they reported a TLF rate of 8.5% and 4.4%, respectively. Of note, the cumulative incidence of definite/probable ST was rather high (3.0% in AMC PCI registry and 2.1% in GHOST-EU registry). GHOST-EU 1-year follow-up data have been presented at EuroPCR Congress 2015.38 The TLF rate was satisfactory, with a cumulative incidence of 5.2%. Definite/probable ST incidence was 2.0%, with a very low rate after 6 months (0.1%). Thrombotic events were mostly clustered in the first month. Tamburino et al recently matched 1-year outcome of GHOST-EU patients with Xience DES USA registry subjects by applying propensity score.39 The primary endpoint was DOCE rate (composite of cardiac death, target vessel MI, and ischemia-driven TLR). Definite/probable device thrombosis was also investigated. No significant difference was detected for DOCE (BVS 5.8% vs DES 7.6%; P=0.12) and ST/stent thrombosis (1.8% vs 1.1%; P=0.23). In the BVS group, cardiac death was less frequent (0.7% vs 1.9%; P=0.03) and a trend toward a reduction in MI rate was also present (2.4% vs 4.0%; P=0.07).

**Table 2** Published meta-analysis on Absorb BVS™

<table>
<thead>
<tr>
<th>Reference</th>
<th>Follow-up†</th>
<th>Number of BVS patients</th>
<th>STEMI (%)</th>
<th>Clinical outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cassese et al59</td>
<td>12 (9–12) months</td>
<td>2,337</td>
<td>4.5</td>
<td>TLR</td>
</tr>
<tr>
<td>Lipinski et al56</td>
<td>6.4±5.1 months</td>
<td>8,351</td>
<td>27</td>
<td>DOCE (cardiac death, TV-MI, and ischemia-driven TLR)</td>
</tr>
<tr>
<td>Stone et al64</td>
<td>1 year</td>
<td>2,164</td>
<td>0</td>
<td>POCE (death, MI, and any revascularization)</td>
</tr>
</tbody>
</table>

**Note:** †Follow-up data shown as number, mean ± SD, or median (interquartile range).

**Abbreviations:** BVS, Absorb bioresorbable vascular scaffold; CI, confidence interval; DES, drug-eluting stent; DOCE, device-oriented composite endpoint; MACE, major adverse cardiovascular event; MI, myocardial infarction; OR, odds ratio; POCE, patient-oriented composite endpoint; STEMI, ST-segment elevation myocardial infarction; TLF, target lesion revascularization; TV-MI, target vessel myocardial infarction.
One-year follow-up

Several series studied 1-year BVS outcome in an all-comers population.40–42 They reported a MACE rate of 4.5%–8%, thus confirming good BVS performance in routine clinical practice.

Gil et al studied 1-year BVS clinical performance in stable CAD.43 They performed a subanalysis for patients treated with the combination of BVS and DES (hybrid revascularization). Results were satisfactory with a MACE rate of 7.2% and 4.5% in whole population and hybrid revascularization subgroup, respectively. There was no device thrombosis in hybrid revascularization subgroup; meanwhile, two cases were reported in the whole population (1.4%), one subacute (0.7%) and one late (0.7%).

Kawamoto et al compared 1-year clinical outcome between BVS patients with “full-plastic jacket” (FPJ) (BVS total length ≥60 mm) and those without FPJ (BVS total length <60 mm).44 Patients were all affected by stable CAD or unstable angina. No difference between the two groups was found in MACE rate (FPJ 19.2% vs NO-FPJ 13.0%; P=0.14). One late ST was reported in the FPJ group (5.3%) in a patient who had stopped double antiplatelet therapy.

Several registries assessed long-term BVS performance in ACS.

Kochman et al in their small series reported a satisfactory 1-year BVS clinical performance in STEMI, with only one nontarget vessel revascularization (5.3%).45 No thrombotic event at follow-up was reported.

Gori et al and POLAR ACS study evaluated the clinical outcomes of BVS in ACS.46,47 At 1-year, MACE incidence was 13.5% and 2%, respectively. Definite/probable ST rate was 3.0% and 1.0%, respectively. STs were all clustered in the first 6 months in both the series.

Long-term follow-up

The BVS EXPAND evaluated BVS performance in subjects suffering from silent ischemia, stable/unstable angina, or non-STEMI.48 Inclusion angiographic criteria were lesion length ≤28 mm and reference vessel diameter in a range between 2.0 and 3.8 mm. The primary outcome was a composite of cardiac death, all MI, and TLR. Median follow-up period was 559 days (interquartile range 371–733 days). BVS performance was satisfactory, with a primary outcome rate of 5.5% at 1-year follow-up. Definite 12-month ST incidence was 1.4%.

The ABSORB EXTEND is a prospective, multicenter registry (NCT01023789).49 It recruited patients with silent ischemia or stable/unstable angina (final planned enrollment 800 subjects). Abizaid et al in their preliminary report of 512 patients reported satisfactory BVS outcome at 1-year follow-up.50 The composite endpoints of ischemia-driven MACE, ischemia-driven TLF, and ischemia-driven target vessel failure were 4.3%, 4.3%, and 4.9%, respectively. Definite/probable ST was also investigated, with a 1-year rate of 0.8%. There was no acute ST case; meanwhile, subacute and late ST rates were 0.4% for both. Three-year follow-up data of the first 250 recruited subjects have been reported at the Transcatheter Cardiovascular Therapeutics meeting 2014 by Pieter Smits.51 The rates of ischemia-driven MACE, ischemia-driven TLF, and ischemia-driven target vessel failure were 9.3%, 8.9%, and 10.1%, respectively. The overall rate of definite/probable ST was 1.2%. Research compared ABSORB EXTEND subjects with a control group of subjects selected from other trials and treated with DES Xience (Abbott Laboratories, Abbott Park, IL, USA) by propensity score matching. There was no difference in 3-year MACE (hazard ratio 0.73; 95% confidence interval [CI] 0.38–1.41), definite/probable device thrombosis (hazard ratio 0.83; 95% CI 0.08–9.15), and MI rate (hazard ratio 1.06; 95% CI 0.41–2.73). Target vessel failure rate was significantly lower in the ABSORB EXTEND group (BVS 8.1% vs DES 14.2%; P=0.0488).

The ABSORB B is a multicenter, prospective, single-arm study. It included patients with de novo coronary lesions and silent ischemia or stable/unstable angina.52 The authors performed a multimodality imaging analysis and the primary clinical outcome measure was a composite of cardiac death, MI, and ischemia-driven TLR. It is the registry with the longest follow-up available for all the subjects (5 years). BVS performance was good, with a 5-year MACE rate of 11.0%. No ST was reported.

Propensity score matching comparisons

Costopoulos et al compared BVS and everolimus-eluting stent 6-month outcome in a real-world population, with the majority being B2/C class lesions according to the classification of the American College of Cardiology/American Heart Association (BVS 83.9% vs DES 77.4%; P=0.19).53 There was no difference between the two groups with respect to MACE (3.3% vs 7.6%; P=0.19) and TLR (3.3% vs 5.4%; P=0.41). No definite/probable device thrombosis was reported.

Sato et al also compared BVS and DES performance in a real-world population.54 Procedure time, total contrast medium administered, and fluoroscopy time were higher in the BVS group (P<0.001, P=0.02, and P<0.001, respectively). BVS delivery was also an independent predictor of long (>2 hours) procedure time in multivariable analysis (odds ratio =7.83%; 95% CI 2.81–25.78; P<0.001). There was no
difference in 1-year MACE (BVS 10.2% vs DES 10.5%; \( P=0.82 \)) and stent thrombosis/ST (1.0% vs 2.1%; \( P=0.58 \)) rates between the two groups.

Muramatsu et al in their retrospective analysis compared BVS performance in diabetic patients and non-diabetic patients.\(^5\) Diabetic BVS patients were also matched and compared with diabetic DES patients of the SPIRIT trials,\(^6\) by applying propensity score matching. The primary outcome measure was 1-year DOCE rate, including cardiac death, target vessel MI, and TLR. Definite/probable device thrombosis incidence did not differ between the two study arms (diabetic BVS 0.7% vs diabetic DES 0.7%; \( P=1.00 \)).

The ABSORB II, ABSORB JAPAN, and ABSORB III trials are three randomized clinical studies, enrolling subjects with silent ischemia or stable/unstable angina.\(^9\) In all trials, patients were randomized to Absorb or DES Xience in a 2:1 ratio. In ABSORB II, the coprimary endpoints were vasomotion (change in mean lumen diameter before and after nitrate administration at 3 years) and difference between minimum lumen diameter (after nitrate administration) after the index procedure and at 3 years. Clinical endpoints were also investigated. Serruys et al recently published a 1-year interim analysis, reporting similar DOCE and MACE rates between the two study arms (BVS 5% vs DES 3%; \( P=0.35 \) for both), mainly driven by MI (4% vs 1%; \( P=0.06 \)) and TLR (1% vs 2%; \( P=0.69 \)).\(^6\) Definite/probable stent thrombosis/ST incidence did not differ between the two groups (0.9% vs 0.0%; \( P=0.55 \)).

The ABSORB JAPAN is single-blind, multicenter trial designed to enable approval of the Absorb BVSTM in Japan.\(^6\) The primary outcome was TLF at 1 year. Definite/probable device thrombosis was also studied. Scaffold proved to be noninferior to DES, both for TLF (BVS 4.2% vs DES 3.8%; \( P<0.0001 \) for noninferiority) and device thrombosis (1.5% vs 1.5%; \( P=1.0 \)).

The ABSORB III is to date the biggest randomized BVS trial published. It investigated as a primary clinical outcome the 1-year TLF rate, investigated for both noninferiority and superiority.\(^6\) Device thrombosis was also studied. The Absorb BVSTM proved to be noninferior to DES Xience, but not superior for the primary endpoint (BVS 7.8% vs DES 6.1%, \( P=0.007 \) for noninferiority, \( P=0.16 \) for superiority). Stent thrombosis/ST frequency did not differ between the two study arms (1.5% vs 0.7%; \( P=0.13 \)), although events were numerically higher in the BVS group.

The ABSORB CHINA has been designed to support regulatory approval of the Absorb BVSTM in People’s Republic of China.\(^6\) Patients with silent ischemia or stable/unstable angina were randomized to Absorb BVSTM or DES.
Xience in a 1:1 ratio and stratified according to diabetes and number of lesions treated. The primary endpoint was in-segment late loss at 1-year. Clinical outcomes were also studied. BVS proved to be noninferior to DES for the angiographic primary outcome ($P=0.01$). POCE (BVS 8.0% vs DES 9.7%; $P=0.51$) and DOCE (3.4% vs 4.2%; $P=0.62$) rates at 1 year were also similar. Device thrombosis did not significantly differ between the two study arms (0.4% vs 0.0%; $P=1.0$).

**Meta-analysis**

Three BVS meta-analyses have been published.$^{16,64,65}$ Stone et al pooled data of ABSORB II, ABSORB III, ABSORB CHINA, and ABSORB JAPAN trials.$^{64}$ They carried out a patient level, intention-to-treat analysis and outcomes analyzed were relative at 1-year POCE (composite of all-cause mortality, all MI, and all revascularization) rate and relative 1-year DOCE (cardiac death, target vessel MI, and ischemia-driven TLR) rate. Primary outcome did not differ between the two groups, both in patient-oriented (BVS 11.9% vs DES 10.6%, relative risk 1.09, 95% CI: 0.89–0.34; $P=0.38$) and in device-oriented (6.6% vs 5.2%, relative risk 1.22, 95% CI: 0.91–1.64; $P=0.17$) analyses. Target vessel MI was more frequent in BVS group (5.1% vs 3.3%, relative risk 1.45, 95% CI: 1.02–2.07; $P=0.04$) and there was a trend in definite/probable device thrombosis incidence (1.3% vs 0.6%, relative risk 2.09, 95% CI: 0.92–4.75; $P=0.08$) (Figure 1). Even if clinical outcomes did not differ between the two groups, technical BVS performance was inferior to the DES one. Actually, post-percutaneous in-device coronary intervention quantitative analysis proved that BVS lesions had lower acute gain (1.41±0.45 vs 1.58±0.45 mm; $P<0.0001$), lower minimal luminal diameter (2.37±0.39 vs 2.53±0.40 mm; $P<0.0001$), and higher diameter stenosis (12.4% vs 7.5%; $P<0.0001$). This could be due to drawbacks that still affect BVS technology. Indeed, even if BVS is clinically noninferior to DES, some technical matters still affect it and its technical performance.

Cassese et al pooled data of trials analyzed by Stone et al, also adding EVERBIO II and TROFI II trials.$^{65}$ The primary efficacy endpoint was TLR and the primary safety outcome was definite/probable device thrombosis. Median follow-up was 12 months (interquartile range 9–12). TLR rate did not differ between the two study groups (odds ratio 0.97, 95% CI: 0.66–1.43; $P=0.87$), even though BVS subjects had a greater risk of device thrombosis (odds ratio 1.99, 95% CI: 1.00–3.98; $P=0.05$), especially in the first month (odds ratio 3.11, 95% CI: 1.24–7.82; $P=0.02$) (Figures 1 and 2).

Lipinski et al pooled data of published randomized trials and also registries, accounting for a total of 10,510 patients treated with BVS ($n=8,351$) and DES ($n=2,159$).$^{16}$ They studied relative risk of device thrombosis at the longest follow-up. Other clinical outcomes, such as death, MI, and MACE rate, were also evaluated. BVS patients proved to have a higher risk of device thrombosis (odds ratio: 2.06, 95% CI: 1.07–3.98; $P=0.03$) and MI (odds ratio: 2.06, 95% CI: 1.31–3.22; $P=0.002$) (Figure 1). MACE (odds ratio: 0.87, 95% CI: 0.66–1.16; $P=0.35$) and cardiovascular death (odds ratio: 0.81, 95% CI: 0.42–1.58; $P=0.54$) rates did not differ between the two groups, even though there was a trend toward decreased all-cause mortality in the BVS arm (odds ratio: 0.40, 95% CI: 0.15–1.06; $P=0.06$).

**Technical issues and scaffold pitfalls**

Published data suggest that implantation of Absorb BVSTM is noninferior to second-generation DES in terms of clinical
outcome for BVS implantation is of great importance. The great benefit with BVS delivery is expected for young patients with long lesions. Due to the bulky structure of the BVS (strut thickness =150 μm), vessels with extreme angulation of the segment proximal to the lesion should be avoided.

Everaert et al gave five simple rules in BVS implantation that could improve scaffold performance. They are summarized in the five golden P for BVS implantation: prepare the lesion, properly size the vessel, pay attention to the expansions limits of the scaffold, postdilate the BVS with a properly sized noncompliant balloon, and pay attention to dual antiplatelet therapy patient compliance.

Adequate lesion preparation is mandatory. Predilation should be performed with increasing balloon size and the final balloon should have a diameter equal or only minimally undersized compared to the diameter of the selected BVS. Noncompliant balloon should be preferred. Full opening of the last balloon with no waist image on balloon profile is the goal that has to be reached.

Correct scaffold sizing is of utmost importance due to limits in scaffold postdilatation. BVS implantation in large vessel (with diameter >4.0 mm) is not allowed. The use of intravascular imaging is greatly encouraged. Optical coherence tomography, with its high resolution, could give important information about lesion characteristics, optimal scaffold dimensions, scaffold implantation results, and scaffold–vessel interactions.

Scaffold implantation has to be performed gradually, pressurizing the system in two atmosphere increments every 5 seconds. Target pressure should be maintained for at least 30 seconds. Due to polymeric backbone of the device, the final scaffold caliber cannot exceed the nominal diameter above 0.5 mm.

Routine postdilatation with noncompliant balloon is greatly encouraged, especially if some waist image is present on device profile. As for scaffold implantation, it is of great importance that the postdilatation balloon caliber does not exceed nominal scaffold diameter above 0.5 mm, in contrast to DESolve™, which has a wide expansion range.

Dual antiplatelet therapy for at least 12 months is suggested in all BVS subjects, both treated for ACS and stable CAD. However, longer dual antiplatelet therapy duration (18–24 months) and/or more potent agents (ticagrelor or prasugrel) can be explored, especially in patients at high risk for thrombotic events.

Major concerns arise from the ST rate (Figure 1). Consistently in randomized trials and registries, ST rate is higher than expected. Moreover, some cases of very late ST have also been reported. ST may be linked to several factors: patient-, lesion-, device-, and procedure-related factors.

Patient-related factors include all patient conditions associated with a higher prothrombotic status (ie, smoking, diabetes mellitus, chronic kidney disease, ACS clinical presentation, etc).

Challenging lesion subsets (ie, small vessels, thrombotic lesions, long lesions, bifurcations, etc) are known to be associated with DES thrombosis and similarly could have a pivotal role in ST.

Absorb BVS™ has greater strut dimensions than second-generation DES. This could create flow disturbances and delay scaffold re-endothelialization. Other factors that can be implied in ST are late-acquired incomplete strut apposition and neo-atherosclerosis.

Procedure-related factors (ie, fracture, incomplete apposition, under-expansion, flow limiting dissection) seem to have an important role in ST, especially in acute ST. The influence of these predisposing factors may be minimized by systematically applying the BVS delivery recommendations. Indeed, Puricel et al recently proved that ST rate can be reduced by the use of a “BVS-specific implantation protocol.”

Future perspective and scaffold evolution: the Absorb GT1 BVS™

BVS is routinely used in clinical practice. The kind of patient who most could benefit from a BVS is a young subject admitted for ACS. Indeed, Absorb BVS™ could perform the best in soft and ruptured plaque and in patients with a high expectancy of life.

Conversely, in calcified and chronic coronary lesions, BVS performance is suboptimal, due to its technologic pitfalls.

The main drawback of BVS backbone is its bulky structure. The considerable thickness of its struts limits the use in bending and calcified vessels. A possible resolution could be to reduce strut thickness so as to improve the navigability and deliverability of the device. However, a good solution could also be the new Absorb GT1 BVS™ (Figure 3).

New Absorb GT1 BVS™ scaffold has the same features of the previous bioresorbable coronary device regarding the
scaffold. All the modifications concern the catheter delivery system.

The Absorb BVSTM delivery system presents three parts: a proximal high supportive jacketed hypotube, a mid shaft (with the skive transition), and the flexible distal shaft, with its distal hydrophilic coating (Figure 3A). The hypotube ends at the hypotube seal, where the outer member starts. The guide wire notch is located at the proximal end of the distal shaft and is ~25.5 cm from the tip of the catheter. The distal shaft presents three seals: from proximal to distal the mid lap seal, the proximal seal and the distal seal. Distally to the mid lap seal, the catheter presents the distal part of the outer member. Between the proximal and the distal seals, we have the scaffold with the balloon, and just distally the distal seal we have the distal balloon shaft with the soft catheter tip.

Compared with the old version of the device, in the Absorb GT1 BVSTM, designers made the hypotube more robust, integrated the skive transition, and optimized the distal catheter (Figure 3B).

The Absorb GT1 BVSTM hypotube has a stronger proximal member and is unjacketed. It has a higher cross-sectional area of the fluid part and wall that allows a faster deflation of the balloon and an increased pushability, respectively.

The skive joint has been simplified and integrated so as to improve push transmission across the material junction and reduce the guide wire notch profile.

The outer member of the distal catheter is now constituted by a single piece with an increase in the outer member diameter. The outer member extends from the hypotube to the proximal balloon seal. The mid shaft and the mid lap seal have been eliminated, improving scaffold control. There has been an increase in the cross-sectional area of the outer member and fluid path, thus allowing a faster deflation and improving the pushability of the system.

The only study evaluating Absorb GT1 BVSTM outcome is the SUGAR-EVE, not recruiting yet. This is a randomized Phase IV clinical trial, comparing the Absorb GT1 BVSTM versus an everolimus-eluting stent in 224 diabetic patients with de novo coronary stenosis. The primary endpoint is in-device late lumen loss at 9-month follow-up. Clinical outcomes will also be evaluated.73

Another important pitfall of the device is the reduced expansion range. This severely limits the use of the device in case of vasoconstriction or wrong vessel diameter evaluation. A greater expansibility could also reduce early ST burden.

The DESolveTM seems to be a valuable alternative. It has a great range of expansion (a 3.0 mm can be postdilated until 4.5 mm) and the property of “self-correction” acute recoil.68,74

However, several coronary scaffolds are currently under clinical development with the main aim to reduce strut thickness and improve scaffold distensibility. The Fortitude (Amaranth Medical, Inc., Mountain View, CA, USA) has a poly-l-lactic acid platform, a strut thickness of 120 μm, and can be postdilated 1 mm above nominal caliber. Another poly-l-lactic acid scaffold, the MeRes (Meril Life Science, Vapi, India), has a strut thickness of 100 μm. The Reva Fantom (REVA Medical, Inc., San Diego, CA, USA), with its tyrosine polycarbonate alloy, and the magnesium backbone Dreams 2G (Biotronik SE & Co. KG, Berlin, Germany) have both lower strut thickness and greater distensibility than Absorb BVSTM. These devices are only at the initial development phase, and large clinical studies with long-term follow-up are awaited to assess clinical performance of these coronary scaffolds.75,76

Conclusion
Available clinical data suggest that the Absorb BVSTM appears to be a safe technology. The main data come from observational registries in which the BVS performance has been satisfactory, even in challenging anatomical and clinical subsets. Recently, the Absorb BVSTM has proved to be
noninferior to second-generation DES also in randomized controlled trials.

Major concerns have arisen about the ST rate. In the registries and randomized trials, it is numerically higher than expected. Moreover, in meta-analysis, it has been significantly more frequent with BVS than with DES.

Refined selection of the lesions to be treated and use of optimal implantation technique may be helpful to prevent the occurrence of thrombotic events. The new Absorb GT1 BVS™ has some technical improvements in the catheter delivery system and could facilitate scaffold implantation.

More randomized clinical trials with longer follow-up are necessary to definitively assess the real BVS performance and pitfalls.

Disclosure

The authors report no conflicts of interest in this work.

References


