Health Policy Advisory Committee on Technology

Technology Brief

Bioresorbable vascular scaffolds for coronary artery disease

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For further information, contact the HealthPACT Secretariat at:

HealthPACT Secretariat
C/o Healthcare Improvement Unit, Clinical Excellence Division
Department of Health, Queensland
Level 2, 15 Butterfield St
HERSTON QLD 4029

Postal Address: GPO Box 48, Brisbane QLD 4001

Email: HealthPACT@health.qld.gov.au  Telephone: +61 7 3328 9180

For permissions beyond the scope of this licence contact: Intellectual Property Officer, Department of Health, GPO Box 48, Brisbane QLD 4001, email ip_officer@health.qld.gov.au, phone (07) 3328 9824.

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This Brief was commissioned by Queensland Health, in its role as the Secretariat of the Health Policy Advisory Committee on Technology (HealthPACT). The production of this Brief was overseen by HealthPACT. HealthPACT comprises representatives from health departments in all States and Territories, the Australian and New Zealand governments and Medical Services Advisory Committee (MSAC). It is a sub-committee of the Australian Health Ministers’ Advisory Council (AHMAC), reporting to AHMAC’s Hospitals Principal Committee (HPC). AHMAC supports HealthPACT through funding.

This brief was prepared by Dr Meegan Vandepeer from ASERNIP-s.
Summary of findings

The only BVS to have TGA approval (Absorb) is being used in several hospitals around Australia. No BVS are listed on the private health system prostheses list in Australia.

Whilst many studies have been published on BVS, the majority are case series studies with short- or mid-term follow-up. In this technical brief, evidence on the use of BVS was provided from the single published RCT and from three retrospective, non-randomised comparative trials comparing patients from different trials matched according to their clinical characteristics. Absorb was the BVS used in all four studies. Three of the studies compared BVS to drug eluting stents (DES), while one of the retrospective comparative studies compared BVS to DES and BMS. The same DES was used as the comparator in all four studies (XIENCE). One of the retrospective comparative studies also included two other types of DES. Three of the studies, including the randomised controlled trial (RCT), had a maximum follow-up of one year. The fourth study had a two-year follow-up.

In general, no significant differences were observed between the BVS and DES groups for most of the parameters measured in all four studies, including procedural and device success, deaths (cardiac and non-cardiac), target vessel revascularisation, target lesion revascularisation, all revascularisation, thrombosis and myocardial infarction. Additional outcomes measured in the RCT included exercise testing and angina status as measured by the Seattle Angina Questionnaire. No differences were observed between the BVS and DES groups for these outcomes, although significantly lower cumulative angina rates at one year were reported in the BVS group.

Conflicts of interest were noted in three of the four studies due to the manufacturer either funding the study and/or providing speakers’ fees and honoraria to the authors.

Thirty-two trials involving BVS were identified, including 11 RCTs. These trials are either ongoing, recruiting or due to start and the majority are analysing the Absorb BVS. Eight of the RCTs are comparing Absorb to a DES with a durable polymer coating.

In summary, the studies on BVS included in this technical brief are limited by their short-term follow-up and potential for bias due to involvement of the manufacturer. Some of the Absorb BVS RCTs identified in the clinical trials database have large patient numbers with long-term follow-ups (up to five years), which will enable future proper assessment of the purported benefits of BVS over DES, given that the bioresorption period for this BVS is 24–48 months.1
**HealthPACT Advice**

HealthPACT noted that the use of bioresorbable stents is widely diffused in the Australian healthcare sector. They have theoretical advantages over metal stents by not producing artefacts on CT and MRI scans and by potentially allowing restenting of coronary arteries if necessary.

HealthPACT noted that drug-eluting stents are already listed on the Australian Government Department of Health and Ageing Private Health Insurance Prosthesis List at a price nearly twice that of bare metal stents. Bioresorbable stents are more expensive than drug-eluting stents but have not as yet demonstrated clinical superiority to justify a higher premium. HealthPACT recommends that the use of bioresorbable stents at a higher cost than already listed stents is not justified. The clinical and cost-effectiveness evidence should be reviewed again in 12 months.
**Technology, Company and Licensing**

**Register ID** WP220  
**Technology name** Bioresorbable vascular scaffolds  
**Patient indication** Patients with coronary artery disease

**Description of the technology**

Bioresorbable vascular scaffolds are the latest development in stent technology for the treatment of coronary artery disease (CAD) (Figure 1). The stents currently used to treat CAD are composed of metal and coated with a polymer containing anti-proliferative drugs such as everolimus or sirolimus that inhibit cell growth to prevent the artery re-narrowing. These drug eluting stents (DES) are permanent and stay in the vessel indefinitely. Bare metal stents (BMS) do not contain anti-proliferative drugs. The polymer coating on DES stents can be durable or biodegradable. Biodegradable polymers break down over time leaving behind only the bare metal stent. Bioresorbable vascular scaffolds (BVS), in comparison, provide a temporary scaffold that gradually dissolves after two to three years.¹ ²

The potential advantages of BVS compared with current stents are:

- restoring the vessel to its natural state making it capable of normal vascular function;
- freeing the vessel for further treatment (further stenting or heart bypass surgery), which would be precluded with the use of permanent metal stents;
- reducing scar tissue growth within the vessel, neoatherosclerosis (atherosclerosis after stenting) and chronic inflammation risk – all problems associated with having a permanent metal implant;
- reducing the risk of late adverse events such as thrombosis, myocardial infarction and sudden death;
- enabling non-invasive imaging, such as coronary computed tomographic angiography and magnetic resonance imaging, without the artefacts (errors) associated with metal stents.² ³

There are several companies developing BVS using a range of different materials, including poly-D-lactic acid, magnesium, rare earth metals and desamino-tyrosine polycarbonate. Some of these BVS contain anti-proliferative drugs, others do not.³

BVS are inserted using a procedure called percutaneous transluminal coronary angioplasty. The patient is given a local anaesthetic and then a guide wire is inserted into an artery in the arm or groin and passed into the blocked segment of the coronary artery under fluoroscopic guidance. The BVS, which is mounted on a balloon catheter, is passed over the guide wire into the artery lesion or blockage.
The balloon is inflated, expanding the BVS. The BVS then locks in place and forms a scaffold that compresses the plaque (the cause of the blockage) and opens the narrowed artery. After the artery has been widened, the balloon is deflated and the guide wire is withdrawn. Additional imaging, such as intravascular ultrasound and optical coherence tomography, is sometimes used to guide the procedure and to optimise positioning and deployment of the BVS in the artery. The average hospital stay depends on the patient’s presenting symptoms. If the patient has stable coronary disease, they are often discharged the following morning, although many interventional services around Australia are routinely discharging patients home on the same day. Patients return to usual functioning after 2 to 3 days (personal communication, Royal Adelaide Hospital).

**Figure 1** The Absorb bioresorbable vascular scaffold by Abbott Vascular (printed with permission by Abbott Vascular)

**Company or developer**

Numerous companies have developed BVS. All the studies included in this technical brief use the Absorb BVS developed by Abbott Vascular, California, USA.

**Reason for assessment**

BVS for CAD are an innovative device that completely resorb and may result in fewer complications than conventional DES and BMS.

**Stage of development in Australia**

- [ ] Yet to emerge
- [ ] Experimental
- [ ] Investigational
- [X] Established
- [ ] Established but changed indication or modification of technique
- [ ] Should be taken out of use
Licensing, reimbursement and other approval

Only the Absorb BVS and the DESolve® BVS (Elixir Medical Corporation, California, USA) have received the CE mark for treatment of CAD. The Absorb BVS is the only one approved by the Australian Therapeutic Goods Administration. None have been approved by the United States Food and Drug Administration. Abbott Vascular is in the process of seeking approval to sell Absorb in the private health care system in Australia (personal communication, Abbott Vascular).

Australian Therapeutic Goods Administration approval

☐ Yes  ARTG number (s) 214148
☐ No
☐ Not applicable

Technology type  Device
Technology use  Therapeutic

Patient Indication and Setting

Disease description and associated mortality and morbidity

CAD, also known as ischaemic heart disease, is the most common form of cardiovascular disease. CAD occurs when the arteries supplying blood to the heart muscle become hardened and narrowed as a result of atherosclerosis, a disease characterised by a build-up of cholesterol and other material, called plaque, on the inner walls of the arteries. As the build-up of cholesterol and plaque grows, the blood flow through the arteries is reduced. A temporary reduction in blood supply can cause chest pain (angina). If a blood vessel becomes completely blocked heart attack occurs. Over time, CAD can weaken the heart muscle and cause heart failure and changes in the normal beating rhythm of the heart (arrhythmias).

CAD is the leading cause of death in Australian men and women, contributing to 20,045 deaths in 2012 (13% of all deaths). It kills 55 Australians each day, or one Australian every 25 minutes. However, deaths resulting from CAD have declined substantially in Australia over the past three decades. Between 1979 and 2010, the age-standardised death rate for CAD fell by 73 per cent for men (from 639 to 170 deaths per 100,000) and by 71 per cent for women (from 325 to 95 deaths per 100,000). The death rate for CAD among Aboriginal and Torres Strait Islander Australians is up to three times higher than for non-indigenous Australians. CAD causes significant illness, disability and poor quality of life. It contributed 7.8 per cent of the total burden of disability-adjusted life years lost in Australia in 2010, the largest of any single condition.
A 2013/2014 health survey in New Zealand reported that one in 20 adults (4.6%) had been diagnosed with CAD. Men were twice as likely as women to have CAD, after adjusting for age differences. In addition, older people were much more likely to have CAD, with 22 per cent of people aged ≥ 75 being affected. CAD was the leading cause of health loss in New Zealand in 2006, accounting for nine per cent of illness, disability and premature mortality.

**Number of patients**

In 2012 to 2013 there were 148,951 hospitalisations in the Australian public hospital system with a principal diagnosis of CAD. Of this number, angina and heart attacks (including subsequent) each accounted for 36 per cent of admissions. Public hospitalisations due to CAD remained relatively stable between 1998/1999 and 2011/2012. In 2012 to 2013, 36,028 transluminal coronary angioplasty procedures with stenting were performed in Australia. In the private hospital system one item number (38306) was identified in relation to the insertion of stents into a coronary artery. From January 2014 to January 2015, a total of 27,122 services were performed for this item.

Similar data for New Zealand were not readily available.

<table>
<thead>
<tr>
<th>Speciality</th>
<th>Cardiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technology setting</td>
<td>General hospital</td>
</tr>
</tbody>
</table>

**Impact**

**Current technology**

BMS or DES with a durable or bioresorbable polymer coating inserted using transluminal coronary angioplasty. Alternatively, a coronary artery bypass graft may be performed (CABG). This is when a healthy artery or vein from the body is connected, or grafted, to the blocked coronary artery. The grafted artery or vein bypasses (that is, goes around) the blocked portion of the coronary artery creating a new path for oxygen-rich blood to flow to the heart muscle.

**Diffusion of technology in Australia**

Absorb is being used in Australian hospitals and in clinical trial settings. There are currently 33 hospitals in Australia that have commercial access to Absorb, with the Eastern Heart Clinic and Sutherland Heart Clinic, NSW, having the most experience with the device (personal communication, Abbott Vascular).

Numerous Australian hospitals have conducted, or are currently involved in, clinical trials of the Absorb BVS, including the ABSORB Cohort B Trial, the ABSORB EXTEND Study and the ABSORB III Randomised Controlled Trial. The hospitals involved...
include: St Vincent’s Hospital, Melbourne; Monash Heart, Melbourne; the Prince of Wales Hospital, Sydney; the Wesley Hospital, Brisbane; Monash Medical Centre, Melbourne; Liverpool Hospital, Sydney; the Prince Charles Hospital, Brisbane; the Royal Brisbane and Women’s Hospital, Brisbane; and the Royal Perth Hospital, Perth. In addition, St Vincent’s Hospital in Sydney is involved in a trial on the ReZolve® BVS (Reva Medical, Inc., California, USA).

International utilisation
Absorb is commercially available in over 60 countries and has been available in Europe since August 2012. Over 100,000 scaffolds have been implanted in greater than 60,000 patients. Upwards of 8,000 patients have been included in clinical trials of BVS. This number will reach 9,700 in 2016 (personal communication, Abbott Vascular).

Cost infrastructure and economic consequences
Absorb, which is currently the only BVS available for clinical use in Australia, is being used under the diagnosis-related group codes F15A and F15B.

Cost of the device is the only expected financial difference between using a BVS or a DES. No additional infrastructure or training is required. The minimum benefit listed for stents on the private health insurance prostheses list is $1,248 for a BMS and $3,450 for a DES (regardless of whether the polymer is bioabsorbable). The cost of DES that many public health departments have been able to negotiate is reported to be significantly less than this (half this amount for the South Australian Health Department) (personal communication, Royal Adelaide Hospital,). The cost of the Absorb BVS is said to vary from state to state, however, on average its price is comparable to the XIENCE DES (Abbott Vascular). At most, Absorb is likely to cost 5 to 10 per cent more than a traditional DES (personal communication, Abbott Vascular).

One of the possible benefits of the Absorb BVS is a reduction in angina after implantation. This would result in lower rates of revascularisation (surgery to open blocked heart arteries) and fewer patient re-admissions, resulting in reduced costs and resource use in the healthcare system. Other financial savings may result from improved patient outcomes and expanded patient treatment strategies. For example, the use of non-invasive imaging techniques, such as coronary computed tomographic angiography, instead of conventional coronary angiography for angina patients with a BVS. Unlike permanent metallic implants, the Absorb BVS does not cause errors during non-invasive imaging (personal communication, Abbott Vascular). Coronary computed tomographic angiography is a cost-effective alternative to invasive coronary angiography.
Ethical, cultural, access or religious considerations
No cultural, religious, or access considerations for BVS were identified.

Evidence and Policy

Safety and effectiveness
Four studies were selected for inclusion in this technology brief. One was a multicentre, randomised controlled trial (RCT) (level II interventional evidence) and the other three were retrospective, non-randomised comparative studies (level III-3 interventional evidence). Three of the studies compared BVS to DES and one of the level III-3 studies compared BVS with DES and BMS. The Absorb BVS was used in all four studies, as was the XIENCE DES. One of the retrospective comparative studies also included two other types of DES. An overview of the studies is provided in Table 1.

Table 1  Included study characteristics

<table>
<thead>
<tr>
<th>Study/Location</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Length of follow up &amp; number of patients</th>
<th>Conflicts of interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serruys et al 2015&lt;sup&gt;22&lt;/sup&gt; RCT Europe and NZ (multicentre)</td>
<td>Patients aged 18 to 85 years with evidence of MI, suitable for CABG and with one or two de novo native lesions in different epicardial vessels</td>
<td>Patients with acute MI before the procedure, unstable arrhythmia or left ventricular ejection fraction &lt;30%</td>
<td>1 year BVS: n=335, DES: n=166 Losses to follow-up: BVS: n=6 (1.8%) DES: n=2 (1.2%)</td>
<td>The manufacturer of the BVS sponsored the study</td>
</tr>
<tr>
<td>Brugaletta et al 2015&lt;sup&gt;23&lt;/sup&gt; III-3 Multicentre (locations not stated)</td>
<td>STEMI patients. DES and BMS patients matched to BVS patients were from the EXAMINATION trial</td>
<td>Not stated</td>
<td>1 year BVS: n=290, DES: n=290 Losses to follow-up: BVS: n=4 (1.4%) DES: n=0</td>
<td>Authors received speaker’s fees and honoraria from the manufacturer of the BVS One author has been a consultant for the manufacturer of the BVS</td>
</tr>
<tr>
<td>Sato et al 2015&lt;sup&gt;21&lt;/sup&gt; III-3 Italy (single centre)</td>
<td>Not stated</td>
<td>Not stated</td>
<td>1 year BVS: n=96, DES: n=96 Losses to follow-up: BVS: n=31 (32%) DES: n=5 (5.2%)</td>
<td>No</td>
</tr>
<tr>
<td>Zhang et al 2014&lt;sup&gt;4,24&lt;/sup&gt; III-3 Multicentre (locations not stated)</td>
<td>All patients recruited in the ABSORB Cohort B and SPIRIT II trials implanted with a single BVS or DES with serial angiographic examinations at baseline and at 2-year follow-up.</td>
<td>Not stated</td>
<td>2 year BVS: n=33, DES: n=26 Losses to follow-up:*</td>
<td>The manufacturer of the BVS sponsored the study The guest editor received research support from the manufacturer of the BVS</td>
</tr>
</tbody>
</table>

*In the non-matched analyses, 30 BVS and 22 DES patients had intravascular ultrasound (IVUS) post-procedure and 32 BVS (97%) and 20 DES (78%) patients had IVUS at the 2-year follow-up. In the matched analyses of quantitative coronary angiography outcomes, 28 BVS and 26 DES patients were included. In the matched analyses of IVUS outcomes 25 BVS and 22 DES patients were included in the post-procedure analyses and 27 BVS (82%) and 20 DES (77%) patients were included in the two-year follow-up analyses. BMS: bare metal stent; BVS: bioresorbable vascular scaffold; CABG: coronary artery bypass graft; DES: drug eluting stent; MI: myocardial ischaemia; NA: not applicable; RCT: randomised controlled trial; STEMI: ST segment elevation myocardial infarction
ABSORB II is a single-blind, multicentre RCT comparing the Absorb everolimus-eluting BVS (Abbott Vascular) to the XIENCE everolimus DES (Abbott Vascular) in patients with myocardial ischaemia (NCT01425281). This study reported on procedural outcomes and one-year clinical outcomes from the trial.

More than 80 per cent of the patients had single-vessel disease and 24 per cent had diabetes. Patients were masked to treatment allocation but the study investigators and physicians doing the procedure were not. However, 37 patients (32 in the BVS group and 5 in the DES group) were potentially unblinded through discharge letters sent to referring physicians.

Initially, 501 patients were enrolled from 46 sites in Europe and New Zealand, with 335 assigned to receive a BVS and 166 a DES. Clinical follow-up was done at 30 days, 180 days and at one year. At the end of one year, 329 patients (98%) in the BVS group and 164 patients (99%) in the DES group were included in the clinical follow-up.

Device success was defined as successful delivery and deployment of the scaffold or stent at the intended target lesion and successful withdrawal of the delivery system. This included attainment of final in-scaffold or in-stent residual stenosis of less than 50 per cent by quantitative coronary angiography. Procedural success was defined as device success without the occurrence of cardiac death, target-vessel myocardial infarction or repeat target-lesion revascularisation during the hospital stay (maximum of seven days).

Effectiveness

The rates of acute device recoil and of device and clinical procedural success did not differ significantly between the two devices ($p>0.05$; Table 2).

Compared to baseline values, substantial improvement was reported in all five domains of the Seattle Angina Questionnaire (angina stability, angina frequency, physical limitation, quality of life and treatment satisfaction) at six and 12 months for both groups. No significant differences were observed between the two groups for any of the five domains of the Questionnaire at six or 12 months ($p>0.05$).

The cumulative rate of recurrent or worsening angina, assessed through adverse event reporting, was significantly lower with the BVS group (22% versus 30%; $p=0.04$). Results from exercise testing at six and 12 months showed no significant differences between the two groups in the number of patients with an ST depression of $\geq 0.1$ mV or with chest pain ($p>0.05$).
No significant differences were observed between the two groups with respect to rates of cardiac death (0% for both groups), myocardial infarction, thrombosis and all target-lesion revascularisation ($p>0.05$, Table 2).

### Table 2  
Comparison of procedure success and clinical outcomes between BVS and DES at one-year follow-up (Serruys et al 2015)\(^{22}\)

<table>
<thead>
<tr>
<th>Procedural details</th>
<th>BVS group*</th>
<th>DES group*</th>
<th>Difference (95% CI)</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute recoil of device following implantation per device (mm)</td>
<td>0.19 (0.19)</td>
<td>0.19 (0.18)</td>
<td>-0.00 [-0.04, 0.03]</td>
<td>0.85</td>
</tr>
<tr>
<td>Clinical device success</td>
<td>361 (99%)</td>
<td>182 (100%)</td>
<td>-0.82% [-2.39, 1.31]</td>
<td>0.55</td>
</tr>
<tr>
<td>Clinical procedural success</td>
<td>322 (96%)†</td>
<td>164 (99%)†</td>
<td>-2.68% [-5.46, 0.80]</td>
<td>0.16</td>
</tr>
<tr>
<td>Cardiac death</td>
<td>0</td>
<td>0</td>
<td>0.00%</td>
<td>1.00</td>
</tr>
<tr>
<td>Myocardial infarction (per protocol)</td>
<td>15 (4%)</td>
<td>2 (1%)</td>
<td>3.32% [-3.25, 6.26]</td>
<td>0.06</td>
</tr>
<tr>
<td>All target-lesion revascularisation</td>
<td>4 (1%)</td>
<td>3 (2%)</td>
<td>-0.61% [-4.08, 1.60]</td>
<td>0.69</td>
</tr>
<tr>
<td>Definite scaffold or stent thrombosis</td>
<td>2 (0.6%)</td>
<td>0</td>
<td>0.61% [-1.72, 2.19]</td>
<td>1.00</td>
</tr>
</tbody>
</table>

* data are n (%) or mean (SD) unless otherwise stated; †Percentage based on number of patients (335 in BVS group, 166 in the metallic stent group); BVS: bioresorbable vascular scaffold; DES: drug eluting stent

**Safety**

One patient in the DES group died due to cancer.

**Brugaletta et al 2015\(^{23}\)**

A retrospective comparative study compared the one-year device orientated endpoint (DOCE), which includes cardiac death, target vessel myocardial infarction and target lesion revascularisation, in patients with ST-segment elevation myocardial infarction (STEMI) who were treated with a BVS (Absorb), a DES (XIENCE V, Abbot Vascular) or a BMS (MULTI-LINK VISION, Abbott Vascular). The 290 consecutive BVS patients recruited from six different centres received a BVS between December 2012 and June 2013. The DES and BMS patients (n=290 in each group) were selected from the multicentre, multinational, prospective, randomised, single-blind, controlled EXAMINATION trial (NCT 00828087). Patients from the different trials were matched using propensity scores to adjust for differences in clinical and procedural parameters.

**Effectiveness**

One-year follow-up data was available in 100 per cent of BMS and DES patients and in 98 per cent of BVS patients. Despite propensity-score matching there were
significant baseline differences between the groups. Significantly more BVS patients had a history of smoking, compared with both the DES and BMS patients ($p<0.05$), and a higher rate of glycoprotein IIb/IIIa inhibitor use than patients in the DES group ($p<0.05$). With respect to procedural characteristics, there was a significantly higher use of pre- and post-dilation in the BVS patients, compared with the DES and BMS patients ($p<0.05$). The thrombolysis in myocardial infarction (TIMI) vessel blood flow was significantly lower in the BVS patients than in the DES patients ($p<0.05$).

No significant differences in DOCE, or any of the components of DOCE, were found between the BVS and DES groups or between the BVS and BMS groups at 30 days or one-year follow-up (Table 3).

Table 3  Clinical outcomes at one year. Values are n (%) (Brugaletta et al 2015)$^{23}$

<table>
<thead>
<tr>
<th></th>
<th>BVS group (n=290)</th>
<th>DES group (n=290)</th>
<th>BMS group (n=290)</th>
<th>HR [95% CI] for BVS vs DES comparison*</th>
<th>$p$ value</th>
<th>HR [95% CI] for BVS vs BMS comparison*</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac death</td>
<td>6 (2.1)</td>
<td>6 (2.1)</td>
<td>6 (2.1)</td>
<td>0.87 [0.08, 9.90]</td>
<td>0.91</td>
<td>2.46 [0.15, 40.43]</td>
<td>0.53</td>
</tr>
<tr>
<td>Target vessel myocardial infarction</td>
<td>6 (2.1)</td>
<td>4 (1.4)</td>
<td>3 (1.0)</td>
<td>1.65 [0.28, 9.90]</td>
<td>0.58</td>
<td>2.52 [0.62, 10.31]</td>
<td>0.20</td>
</tr>
<tr>
<td>Target lesion revascularisation</td>
<td>5 (1.7)</td>
<td>4 (1.4)</td>
<td>10 (3.4)</td>
<td>1.93 [0.25, 14.91]</td>
<td>0.53</td>
<td>0.95 [0.15, 5.85]</td>
<td>0.96</td>
</tr>
<tr>
<td>Definite device thrombosis</td>
<td>5 (1.7)</td>
<td>2 (0.7)</td>
<td>2 (0.7)</td>
<td>1.10 [0.70, 17.66]</td>
<td>0.94</td>
<td>1.19 [0.74, 19.03]</td>
<td>0.90</td>
</tr>
<tr>
<td>Definite/probable device thrombosis</td>
<td>7 (2.4)</td>
<td>4 (1.4)</td>
<td>5 (1.7)</td>
<td>1.10 [0.69, 17.54]</td>
<td>0.95</td>
<td>0.79 [0.07, 9.20]</td>
<td>0.85</td>
</tr>
</tbody>
</table>

*HRs have been estimated in the timeframe after 30 days up to one year; BMS: bare metallic stent; BVS: bioresorbable vascular scaffold; CI: confidence interval; DES: drug eluting stent; HR: hazard ratio

Safety

No safety outcomes were reported.

Sato et al 2015$^{21}$

A second retrospective comparative study compared patients with predominantly complex lesions treated with a BVS (Absorb) with those treated with a DES (XIENCE Prime or XIENCE V, Abbott Vascular; Promus or Promus Element, Boston Scientific; or Nobori, Terumo Medical Corporation). Using propensity-score matching to adjust for differences in baseline clinical characteristics, 96 of 99 consecutive patients treated with BVS between May 2012 and May 2014 were matched with 96 of 193 consecutive patients who received a DES from a single centre in Italy.

Procedural success was defined as angiographic success (residual diameter stenosis after stent or scaffold implantation <20%) without in-hospital major adverse cardiac
events (MACE). MACE was defined as the composite of all-cause death, follow-up myocardial infarction (MI), and target vessel revascularisation. Deaths that could not be attributed to another cause were considered to be heart related.

**Effectiveness**

Procedural success did not differ significantly between the BVS and DES groups (94% versus 96%; \( p = 0.51 \)). However, significantly greater values (\( p < 0.05 \)) were recorded for the BVS group, compared with the DES group, with respect to the total procedure and fluoroscopy time and the number of balloon dilations before and after the procedure.

One-year follow-up was available in 65 (68%) of the BVS patients and 91 (95%) of the DES patients. There was no significant difference in the one-year estimated cumulative MACE incidence between the BVS and DES groups (10.2% vs 10.5%). Similarly, there were no significant differences in the rates of estimated composite endpoint of all-cause death and follow-up myocardial infarction (2.8% vs 3.5%), target vessel revascularisation (9.0% vs 8.6%) or target lesion revascularisation (8.2% vs 5.7%).

**Safety**

During the follow-up time one case of acute stent thrombosis occurred in the BVS group two hours after treatment for ST-elevation MI. Two probable stent thrombosis cases occurred in the DES group (one acute and one late).

Zhang et al 2014

A third retrospective comparative study reported post-device implantation and two-year outcomes for patients treated with BVS (Absorb) or DES (XIENCE V, Abbott Vascular). The present study was a pooled analysis of a subset of patients from the non-randomised, multicentre ABSORB Cohort B trial (n=101; NCT00856856) and the multicentre, randomised SPIRIT II trial (n=300; NCT00180310) who underwent angiographic examination at baseline and at two-year follow-up. Both trials included patients with de novo lesions.

In total, 33 patients with 33 lesions (the BVS group) from a subset of 45 patients in the ABSORB Cohort B trial and 26 patients with 28 lesions (the DES group) from a subset of 113 patients in the SPIRIT II trial were included in the study. The investigators conducted a range of analyses including quantitative coronary angiography (QCA), intravascular ultrasound (IVUS) and an assessment of MACE. MACE included a composite of cardiac death, any myocardial infarction and ischaemia-driven target lesion revascularisation (ID-TLR).
As the two populations had different baseline and angiographic characteristics, the QCA and IVUS measurements were repeated after matching the two populations for the following variables: diabetes mellitus, reference vessel diameter, pre-procedural minimal vessel lumen diameter and lesion length. After matching, 28 patients with 28 lesions in the BVS group and 26 patients with 28 lesions in the DES group were analysed.

**Effectiveness**

The two patient groups were similar at baseline with respect to diabetes mellitus, hypertension, hypercholesterolaemia, and angiographic characteristics. However, patients treated with DES were more likely to have two-vessel CAD and unstable angina ($p<0.05$)

From the QCA analyses, the only parameters that differed significantly between the two groups at the two-year follow-up were the mean in-stent/in-scaffold minimum vessel lumen diameter, which was significantly higher in the DES group, and the mean in-stent/in-scaffold diameter stenosis, which was significantly higher in the BVS group ($p<0.05$). These results were observed in both the unmatched and the matched comparisons.

Results from the IVUS analyses revealed that the two-year projected mean minimum lumen diameter was significantly higher in the DES group ($p<0.05$) in both the matched and the unmatched comparisons.

**Safety**

During the two-year follow-up, two patients developed ID-TLR in the BVS group. One patient had in-scaffold restenosis at 168 days of follow-up, while the other patient had in-scaffold restenosis at 383 days of follow-up. Two patients in the BVS group, but no patients in the DES group, experienced non-Q-wave MI at two-year follow-up. No death was reported in either treatment group.

**Economic evaluation**

No economic evaluation studies on BVS were identified. Abbott Vascular are in the process of investigating the economic benefits that may potentially arise from use of the Absorb BVS (personal communication, Abbott Vascular).

**Ongoing research**

A total of 32 trials involving BVS that were either ongoing, recruiting, or due to start, were identified from a search of ClinicalTrials.gov and the Australian and New Zealand Clinical Trials Registry (Table 4). Of the trials identified, 24 analysed Absorb, three analysed DESolve (Elixir Medical), two each analysed ReZolve (REVA Medical Inc.) and FORTITUDE™ (Amaranth Medical, Inc., California, USA) and one analysed
the DREAMS 2 BVS (BIOTRONIK SE & Co. KG, Berlin, Germany). The 11 RCTS and single non-randomised comparative trial identified, all analysed the Absorb BVS. The remaining 20 trials were all case series studies.

Other issues

Conflicts of interest were identified in three of the four studies. Two of the included studies, the RCT by Serruys et al (2015)\textsuperscript{22} and the non-randomised comparative study by Zhang et al (2014),\textsuperscript{24} were funded by Abbott Vascular. In addition, Abbott Vascular was involved in the study design, data collection, data analyses, data interpretation and writing of the RCT, and provided research support to the guest editor of the Zhang et al (2014)\textsuperscript{24} study. With respect to the Brugaletta et al (2015) study\textsuperscript{23}, three of the authors received speakers’ honoraria from Abbott Vascular and a fourth served as a consultant for the company. Only the study by Sato et al (2015)\textsuperscript{21} reported no conflict of interest.
<table>
<thead>
<tr>
<th>Study Location</th>
<th>Design</th>
<th>Number of patients</th>
<th>Intervention</th>
<th>Primary outcomes</th>
<th>Trial status (Estimated completion date)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absorb BVS</td>
<td></td>
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<tr>
<td>NCT02171065</td>
<td>RCT</td>
<td>900</td>
<td>Absorb BVS plus guideline directed medical therapy</td>
<td>Patient level non-culprit lesion related MACE through 2 years post-procedure</td>
<td>Recruiting (December 2018)</td>
</tr>
<tr>
<td>Sweden</td>
<td>Multicentre</td>
<td></td>
<td>Guideline directed medical therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01986803</td>
<td>RCT</td>
<td>190</td>
<td>Absorb BVS</td>
<td>Healing score at 6 months post-procedure</td>
<td>Ongoing, not recruiting (March 2015)</td>
</tr>
<tr>
<td>Denmark, Netherlands, Spain, Switzerland</td>
<td>Multicentre</td>
<td></td>
<td>XIENCE Xpedition stent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT0185077</td>
<td>RCT</td>
<td>2,690</td>
<td>Absorb BVS</td>
<td>Target vessel failure at 2 years post-procedure</td>
<td>Recruiting (September 2017)</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Multicentre</td>
<td></td>
<td>XIENCE stent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01844284</td>
<td>RCT</td>
<td>400</td>
<td>Absorb BVS</td>
<td>Target lesion failure, non-inferiority against the active control</td>
<td>Ongoing, not recruiting (May 2015)</td>
</tr>
<tr>
<td>Japan</td>
<td>Multicentre</td>
<td></td>
<td>XIENCE PRIME/XIENCE Xpedition stent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT01751906</td>
<td>RCT</td>
<td>2,250</td>
<td>Absorb BVS</td>
<td>Target lesion failure and non-inferiority against the control at 1 year post-procedure</td>
<td>Recruiting (August 2015)</td>
</tr>
<tr>
<td>USA, Australia, Canada, Puerto Rico</td>
<td>Multicentre</td>
<td></td>
<td>XIENCE V, XIENCE PRIME or XIENCE Xpedition stent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT0142581</td>
<td>RCT</td>
<td>501</td>
<td>Absorb BVS</td>
<td>Vasomotion assessed by change in mean lumen diameter between pre- and post-nitrate QCA at 3 years post-procedure</td>
<td>Ongoing, not recruiting</td>
</tr>
<tr>
<td>NCT02173379</td>
<td>RCT</td>
<td>3,000</td>
<td>Absorb BVS</td>
<td>Percentage of patients experiencing angina within 1 year and TLF (composite of cardiac death, MI attributable to target vessel, or ischaemia-driven target lesion revascularisation) between 1 and 5 years post-procedure</td>
<td>Recruiting</td>
</tr>
<tr>
<td></td>
<td>Multicentre</td>
<td></td>
<td>XIENCE V, XIENCE PRIME or XIENCE Xpedition stent</td>
<td></td>
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<tr>
<td>Study Location</td>
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<tr>
<td>Spain</td>
<td>RCT</td>
<td>Single centre</td>
<td>Clopidogrel plus Absorb BVS</td>
<td>Difference in increase of coronary blood flow under adenosine administration from baseline in the coronary segment distal to the scaffold immediately after intervention</td>
<td>Not yet open (May 2019)</td>
</tr>
<tr>
<td>Germany</td>
<td>RCT</td>
<td>Single centre</td>
<td>Absorb BVS XIENCE stent</td>
<td>Percentage diameter stenosis at 6-8 months post-procedure</td>
<td>Recruiting (March 2015)</td>
</tr>
<tr>
<td>Poland</td>
<td>RCT</td>
<td>Single centre</td>
<td>Absorb BVS CABG</td>
<td>Extent of ischaemic and left ventricular ejection fraction in cardiac MR at 12 months post-procedure</td>
<td>Not yet open (September 2017)</td>
</tr>
<tr>
<td>USA</td>
<td>RCT</td>
<td>NR</td>
<td>Absorb BVS XIENCE V stent</td>
<td>In-segment late loss from index procedure to 1 year post-procedure</td>
<td>Ongoing, not recruiting</td>
</tr>
<tr>
<td>Austria</td>
<td>Non randomised comparative</td>
<td>60</td>
<td>Absorb BVS XIENCE stent</td>
<td>Adverse post-stenting results at 1 year post-procedure (malapposition, under-expansion and edge dissections)</td>
<td>Recruiting (December 2014)</td>
</tr>
<tr>
<td>Belgium</td>
<td>Case series Multicentre registry</td>
<td>1,802</td>
<td>Absorb BVS</td>
<td>Cardiac death, target vessel MI, ischaemic-driven TLR, TLF at 1 year in the 12 mm or shorter group compared to the 18 mm group</td>
<td>Ongoing, not recruiting (August 2015)</td>
</tr>
<tr>
<td>Italy, Netherlands</td>
<td>Case series Multicentre</td>
<td>30</td>
<td>Absorb BVS</td>
<td>Restenosis rate by QCA</td>
<td>Recruiting (December 2016)</td>
</tr>
<tr>
<td>Germany</td>
<td>Case series Post-marketing surveillance registry</td>
<td>180</td>
<td>Absorb BVS</td>
<td>MACE at 6, 12, 24 and 36 months post-procedure</td>
<td>Ongoing, not recruiting (March 2013)</td>
</tr>
<tr>
<td>Study Location</td>
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<tr>
<td>NCT02004730 Italy</td>
<td>Case series Multicentre registry</td>
<td>1,000</td>
<td>Absorb BVS</td>
<td>MACE at 30 days, 6 months, 1 year and then yearly to 5 years post-procedure</td>
<td>Recruiting (December 2014)</td>
</tr>
<tr>
<td>NCT02229864 USA</td>
<td>Case series Multicentre</td>
<td>12</td>
<td>Absorb BVS</td>
<td>To assess pharmacokinetics of tmax, Cmax, AUCO-24 hours, AUCO-t, AUCO-∞, k1/2 , CL within a 30-day period post-procedure</td>
<td>Ongoing, not recruiting (December 2014)</td>
</tr>
<tr>
<td>NCT02238054 France</td>
<td>Case series Multicentre</td>
<td>2,000</td>
<td>Absorb BVS</td>
<td>MACE at 1 year post-procedure</td>
<td>Recruiting (September 2021)</td>
</tr>
<tr>
<td>NCT01977534 United Kingdom</td>
<td>Case series Multicentre post-market surveillance registry</td>
<td>1,000</td>
<td>Absorb BVS</td>
<td>Acute Success: device success and procedural success, death (cardiovascular and non-cardiovascular), MI, TLR (all and ischaemic-driven), TVR (all and ischaemic-driven), cardiac death/TV-MI/ischaemia-driven TLR, cardiac death/TV-MI/ischaemia-driven TVR, scaffold/stent thrombosis (definite and probable)</td>
<td>Recruiting (September 2018)</td>
</tr>
<tr>
<td>NCT02066623 Germany, Austria</td>
<td>Case series Multicentre registry</td>
<td>5,000</td>
<td>Absorb BVS</td>
<td>Number of serious adverse cardiac events up to 5 years post-procedure</td>
<td>Recruiting (April 2020)</td>
</tr>
<tr>
<td>NCT01023789 Argentina, Australia, Austria, Belgium, Brazil, Canada, China, Denmark, France, Germany, India, Israel, Italy, Japan, Malaysia, Netherlands, New Zealand, Poland, Singapore, South Africa, Spain</td>
<td>Case series Multicentre</td>
<td>807</td>
<td>Absorb BVS</td>
<td>Device and procedure success (acute)</td>
<td>Ongoing, not recruiting (October 2016)</td>
</tr>
<tr>
<td>Study Location</td>
<td>Design</td>
<td>Number of patients</td>
<td>Intervention</td>
<td>Primary outcomes</td>
<td>Trial status (Estimated completion date)</td>
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<tr>
<td><strong>Sweden, Switzerland, Taiwan, United Kingdom</strong></td>
<td>Case series</td>
<td>101</td>
<td>Absorb BVS</td>
<td>In-stent LL, in-segment LL, proximal LL, Distal LL, in-stent and in-segment angiographic binary restenosis rate, in-stent % volume obstruction, persisting incomplete apposition, late incomplete apposition, aneurysm, thrombus, persisting dissection, ischaemia-driven MACE. Acute success (device and procedure), ischaemia-driven TLR and TVR</td>
<td>Ongoing, not recruiting (December 2014)</td>
</tr>
<tr>
<td><strong>Australia, Belgium, Denmark, France, Netherlands, New Zealand, Poland, Switzerland</strong></td>
<td>Case series</td>
<td>2,000</td>
<td>Absorb BVS</td>
<td>Scaffold thrombosis (acute, subacute, late and very late) and TLR (ischaemia- or angiographic-driven), MACE (5 year follow-up), cardiac death, TLR, MI</td>
<td>Recruiting (May 2016)</td>
</tr>
<tr>
<td><strong>Italy</strong></td>
<td>Case series</td>
<td>300</td>
<td>Absorb BVS</td>
<td>MACE (1 year after procedure) and MACE at 30 days and 1 year post procedure and thrombosis in patients with acute coronary syndrome</td>
<td>Recruiting September 2014</td>
</tr>
<tr>
<td><strong>DESolve® BVS</strong></td>
<td>Case series</td>
<td>126</td>
<td>DESolve BVS</td>
<td>MACE at 1 and 6 months and 1, 2, 3, 4 and 5 years post-procedure</td>
<td>Ongoing, not recruiting (June 2013)</td>
</tr>
<tr>
<td><strong>NCT02013349</strong></td>
<td>Case series</td>
<td>200</td>
<td>DESolve BVS</td>
<td>MACE at 1 and 6 months and 1, 2, 3, 4 and 5 years post-procedure</td>
<td>Recruiting (July 2015)</td>
</tr>
<tr>
<td>Study Location</td>
<td>Design</td>
<td>Number of patients</td>
<td>Intervention</td>
<td>Primary outcomes</td>
<td>Trial status (Estimated completion date)</td>
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<tr>
<td>Belgium, New Zealand</td>
<td>Case series</td>
<td>16</td>
<td>DESolve BVS</td>
<td>Procedure and device success (time frame: 7 days post-procedure). MACE, TLF, TVF, TVR, stent thrombosis (up to 5 years follow-up)</td>
<td>Ongoing, not recruiting (March 2012)</td>
</tr>
<tr>
<td>Australia, Brazil, Germany</td>
<td>Case series Multicentre</td>
<td>125</td>
<td>ReZolve BVS</td>
<td>MACE (at 6 and 12 months), late lumen loss</td>
<td>Ongoing, not recruiting (September 2014)</td>
</tr>
<tr>
<td>Brazil</td>
<td>Case series NR</td>
<td>50</td>
<td>ReZolve BVS</td>
<td>Ischaemia-driven TLR (at 6 months post-procedure)</td>
<td>Ongoing, not recruiting (September 2014)</td>
</tr>
<tr>
<td>Italy</td>
<td>Case series Multicentre</td>
<td>120</td>
<td>FORTITUDE BVS</td>
<td>In-scaffold late lumen loss and incidence of target vessel failure (at 9 months post-procedure)</td>
<td>Not yet open (September 2016)</td>
</tr>
<tr>
<td>Colombia</td>
<td>Case series Multicentre</td>
<td>50</td>
<td>FORTITUDE BVS</td>
<td>Incidence of target vessel failure and in-scaffold late lumen loss (at 9 months post-procedure)</td>
<td>Recruiting (October 2015)</td>
</tr>
<tr>
<td>Belgium, Brazil, Denmark, Germany, Netherlands, Singapore, Spain, Switzerland</td>
<td>Case series Multicentre</td>
<td>121</td>
<td>DREAMS 2nd generation BVS</td>
<td>In-segment late lumen loss (at 6 months post-procedure)</td>
<td>Ongoing, not recruiting (October 2015)</td>
</tr>
</tbody>
</table>

BVS: bioresorbable vascular scaffolds; CABG: coronary artery bypass grafting; LL: late loss; MACE: major adverse cardiac event; MI: myocardial infarction; MR: magnetic resonance; NR: not reported; QCA: quantitative coronary angiography; RCT: randomised controlled trial; TLF: target lesion failure; TLR: target lesion revascularisation; TV-MI: target vessel-myocardial infarction; TVR: target vessel revascularisation; USA: United States of America.
Number of studies included

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

Total number of studies: 4
Total number of Level II studies: 1
Total number of Level III-3 studies: 3

Search criteria to be used (MeSH terms)

Searches were conducted using the following search strategy:

1. bio-resorbable scaffold
2. bioresorbable scaffold
3. bioresorbable vascular scaffold
4. bio-resorbable vascular scaffold
5. bioabsorbable scaffold
6. 1 OR 2 OR 3 OR 4 OR 5
7. (Igaki-Tamai) OR Igaki Tamai
8. DREAMS
9. ABSORB
10. (RESTORE) AND Sirolimus
11. ReZolve
12. (IDEAL) AND Sirolimus
13. DeSolve
14. ART FIM
15. ART-FIM
16. EVOLVE
17. Synergy
18. GHOST
19. Zorion
20. MeRes
21. Avatar
22. Sahajanand
23. (Acute) AND CD34
24. Xinsorb
25. amaranth
26. 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25
27. stent* OR scaffold*
28. 26 AND 27
29. 6 OR 28

Literature search date
23/02/2015

References


