JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 10, NO. 18, 2017

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcin.2017.07.023

A Prospective Evaluation of a Pre-Specified Absorb BVS Implantation Strategy in ST-Segment Elevation Myocardial Infarction

The BVS STEMI STRATEGY-IT Study

Alfonso Ielasi, MD,[a] Gianluca Campo, MD, PhD,[b] Claudio Rapetto, MD,[c] Attilio Varricchio, MD, PhD,[d] Bernardo Cortese, MD,[e] Salvatore Brugaletta, MD, PhD,[f] Salvatore Geraci, MD,[g] Paolo Vicinelli, MD,[h] Fortunato Scotto di Uccio, MD,[i] Gioel Gabrio Secco, MD,[j] Arnaldo Poli, MD,[k] Elisa Nicolini, MD,[l] Kohki Ishida, MD,[f] Azeem Latib, MD,[m,n] Maurizio Tespili, MD[a]

ABSTRACT

OBJECTIVES The aim of this study was to assess the feasibility and clinical results following a pre-specified bioresorbable scaffold (Absorb BVS) implantation strategy in patients with ST-segment elevation myocardial infarction (STEMI).

BACKGROUND Concerns were raised about the safety of Absorb because a non-negligible rate of thrombosis was reported within 30 days and at midterm follow-up after primary percutaneous coronary intervention.

METHODS This was a prospective, multicenter study of patients with STEMI (<75 years of age with symptom onset <12 h) undergoing primary percutaneous coronary intervention with Absorb following a dedicated implantation protocol. The primary endpoint was a device-oriented composite endpoint of cardiac death, target vessel myocardial infarction, and ischemia-driven target lesion revascularization within 30 days.

RESULTS During the study period, 505 patients with STEMI (16.9% of the overall STEMI population) were treated with the Absorb BVS. The mean age was 56.6 ± 9.4 years, and 487 patients (96.4%) were in Killip class I or II at admission. According to the study protocol, direct Absorb implantation was feasible in 47 patients (9.3%), whereas post-dilatation was performed in 468 cases (92.7%). Procedural success was attained in 94.8% of the cases. Dual antiplatelet therapy with ticagrelor or prasugrel was administered at discharge in 481 patients (95.1%). At 30-day follow-up, the hierarchical device-oriented composite endpoint rate was 0.6% (0.4% cardiac death, 0.2% target vessel myocardial infarction and ischemia-driven target lesion revascularization). One episode (0.2%) of probable scaffold thrombosis was reported.

CONCLUSIONS A pre-specified Absorb implantation strategy in real-world patients with STEMI undergoing primary percutaneous coronary intervention was feasible and associated with a low 30-day device-oriented composite endpoint rate. Mid- and long-term follow-up is strongly needed to eventually confirm these early results. (Use of BVS in ST-Segment Elevation Myocardial Infarction [STEMI]: The BVS STEMI STRATEGY-IT Prospective Registry [STRATEGY-IT]; NCT02601781) (J Am Coll Cardiol Intv 2017;10:1855–64) © 2017 by the American College of Cardiology Foundation.

From the [a]Cardiology Division, ASST Bergamo Est, Bolognini Hospital Seriate, Seriate, Italy; [b]Cardiovascular Section, Medical Sciences Department, Azienda Ospedaliera Universitaria S. Anna, Ferrara, Italy; [c]Cardiology Division, Sanremo Hospital, Sanremo, Italy; [d]Cardiology Division, Santa Maria Della Pietà Hospital, Nola, Italy; [e]Cardiac Department, ASST Fatebenefratelli/Sacco, Fatebenefratelli Hospital, Milan, Italy; [f]Cardiology Department, Thorax Institute, IDIBAPS, University of Barcelona, Hospital Clinic, Barcelona, Spain; [g]Cardiology Division San Giovanni di Dio Hospital, Agrigento, Italy; [h]Cardiology Division, ASST Milanese Ovest, Fornaroli Hospital, Magenta, Italy; [i]Cardiology Division, Santa Maria Loreto Mare Hospital, Naples, Italy; [j]Cardiology Division, Santi Antonio, Biagio e Cesare Arrigo Hospital, Alessandria, Italy; [k]Cardiology Division, ASST Milanese Ovest, Legnano

ABBREVIATIONS AND ACRONYMS

BVS = bioresorbable scaffold

DAPT = dual antiplatelet therapy

DES = drug-eluting stent(s)

DOCE = device-oriented composite endpoint

DS = diameter stenosis

EES = everolimus-eluting stent(s)

ID-TLR = ischemia-driven target lesion revascularization

NC = noncompliant

PCI = percutaneous coronary intervention

pPCI = primary percutaneous coronary intervention

RVD = reference vessel diameter

ScT = scaffold thrombosis

STEMI = ST-segment elevation myocardial infarction

TV-MI = target vessel myocardial infarction

ST-segment elevation myocardial infarction (STEMI) might represent an attractive subset for bioresorbable vascular scaffold (BVS) technology. Specifically, the "culprit" lesion consists primarily of a soft, lipid-rich necrotic core that is easy to expand. Furthermore, STEMI occurs predominantly in relatively young subjects with long life expectancy, fewer previous cardiac events, and less previous revascularization (1). However, STEMI lesions have a much higher prothrombotic milieu, which might increase the risk for thrombotic recurrence on the larger struts of current scaffolds compared with the newer generation drug-eluting stent (DES). Data from the initial clinical experiences with a polymeric everolimus-eluting BVS (Absorb BVS, Abbott Vascular, Santa Clara, California) in patients with STEMI were encouraging. However, concerns were raised about device safety because a non-negligible rate of scaffold thrombosis (ScT) was reported within 30 days and at midterm follow-up after primary percutaneous coronary intervention (pPCI) (2,3).

SEE PAGE 1865

Technical issues specifically related to the structural features of the Absorb BVS (i.e., thicker polymeric struts, maximal post-expansion scaffold limits) were advocated as probable causes for these early events. Nevertheless, pre-specified technical suggestions in order to perform an optimal Absorb procedure in the STEMI subset have been lacking in each of the studies performed to date (2–5). The aim of the present study was to prospectively assess the feasibility and clinical results following a pre-specified Absorb BVS implantation strategy for patients with STEMI undergoing pPCI.

METHODS

The rationale and design of the BVS STEMI STRATEGY-IT study has been extensively described elsewhere (6). The study is registered as NCT02601781. Briefly, BVS STEMI STRATEGY-IT is an investigator-owned and investigator-directed, prospective, nonrandomized, single-arm, multicenter study intended to obtain data from 500 consecutive patients with STEMI eligible to undergo pPCI with Absorb BVS (1.1 or GT1) implantation on the basis of pre-specified inclusion and exclusion criteria. The main inclusion criterion was the presence of STEMI with symptom onset <12 h. Exclusion criteria were common to most Absorb studies (6) except for: 1) age >75 years; and 2) infarct-related artery maximal diameter (within planned device deployment segment) <2.5 or >3.7 mm. A screening log form was prospectively completed by each participating center to track the eligibility status of the patients with STEMI treated within the study period. Included in the form was specifically collected information about the stent implanted (DES or bare-metal stent) and the reason why (i.e., a specific exclusion criterion) a stent rather than an Absorb BVS was selected during pPCI.

A total of 22 Italian centers were involved in the study (Online Appendix). All centers had approval from their medical ethics committees.

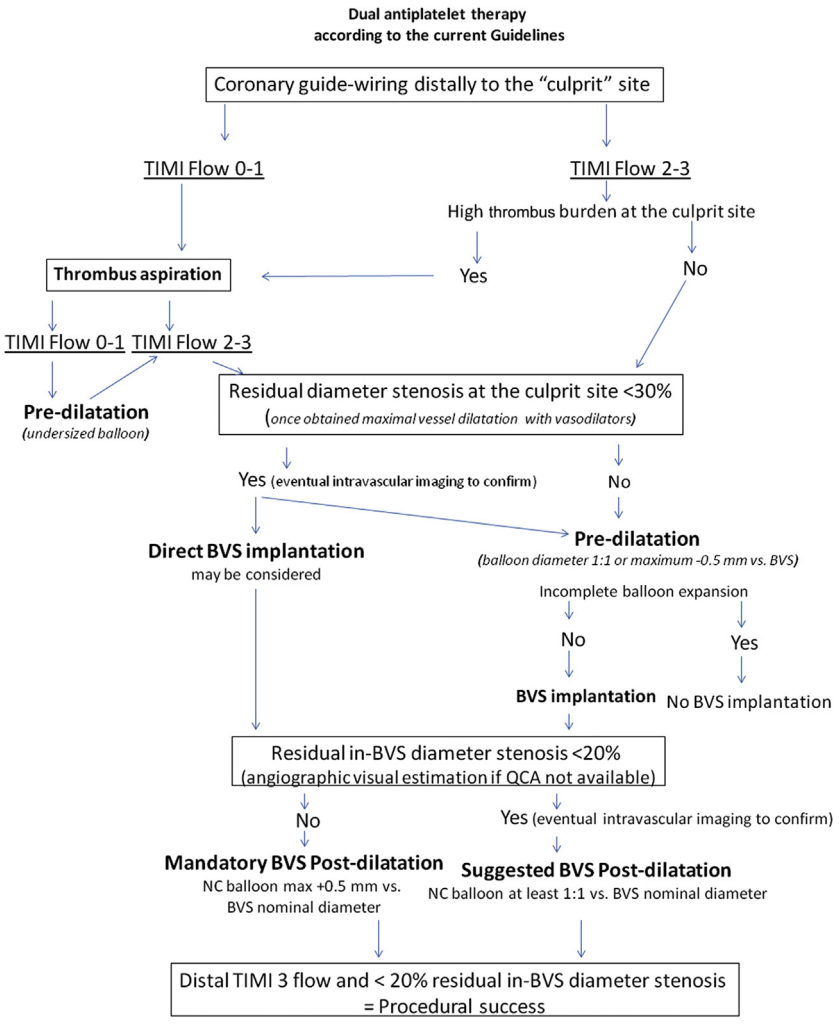
CLINICAL ENDPOINTS. Study endpoints have been previously described (6). In summary, the primary endpoint of the study is a device-oriented composite endpoint (DOCE) of cardiac death, target vessel myocardial infarction (TV-MI), and ischemia-driven target lesion revascularization (ID-TLR) within 30 days after the index procedure. The secondary endpoints are: 1) procedural success, defined as Absorb implantation at the "culprit" lesion site with <20% final in-BVS percentage diameter stenosis (DS) and distal TIMI (Thrombolysis In Myocardial Infarction) flow grade 3; 2) DOCE at 6 months and 1-, 3-, and 5-year follow-up; 3) any definite or probable ScT (in-hospital, within 7 days after pPCI, and at follow-up); 4) any bleeding (in-hospital, within 7 days after pPCI, and at follow-up); 5) cardiac death, TV-MI, ID-TLR, and target vessel revascularization (as singular endpoints) in-hospital, within 7 days after pPCI, or at follow-up; and 6) ST-segment resolution on electrocardiography within 60 min of pPCI.

CLINICAL FOLLOW-UP. Clinical data at follow-up were collected by the medical staff of each participating center by hospital visit or telephone contact at 30 days. Angiographic follow-up was not mandatory

Hospital, Legnano, Italy; [l]Interventional Cardiology Unit, Riuniti Hospital, Ancona, Italy; [m]Interventional Cardiology Unit, EMO-GVM Centro Cuore Columbus, Milan, Italy; and the [n]Interventional Cardiology Unit, San Raffaele Scientific Institute, Milan, Italy. This work was supported by a research grant from Abbott Vascular. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received June 11, 2017; revised manuscript received July 10, 2017, accepted July 19, 2017.

FIGURE 1 Flowchart Illustrating the Absorb Implantation Strategy in Patients With ST-Segment Elevation Myocardial Infarction

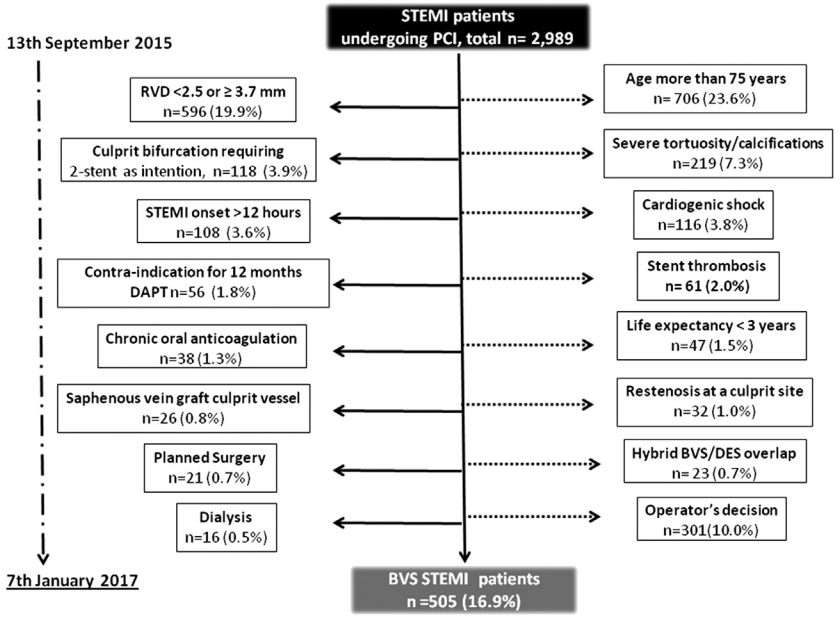


BVS = bioresorbable vascular scaffold; NC = noncompliant; QCA = quantitative coronary angiography; TIMI = Thrombolysis In Myocardial Infarction.

but performed only in case of planned "step" revascularization or if clinically indicated at follow-up. Clinical, lesion, and procedural data and follow-up outcomes of patients who provided written informed consent were entered into a Web-based case report form managed by Cardiogroup.org. The safety monitoring of the study and the data entry were continuously supervised by the study steering committee. Source document verification was routinely performed for 100% of all reported events. All clinical endpoints were adjudicated by an independent clinical event adjudication committee. Clinical and procedural source document verification was performed in a random 25% of all enrolled patients.

THE "BVS STEMI STRATEGY." The pre-specified BVS implantation protocol during pPCI was previously and extensively described elsewhere (6). pPCI was performed according to standard practice (7). A loading dose of the strongest dual-antiplatelet therapy (DAPT) regimen actually available (i.e., aspirin 250 to 500 mg intravenous bolus and ticagrelor 180 mg or prasugrel 60 mg or clopidogrel 600 mg when ticagrelor or prasugrel were not available) has been suggested to be administered as soon as possible before pPCI and followed for at least 12 months by a maintenance dose (aspirin 100 mg/day, ticagrelor 180 mg twice daily, prasugrel 10 mg/day, clopidogrel 75 mg/day). Unfractionated heparin (70/100 IU/kg)

FIGURE 2 Study Diagram According to the Exclusion Criteria



BVS = bioresorbable vascular scaffold; DAPT = dual antiplatelet therapy; DES = drug-eluting stent(s); PCI = percutaneous coronary intervention; RVD = reference vessel diameter; STEMI = ST-segment elevation myocardial infarction.

was the parenteral anticoagulant agent suggested during pPCI. After distal TIMI flow grade 2 or 3 restoration (with or without manual thrombus aspiration), the maximum culprit vessel dilatation by the administration of an intracoronary bolus of vasodilator drugs was recommended (whether clinically feasible) in order to accurately select the BVS diameter according to the maximal vessel diameter (visually estimated by the operator if quantitative coronary angiography was unavailable, whereas intracoronary imaging was left to the operator's discretion) assessed immediately (5 to 10 mm) proximal to the culprit lesion site (in 2 orthogonal angiographic views). Direct BVS implantation was allowed in case of successful distal TIMI flow grade 2 or 3 restoration with residual DS at the culprit site <30%. In the other cases, pre-dilatation with semicompliant or noncompliant (NC) balloons (ratio 1:1 compared with the nominal diameter of the selected BVS or undersized of a maximum of 0.5 mm less than the nominal diameter of the selected BVS) was recommended. The full and homogeneous expansion of the pre-dilatation balloon (1:1 sizing) was considered as a crucial sign to proceed to BVS implantation. BVS deployment was performed gradually according to the instructions for use, and once reached, the target pressure was maintained (if tolerated by the patient) for at least 30 s to favor device expansion. Even if post-dilatation is not routinely performed during pPCI with new-generation DES (15% to 20% of cases) (8), it was strongly encouraged for BVS implantation in this study. In particular, the inflation of a NC balloon (for 10 to 60 s if tolerated by the patient) with a maximum diameter 0.5 mm more than the nominal BVS diameter implanted is needed in case of TIMI flow grade 3 and more than 20% in-BVS residual DS at the culprit site. In case of TIMI flow grade 3 and <20% residual in-BVS DS, the decision to post-dilate (NC balloon diameter ratio at least 1:1 with the nominal diameter of the BVS implanted) was left to the operator's discretion but strongly encouraged, particularly in case of reference vessel diameter (RVD) of 2.5 to 2.6 mm. Post-dilatation could be avoided in case of: 1) no residual stenosis associated with adequate BVS expansion and apposition (preferably confirmed by intravascular imaging; or 2) persistent slow flow or no-reflow during BVS implantation (although it was still encouraged in case of TIMI flow grade 3 restoration). Figure 1 shows the BVS implantation strategy flowchart. Quantitative coronary angiographic analysis immediately before and after BVS implantation were analyzed offline by an expert independent operator at a central core laboratory of the Thorax Institute IDIBAPS, University of Barcelona.

STATISTICAL ANALYSIS. Statistical analysis for primary and secondary endpoints were performed for the overall population. Numeric data are presented as mean ± SD or median (interquartile ranges). Categorical data are presented as counts and percentages of the total. All data were analyzed using descriptive statistical methods. All analyses were performed using SPSS version 21.0 software (SPSS, Chicago, Illinois). Given that this was an observational study, we relied on confidence interval profiling for sample size justification, without proceeding with formal power analysis. Accordingly, we computed that a target sample of 500 patients would enable the computation of reasonably precise 95% confidence intervals. Specifically, assuming the rate of 3.1% DOCE at 30 days (in keeping with the BVS-EXAMINATION data), confidence intervals computed with the Wilson score would be from 2.0% to 5.1% (16 of 500).

RESULTS

Between September 13, 2015, and January 7, 2017, a total of 2,989 patients with STEMI underwent pPCI at 22 Italian centers (80% of them simultaneously active in the enrollment only from July 2016). Among these patients, 505 (16.9%) were treated with at least 1 BVS implantation. Major exclusion criteria were age >75 years and reference diameter at the culprit site <2.5 mm or >3.7 mm (23.6% and 19.9%, respectively, of the excluded patients). Figure 2 shows the study flowchart. Baseline patient characteristics are shown in Table 1. The mean age was 56.6 ± 9.4 years. Sixty-nine patients (13.7%) had diabetes, and 487 (96.4%) were in Killip class I or II at admission. Lesion and procedural characteristics are described in Table 2. Of the 505 patients with STEMI, the majority of infarctions (228 [45.1%]) involved the anterior myocardial wall. Manual thrombectomy was performed in 227 patients (45%), and intracoronary vasodilator drugs were administered after flow restoration (≥1) in 351 patients (69.5%). According to the study protocol, direct BVS implantation was feasible in 47 patients (9.3%). Pre-dilatation was performed in 458 patients (90.7%), in 282 (61.6%) with "undersized" balloons. About 90% of the BVS implanted were 3.0 and 3.5 mm in diameter. Intracoronary imaging before and after BVS implantation was used in 26 patients (5.1%). BVS post-dilatation was performed in 468 patients (92.7%) and in the vast majority (411 of 468 [87.8%]), even in case of in-BVS DS <20% (not mandatory but suggested by the protocol in this specific situation). The DAPT bolus was administered in 230 patients (45.5%) at the first

TABLE 1 Baseline Patient Characteristics (N = 505)

Demographic characteristics	
Age (yrs)	56.6 ± 9.4
Male	410 (81.2)
Cardiovascular risk factors	
Hypertension	241 (47.7)
Diabetes mellitus	69 (13.7)
Hypercholesterolemia	238 (47.1)
Family history of CAD	156 (30.9)
Smoking history	273 (54.2)
Clinical characteristics	
Killip class I or II at presentation	487 (96.4)
Multivessel CAD	137 (27.1)
Previous myocardial infarction	19 (3.8)
Previous PCI	22 (4.4)
LV ejection fraction	50.7 ± 7.4
COPD	18 (3.6)
Chronic kidney disease (eGFR <60 ml/min)	12 (2.4)
Peripheral artery disease	10 (2.0)

Values are mean ± SD or n (%).

CAD = coronary artery disease; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; PCI = percutaneous coronary intervention.

TABLE 2 Lesion and Procedural Characteristics (N = 505)

Radial access	455 (90.1)
Symptom-to-balloon time (min)	168.5 (117.5–260.0)
Door-to-balloon time (min)	40 (30–60)
Off-duty primary PCI	261 (51.7)
"Culprit" LAD	228 (45.1)
Intracoronary vasodilator administration after flow restoration	351 (69.5)
Manual thrombectomy	227 (45.0)
Direct BVS implantation	47 (9.3)
Pre-dilatation balloon diameter sized 1:1 vs. artery diameter/BVS implanted	176 (38.4)
"Undersized" pre-dilatation	282 (61.6)
"Culprit" bifurcation with SB >2 mm	96 (19.0)
BVS diameter (mm)	3.2 ± 0.3
At least 1 BVS (2.5 mm) implanted	51 (10.1)
BVS length (mm)	22.8 ± 4.8
BVS overlap	109 (21.6)
Intracoronary imaging before and after BVS implantation	26 (5.1)
Intracoronary imaging at least after BVS implantation	52 (10.2)
Post-dilatation	468 (92.7)
Post-dilatation despite in-BVS %DS <20%	411 (87.8)
Post-dilatation balloon diameter (mm)	3.42 ± 0.38
Post-dilatation balloon pressure (atm)	18.2 ± 6.1
Post-dilatation balloon diameter +0.50 mm vs. BVS nominal diameter	185 (39.5)
Post-dilatation balloon diameter +0.25 mm vs. BVS nominal diameter	98 (20.9)
BVS number per patient	1.45 ± 0.77

Values are n (%), median (interquartile range), or mean ± SD.

BVS = bioresorbable vascular scaffold; DS = diameter stenosis; LAD = left anterior descending coronary artery; SB = side branch.

TABLE 3 Periprocedural Antithrombotic and Antiplatelet Drug Regimen (N = 505)

Periprocedural antiplatelet agent administration	
First medical contact	230 (45.5)
Immediately pre-PCI	207 (41.0)
Immediately post-PCI	69 (13.5)
Aspirin and ticagrelor or prasugrel	483 (95.6)
Dual antiplatelet regimen at discharge	
Aspirin and ticagrelor	367 (72.6)
Aspirin and prasugrel	114 (22.5)
Aspirin and clopidogrel	25 (4.9)
Periprocedural antithrombotic regimen	
Unfractionated heparin	503 (99.6)
Bivalirudin	2 (0.4)
GP IIb/IIIa inhibitors	204 (40.3)

Values are n (%).
GP = glycoprotein; PCI = percutaneous coronary intervention.

TABLE 4 Angiographic Characteristics and Quantitative Coronary Angiography (N = 505)

Baseline TIMI flow grade 0 or 1	310 (61.2)
Baseline TIMI flow grade 2 or 3	196 (38.8)
Final TIMI flow grade 3	482 (95.4)
TIMI thrombus scale 4 or 5	256 (50.7)
Pre-procedure	
Lesion length (mm)	18.6 ± 10.7
Reference diameter (mm)	2.72 ± 0.41
MLD (mm)	0.44 ± 0.51
DS (%)	84.5 ± 11.7
Post-procedure	
Device length (mm)	27.1 ± 12.2
Reference diameter (mm)	3.0 ± 0.57
MLD (mm)	2.65 ± 1.43
DS (%)	14.5 ± 6.3
Acute gain (mm)	2.36 ± 2.32

Values are n (%) or mean ± SD.
DS = diameter stenosis; MLD = minimal luminal diameter; TIMI = Thrombolysis In Myocardial Infarction.

medical contact, and 481 patients (95.1%) received aspirin in addition to ticagrelor or prasugrel (Table 3). Quantitative coronary angiographic data are reported in Table 4.

OUTCOMES. Procedural and clinical endpoints are shown in Table 5. Procedural success (by visual estimation) was obtained in 479 patients (94.8%) and by off-line quantitative coronary angiographic measurements in 445 patients (88.1%). BVS implantation failure was reported in 3 patients (0.6%) because of unsuccessful device delivery at the culprit site. Thirty-day follow-up was available for all eligible patients. At 30-day follow-up, the hierarchical DOCE rate was 0.6% (3 events). Two patients (0.4%) died. One died suddenly (abrupt asystole probably related to cardiac rupture but classified as probable ScT) 2 days after the index procedure (manual thrombectomy, 2.5-mm balloon pre-dilatation, 3.0 × 28.0 mm BVS implantation at the left anterior descending coronary artery-diagonal bifurcation, then post-dilatation with a 3.5-mm NC balloon), whereas another patient died during hospitalization 26 days after the index procedure (pre-dilatation with a 2.0-mm balloon, 2.5 × 28.0 mm BVS implanted at the left circumflex coronary artery-obtuse marginal bifurcation, then post-dilatation with a 2.5-mm NC balloon at 20 atm) following a systemic infection (orotracheal intubation was required during the index procedure because of multiple cardiac arrests). TV-MI and ID-TLR occurred in 1 patient (0.2%). In detail, the subject underwent emergent coronary angiography 3 days after the index procedure because of transient inferior ST-segment elevation. Reversible coronary spasm was revealed in the segments proximal to the 3.5 × 28.0 mm BVS implanted (during the index procedure after manual thrombectomy, pre-dilatation with a 3.0-mm semi-compliant balloon, then post-dilatation with a 3.5-mm NC balloon at 20 atm) in the distal right coronary artery. However, after intracoronary imaging evaluation demonstrating BVS malapposition, percutaneous coronary intervention (PCI) with a 4.0-mm NC balloon at 20 atm was performed. The patient was then discharged 1 week later uneventfully. No episodes of definite ScT were reported, whereas 7 patients experienced bleeding, classified as Bleeding Academic Research Consortium grade 3b in 2 (0.4%), grade 2 in 3 (0.6%), and grade 1 in 2 (0.4%).

DISCUSSION

The main findings of this study of patients with STEMI younger than 75 years treated by pPCI with BVS are as follows: 1) feasibility of a pre-specified Absorb implantation strategy demonstrated by 94.8% procedural success; and 2) a lower 30-day DOCE rate (0.6%) compared with historical STEMI cohorts treated with the Absorb without a specific implantation strategy (Table 6).

Advances in antiplatelet agents, interventional techniques, and DES design have improved the outcomes of patients with acute coronary syndromes treated with PCI. Even if the newer generation DES are associated with excellent clinical performance in patients with STEMI (9), they all have potential shortcomings related to the permanent caging of the coronary wall at the original "culprit" site. The BVS technology represents the last frontier in interventional cardiology, with theoretical advantages over

TABLE 5 Procedural and Clinical Endpoints (N = 505)

BVS implantation failure	3 (0.6)
Primary endpoints at 30 days	
Hierarchical DOCE	3 (0.6)
Secondary endpoints	
Procedural success	479 (94.8)
ST-segment resolution >70% within 60 min after pPCI	299 (59.2)
Cardiac death	2 (0.4)
All cause death	2 (0.4)
ID-TLR	1 (0.2)
All TLR	2 (0.4)
TV-MI	1 (0.2)
Definite/probable scaffold thrombosis	1 (0.2)
Overall bleeding events	7 (1.4)
BARC grade 3b	2 (0.4)
BARC grade 2	3 (0.6)

Values are n (%).

BARC = Bleeding Academic Research Consortium; BVS = bioresorbable vascular scaffold; DOCE = device-oriented composite endpoint; ID-TLR = ischemia-driven target lesion revascularization; pPCI = primary percutaneous coronary intervention; TLR = target lesion revascularization; TV-MI = target vessel myocardial infarction.

metallic prosthesis to be assessed at long-term follow-up.

Data from randomized trials comparing Absorb with a cobalt-chromium everolimus-eluting stent (EES) at 1 year showed similar clinical (albeit inferior angiographic) efficacy as well as increased rates of TV-MI and ScT (10,11).

More recently, 3-year data from the ABSORB II trial demonstrated no differences in vasomotion and a significantly higher rate of late lumen loss in Absorb-treated lesions. Moreover, Absorb implantation was clinically inferior (although the trial was not powered for clinical endpoints) to the counterpart because of higher TV-MI and very late ScT rates (12). Similar clinical results were also reported in the 2-year data from the AIDA (Amsterdam Investigator-Initiated Absorb Strategy All-Comers) randomized trial assessing BVS performance (vs. metallic EES) in routine PCI (13). Absorb implantation techniques in the early post-procedural period, along with device characteristics related to the degradation process late or very late at follow-up (i.e., late structural discontinuity and malapposed or uncovered BVS struts) (14), could be advocated as potential causes for these results.

On the basis of this evidence, the question regarding both the real benefit of Absorb over DES and the optimal patient or lesion subset in which this device could maximally express its performance remains open. Acute coronary syndromes at admission and particularly STEMI were an exclusion criterion for all the aforementioned trials, whose results cannot be extended beyond subjects with stable de novo coronary artery disease. An interesting question is whether STEMI represents an intriguing target for Absorb implantation. Theoretically it does, because of the unique characteristics of the patients and lesions involved. Patients with STEMI are usually younger with fewer comorbidities compared with patients in stable condition and thus better tolerate a stronger DAPT regimen. The softer "culprit" lesion (compared with a stable one) appears more easily expandable by the Absorb, resulting in more complete strut embedding to the vessel wall. Furthermore, the thrombotic material superimposing the culprit plaque may be trapped behind the large Absorb struts, reducing the risk for distal embolization (i.e., the concept of snowshoes vs. ice skates) (15). In contrast, BVS implantation in a thrombotic setting could be associated with higher risk (compared with DES) of incomplete (early and/or late) strut apposition, potentially leading to hard clinical events (i.e., TV-MI and ScT).

The only randomized study comparing Absorb with EES in STEMI (although not powered for clinical endpoints) showed similar results in terms of 6-month vascular healing. Furthermore, the acute gain and post-procedural minimal luminal diameter were identical in both arms, supporting the concept that thrombotic lesions could be more amenable (compared with stable lesions) to Absorb treatment (1). In contrast, 2 propensity matched-analyses of Absorb (implanted without a specific strategy) versus cobalt-chromium EES raised concerns about Absorb safety in the STEMI setting because of a non-negligible ScT rate within the first 30 days (2.1%) (2) after implantation up to 18-month follow-up (4.3%) (3). Data from a retrospective all-comers cohort of 1,305 Absorb-treated patients (16) and from the "PSP" analysis of the GHOST-EU study (17) clearly showed that a tailored Absorb implantation technique could significantly reduce the early and midterm incidence of scaffold failures. However, the vast majority of the Absorb-treated patients in the aforementioned studies had no STEMI at admission, and it is unknown whether the techniques proposed could be different for this setting.

The present study represents the first prospective evaluation of a pre-defined Absorb implantation strategy in the complex STEMI scenario. The high procedural success rate reported supports the feasibility of the proposed strategy that mixed the strongest DAPT regimen actually available with specific procedural steps in association with reasonable patient selection. The latter point appears of equal importance as well as the implantation strategy, because the current BVS generation does not fit for an all-comers patient or lesion population (i.e., older

TABLE 6 Comparison of the Main Studies Assessing Absorb Performance in ST-Segment Elevation Myocardial Infarction

	BVS STEMI STRATEGY-IT	BVS EXAMINATION (2)	BVS STEMI First (3)	TROFI II (1)
N	505	290 (BVS arm)	151 (BVS arm)	95 (BVS arm)
Type	Registry	Propensity match	Propensity match	Randomized
Recruitment period	September 2015 to January 2017	December 2012 to June 2013	November 2012 to April 2013	January 2014 to September 2014
Thrombus aspiration, %	45.0	75.0	76.7	81.0
Pre-dilatation, %	90.7	81.0	54.1	56.0
Post-dilatation, %	92.7	36.0	39.7	50.0
DAPT including prasugrel and ticagrelor, %	95.1	66.7	NA	63.1
Intravascular imaging at baseline procedure, %	10.2	NA	NA	NP
30-day definite/probable ScT	0.2	2.1	2.8	0.0
30-day DOCE	0.6	3.1	NA	0.0

DAPT = dual antiplatelet therapy; DOCE = device-oriented composite endpoint; NA = not available; NP = not performed (optical coherence tomography was done only at 6-month follow-up, not at the index procedure to guide BVS implantation); ScT = scaffold thrombosis.

patients, "late comers STEMI," RVD at the culprit site <2.5 or >3.7 mm, "tapered" vessels, cardiogenic shock, contraindications to prolonged DAPT), limiting its use to a relatively restrained number of patients (16.9% of the overall population treated during the study period). However, patient selection did not automatically translate into treating simple lesions, as demonstrated by the high thrombus burden at the culprit site (51% of TIMI thrombus scale 4 to 5), the 21% of overlapping BVS (maximum of 5 in a single patient) and the 19% of bifurcations involved. The hierarchical DOCE rate of 0.6% and the ScT rate of 0.2% reported within 30 days were significantly lower compared with the 3.1% and 2.1% rates reported in the scaffold cohort (n = 290 patients) of the BVS EXAMINATION study, in which no specific implantation strategies were used in patients with STEMI. In detail, vessel sizing and percentage DS assessment after flow restoration (TIMI flow grade ≥1), with or without manual thrombectomy, was the first important step in our strategy. To reduce the vasoconstriction typical of the acute phase, administration of intracoronary vasodilator drugs was strongly suggested (administered in 70% of the cases) to properly size the vessel after maximal dilatation. This step assumed the hemodynamic stability of the patient, as predominantly was the case in our STEMI cohort. Absorb diameter selection was based mostly, as per routine clinical practice, on the angiographic images (mostly estimated visually by the operator) according to the maximal vessel diameter proximal to the culprit lesion site. In case of excessive vessel tapering (i.e., more than 0.25 mm) at the distal landing zone, BVS implantation was not considered to avoid significant mismatch or vessel dissection. The slight Absorb diameter overestimation, suggested to overcome the risk for BVS undersizing, compared with the proximal estimated RVD was reflected by the low rate (10%) of 2.5-mm BVS implanted that were selected only for vessels with RVDs between 2.5 and 2.6 mm.

According to the study protocol, DS <30% at the culprit site (after flow restoration and maximal dilatation) was adopted as a cutoff value to allow direct Absorb implantation (feasible in 9.3% of cases). Post-dilatation with an NC balloon (maximum +0.5 mm compared with the nominal diameter of the Absorb implanted) was mandatory in case of >20% in-Absorb DS and strongly suggested in case of <20% in-Absorb DS (except in case of intracoronary imaging demonstrating a perfect embedment of the Absorb struts into the vessel wall). These pre-specified recommendations resulted in 90.7% pre-dilatation (62% with an undersized balloon) and 92.7% post-dilatation rates, both higher not only compared with those of historical DES cohorts implanted in all-comers STEMI studies (pre-dilatation, 40% and 62% [8,18]; post-dilatation, 16%) (8) but also compared with those of the scaffold arms from the BVS EXAMINATION (pre-dilatation, 81%; post-dilatation, 36.3%) and the BVS STEMI First (pre-dilatation, 54.1%; post-dilatation, 39.7%) studies. The 87.8% post-dilatation rate reported despite the in-Absorb DS of <20% was probably led by the prevalent angiographically guided BVS implantation strategy with a high rate of overlapping BVS. However, post-dilatation was not associated with a particular risk for no-reflow, as demonstrated by the final TIMI flow grade 3 rate of 95.4%. The protective impact of thicker versus thinner struts on thrombus prolapse and distal embolization was previously demonstrated in a small cohort of patients with STEMI (19).

Along with the dedicated implantation techniques aiming to reduce shear stress on top of the BVS struts, even the DAPT regimen may play an important role in

mitigating the risk for early ScT and clinical events, particularly in relatively young patients with STEMI (20). The vast majority of our patients (95%) received prasugrel and ticagrelor (in association with aspirin), which achieve more prompt and potent platelet inhibition (compared with clopidogrel) and are associated with low rates of stent thrombosis in patients with acute coronary syndromes treated with PCI (21,22). Furthermore, 45.5% of our patients with STEMI received a pre-hospital bolus of ticagrelor, which has been demonstrated to reduce rates of stent thrombosis and myocardial infarction (compared with in-hospital bolus) within 24 h after pPCI with stent implantation (23). In contrast, intravenous glycoprotein IIb/IIIa inhibitors were administered to 40.3% of our BVS patients with STEMI in case of potential delayed antiplatelet effect due to absence of pretreatment with both antiplatelet agents. Whether our strategy of combining the optimal DAPT regimen and a tailored BVS implantation strategy might affect the mid- and long-term outcomes of patients with STEMI remains to be investigated.

STUDY LIMITATIONS. The observational nature of the study, the lack of a direct comparison with a current-generation DES, and the short follow-up period represent the major limitations. All these aspects preclude reaching definitive conclusions in terms of clinical outcomes. Although our inclusion criteria were broader than those of other BVS studies, our cohort was inherently less "complex" than a "real-world" all-comers population, precluding generalization of the outcomes reported in the overall STEMI population. Furthermore, the proposed strategy was tested using the Absorb polymeric scaffold, and our results cannot be extended to other polymeric or metallic scaffolds actually available on the market.

CONCLUSIONS

Our study represents the first prospective evaluation demonstrating the feasibility of a pre-specified BVS implantation technique in patients with STEMI younger than 75 years undergoing pPCI. Although the proposed strategy was associated with a lower 30-day DOCE rate compared with historical BVS STEMI cohorts, its potential impact on mid- and long-term outcomes needs to be determined.

ADDRESS FOR CORRESPONDENCE: Dr. Alfonso Ielasi, Cardiology Department, Azienda Socio Sanitaria Territoriale Bergamo Est, Bolognini Hospital Seriate, Via Paderno 21, 24068 Seriate (BG), Italy. E-mail: alielasi@hotmail.com.

PERSPECTIVES

WHAT IS KNOWN? Concerns have been raised about the safety of the Absorb BVS in the attractive STEMI subset because a non-negligible rate of ScT was reported early and at midterm follow-up after pPCI. Technical issues specifically related to the structural features of Absorb were advocated as probable causes for the early events.

WHAT IS NEW? This study represents the first prospective evaluation of a pre-defined Absorb implantation strategy in selected patients with STEMI undergoing pPCI. The high procedural success rate reported supports the feasibility of the proposed strategy that mixed the strongest DAPT regimen actually available with specific procedural steps in association with a reasonable patient selection.

WHAT IS NEXT? Although the proposed strategy was associated with lower 30-day DOCE and ScT rates compared with historical BVS STEMI cohorts, its potential impact on mid- and long-term outcomes needs to be determined. Randomized studies comparing Absorb (implanted according to the strategy proposed) versus EES may be needed to assess the potential role of this polymeric BVS in selected subjects with STEMI.

REFERENCES

1. Sabatè M, Windecker S, Iñiguez A, et al. Everolimus-eluting bioresorbable stent vs. durable polymer everolimus-eluting metallic stent in patients with ST-segment elevation myocardial infarction: results of the randomized ABSORB ST-segment elevation myocardial infarction-TROFI II trial. Eur Heart J 2016;37:229–40.

2. Brugaletta S, Gori T, Low AF, et al. Absorb bioresorbable vascular scaffold versus everolimus-eluting metallic stent in ST-segment elevation myocardial infarction: 1-year results of a propensity score matching comparison: the BVS-EXAMINATION study (bioresorbable vascular scaffold—a clinical evaluation of everolimus eluting coronary stents in the treatment of patients with ST-segment elevation myocardial infarction). J Am Coll Cardiol Intv 2015;8:189–97.

3. Fam JM, Felix C, van Geuns RJ, et al. Initial experience with everolimus-eluting bioresorbable vascular scaffolds for treatment of patients presenting with acute myocardial infarction: a propensity-matched comparison to metallic drug eluting stents 18-month follow-up of the BVS STEMI First study. EuroIntervention 2016;12:30–7.

4. Kocka V, Maly M, Tousek P, et al. Bioresorbable vascular scaffolds in acute ST-segment elevation myocardial infarction: a prospective multicentre study "Prague 19." Eur Heart J 2014;35:787–94.

5. Ielasi A, Cortese B, Varricchio A, et al. Immediate and midterm outcomes following primary PCI

with bioresorbable vascular scaffold implantation in patients with ST-segment myocardial infarction: insights from the multicentre "Registro ABSORB Italiano" (RAI registry). EuroIntervention 2015;11:157–62.

6. Ielasi A, Varricchio A, Campo G, et al. A prospective evaluation of a standardized strategy for the use of a polymeric everolimus-eluting bioresorbable scaffold in ST-segment elevation myocardial infarction: rationale and design of the BVS STEMI STRATEGY-IT study. Catheter Cardiovasc Interv 2017;89:1129–38.

7. Windecker S, Kolh P, Alfonso F, et al. 2014 ESC/EACTS guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2014;35:2541–619.

8. Sabatè M, Cequier A, Iniguez A, et al. Everolimus-eluting stent versus bare-metal stent in ST-segment elevation myocardial infarction (EXAMINATION): 1 year results of a randomised controlled trial. Lancet 2012;380:1482–90.

9. Sabaté M, Räber L, Heg D, et al. Comparison of newer-generation drug-eluting with bare-metal stents in patients with acute ST-segment elevation myocardial infarction: a pooled analysis of the EXAMINATION (Clinical Evaluation of the Xience-V Stent in Acute Myocardial Infarction) and COMFORTABLE-AMI (Comparison of Biolimus Eluted From an Erodible Stent Coating With Bare Metal Stents in Acute ST-Elevation Myocardial Infarction) trials. J Am Coll Cardiol Intv 2014;7:55–63.

10. Cassese S, Byrne RA, Ndrepepa G, et al. Everolimus-eluting bioresorbable vascular scaffolds versus everolimus-eluting metallic stents: a meta-analysis of randomised controlled trials. Lancet 2016;387:537–44.

11. Stone GW, Gao R, Kimura T, et al. 1-Year outcomes with the Absorb bioresorbable scaffold in patients with coronary artery disease: a patient-level, pooled meta-analysis. Lancet 2016;387:1277–89.

12. Serruys PW, Chevalier B, Sotomi Y, et al. Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II): a 3 year, randomised, controlled, single-blind, multicentre clinical trial. Lancet 2016;388:2479–91.

13. Wykrzykowska JJ, Kraak R, Hofma S, et al. Bioresorbable scaffold versus metallic stent in routine PCI. N Engl J Med 2017;376:2319–28.

14. Raber L, Brugaletta S, Yamaji K, et al. Very late scaffold thrombosis: intracoronary imaging and histopathological and spectroscopic findings. J Am Coll Cardiol 2015;66:1901–14.

15. Serruys PW, Suwannasom P, Nakatani S, et al. Snowshoe versus ice skate for scaffolding of disrupted vessel wall. J Am Coll Cardiol Intv 2015;8:910–3.

16. 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 2016;67:921–31.

17. Ortega-Paz L, Capodanno D, Gori T, et al. Predilation, sizing and post-dilation scoring in patients undergoing everolimus-eluting bioresorbable scaffold implantation for prediction of cardiac adverse events: development and internal validation of the PSP score. EuroIntervention 2017;12:2110–7.

18. Räber L, Kelbaek H, Ostoijc M, et al. Comparison of biolimus eluted from an erodible stent coating with bare metal stents in acute ST-elevation myocardial infarction (COMFORTABLE AMI trial): rationale and design. EuroIntervention 2012;7:1435–43.

19. Diletti R, van der Sijde J, Karanasos A, et al. Differential thrombotic prolapse burden in either bioresorbable vascular scaffolds or metallic stents implanted during acute myocardial infarction: the snowshoe effect: insights from the maximal footprint analysis. Int J Cardiol 2016;220:802–8.

20. Montalescot G, van 't Hof AW, Lapostolle F, et al., for the ATLANTIC Investigators. Prehospital ticagrelor in ST-segment elevation myocardial infarction. N Engl J Med 2014;371:1016–27.

21. Wiviott SD, Braunwald E, McCabe CH, et al., for the TRITON-TIMI 38 Investigators. Intensive oral antiplatelet therapy for reduction of ischaemic events including stent thrombosis in patients with acute coronary syndromes treated with percutaneous coronary intervention and stenting in the TRITON-TIMI 38 trial: a subanalysis of a randomised trial. Lancet 2008;371:1353–63.

22. Steg PG, Harrington RA, Emanuelsson H, et al., for the PLATO Study Group. Stent thrombosis with ticagrelor versus clopidogrel in patients with acute coronary syndromes: an analysis from the prospective, randomized PLATO trial. Circulation 2013;128:1055–65.

23. Montalescot G, van't Hof AW, Bolognese L, et al., for the ATLANTIC Investigators. Effect of pre-hospital ticagrelor during the first 24 h after primary percutaneous coronary intervention in patients with ST-segment elevation myocardial infarction: the ATLANTIC-H^2? analysis. J Am Coll Cardiol Intv 2016;9:646–56.

KEY WORDS bioresorbable scaffold, primary PCI, STEMI

APPENDIX For a list of collaborators, please see the online version of this article.