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Bioresorbable Everolimus-Eluting Vascular Scaffold for Long Coronary Lesions

A Subanalysis of the International, Multicenter GHOST-EU Registry

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ABSTRACT

OBJECTIVES The authors sought to investigate 1-year outcomes in patients treated with bioresorbable everolimus-eluting vascular scaffolds (BVS) for "long coronary lesions."

BACKGROUND The present substudy derived from the GHOST-EU registry included 1,722 lesions in 1,468 consecutive patients, enrolled between November 2011 and September 2014 at 11 European centers.

METHODS The lesions were divided into 3 groups according to continuous BVS length: 1) shorter than 30 mm; 2) between 30 and 60 mm; and 3) longer than 60 mm. Primary device-oriented endpoint (target lesion failure [TLF]) was defined as a combination of cardiovascular death, target vessel myocardial infarction, or clinically driven target lesion revascularization.

RESULTS Patients with lesions ≥60 mm had more comorbidities and more complex lesion characteristics, including chronic total occlusions (37%), bifurcation lesions (40.3%), higher Syntax score (16.4 ± 7.8), and higher number of scaffolds implanted per lesion (3.3 ± 0.9 mm). The main target vessel was the left anterior coronary artery in all groups. Median follow-up was 384 (interquartile range: 359 to 459) days. One-year follow-up was completed in 70.3% of patients. TLF at 1 year was significantly higher in group C (group A 4.8%, group B 4.5%, group C 14.3%; overall $p = 0.001$), whereas there were no significant differences between groups A and B. Finally, a numerically higher (but not statistically significant) number of scaffold thromboses were observed in group C when compared with shorter lesions (group A 2.1%, group B 1.1%, group C 3.8%; overall $p = 0.29$).

CONCLUSIONS In a real-world setting, treatment of long coronary lesions with BVS ≥60 mm was associated with a higher TLF rate, driven by myocardial infarction and clinically driven target lesion revascularization.
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Percutaneous treatment of long coronary artery lesions remains a challenge despite recent technical advances in the field. The optimal management of these lesions is becoming more important due to a rising incidence of long and complex lesions in an increasingly elderly and comorbid population (1).

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The advent of drug-eluting stents (DES) has dramatically reduced the rates of restenosis and target lesion revascularization (TLR) and has further improved outcomes compared with bare-metal stents (BMS) (2,3). However, multiple DES implantation (full metal jacket) for diffuse coronary lesions remains associated with high rates of restenosis and stent thrombosis due to several factors including delayed arterial healing, inflammation, and malapposition or incomplete stent apposition) (4,5). Furthermore, the presence of a permanent metallic cage of long coronary segments with DES precludes future surgical revascularization if needed and is associated with a risk of very late stent thrombosis.

Bioresorbable vascular scaffold (BVS) treatment of long coronary lesions is particularly attractive due to its complete resorption within 3 to 4 years, allowing for the possibility of positive vessel remodeling and restoration of vasomotor and endothelial function. Furthermore, this approach does not preclude future surgical or percutaneous revascularization, allows for follow-up with noninvasive imaging, and possibly reduces the risk of very late stent thrombosis. Several pivotal studies have demonstrated the safety and efficacy of this novel technology; however, there are limited data on outcomes following BVS implantation in this patient group.

The aim of this study was therefore to analyze 1-year outcomes following BVS implantation in long coronary artery lesions.

METHODS

STUDY DESIGN AND PATIENT POPULATION. The GHOST-EU (Gauging coronary Healing with bioresorbable Scaffolding plaTforms in EUrope) registry is an investigator-initiated, retrospective, multicenter registry conducted in 11 European centers in Italy, Germany, Poland, Spain, and the United Kingdom; specific details about this registry are described in a previous publication, reporting 30-day and 6-month outcomes (6). This study was an "all-comer" registry including consecutive patients who were treated with at least 1 Absorb BVS (Abbott Vascular, Santa Clara, California) for the treatment of coronary artery lesions. The present substudy included a total of 1,722 lesions in 1,468 patients, enrolled between November 2011 and September 2014. All lesions were divided into 3 groups according to continuous BVS length: 1) <30 mm; 2) 30 to 60 mm; and 3) ≥60 mm.

PROCEDURES AND FOLLOW-UP. All interventions were performed according to current best practice. The decision to perform post-dilation and intracoronary imaging, the choice of antithrombotic/antiplatelet therapy, and the choice of metallic DES or BMS implantation, when required, was not prespecified and was left to the operators' discretion. A loading dose of aspirin 250 to 500 mg was administered before percutaneous coronary intervention (PCI), unless patients were already on chronic aspirin therapy, followed by 75 to 100 mg oral daily lifelong. A loading dose of clopidogrel (300 to 600 mg), prasugrel (60 mg), or ticagrelor (180 mg) was administered before or immediately after PCI, unless patients

ABBREVIATIONS AND ACRONYMS

BMS = bare-metal stent(s)
BVS = bioresorbable vascular scaffold(s)
CI = confidence interval
DES = drug-eluting stent(s)
HR = hazard ratio
MI = myocardial infarction
PCI = percutaneous coronary intervention
QCA = quantitative coronary angiography
TLF = target lesion failure
TLR = target lesion revascularization

TABLE 1 Patient Characteristics

	BVS Length			
	<30 mm (n = 1,111)	30–60 mm (n = 276)	≥60 mm (n = 81)	p Value
Age, yrs	62.2 ± 11.1	62.1 ± 10.1	59.3 ± 27.2	0.12
Male	876 (78.8)	224 (81.2)	73 (90.1)	0.04
Current smoker	350 (31.5)	72 (26.1)	24 (29.6)	0.21
DM	267 (24.0)	85 (30.8)	28 (34.6)	0.01
Insulin-dependent DM	95 (8.7)	29 (10.8)	9 (11.3)	0.47
Hypertension	810 (72.9)	194 (70.3)	62 (76.5)	0.49
Dyslipidemia	573 (51.6)	149 (54.0)	49 (60.5)	0.26
Family history of CAD	329 (29.6)	94 (34.1)	32 (39.5)	0.08
Previous PCI	353 (31.8)	107 (38.8)	35 (43.2)	0.02
Previous CABG	51 (4.6)	15 (5.4)	4 (4.9)	0.84
Previous TIA/stroke	39 (3.5)	10 (3.6)	3 (3.7)	0.99
eGFR, ml/min/1.73 m^2	85.5 ± 27.2	87.1 ± 27.1	92.1 ± 26.3	0.03
Stable angina/silent ischemia	528 (47.5)	180 (65.2)	63 (77.8)	<0.001
Acute coronary syndrome	583 (52.5)	96 (34.8)	18 (22.2)	<0.001
Unstable angina	148 (13.3)	36 (13.0)	6 (7.4)	0.31
NSTEMI	223 (20.1)	26 (9.4)	10 (12.3)	<0.001
STEMI	212 (19.1)	34 (12.3)	2 (2.5)	<0.001
LVEF, %	54.0 ± 9.6	54.2 ± 8.1	52.8 ± 10.9	0.96
Multivessel disease	396 (35.6)	133 (48.2)	40 (49.4)	<0.001
Prasugrel use	246 (22.5)	57 (22.5)	20 (25.6)	0.82
Ticagrelor use	3 (0.3)	3 (1.2)	1 (1.3)	0.09

Values are mean ± SD or n (%).

BVS = bioresorbable vascular scaffolds; CABG = coronary artery bypass graft; CAD = coronary artery disease; PCI = percutaneous coronary intervention; DM = diabetes mellitus; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; NSTEMI = non-ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction; TIA = transient ischemic attack.

TABLE 2 Lesion and Procedural Characteristics

	BVS Length			
	<30 mm (n = 1,348 Lesions)	30-60 mm (n = 293 Lesions)	≥60 mm (n = 81 Lesions)	p Value
Target vessel				
LAD	611 (45.8)	168 (57.5)	42 (53.2)	0.001
LCX	356 (26.7)	56 (19.2)	7 (8.9)	<0.001
RCA	355 (26.6)	64 (21.9)	29 (36.7)	0.03
Type B2/C	571 (45.6)	209 (74.9)	68 (86.1)	<0.001
In-stent restenosis	38 (2.8)	16 (5.5)	2 (2.5)	0.06
Chronic total occlusion	45 (3.3)	33 (11.3)	30 (37.0)	<0.001
Ostial lesion	74 (6.2)	7 (2.6)	8 (10.5)	0.02
Bifurcation lesion	260 (25.0)	92 (38.8)	29 (40.3)	<0.001
Thrombotic lesion	268 (20.4)	23 (8.0)	1 (1.2)	<0.001
Syntax score	10.4 ± 7.2	14.6 ± 8.6	16.4 ± 7.8	<0.001
Pre-dilation	1,284 (95.3)	291 (99.3)	81 (100)	0.001
Number of BVS implanted	1.0 ± 0.1	2.0 ± 0.4	3.3 ± 0.9	<0.001
Total BVS length, mm	20.7 ± 5.5	45.4 ± 8.4	85.9 ± 7.2	<0.001
Average BVS diameter, mm	3.05 ± 0.40	3.09 ± 0.28	3.06 ± 0.24	0.25
Post-dilation	608 (45.1)	225 (76.8)	67 (82.7)	<0.001
IVUS	127 (10.9)	83 (29.2)	30 (37.0)	<0.001
OCT	116 (10.0)	67 (23.6)	33 (40.7)	<0.001
Overlap	33 (2.4)	252 (86.0)	78 (96.3)	<0.001

Values are n (%) or mean ± SD.

BVS = bioresorbable vascular scaffold; IVUS = intravascular ultrasound; LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; OCT = optical coherence tomography; RCA = right coronary artery.

were already on chronic therapy, followed by a maintenance dose of clopidogrel (75 mg once daily), prasugrel (10 mg once daily), or ticagrelor (90 mg twice daily) for 6 to 12 months. Cardiac enzymes (creatine kinase, creatine kinase-myocardial band, and troponin) were measured after the procedure in accordance with the practice at each participating center. Clinical follow-up was obtained by clinical visit or phone call, according to a time schedule specific for each hospital. Quantitative coronary angiography (QCA) was performed using standard methods and definitions at each institution (7). Procedural data at baseline and 6 and 12 months were collected.

TABLE 3 QCA Results

	BVS Length			
	<30 mm (n = 1,348 Lesions)	30-60 mm (n = 293 Lesions)	≥60 mm (n = 81 Lesions)	p Value
Baseline				
RVD, mm	2.91 ± 0.51	2.89 ± 0.49	2.89 ± 0.51	0.96
MLD, mm	0.81 ± 0.59	0.86 ± 0.49	0.79 ± 0.53	<0.001
%DS	72.4 ± 18.6	69.9 ± 17.3	70.7 ± 20.8	<0.001
Lesion length, mm	13.7 ± 7.1	28.6 ± 15.3	47.2 ± 23.5	<0.001
Post-procedure				
RVD, mm	3.05 ± 0.46	3.13 ± 0.43	3.09 ± 0.50	0.40
MLD, mm	2.67 ± 0.52	2.67 ± 0.44	2.68 ± 0.55	0.84
Acute gain, mm	1.86 ± 0.69	1.81 ± 0.57	1.89 ± 0.67	0.35
Residual %DS	12.5 ± 11.7	14.5 ± 10.0	13.4 ± 9.3	0.02

Values are mean ± SD.

BVS = bioresorbable vascular scaffold; DS = diameter stenosis; MLD = minimal lumen diameter; QCA = quantitative coronary angiography; RVD = reference vessel diameter.

OUTCOMES AND DEFINITIONS. The primary endpoint was a device-oriented composite endpoint (target lesion failure [TLF]) defined as a combination of cardiac death, target vessel myocardial infarction and clinically driven TLR at 1 year. Secondary endpoints included each component of TLF target vessel failure (defined as acombination of cardiac death, target vessel myocardial infarction [MI], and clinically driven target vessel revascularization), and scaffold thrombosis.

Scaffold thrombosis was classified according to the Academic Research Consortium criteria (8). Deaths not attributed to a specific cause were considered to be cardiac in etiology. Recurrent MI was defined according to the universal definition (9).

STATISTICAL ANALYSIS. All continuous variables were checked using the Kolmogorov-Smirnov test to evaluate normality of distribution. Differences in continuous variables among groups were compared using the Student *t* or Mann-Whitney *U* test appropriately. Categorical variables are presented as numerical values and percentages, and were compared using the chi-square or Fisher exact test. The cumulative event rates were estimated on a per-patient basis using Kaplan-Meier analysis, and the significance of differences between groups was assessed with the log rank test. Cox proportional hazards regression analysis was performed to identify predictors of TLF in the univariate analysis. Covariates with a $p < 0.10$ on the univariate analysis or judged to be of clinical importance were included in a multivariate model to investigate the independent predictors of TLF. The number of independent variables was limited to 1 for every 8 to 10 events. All p values were 2-sided, and values of $p < 0.05$ were considered as statistically significant. Analyses were performed with SPSS version 21.0 (SPSS, Chicago, Illinois).

RESULTS

BASELINE CLINICAL CHARACTERISTICS. There were 1,348 lesions in 1,111 patients (75.7%) in group A, 293 lesions in 276 patients (18.8%) in group B, and 81 lesions in 81 patients (5.5%) in group C. Patient characteristics are summarized in Table 1.

TABLE 4 Clinical Outcomes at 1 Year

	BVS Length				Pairwise Analysis		
	<30 mm (Group A) (n = 1,111)	30–60 mm (Group B) (n = 276)	≥60 mm (Group C) (n = 81)	Overall p Value	Group A vs. B	Group B vs. C	Group A vs. C
TLF				0.001	0.71	0.001	<0.001
6 months	37 (3.4)	4 (1.5)	7 (8.9)				
12 months	50 (4.8)	11 (4.5)	11 (14.3)				
TVF				0.001	0.52	0.001	<0.001
6 months	49 (4.5)	7 (2.7)	9 (11.6)				
12 months	68 (6.5)	14 (5.6)	13 (16.9)				
All-cause death				0.40	0.17	0.36	0.93
6 months	14 (1.3)	1 (0.4)	0				
12 months	15 (1.4)	1 (0.4)	1 (1.4)				
Cardiac death				0.22	0.09	0.07	0.90
6 months	12 (1.1)	0	0				
12 months	12 (1.1)	0	1 (1.4)				
Target vessel MI				0.01	0.10	0.002	0.02
6 months	20 (1.9)	1 (0.4)	5 (6.4)				
12 months	25 (2.4)	2 (0.8)	5 (6.4)				
CD-TLR				0.01	0.60	0.04	0.003
6 months	24 (2.2)	4 (1.5)	5 (6.4)				
12 months	37 (3.6)	11 (4.5)	8 (10.4)				
ST (definite or probable)				0.29	0.28	0.10	0.32
6 months	22 (2.0)	3 (1.1)	3 (3.8)				
12 months	23 (2.1)	3 (1.1)	3 (3.8)				

Values are n (cumulative event rates). The cumulative event rates were calculated with Kaplan-Meier analysis.

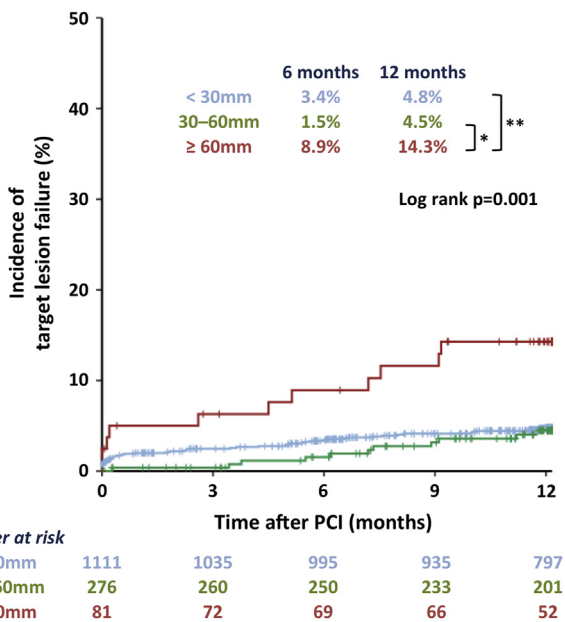
BVS = bioresorbable vascular scaffold; CD-TLR = clinically driven target lesion revascularization; MI = myocardial infarction; ST = scaffold thrombosis; TLF = target lesion failure; TVF = target vessel failure.

Patients with very long lesions (group C) had more clinical comorbidities (e.g., diabetes mellitus, multivessel disease, and prior coronary revascularization) compared with the patients in the other groups.

LESION COMPLEXITY AND PROCEDURAL CHARACTERISTICS. Lesion and procedural characteristics are summarized in Table 2. The main target vessel was the left anterior coronary artery in all groups. The Syntax score was higher in patients with longer scaffold length (group A 10.4 ± 7.2 vs. group B 14.6 ± 8.6 vs. group C 16.4 ± 7.8; $p < 0.001$). Furthermore, longer lesions more frequently included chronic total occlusions (3.3% vs. 11.3% vs. 37.0%; $p < 0.001$), bifurcations (25.0% vs. 38.8% vs. 40.3%; $p < 0.001$), and ostial lesions (6.2% vs. 2.6% vs. 10.5%; $p = 0.02$) in groups A, B, and C, respectively. Total scaffold length in each group was 20.7 ± 5.5 mm in group A, 45.4 ± 8.4 mm in group B, and 85.9 ± 7.2 mm in group C ($p < 0.001$). The maximum scaffold length was 28 mm, 58 mm, and 132 mm in groups A, B, and C, respectively.

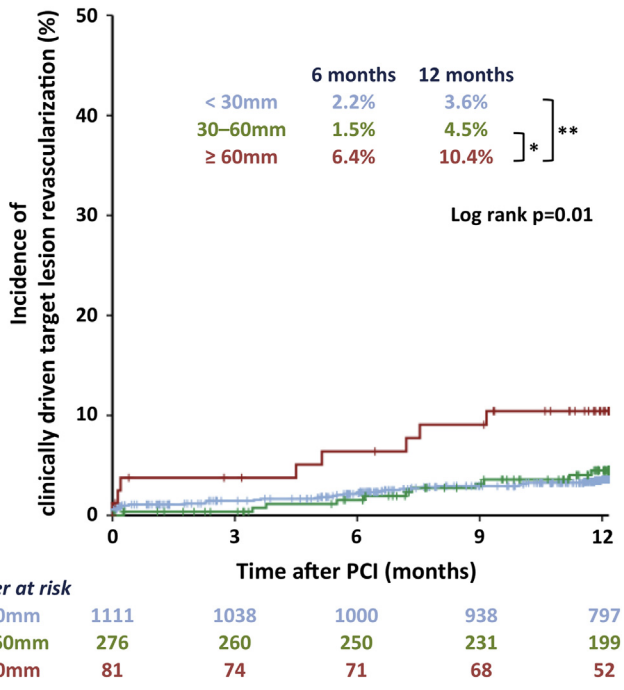
Procedurally, the rates of pre-dilation (group A 95.3% vs. group B 99.3% vs. group C 100%; $p = 0.001$) and post-dilation (group A 45.1% vs.

FIGURE 1 The 1-Year Primary Composite Endpoint TLF



Kaplan-Meier curves of 1-year primary composite endpoint (target lesion failure [TLF]) between the 3 groups. TLF at 1 year was significantly higher in group C (≥60 mm). * and ** indicate log rank test with p = 0.001 performed respectively in groups B to C and A to C. PCI = percutaneous coronary intervention.

FIGURE 2 Outcomes in CD-TLR



Kaplan-Meier curves demonstrate worse outcomes in clinically driven target lesion revascularization (CD-TLR) of group C patients (≥60 mm) compared with groups A and B (≤60 mm). * and ** indicate log rank test with p = 0.01 performed respectively in groups B to C and A to C. PCI = percutaneous coronary intervention.

group B 76.8% vs. group C 82.7%; p = 0.001) were higher in the long lesion group. Intravascular ultrasound optical coherence tomography was also more frequently performed as scaffold length increased (group A 10.9%/10.0% vs. group B 29.2%/23.6% vs. group C 37.0%/40.7%; p < 0.001). Unsurprisingly, there were a higher number of overlap sites in group C (2.2 ± 1.2 vs. group B 0.9 ± 0.5 and group A 0.01 ± 0.1).

QUANTITATIVE CORONARY ANALYSIS RESULTS. Lesion length in each group was 13.7 ± 7.1 mm (group A), 28.6 ± 15.3 mm (group B), and 47.2 ± 23.5 mm (group C) (Table 3). Baseline reference vessel diameter was comparable among groups (group A 2.91 ± 0.51 mm, group B 2.89 ± 0.49 mm, and group C 2.89 ± 0.51 mm; p = 0.96). Post-procedural QCA results demonstrated comparable results among groups in terms of final minimal lumen diameter and percent diameter stenosis.

CLINICAL OUTCOMES. Clinical outcomes at 1 year are summarized in Table 4. Median follow-up period was 384 (interquartile range: 359 to 459) days. One-year follow-up was completed in 70.3% without significant differences among groups (group A 70.7%, group B 69.9%, group C 66.7%; p = 0.74). The primary composite endpoint (TLF) at 1 year was significantly higher in group C (group A 4.8%, group B 4.5%, and group C 14.3%; overall p = 0.001) (Figure 1). The interaction test for treatment group (group A, B, or C) by each center yielded a p value of 0.83 for TLF at 1 year, indicating that there was no center bias accounting for the observed results.

Among the components of TLF, group C had worse outcomes with regard to MI (group A 3.2%, group B 1.2%, and group C 6.4%; overall p = 0.01) and clinically driven TLR (group A 3.6%, group B 4.5%, and group C 10.4%; overall p = 0.01) (Figure 2), whereas there were no significant differences in cardiac death (group A 1.1%, group B 0%, and group C 1.4%; overall p = 0.22). The rate of target vessel failure in group C was also higher compared with groups A and B (group A 6.5%, group B 5.6%, group C 16.9%; p = 0.001). The rate of scaffold thrombosis was numerically higher in group C; however, this did not reach statistical significance at 1 year (group A 2.1%, group B 1.1%, group C 3.8%; overall p = 0.29) (Figure 3).

INDEPENDENT PREDICTORS FOR TLF. Univariate Cox regression analysis revealed diabetes mellitus (hazard ratio [HR]: 1.87, 95% confidence interval [CI]: 1.24 to 2.80; p = 0.003), acute coronary syndrome (HR: 1.77, 95% CI: 1.17 to 2.65; p = 0.006), and ostial lesions (HR: 2.06, 95% CI: 1.03 to 4.10; p = 0.04) as predictors for TLF at 1 year (Table 5). The covariates entered into the final multivariate model included diabetes mellitus, acute coronary syndrome, intravascular ultrasound, total scaffold length (per 30-mm increase), post-dilation, and ostial lesions. Multivariable analysis revealed diabetes mellitus (HR: 1.84, 95% CI: 1.10 to 3.07; p = 0.02), acute coronary syndrome (HR: 2.22, 95% CI: 1.29 to 3.81; p = 0.004), and ostial lesions (HR: 2.32, 95% CI: 1.04 to 5.17; p = 0.04) to be independent predictors. Total scaffold length (per 30-mm increase) was also found to be an independent predictor for TLF at 1 year (HR: 1.54, 95% CI: 1.04 to 5.17; p = 0.04).

DISCUSSION

The current data report 1-year outcomes following Absorb BVS implantation for the treatment of long coronary lesions in a "real-world" population. The main findings of this study are the following: 1) clinical outcomes following (BVS) implantation were comparable between short (scaffold length <30 mm) and moderate (scaffold

length 30 to 60 mm) lesions; 2) PCI with BVS for long lesions (scaffold length ≥60 mm) was associated with worse clinical outcomes despite a higher rate of post-dilation and intravascular imaging use; and 3) there were no statistical differences with regard to the rate of scaffold thrombosis between groups.

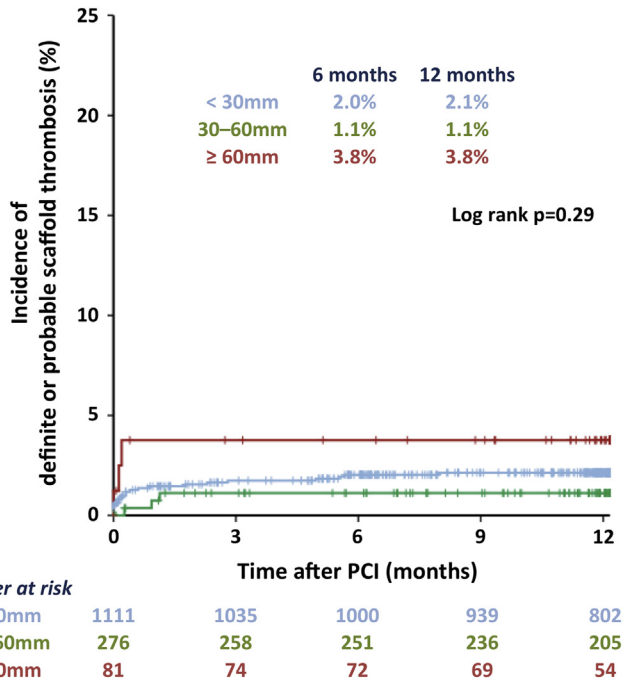
PCI for long lesions remains a challenge due to the higher event rates observed compared with short lesions. A number of studies have demonstrated that lesion/stent length is an independent predictor of adverse events (10-12). BVS is theoretically advantageous over metallic stents in this setting due to the total bioresorption of struts resulting in the recovery of vasomotor and endothelial function. The absence of a permanent metallic cage removes the risk of very late stent thrombosis; furthermore, this approach may allow future surgical or percutaneous revascularization, although this hypothesis remains to be proven by large series.

In this study, clinical outcomes were comparable in patients presenting with short (<30 mm) and intermediate (30 to 60 mm) coronary lesions treated with BVS. However, the treatment of very long coronary lesions (≥60 mm) with BVS was associated with worse event rates despite greater post-dilation and intravascular imaging use. There are some possible explanations for these findings. First, the long coronary lesion group more frequently included the use of 2.5-mm BVS (group A 23.9%, group B 38.6%, and group C 61.7%; overall $p < 0.001$). As demonstrated by the ABSORB III substudy (13,14), small diameter BVS are associated with worse outcomes. Second, the greater lesion complexity in group C may have accounted for worse outcomes, even though each individual variable was not found to be a predictor for TLR in this study.

Recent meta-analyses have confirmed that the current-generation BVS is associated with higher rates of scaffold thrombosis before absorption of BVS struts (15) compared with contemporary metallic stents. In this study, although there were no statistical differences with regard to the rates of scaffold thrombosis, group C had a numerically higher rate of scaffold thrombosis (3.8% at 1 year). Furthermore, the rates in groups A and B were high compared with historical series of PCI with DES, as reported in previous papers on the GHOST-EU registry.

Due to the physical properties of the materials used to manufacture the current generation Absorb BVS, an increased strut thickness (150 μm) and width is required to ensure sufficient radial strength and to prevent acute recoil. Furthermore, the rectangular-shaped strut of BVS results in greater flow disturbances compared with the oval- or round-shaped strut (16).

FIGURE 3 Incidence of Definite and Probable ST



Kaplan-Meier curves illustrate the incidence of definite and probable scaffold thrombosis (ST) over time up to 1 year: ST was numerically higher in group C, but when compared with the other groups, it did not reach statistical significance. PCI = percutaneous coronary intervention.

Therefore, when treating long lesions with multiple BVS, the scaffolds should be implanted with minimal overlap and without gaps to minimize thrombogenicity and delayed neointimal coverage (17) of the struts. As mentioned before, the true benefits of long BVS implantation can be obtained after complete absorption of the strut material (poly-L-lactic acid). However, the major concern with regard to long segments treated with BVS is the short- and mid-term outcomes before full strut absorption. **Table 6** summarizes the pivotal studies investigating outcomes following DES implantation for long coronary lesions. A recent randomized trial conducted by Ahn et al. (18) compared second-generation zotarolimus-eluting stents and sirolimus-eluting stents in de novo long coronary lesions. At 12-month follow-up, both zotarolimus-eluting stents and sirolimus-eluting stents had favorable outcomes without significant differences between the 2 groups. The composite endpoint (defined as death, MI, and TLR) in the current study are similar

TABLE 5 Independent Predictors for TLF at 1 Year

	Univariate			Multivariate		
	HR	95% CI	p Value	HR	95% CI	p Value
Male	0.96	0.59–1.57	0.86			
Age, yrs	1.00	0.98–1.02	0.98			
DM	1.87	1.24–2.80	0.003	1.84	1.10–3.07	0.02
Current smoking	1.07	0.69–1.64	0.77			
Prior CABG	1.16	0.51–2.66	0.72			
Prior PCI	1.28	0.86–1.93	0.23			
Prior stroke	1.21	0.45–3.29	0.71			
CKD	1.14	0.62–2.10	0.67			
Low LVEF (<30%)	1.35	0.42–4.27	0.62			
ACS	1.77	1.17–2.65	0.006	2.22	1.29–3.81	0.004
Syntax score	1.01	0.98–1.04	0.51			
IVUS or OCT use	1.11	0.66–1.87	0.71	0.95	0.50–1.78	0.86
Type B2/C lesion	1.01	0.67–1.51	0.97			
In-stent restenosis	1.88	0.76–4.62	0.17			
CTO	0.70	0.28–1.71	0.43			
Total scaffold length (per 30-mm increase)	1.31	0.96–1.79	0.09	1.54	1.03–2.31	0.04
RVD <2.5 mm	1.31	0.74–2.35	0.36			
Mean scaffold diameter	0.88	0.59–1.32	0.54			
Pre-dilation	0.68	0.28–1.67	0.40			
Post-dilation	0.82	0.55–1.23	0.34	1.13	0.65–1.96	0.67
Bifurcation lesions	1.17	0.74–1.84	0.51			
Prasugrel or ticagrelor	0.99	0.88–1.11	0.86			
Ostial lesion	2.06	1.03–4.10	0.04	2.32	1.04–5.17	0.04

ACS = acute coronary syndrome(s); CI = confidence interval; CKD = chronic kidney disease; CTO = chronic total occlusion; HR = hazard ratio; other abbreviations as in Tables 1 to 4.

to those of the first- and second-generation DES; however, the rates of thrombosis, TLR, and target vessel revascularization are numerically higher. These data imply that further efforts to optimize BVS implantation (optimal sizing, pre- and post-dilation, and intravascular imaging) and improvements in BVS design are required to further improve procedural and clinical outcomes.

With regard to dual-antiplatelet therapy, the optimal combination of agents and duration following BVS implantation is currently unclear. In the long BVS subset, there were 3 thrombosis cases within 1 year. Each of these patients were treated with multiple BVS in the setting of acute coronary syndrome (unstable angina n = 2, and non-ST-segment elevation MI n = 1) and were still on dual-antiplatelet therapy. Acute thrombosis occurred in a patient presenting with unstable angina treated with ticagrelor, and subacute thrombosis was observed in the remaining patients (4 and 6 days, respectively).

BVS PROCEDURES COST-EFFECTIVENESS. BVS are priced differently among European countries, are more expensive than DES, and their price has decreased over the years during the GHOST-EU registry period. The cost of PCI with BVS is undoubtedly higher compared with DES; apart from the cost of the scaffold, we should take into consideration the increased procedural duration, increased number of guide wires, balloons, and scoring devices used, increased invasive imaging, and different catheterization lab's technical equipment and operator experience among the centers involved in this registry (19). It should also be remembered that the GHOST-EU registry included the initial experiences with BVS implantation in Europe in an all-comers population. For these reasons, we could not perform a reliable estimate of the difference in costs between BVS and DES strategies. Although unproven, the potential long-term benefits of BVS and the gradual acquisition of experience with implantation techniques may overcome the initial gap in procedural costs.

STUDY LIMITATIONS. This was a nonrandomized retrospective study, and so selection bias cannot be excluded. Furthermore, procedures were not standardized (e.g., use of pre- and post-dilation, intravascular imaging), and there were substantial differences in deployment and post-dilation practice

TABLE 6 Previous Reports on the Clinical Outcomes Following Metallic DES Implantation for Diffuse Lesions

	Kim et al. 2006*		LONG DES III†		LONG DES IV‡		GHOST-EU
Follow-up period	9 months		12 months		12 months		12 months
Stent/scaffold type	SES	PES	SES	EES	SES	ZES	Absorb BVS
Number of patients	250	250	226	224	250	250	
Mean stent/scaffold length, mm	40.6 ± 13.2	41.1 ± 13.4	46.4 ± 17.4	46.5 ± 16.9	44.8 ± 16.9	45.9 ± 17.1	
Clinical outcomes, %							
Stent/scaffold thrombosis	0.8	0	0	0.4	0.8	0	<30 mm: 2.1 30–60 mm: 1.1 ≥60 mm: 3.8
MI	8.8	10.8	8.0	9.8	13.6	11.6	<30 mm: 2.4 30–60 mm: 0.8 ≥60 mm: 6.4
TLR	2.4	7.2	2.2	3.1	2.4	1.6	<30 mm: 3.6 30–60 mm: 4.5 ≥60 mm: 10.4
TVR	3.2	7.6	2.7	4.0	2.4	2.0	<30 mm: 5.7 30–60 mm: 5.5 ≥60 mm: 17.4
MACE	11.2	16.5	10.2	14.3	16.0	14.4	<30 mm: 4.8 30–60 mm: 4.5 ≥60 mm: 14.3

MACE was defined as a composite of death, MI, and TLR. *Kim et al. Sirolimus-eluting stent versus paclitaxel-eluting stent for patient with long coronary artery disease. Circulation 2006;114:2148-53. †Park et al. Comparison of everolimus- and sirolimus-eluting stents in patients with long coronary lesions: a randomized LONG-DES-III (Percutaneous Treatment of LONG Native Coronary Lesions With Drug-Eluting Stent-III) Trial). J Am Coll Cardiol Intv 2011;4:1096-103. ‡Ahn et al. Comparison of resolute zotarolimus-eluting stents and sirolimus-eluting stents in patients with de novo long coronary artery lesions: a randomized LONG-DES IV trial. Circ Cardiovasc Interv 2012;5:633-40.

DES = drug-eluting stent(s); EES = everolimus-eluting stent(s); GHOST-EU = Gauging coronary Healing with bioresorbable Scaffolding plaTforms in EUrope; MACE = major adverse cardiac event(s); PES = paclitaxel-eluting stent(s); SES = sirolimus-eluting stent(s); TLR = target lesion revascularization; TVR = target vessel revascularization; ZES = zotarolimus-eluting stent(s); other abbreviations as in Table 4.

compared with current recommendations, which may have affected the results of this study (20). A recent multicenter analysis from Puricel et al. (21) showed how scaffold thrombosis could be significantly reduced employing an optimized and standardized implantation strategy.

To maintain consistency with previous publications (Table 6), we grouped the patients according to the scaffold length and not the lesion length, because lesion length as measured by QCA was not available in 30% of cases. All data were site-reported without central core laboratory evaluation. There were no data available about type of metallic DES/BMS implanted, when required, and overlap between BVS and metallic DES/BMS in this study. Therefore, detailed information with regard to the degree of BVS overlap was not available. Furthermore, implantation technique for multiple BVS implantation was not reported in the current study, although to minimize scaffold damage and avoid strut disruption, distal to proximal BVS implantation is preferable. Finally, even though this study included a large number of patients, the number of patients treated with continuous and long BVS implantation was relatively small. Finally, the follow-up period was limited to 1 year, before full absorption of BVS. Larger randomized studies with longer follow-up are required to investigate the possible longer-term benefits of BVS in comparison to current-generation metallic DES.

CONCLUSIONS

Treatment of very long coronary lesions (scaffold length ≥60 mm) with BVS was associated with a high TLF rate, which was driven by MI and clinically driven TLR. Although there was a numerically higher incidence of scaffold thrombosis when treating long segments, this did not reach statistical significance. Careful patient and lesion selection, including vessel size; meticulous implantation techniques; including adequate lesion preparation, the use of intravascular imaging, and post-dilation; and perhaps more potent antiplatelet therapy may be required to optimize clinical outcomes.

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PERSPECTIVES

WHAT IS KNOWN? The length of a metallic stent is a known predictor of stent thrombosis and in-stent restenosis. Bioresorbable vascular scaffolds are potentially advantageous by virtue of complete absorption of struts, which may result in the recovery of vasomotor function and a potential reduction of very late clinical adverse events. However, pivotal randomized studies and real-world registries have demonstrated a high incidence of scaffold thrombosis.

WHAT IS NEW? Treatment of lesions requiring BVS length <60 mm has acceptable clinical outcomes; conversely, treatment of very long coronary lesions (BVS length >60 mm) was associated with a higher TLF rate and a numerically higher, but nonsignificant, rate of scaffold thrombosis.

WHAT IS NEXT? To optimize clinical outcomes, a standardized implantation technique, consisting of meticulous vessel sizing, mandatory pre-dilation, and post-dilation, is advisable. Liberal use of intracoronary imaging is recommended, as well as more potent antiplatelet therapy, especially for the first month's use in complex lesions. Randomized studies with pre-specified implantation technique and longer follow-up are required to better clarify the longer-term benefits of BVS in diffuse disease in comparison to current metallic DES.

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