




ORIGINAL STUDY

Five-year angiographic, OCT and clinical outcomes of a randomized comparison of everolimus and biolimus-eluting coronary stents with everolimus-eluting bioresorbable vascular scaffolds

Sara Schukraft MD  | Diego Arroyo MD | Mario Togni MD |
Jean-Jacques Goy MD  | Peter Wenaweser MD | Mathieu Stadelmann MD |
Gerard Baeriswyl MD | Olivier Muller MD | Jean-Christophe Stauffer MD |
Serban Puricel MD | Stéphane Cook MD 

Cardiology, University & Hospital Fribourg,
Fribourg, Switzerland

Correspondence

Sara Schukraft, Department of Cardiology
University & Hospital Fribourg, CH-1708
Fribourg, Switzerland.

Email: sara.schukraft@yahoo.com

Funding information

Fonds Scientifique Cardiovasculaire

Abstract

Aims: To compare 5-year angiographic, optical coherence tomography (OCT), and clinical outcomes between patients treated with bioresorbable vascular scaffolds (BVS) and drug-eluting stents (DES).

Methods: The EverBio-2 trial (Comparison of Everolimus- and Biolimus-Eluting Coronary Stents with Everolimus-Eluting Bioresorbable Vascular Scaffold) was a single-center, assessor-blinded, randomized controlled trial in which 240 patients were randomly allocated (1:1:1) to BVS, everolimus-eluting (EES) or biolimus-eluting (BES) DES. Clinical follow-up was scheduled up to 5 years. All patients, alive and who did not have repeat revascularization of the target lesion during follow-up were asked to return for angiographic follow-up at 5 years.

Results: Five-year angiographic follow-up was completed in 122 patients (51%) and OCT analysis was performed in 86 (36%) patients. In-stent late lumen loss was similar in both groups with 0.50 ± 0.38 mm in BVS versus 0.58 ± 0.36 mm in EES/BES, $p = 0.20$. Clinical follow-up was complete in 232 patients (97%) at 5 years. The rate of the device-oriented endpoint was 22% in the BVS and 18% in the EES/BES group ($p = 0.49$). The patient-oriented composite endpoint occurred in 40% of BVS- and 43% of EES/BES-treated patients ($p = 0.72$) at 5 years. No acute coronary syndrome due to stent thrombosis was detected after 2 years. Complete BVS strut resorption was observed at 5 years in the OCT subgroup.

Conclusion: Five-year clinical outcomes were similar between BVS and DES patients as well as angiographic outcomes in a selected subgroup. However, a definitive con-

Abbreviations: BES, biolimus-eluting stent; BVS, bioresorbable vascular scaffold; DES, drug-eluting stent; EES, everolimus-eluting stent; LLL, late lumen loss; OCT, optical coherence tomography; TLF, target lesion failure.

Serban Puricel and Stéphane Cook contributed equally to this article

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2021 The Authors. *Catheterization and Cardiovascular Interventions* published by Wiley Periodicals LLC.

clusion cannot be drawn because the EverBio-2 trial was not powered for clinical and angiographic endpoints at 5 years of follow-up.

KEYWORDS

BVS, drug eluting stent, percutaneous coronary intervention, stent thrombosis

1 | INTRODUCTION

Metallic coronary stents are associated with persistent physical and biochemical stresses that impact long-term outcomes. Bioresorbable vascular scaffolds (BVS) were developed to overcome these limitations in the long run. While preliminary studies in low-risk patients with simple lesions reported excellent results, later trials were more nuanced.¹

In the EverBio-2 randomized controlled trial, clinical and angiographic outcomes with BVS were satisfactory, with comparable in-stent late-lumen loss (LLL) at 9 months between BVS, everolimus-eluting (EES), and biolimus-eluting (BES) metallic stents.² Soon thereafter, safety concerns emerged with data from several registries reporting increased rates of stent thrombosis (ST) up to 2% at 1 year.^{3–6} The interim results of the ABSORB III study showed an increased risk for target-vessel myocardial infarction (MI) and ST in BVS compared to EES at 2 years.⁷ Based on these safety concerns and low commercial sales, the BVS was removed from the market mid-2017. The 3-year ABSORB III and the 4-year ABSORB II data confirmed the BVS's inferiority to 2nd generation DES.⁸

The reasons for BVS failure are thought to be diverse, and may include both biochemical, inflammatory, as well as pure mechanical causes.⁹ Some of these may be overcome by strict implantation protocols,¹⁰ and most causes are thought to disappear over time. Given that more than a million patients have been treated with BVS, the assessment of long-term outcomes is paramount.

We sought to investigate the 5-year angiographic, optical coherence tomography (OCT) and clinical outcomes of patients enrolled in the EverBio-2 trial. The population included in the angiographic follow-up consists of low-risk patients, in whom the target lesion had not been revascularized.

2 | METHODS

2.1 | Study population and data collection

The EverBio-2 trial is a single-center, assessor-blinded, randomized study. Between November 2012 and November 2013, 240 patients were allocated to either BVS ($n = 80$), BES ($n = 80$), or EES ($n = 80$). Trial protocol details have been published previously.¹¹ Clinical follow-up was performed at 9 months, 1, 2, and 5 years. For the present study, all patients who were alive and who did not have repeat revascularization of the target lesion were considered for angiographic follow-up at 5 years. Patients with moderate to severe renal failure,

repeat coronary angiography during the previous year, as well as those unable or unwilling to participate in angiographic follow-up were excluded from angiographic follow-up. The EverBio-2 study complied with the Helsinki Declaration and was approved by the local ethics committees of Fribourg and Vaud (043/12-CER-FR/PB_2017-00237). All patients provided written, informed consent for participation.

2.2 | Quantitative coronary angiography

Coronary angiograms were repeated and performed via the femoral or radial artery with a 5-6F guiding catheter as per clinical practice. Coronary angiograms were recorded in the same projections as during the index procedure and 9-month angiographic follow-up. All patients received 200 μg of i.c. nitroglycerin before acquisition. Coronary angiograms were analyzed with the use of an automated edge detection system (CAAS II, Pie Medical, Netherlands) at the angiographic core laboratory of the University of Fribourg.

2.3 | Primary endpoint

The primary endpoint was in-stent LLL defined as the difference between the minimal lumen diameter after the procedure and the minimal lumen diameter at 5-year follow-up. Secondary angiographic endpoints were in-segment LLL, binary restenosis, minimal lumen diameter, and percent diameter stenosis.

2.4 | Clinical endpoints

Clinical outcomes were compared using the Academic Research Consortium (ARC)-defined device-oriented composite endpoint (composite of cardiac death, MI of the target vessel, and target lesion revascularization [TLR]) and patient-oriented composite endpoint (composite of death, MI, and any revascularization), as well as acute coronary syndrome due ST at 5 years.¹²

2.5 | OCT imaging and analysis

OCT was performed with the Optis Illumen system (Abbott Vascular) using the Dragonfly Duo OCT Imaging Catheter with "75 mmHR mode" pullback, the non-occlusive flushing technique at 36 mm/s.

OCT pullbacks were assessed offline using a proprietary software (Lightlab, Abbott Vascular). Quantitative analysis was performed at 1-mm intervals within the stent and 5-mm proximal and distal to the stent edges. Advanced OCT image analysis included luminal morphometry and symmetry at 5 years. Lumen area was delineated in stent and in segment. Strut analysis was performed according to Nakatani and al.¹³ The so-called “Golden Tube” appearance was defined as: (1) vessel without visible scaffold, (2) the presence of progressive lumen enlargement, and (3) the development of a signal-rich, low-attenuating tissue layer in absence of thin-cap fibroatheroma. Peristrut low-intensity area was defined as a region around scaffolds with a homogenous lower intensity appearance than the surrounding tissue without significant signal attenuation behind the area.

2.6 | Statistical analysis

Categorical variables are reported as counts and percentages; continuous variables are reported as mean and SD. Normality was assessed by visual inspection of histograms and the computation of Q-Q plots. Continuous variables are analyzed using the Student t-test or the Wilcoxon rank-sum test per distribution. Categorical variables were compared using chi-square or Fisher exact test as appropriate.

The primary endpoint was compared using a Wilcoxon rank-sum test. A multivariate linear regression was computed to rid the analysis of the primary endpoint of the potential bias arising from imbalance in pretreatment variables. Survival free from the occurrence of clinical end points was assessed by computation of the Kaplan–Meier curves.

Survival was compared using the log-rank test. Landmark analysis was performed in setting the landmark at 2 years. To fully disclose the results, post-hoc inferential statistics were performed comparing BVS to the individual DES. All statistical analyses were performed using dedicated software (Stata 14, Texas) at a 2-tailed significance level of $\alpha = 0.05$.

3 | RESULTS

3.1 | Baseline patient and procedural characteristics

A total of 240 patients were randomly assigned to BVS, EES, or BES implantation. Angiographic follow-up was completed in 122 (51%) patients and OCT analysis was performed in 86 (36%) patients at 5 years (Figure 1). There were significant differences regarding baseline characteristics between patients who participated in 5-year angiographic follow-up and those who did not (Supplementary Tables 1 and 2). Patients undergoing paired angiographies were younger (63 ± 10 vs. 67 ± 11 year, $p = 0.02$) and less frequently diabetics (16% vs. 32%, $p < 0.01$) than patients not undergoing paired angiographies.

Baseline characteristics of all patients vs. patient included in the late angiographic follow-up were similar (Supplementary Tables 3 and 4). Baseline and procedural characteristics of patients participating in 5-year angiographic follow-up are summarized in Tables 1 and 2. No patient in the BVS group, but 9 EES/BES-treated patients (11%) had previously undergone coronary artery bypass grafting (CABG) ($p = 0.03$).

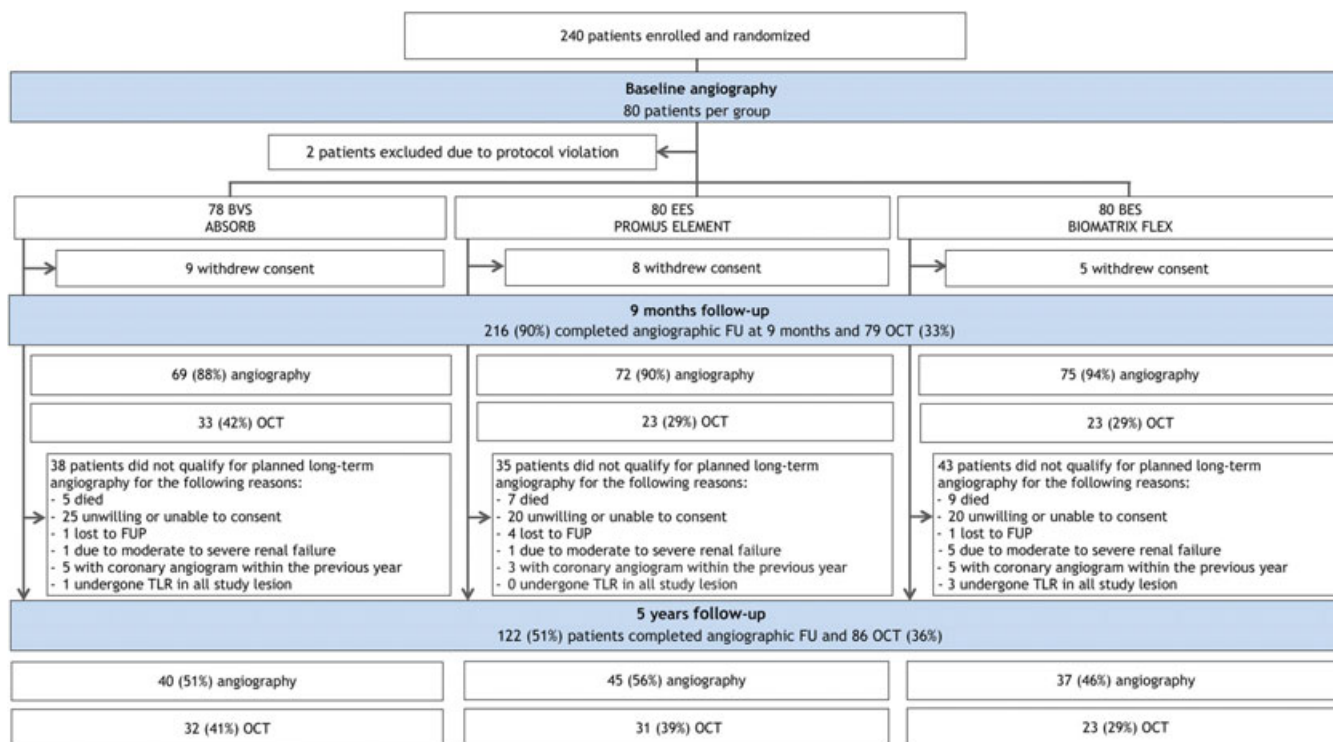


FIGURE 1 Patient flowchart. BES, biolimus-eluting stent; BVS, bioresorbable vascular scaffold; EES, everolimus-eluting stent; FU, follow-up; OCT, optical coherence tomography [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Late angiographic follow-up—patient characteristics

	BVS (n = 40)	EES/BES (n = 82)	EES (n = 45)	BES (n = 37)	p-value		
					BVS versus EES/BES	BVS versus EES	BVS versus BES
Male	34 (85)	65 (78)	38 (84)	27 (73)	0.62	1.00	0.52
Age, year	64 ± 11	63 ± 10	63 ± 11	63 ± 9	0.79	1.00	1.00
Hypertension	23 (57)	51 (62)	30 (67)	21 (57)	0.69	1.00	1.00
Diabetes mellitus	5 (13)	14 (17)	6 (13)	8 (21)	0.60	1.00	0.74
Non-insulin dependent	5 (12)	9 (11)	2 (4)	7 (19)	0.77	0.50	1.00
Smoking	16 (40)	33 (40)	22 (49)	11 (30)	1.00	1.00	0.94
Dyslipidemia	24 (60)	51 (62)	30 (66)	21 (57)	0.84	1.00	1.00
Family history of CAD	10 (25)	23 (28)	12 (27)	11 (30)	0.83	1.00	1.00
Previous PCI	13 (32)	27 (33)	16 (36)	11 (30)	1.00	1.00	1.00
Previous CABG	0 (0)	9 (11)	5 (11)	4 (11)	0.03	0.12	0.09
Previous MI	8 (21)	18 (22)	10 (22)	8 (21)	1.00	1.00	1.00
Indication for index procedure							
Unstable angina	2 (5)	10 (12)	4 (9)	6 (16)	0.33	1.00	0.30
NSTEMI	4 (10)	18 (22)	8 (18)	10 (27)	0.14	0.72	0.16
STEMI	6 (15)	7 (8)	4 (9)	3 (8)	0.35	1.00	0.96
Stable angina	26 (65)	35 (43)	23 (51)	12 (32)	0.03	0.54	0.01
Silent ischemia	2 (5)	12 (14)	6 (13)	6 (16)	0.14	0.54	0.28
LVEF, %	60 (45–65)	60 (50–68)	60 (55–68)	59 (45–65)	0.43	0.54	1.00

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

Abbreviations: BES, biolimus-eluting stent; BVS, bioresorbable vascular scaffold; CABG, coronary artery bypass grafting; CAD, coronary artery disease; EES, everolimus-eluting stent; LAD, left anterior descending; LCX, left circumflex artery; LM, left main coronary artery; NSTEMI, non-ST-elevation myocardial infarction; RCA, right coronary artery; STEMI, ST-elevation myocardial infarction.

3.2 | Angiographic outcomes

Angiographic findings are presented in Table 3. In-stent LLL at 5 years was 0.50 ± 0.38 mm in BVS-treated and 0.58 ± 0.36 mm in EES/BES-treated patients ($p = 0.20$). Patients treated with BES had a lower percentage of in-stent diameter stenosis than those allocated to EES ($p = 0.03$). Figure 2 depicts the cumulative frequency distribution of in-stent LLL at 9-months and 5-years. In-segment LLL was 0.43 ± 0.58 mm in BVS and 0.45 ± 0.38 mm in EES/BES ($p = 0.66$). After multivariate adjustment, the difference between in-stent ($p = 0.11$) and in-segment ($p = 0.76$) LLL was not statistically significant (Supplementary Table 5). 9-months angiographic outcomes of patients included in the present analysis are provided in Supplementary Table 6.

3.3 | OCT results

OCT analysis is summarized in Table 4. Baseline patient characteristics of the 5 years OCT follow-up are summarized in Supplementary Table 7. There was complete strut resorption in all BVS patients (Figure 3). Mean lumen area was significantly higher in BVS (7.05 ± 2.45 mm²) than in

EES/BES (5.87 ± 2.21 mm², $p = 0.04$). The BVS showed a trend toward a wider external elastic membrane area (12.86 ± 3.25 mm²) when compared with EES/BES (11.58 ± 3.69 mm²; $p = 0.11$). In-stent eccentricity and asymmetry index were similar between the groups. Paired OCT measurements between 9 months and 5 years were available in 24 (30%) patients. Data demonstrated a trend toward an increase in mean lumen area (1.49 ± 3.52 mm²) in BVS compared with EES/BES (-0.53 ± 1.33 mm²) between 9 months and 5 years (Supplementary Table 8).

3.4 | Clinical outcomes

Clinical follow-up at 5 years as available in 99% ($n = 77$) of patients in the BVS group, 95% ($n = 76$) in the EES group, and 99% ($n = 79$) in the BES group, and is presented in Table 5. The device-oriented composite end point occurred in 17 BVS- (22%) and 29 (18%) EES/BES-treated patients ($p = 0.49$). Cardiac death occurred in 2 (3%) patients with BVS and 7 (4%) patients with EES/BES ($p = 0.48$). Clinical outcome at 5 years of all patients versus patient included in the late angiographic follow-up are presented in Supplementary Table 9.

TABLE 2 Late angiographic follow-up—procedural characteristics

	BVS (n = 40)	EES/BES (n = 82)	EES (n = 45)	BES (n = 37)	p-value		
					BVS versus EES/BES	BVS versus EES	BVS versus BES
Vessels diseased per patient	1.8 ± 0.7	1.8 ± 0.8	1.9 ± 0.8	1.7 ± 0.7	0.74	1.00	0.64
Vessels treated per patient	1.1 ± 0.3	1.1 ± 0.4	1.1 ± 0.3	1.1 ± 0.4	0.98	1.00	1.00
Lesions per patient	2.2 ± 1.0	2.0 ± 1.2	2.1 ± 1.2	2.0 ± 1.2	0.32	1.00	0.54
Lesions treated per patient	1.4 ± 0.6 (n = 45)	1.4 ± 0.7 (n = 106)	1.5 ± 0.7 (n = 62)	1.2 ± 0.4 (n = 44)	0.40	1.00	0.08
Target coronary artery							
LM	0 (0)	1 (1)	1 (2)	0 (0)	1.00	1.00	-
LAD	19 (42)	34 (32)	19 (31)	15 (34)	0.27	0.46	1.00
LCX	13 (29)	21 (20)	13 (21)	8 (18)	0.29	0.74	0.64
RCA	13 (29)	47 (44)	28 (45)	19 (43)	0.10	0.22	0.38
Arterial graft	0 (0)	0 (0)	0 (0)	0 (0)	-	-	-
Vein graft	0 (0)	3 (3)	1 (2)	2 (5)	0.55	1.00	0.48
Type of intervention per lesion							
Pure stent implantation	43 (96)	105 (99)	61 (98)	44 (100)	0.21	0.76	0.32
Hybrid with other DES implantation	2 (4)	1 (1)	1 (2)	0 (0)	0.21	0.76	0.32
Hybrid with BMS implantation	0	0	0	0	-	-	-
Lesion complexity							
A	9 (20)	27 (25)	17 (27)	10 (23)	0.54	0.76	1.00
B1	22 (49)	45 (42)	20 (32)	25 (57)	0.48	0.16	0.90
B2	7 (16)	16 (15)	12 (19)	4 (9)	1.00	1.00	0.70
C	7 (15)	18 (17)	13 (21)	5 (11)	1.00	1.00	1.00
Baseline TIMI flow per lesion							
TIMI 0	0 (0)	3 (3)	2 (3)	1 (2)	0.56	0.44	0.62
TIMI 1	0 (0)	0 (0)	0 (0)	0 (0)	-	-	-
TIMI 2	1 (2)	0 (0)	0 (0)	0 (0)	0.30	0.48	0.64
TIMI 3	44 (98)	103 (97)	60 (97)	43 (97)	1.00	1.00	1.00
TIMI flow post-intervention per lesion							
TIMI 0	0 (0)	0 (0)	0 (0)	0 (0)	-	-	-
TIMI 1	0 (0)	0 (0)	0 (0)	0 (0)	-	-	-
TIMI 2	0 (0)	1 (1)	1 (2)	0 (0)	1.00	1.00	-
TIMI 3	45 (100)	105 (99)	61 (98)	44 (100)	1.00	0.78	-
Restenotic lesion	1 (2)	2 (2)	1 (2)	1 (2)	1.00	1.00	1.00
Chronic total occlusion	1 (2)	5 (5)	4 (7)	1 (2)	0.67	0.78	1.00
Thrombus aspiration	5 (11)	8 (8)	4 (6)	4 (9)	0.53	0.98	1.00
Number of stent per lesion	1.3 ± 0.6	1.2 ± 0.6	1.3 ± 0.7	1.1 ± 0.4	0.50	1.00	0.42
Lesion length, mm	12.1 ± 7.8	8.9 ± 4.9	8.3 ± 4.4	9.7 ± 5.4	<0.01	<0.01	0.24
Maximum pressure per lesion, atm	13.6 ± 3.1	14.0 ± 3.2	14.8 ± 2.7	13 ± 3.5	0.52	0.02	0.80
Overlapping stents per lesion	10 (22)	19 (18)	11 (12)	8 (18)	0.65	1.00	1.00
Direct stenting per lesion	3 (7)	17 (16)	9 (15)	8 (18)	0.19	0.46	0.24
Post-dilatation per lesion	17 (38)	30 (28)	15 (24)	15 (34)	0.28	0.28	1.00
Time to angiographic follow-up, years	5.1 ± 0.4	5.2 ± 0.4	5.0 ± 0.4	5.3 ± 0.4	0.67	0.26	0.80

Note: Values are mean ± SD or n (%).

Abbreviations: BES, biolimus-eluting stent; BVS, bioresorbable vascular scaffold; EES, everolimus-eluting stent; LAD, left anterior descending; LCX, left circumflex artery; LM, left main coronary artery; RCA, right coronary artery.

TABLE 3 Late angiographic follow-up—quantitative coronary angiography measurements

	BVS (n = 45)	EES/BES (n = 106)	EES (n = 62)	BES (n = 44)	p-value		
					BVS versus EES/BES	BVS versus EES	BVS versus BES
MLD, in-stent, mm	2.05 ± 0.55	2.15 ± 0.47	2.10 ± 0.43	2.22 ± 0.52	0.27	1.00	0.28
MLD, in-segment, mm	1.90 ± 0.53	1.81 ± 0.43	1.75 ± 0.37	1.88 ± 0.49	0.40	0.40	1.00
Diameter stenosis, in-stent	15.26 ± 13.49	12.24 ± 11.86	14.05 ± 11.64	9.56 ± 11.79	0.18	1.00	0.03
Diameter stenosis, in-segment	20.15 ± 14.04	17.49 ± 14.53	19.92 ± 15.30	14.06 ± 12.77	0.20	1.00	0.05
Binary restenosis in-stent	1 (2)	0 (0)	0 (0)	0 (0)	0.29	0.82	1.00
Binary restenosis in-segment	1 (2)	3 (3)	3 (5)	0 (0)	1.00	1.00	1.00
RVD, mm	2.78 ± 0.68	2.52 ± 0.76	2.44 ± 0.70	2.64 ± 0.82	0.04	0.03	0.64
Late loss, in-stent, mm	0.50 ± 0.38	0.58 ± 0.36	0.59 ± 0.38	0.57 ± 0.34	0.20	0.54	0.48
Late loss, in-segment, mm	0.43 ± 0.58	0.45 ± 0.38	0.41 ± 0.32	0.50 ± 0.44	0.66	1.00	0.92

Note: Values are mean ± SD or n (%).

Abbreviations: BES, biolimus-eluting stent; BVS, bioresorbable vascular scaffold stent; EES, everolimus-eluting stent; MLD, minimum lumen diameter; RVD, reference vessel diameter.

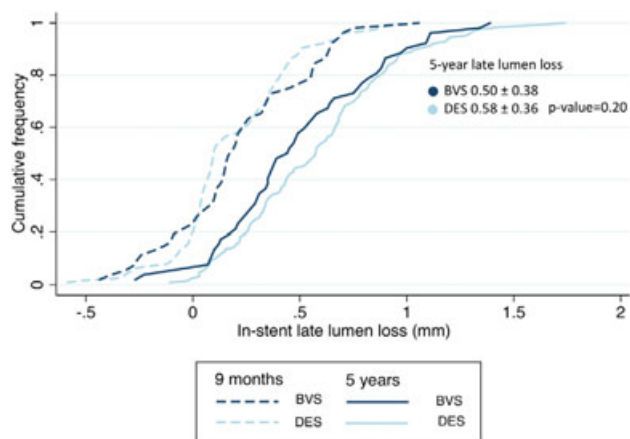


FIGURE 2 Cumulative frequency distribution of in-stent LLL. BVS, bioresorbable vascular scaffold; DES, drug-eluting stent; LLL, late lumen loss [Color figure can be viewed at wileyonlinelibrary.com]

Landmark analysis between 2 and 5 years did not show significant differences in clinical outcomes between years 2 and 5 of follow-up (Figure 4). No acute coronary syndrome due to ST was detected beyond 9 months.

4 | DISCUSSION

The key findings of the 5-year late angiographic and clinical follow-up of the EverBio-2 trial are: (a) similar patient and device-oriented clinical outcomes in the overall population, (b) no significant difference in in-stent LLL between BVS and EES/BES treated patients in a selected

angiographic subgroup, (c) complete BVS strut resorption in the OCT subgroup.

4.1 | Angiographic findings

Repeat angiography was completed in 122 of 240 patients (51%) at 5 years, which is comparable to previous trials studying long-term angiographic follow-up.^{14,15} The angiographic in-stent LLL at 5 years was similar between patients treated with BVS and those treated with EES/BES. In-stent (0.50 ± 0.38 mm) LLL at 5 years was considerably higher than in patients enrolled in the ABSORB Cohort B (0.16 ± 0.32 mm)¹⁶ or ABSORB EXTEND (0.26 ± 0.54 mm).¹⁷ The higher patient and lesion complexity in the present trial may explain this difference. To our knowledge, no systematic 5-year angiographic follow-up assessing LLL has been performed for either EES or BES.

The current analysis likely underestimates the true in-stent LLL of the patient population enrolled in the EverBio-2 trial, given that patients who died or had undergone TLR at 5 years were excluded from angiographic follow-up. However, the presented data is the only available long-term head-to-head comparison of BVS and metallic DES for angiographic endpoints. While angiographic LLL at 9 months and 1-year is believed to be a robust marker of the ultimate need for TLR,¹⁸ the significance of 5-year LLL in regard to very long-term outcomes remains uncertain.

4.2 | OCT findings

During the first few months, the poly-L-lactic acid backbone is hydrolyzed and progressively substituted by a provisional acellular

TABLE 4 OCT substudy—endovascular findings at 5-year follow-up

	BVS (n = 34)	EES/ BES (n = 54)	EES (n = 31)	BES (n = 23)	p-value		
					BVS versus EES/BES	BVS versus EES	BVS versus BES
Reference lumen area, mm ²	6.79 ± 2.41	6.16 ± 2.30	5.79 ± 2.07	6.64 ± 2.65	0.19	0.20	1.00
Mean lumen area, mm ²	7.05 ± 2.45	5.87 ± 2.21	5.23 ± 1.87	6.73 ± 2.38	0.04	<0.01	1.00
Minimal lumen area, mm ²	4.90 ± 1.93	4.29 ± 2.04	3.78 ± 1.66	4.97 ± 2.33	0.14	0.06	1.00
Mean external elastic membrane, mm ²	12.86 ± 3.25	11.58 ± 3.69	10.37 ± 3.15	13.21 ± 3.81	0.11	0.01	1.00
Minimal external elastic membrane, mm ²	9.81 ± 2.81	8.33 ± 3.54	7.26 ± 2.49	9.77 ± 4.24	0.03	<0.01	1.00
Eccentricity index	0.84 ± 0.04	0.83 ± 0.09	0.83 ± 0.11	0.84 ± 0.55	0.88	1.00	1.00
Symmetry index	0.42 ± 0.10	0.39 ± 0.12	0.40 ± 0.13	0.37 ± 0.10	0.07	0.36	0.16
Number of struts per patients	0	165 ± 69	163 ± 74	168 ± 63	<0.01	<0.01	<0.01
Total number of struts	0	8937	5067	3869	<0.01	<0.01	<0.01
Number of malapposed struts	0	128	91	37	<0.01	<0.01	<0.01

Note: Values are mean ± SD.

Abbreviations: BES, biolimus-eluting stent; BVS, bioresorbable vascular scaffold stent; EES, everolimus-eluting stent.

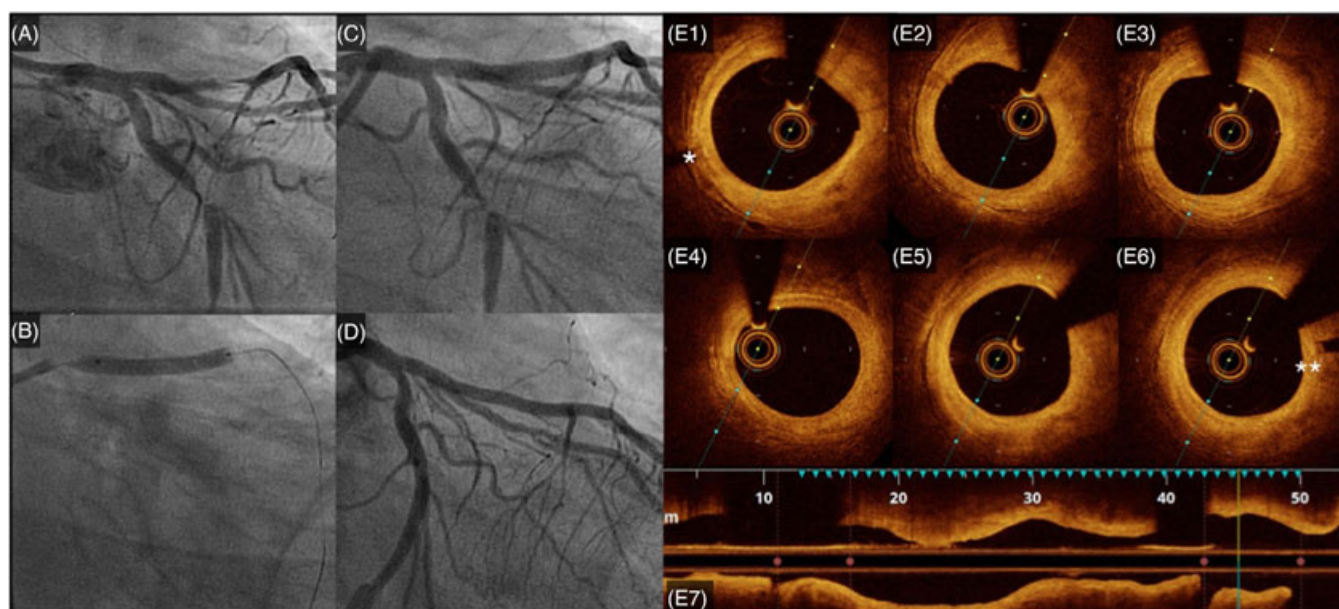


FIGURE 3 “Golden Tube” with complete resorption of the scaffold. A 50-year-old male patient presented with chest pain and anterior ST-elevation myocardial infarction (STEMI). Diagnostic angiography revealed a 3-vessel disease with acute thrombotic occlusion of the proximal left anterior descending artery (LAD) (A). The lesion was treated with a BVS 3.0/28 mm (B) with a good immediate result (C). Five-years later, the angiogram showed an excellent result (D). Optical coherence tomography (OCT) cross sections between proximal (*) and distal (**) markers at 5 years revealed a “Golden Tube” with complete resorption of the scaffold (E) [Color figure can be viewed at wileyonlinelibrary.com]

matrix that is secondarily cellularized into intima.¹⁹ Between the 1st and 3rd year, programmed disintegration of the polymeric scaffold struts occurs, and OCT images may show scaffold discontinuities, endoluminal dislocation, and peristrut low-intensity area, which are signs of a fragilized backbone.²⁰ No intraluminal material was found in the current analysis at 5 years. In all studied segments, the struts were no longer visible with normalized light intensity. While OCT is not capable of measuring polymer resorption, these results support that resorption and tissue replacement

of struts is complete by 5 years post implantation in this selected patient population.²¹

Furthermore, once the BVS is resorbed, the artery can behave more freely, unlike metallic DES, whose backbone constraints the vascular remodeling capacities. OCT follow-up showed a significantly higher mean lumen area in BVS than in metallic stent at 5 years. Moreover, we observed a trend toward late luminal enlargement in BVS and shrinking in DES in 24 paired OCT measurement between 9 months and 5 years. Our results are in line with a previous report comparing the remodeling

TABLE 5 Clinical outcome at 5 years

	BVS (n = 78)	EES/BES (n = 160)	EES (n = 80)	BES (n = 80)	p-value		
					BVS versus EES/BES	BVS versus EES	BVS versus BES
Device-oriented composite	17 (22)	29 (18)	18 (23)	11 (14)	0.49	1.00	0.34
Cardiac death	2 (3)	7 (4)	2 (3)	5 (6)	0.48	1.00	0.52
MI of the target vessel	3 (4)	1 (1)	1 (1)	0 (0)	0.07	0.62	0.16
TLR	15 (19)	23 (14)	15 (19)	8 (10)	0.37	1.00	0.20
Patient-oriented composite	31 (40)	69 (43)	37 (46)	32 (40)	0.72	0.76	1.00
All-cause mortality	4 (5)	16 (10)	7 (9)	9 (11)	0.20	0.72	0.32
Any MI	6 (8)	6 (4)	5 (6)	1 (1)	0.19	1.00	0.10
Any revascularization	28 (36)	58 (36)	32 (40)	26 (33)	0.97	1.00	1.00

Note: Values are n (%), p-values are derived from log-rank test.

Abbreviations: BES, biolimus-eluting stent; BVS, bioresorbable vascular scaffold stent; EES, everolimus-eluting stent; MI, myocardial infarction; TLR, target lesion revascularization.

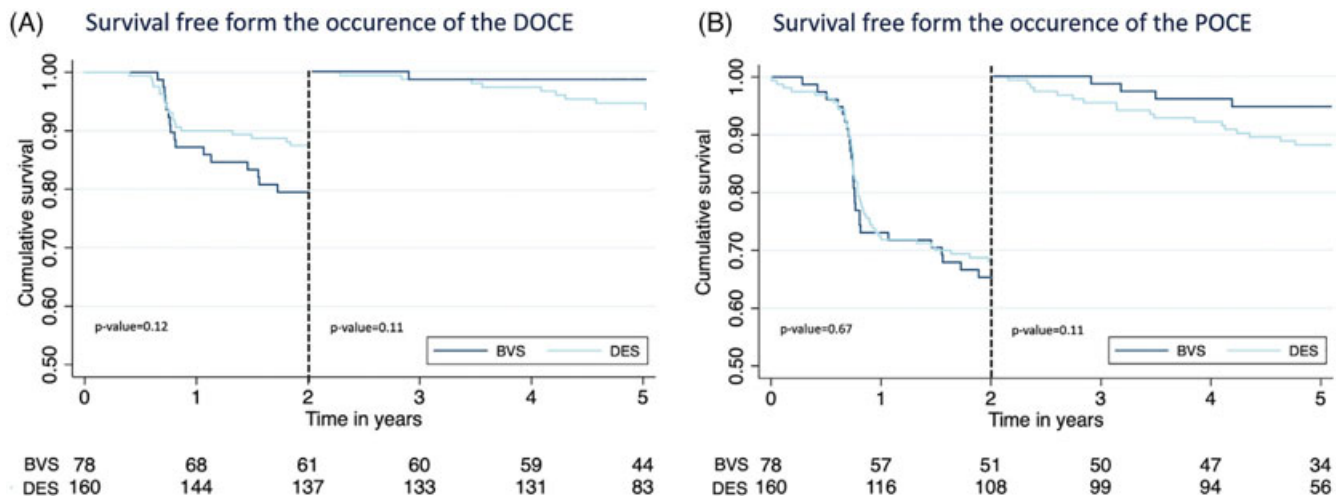


FIGURE 4 Landmark analysis for device-oriented (A) and patient-oriented (B) composite endpoints per implanted device. DES, drug-eluting stent; DOCE, device-oriented composite endpoint; EES, everolimus-eluting stent; POCE, patient-oriented composite endpoint [Color figure can be viewed at wileyonlinelibrary.com]

of BVS with DES.²² Indeed, Nakatani et al. demonstrated a relationship between the strut integration process and late luminal enlargement.²⁰ In 5 out of 10 paired OCT of the BVS group, we observed a perfect “Golden Tube” as described by Serruys et al.²¹ (Figure 3). Although our OCT findings are difficult to generalize due to the limited number of patients, serial angiographic and OCT data are nonetheless useful and support the hypothesis of positive vascular remodeling.

4.3 | Clinical outcomes

The 5-year clinical outcomes between BVS and EES/BES were similar. Device-oriented composite end point occurred in 22% of patients in the BVS arm and in 18% of patients in the EES/BES arm ($p = 0.49$).

Although BVS was clearly associated with increased rates of major clinical events up to 3 years,^{7,23} data beyond 3 years are limited. Lower major adverse cardiac events rates have been reported after 3 years in a recent meta-analysis²⁴ showing no differences for TLR (OR = 1.23, 95% CI = 0.73–2.07, $p = 0.44$), target vessel MI (OR = 1.03, 95% CI 0.42–2.53, $p = 0.95$), TLR (OR = 1.61, 95% CI 0.77–3.33, $p = 0.20$), and ST (OR = 0.71, 95% CI 0.10–5.07, $p = 0.74$).

5 | LIMITATIONS

The EverBio-2 trial was not powered for clinical and angiographic endpoints at 5-year follow-up. The results of the 5-year angiographic analysis are restricted to relatively low-risk patient

population without TLF. Implementation of protocol-mandated angiography at 9 months likely inflated the rates of repeat revascularization. There was no BVS-specific implantation protocol. Therefore, procedural heterogeneity and low rates of postdilatation may have led to different angiographic and clinical outcomes than reported in large-scale more recent trials with dedicated implantation protocols. The observational data from paired OCT was only possible in a small number of patients with inherent selection bias, as OCT could not technically be performed in all lesions, particularly in more peripheral lesions.

6 | CONCLUSION

Clinical outcomes were similar between BVS and DES patients at 5 years of follow-up. In a low-risk population, angiographic and OCT outcomes were similar between BVS and EES/BES drug-eluting stents. Complete BVS strut resorption was observed in the OCT subgroup. However, a definitive conclusion cannot be drawn because the EverBio-2 trial was not powered for the clinical and angiographic endpoints at 5 years of follow-up.

ACKNOWLEDGMENTS

The authors would like to acknowledge Sonia Lehmann, Estelle Boute and Yannick Faucherre for their constant dedication to the clinical follow-up.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

DATA AVAILABILITY STATEMENT

The datasets used and/or analysed for the current study are available from the corresponding author on reasonable request.

ORCID

Sara Schukraft  <https://orcid.org/0000-0002-1882-9015>

Jean-Jacques Goy  <https://orcid.org/0000-0003-3721-0661>

Stéphane Cook  <https://orcid.org/0000-0003-1221-2978>

REFERENCES

- 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. *The Lancet*. 2016;388:2479-2491.
- Puricel S, Arroyo D, Corpataux N, et al. Comparison of Everolimus- and Biolimus-eluting coronary stents with Everolimus-eluting bioresorbable vascular scaffolds. *J Am Coll Cardiol*. 2015;65:791-801.
- 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). *JACC: Cardiovasc Interventions*. 2015;8:189-197.
- Dudek D, Rzeszutko Ł, Zasada W, et al. Bioresorbable vascular scaffolds in patients with acute coronary syndromes: the POLAR ACS study. *Pol Arch Med Wewn*. 2014;124:669-677.
- Jaguszewski M, Wyss C, Alibegovic J, Lüscher TF, Templin C. Acute thrombosis of bioabsorbable scaffold in a patient with acute coronary syndrome. *Eur Heart J*. 2013;34:2046-2046.
- Serruys PW, Chevalier B, Dudek D, et al. A bioresorbable everolimus-eluting scaffold versus a metallic everolimus-eluting stent for ischaemic heart disease caused by de-novo native coronary artery lesions (ABSORB II): an interim 1-year analysis of clinical and procedural secondary outcomes from a randomised controlled trial. *The Lancet*. 2015;385:43-54.
- Kereiakes DJ, Ellis SG, Metzger C, et al. 3-year clinical outcomes with Everolimus-eluting bioresorbable coronary scaffolds: the ABSORB III trial. *J Am Coll Cardiol*. 2017;70:2852-2862.
- Chevalier B, Cequier A, Dudek D, et al. Four-year follow-up of the randomised comparison between an everolimus-eluting bioresorbable scaffold and an everolimus-eluting metallic stent for the treatment of coronary artery stenosis (ABSORB II trial). *EuroIntervention*. 2018;13:1561-1564.
- Yamaji K, Ueki Y, Souteyrand G, et al. Mechanisms of very late bioresorbable scaffold thrombosis: the INVEST registry. *J Am Coll Cardiol*. 2017;70:2330-2344.
- Ortega-Paz L, Brugaletta S, Sabaté M. Impact of PSP technique on clinical outcomes following bioresorbable scaffolds implantation. *J Clin Med*. 2018;7:27.
- Arroyo D, Togni M, Puricel S, et al. Comparison of everolimus-eluting and biolimus-eluting coronary stents with everolimus-eluting bioresorbable scaffold: study protocol of the randomized controlled EVERBIO II trial. *Trials*. 2014;15:9.
- Cutlip DE, Windecker S, Mehran R, et al. Serruys PW and academic research C clinical end points in coronary stent trials: a case for standardized definitions. *Circulation*. 2007;115:2344-2351.
- Nakatani S, Sotomi Y, Ishibashi Y, et al. Comparative analysis method of permanent metallic stents (XIENCE) and bioresorbable poly-L-lactic (PLLA) scaffolds (absorb) on optical coherence tomography at baseline and follow-up. *EuroIntervention*. 2016;12:1498-1509.
- Alderman EL, Corley SD, Fisher LD, et al. Five-year angiographic follow-up of factors associated with progression of coronary artery disease in the coronary artery surgery study (CASS). CASS participating Investigators and staff. *J Am Coll Cardiol*. 1993;22:1141-1154.
- Räber L, Wohlwend L, Wigger M, et al. Five-year clinical and angiographic outcomes of a randomized comparison of sirolimus-eluting and paclitaxel-eluting stents. *Circulation*. 2011;123:2819-2828.
- Bruyne BD, Toth GG, Onuma Y, Serruys PW. TCT-619 ABSORB cohort B trial: five year angiographic results of the ABSORB Everolimus eluting Bioresorbable vascular scaffold. *J Am Coll Cardiol*. 2019;64:B181.
- Moriyama N, Shishido K, Tanaka Y, et al. Neoatherosclerosis 5 years after bioresorbable vascular scaffold implantation. *J Am Coll Cardiol*. 2018;71:1882-1893.
- Asano T, Serruys PW, Collet C, et al. Angiographic late lumen loss revisited: impact on long-term target lesion revascularization. *Eur Heart J*. 2018;39:3381-3389.
- Vorpahl M, Finn AV, Nakano M, Virmani R. The bioabsorption process: tissue and cellular mechanisms and outcomes. *EuroIntervention*. 2009;5(suppl F):F28-F35.
- Nakatani S, Ishibashi Y, Sotomi Y, et al. Bioresorption and Vessel Wall integration of a fully Bioresorbable polymeric Everolimus-eluting scaffold: optical coherence tomography, intravascular ultrasound, and histological study in a porcine model with 4-year follow-up. *JACC Cardiovasc Interv*. 2016;9:838-851.

21. Otsuka F, Pacheco E, Perkins LE, et al. Long-term safety of an everolimus-eluting bioresorbable vascular scaffold and the cobalt-chromium XIENCE V stent in a porcine coronary artery model. *Circ Cardiovasc Interv.* 2014;7:330-342.
22. Serruys PW, Katagiri Y, Sotomi Y, et al. Arterial remodeling after Bioresorbable scaffolds and metallic stents. *J Am Coll Cardiol.* 2017;70:60-74.
23. Wykrzykowska JJ, Kraak RP, Hofma SH, et al. Bioresorbable scaffolds versus metallic stents in routine PCI. *New England J Med.* 2017;376:2319-2328.
24. Goel S, Pasam RT, Chava S, et al. Three to four years outcomes of the absorb bioresorbable vascular scaffold versus second-generation drug-eluting stent: a meta-analysis. *Catheter Cardiovasc Interv.* 2020;95(2):216-223.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Schukraft S, Arroyo D, Togni M, et al. Five-year angiographic, OCT and clinical outcomes of a randomized comparison of everolimus and biolimus-eluting coronary stents with everolimus-eluting bioresorbable vascular scaffolds. *Catheter Cardiovasc Interv.* 2022;99:523-532. <https://doi.org/10.1002/ccd.29837>