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Coronary artery disease

A randomized trial evaluating everolimus-eluting Absorb bioresorbable scaffolds vs. everolimus-eluting metallic stents in patients with coronary artery disease: ABSORB Japan

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Aims Theoretically, bioresorbable vascular scaffolds (BVSs) may provide superior long-term results compared with permanent metallic drug-eluting stents (DESs). However, whether BVSs are as safe and effective as metallic DESs prior to complete bioresorption is unknown.

Methods and results ABSORB Japan was a single-blind, multicentre, active-controlled, randomized trial designed to support regulatory approval of the Absorb BVS in Japan. Eligible patients with one or two *de novo* lesions in different epicardial vessels were randomized at 38 Japanese sites in a 2:1 ratio to Absorb BVS vs. cobalt-chromium everolimus-eluting stents (CoCr-EESs). The primary endpoint was target lesion failure [TLF: a composite of cardiac death, myocardial infarction attributable to target vessel, or ischaemia-driven target lesion revascularization (ID-TLR)] at 12 months, powered for non-inferiority. The major secondary endpoint was angiographic in-segment late lumen loss (LLL) at 13 months. A total of 400 patients were randomized to BVSs (266 patients and 275 lesions) or CoCr-EESs (134 patients and 137 lesions). TLF through 12 months was 4.2% with BVSs and 3.8% with CoCr-EESs [difference (upper one-sided 95% confidence limit) = 0.39% (3.95%); $P_{\text{non-inferiority}} < 0.0001$]. Definite/probable stent/scaffold thrombosis at 12 months occurred in 1.5% of the patients with both devices ($P = 1.0$), and ID-TLR for restenosis was infrequent (1.1% with BVSs and 1.5% with CoCr-EESs, $P = 1.0$). With 96.0% angiographic follow-up, in-segment LLL at 13 months was 0.13 ± 0.30 mm with BVSs and 0.12 ± 0.32 mm with CoCr-EESs [difference (upper one-sided 95% confidence limit) = 0.01 (0.07); $P_{\text{non-inferiority}} < 0.0001$].

Conclusion In the ABSORB Japan randomized trial, 12-month clinical and 13-month angiographic outcomes of BVSs were comparable to CoCr-EESs.

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Keywords Bioresorbable scaffold • Coronary stent • Restenosis • Thrombosis

Introduction

By providing antiproliferative drug-eluting capability without the chronic limitations of permanent metallic implants, bioresorbable vascular scaffolds (BVSs) may provide long-term benefits over metallic stents.[1] Imaging studies for up to 5 years after Absorb BVS implantation have suggested favourable vascular responses, including restoration of vasomotion and endothelium-dependent vasodilation, late lumen enlargement with plaque regression and vessel remodelling, and formation of a stable-appearing neointima.[1–3] Studies are ongoing to determine whether these long-term changes after BVS implantation might mitigate the risk of very late (>1 year) adverse events reported after metallic drug-eluting stent (DES) implantation, namely, very late stent thrombosis and restenosis (for example, due to neoatherosclerosis).[4] However, even if BVS demonstrates long-term advantages compared with metallic DES, it is important to ensure at least comparable (non-inferior) short- and mid-term (i.e. 1-year) safety and efficacy profiles. Currently, two moderate-sized randomized controlled trials in which Absorb BVSs were compared with newer generation metallic DESs have suggested comparable 9-month angiographic and 1-year clinical results.[5,6] To further examine the relative clinical and angiographic outcomes of Absorb BVSs, a randomized, controlled trial comparing the Absorb BVS with cobalt-chromium everolimus-eluting stents (CoCr-EESs) was designed to support regulatory approval of the Absorb BVS in Japan. This report describes the 12-month primary clinical endpoint results and the major secondary 13-month angiographic results from the ABSORB Japan randomized trial.

Methods

Study design

ABSORB Japan was a prospective, multicentre, randomized, single-blind, active-controlled clinical trial in which 400 patients undergoing coronary stent implantation in Japan were randomized in a 2:1 ratio to treatment with the Absorb everolimus-eluting BVS or the XIENCE Prime/Xpedition CoCr-EES (both Abbott Vascular, Santa Clara, CA, USA).

A total of 38 investigational sites in Japan participated in the study. The study was conducted according to the Declaration of Helsinki. Prior to initiating the study, the Institutional Review Board at each investigational site approved the clinical trial protocol. The protocol summary is provided in the Supplementary material online, Appendix. All patients provided written informed consent before enrolment.

Patients

Patients were eligible if they were ≥20 years of age and had evidence of myocardial ischaemia (stable angina, unstable angina, or silent ischaemia). We excluded patients with left ventricular ejection fraction <30%, estimated glomerular filtration rate <30 mL/min/1.73m^2, recent myocardial infarction (MI), and those at high bleeding risk. The study allowed treatment of up to two *de novo* native lesions in separate epicardial coronary arteries. Key angiographic inclusion criteria included reference vessel diameter ≥2.5 to ≤3.75 mm, lesion length ≤24 mm, and diameter stenosis (DS) ≥50 to <100%. Key angiographic exclusion criteria included left main or ostial location; excessive vessel tortuosity or extreme lesion angulation; heavy calcification proximal to or within the target lesion; myocardial bridge; restenotic lesion; target vessel (TV) containing thrombus; and bifurcation lesion with side branch ≥2 mm in diameter, requiring protection guidewire or dilatation. Full inclusion and exclusion criteria are provided in the Supplementary material online, Appendix.

Randomization and blinding

Patients were randomized in a 2:1 ratio to BVSs vs. CoCr-EESs using a central randomization service. Randomization was stratified by the presence of diabetes mellitus and the number of lesions to be treated. Patients were also allocated randomly to one of the three intravascular imaging subgroups: intravascular ultrasound (IVUS) group (150 patients), optical coherence tomography (OCT) group 1 (125 patients), or OCT group 2 (125 patients), based on the schedules of intravascular imaging. Additional details on randomization processes are provided in the Supplementary material online, Appendix. Patients were blinded to their treatment assignment through the completion of 5-year follow-up. Study investigators doing the procedure were not blinded. However, blinded site personnel were assigned to conduct scheduled clinical follow-up visits in order to reduce ascertainment and/or treatment bias and to maintain patient blinding. Imaging follow-up could be performed by the unblinded physician.

Study procedure

The study allowed treatment of up to two *de novo* native coronary artery lesions. If a patient had two lesions in separate vessels and only one lesion was eligible for randomization, the second lesion could be treated as a non-study lesion. The non-study lesion had to be treated successfully prior to treatment of the study target lesion. Successful predilatation of the target lesion was mandatory. Sizes of the BVSs available in the study were: 2.5, 3.0, and 3.5 mm in diameter and 8, 12, 18, and 28 mm in length. Treatment with the same size matrix was required for patients assigned to the CoCr-EES arm. The target lesion had to be treated with a single study device, and planned overlapping was not allowed. Post-dilatation of BVSs was not mandatory but was allowed, using a low profile, high-pressure, non-compliant balloon with diameter ≤0.5 mm larger than the nominal BVS size. Post-dilatation of CoCr-EESs was per standard of care. If a bailout device was required for the study target lesion, the same study device as the implanted device had to be used. Post-procedural intravascular imaging with the assigned modality was to be performed in the IVUS and OCT-1 groups, whereas it was not allowed in the OCT-2 group.

All patients were maintained on a thienopyridine for at least 12 months and aspirin indefinitely. Clinical follow-up was scheduled up to 5 years. Follow-up angiography was planned in all patients at 13 months.

Endpoints and definitions

The primary endpoint of the study was target lesion failure [TLF: a composite of cardiac death, MI attributable to TV (TV-MI), or ischaemia-

driven target lesion revascularization (ID-TLR)] at 1 year, powered for non-inferiority of BVSs vs. CoCr-EESs. The major secondary endpoint was angiographic in-segment late lumen loss (LLL) at 13 months. Clinical endpoint definitions, including stent/scaffold thrombosis (ST), were based on the Academic Research Consortium definitions,[7] other than peri-procedural non-Q-wave MI, which was defined as a post-procedural creatine kinase (CK)-MB >5× upper limit of normal, similar to the definition used in the ABSORB III US trial and the ABSORB China trial, which were planned in parallel to our study. Device success is defined as successful deployment of the assigned device with attainment of final in-device DS <30% by quantitative coronary angiography (QCA). Procedure success is defined as successful deployment of the assigned device with attainment of final in-device DS <30% by QCA without the occurrence of TLF during the hospital stay (maximum of 7 days). A complete list of endpoints is provided in the Supplementary material online, Appendix.

The sponsor performed on-site monitoring of 100% of case report form data against source documents. Pre-specified adverse cardiac events of death, MI, TLR/TV revascularization (TVR), and ST were adjudicated by an independent blinded clinical events committee. An angiographic core laboratory performed quantitative angiographic analysis (MEDIS QAngio XA 7.3) and, if revascularization occurred during follow-up, adjudicated whether it was done for the target lesion, TV, or non-TV. If an ST was suspected, the angiographic core laboratory assessed whether thrombus was present. The ABSORB Japan organizational structure is detailed in the Supplementary material online, Appendix.

Statistical methods

Twelve-month events were counted through 393 days as a conservative approach to include events occurring through the end of the 1-year (±28 day) follow-up window. The primary endpoint of 12-month TLF was evaluated using the difference in the event rates (BVS minus CoCr-EES) in the intention-to-treat (ITT) population. The hypothesis test was designed to evaluate non-inferiority of BVS to CoCr-EES (margin of 8.6% for a 9.0% assumed event rate in both groups that was agreed upon with the Pharmaceutical and Medical Device Agency in Japan) using the likelihood score method by Farrington and Manning.[8] Randomizing 400 patients 2:1 to BVSs vs. CoCr-EESs, with an anticipated 1-year follow-up rate of 97%, provided 90% power to demonstrate non-inferiority of BVSs for TLF at a one-sided significance level of 0.05. The

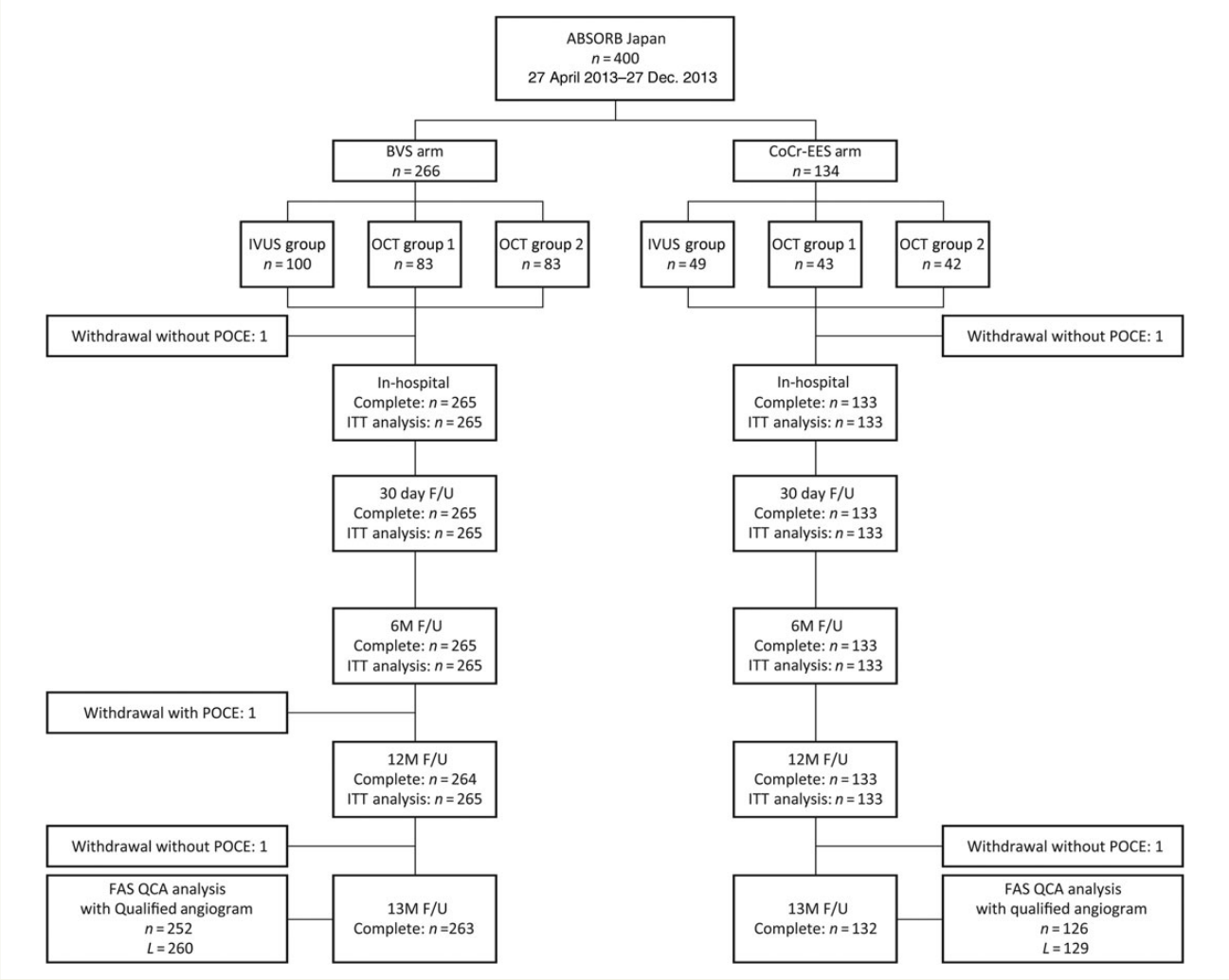


Figure 1 Patient enrolment and disposition. BVS, bioresorbable vascular scaffold; CoCr-EES, cobalt-chromium everolimus-eluting stent; FAS, full-analysis set; F/U, follow-up; ITT, intention-to-treat; IVUS, intravascular ultrasound; OCT, optical coherence tomography; POCE, patient-oriented composite endpoint; QCA, quantitative coronary angiography.

major secondary endpoint of in-segment LLL was tested for non-inferiority (margin of 0.195 mm and SD of 0.5 mm for both arms) using an asymptotic *Z*-test statistic at a one-sided significance level of 0.05. Randomizing 400 patients 2:1 to BVSs vs. CoCr-EESs (assuming that 15% of the patients would have two target lesions), with an anticipated angiographic follow-up rate of 90% at 13 months, provided 98% power to demonstrate non-inferiority of BVSs for LLL. For this angiographic endpoint, the full-analysis-set population, defined as patients who received the assigned study device at the target lesion, was used on a per lesion basis.

For binary variables, counts and percentages were calculated, and the *P*-value based on Pearson's χ^2 test was used when Cochran's rule was met.[9] Otherwise, Fisher's exact test was used. Relative risks and 95% confidence interval (CI) were calculated for clinical outcomes. For continuous variables, means, standard deviations, and *t*-tests were performed when appropriate. For analysis of multiple lesions per patient, generalized estimating equations were used to account for clustering effects. Survival curves were constructed using Kaplan–Meier estimates and were compared by the log-rank test. Subjects were excluded from the analysis population only if they withdrew consent for trial participation prior to the occurrence of death, MI, or revascularization. The power calculations were performed with PASS version 11 (NCSS LLC, Kaysville, UT, USA), and all statistical analyses were performed using SAS versions 9.2 and 9.3 (SAS Institute Inc., Cary, NC, USA). A comprehensive summary of the statistical design and *post hoc* analyses appears in the Supplementary material online, Appendix.

Role of the funding source

The sponsor was involved in study design, data collection, data analysis, data interpretation, and writing of this report. The corresponding author had full access to the analysed data in the study and accepts full responsibility for the integrity of the study and the decision to submit for publication.

Results

Patient disposition

Between 27 April 2013 and 27 December 2013, 400 patients were enrolled and randomly assigned to BVSs (266 patients) or CoCr-EESs (134 patients). Clinical follow-up at 12 months was available in 264 (99.2%) patients in the BVS arm and 133 (98.8%) patients in the CoCr-EES arm (*Figure 1*).

Baseline features and procedures

Baseline demographic variables, risk factors, and lesion characteristics were comparable between the treatment arms (*Table 1*). Mean age was 67.2 years, and 36.0% of the patients had diabetes. Stable coronary artery disease (CAD) was present in 88.0% of the patients. Ninety-seven per cent of patients had treatment of one study target lesion only.

Pre-dilatation was performed using slightly undersized balloons with moderate inflation pressures. The rates of clinical device and procedural success were similar in both groups, with slightly longer procedure duration in the BVS arm (*Table 2*). Of three acute device failures in the BVS arm, two were deployment failures (lesions subsequently treated with CoCr-EESs), and one lesion had in-device DS of ≥30% after BVS implantation. The use of bailout devices was infrequent in both groups. Of five BVS patients who required bailout, four were successfully treated with BVSs and one was treated with CoCr-EES. Nominal device diameter and expected final balloon diameter were similar between the two arms, with post-dilatation performed in a similar proportion of patients but at slightly lower inflation pressure with BVS. In-device acute gain and minimal luminal diameter (MLD) were significantly smaller in the BVS arm than in the CoCr-EES arm. However, in-segment MLD and DS were similar between the two arms (*Table 3*).

Table 1 Baseline characteristics of the study population

	BVS	CoCr-EES
Patients		
Number of patients	266	134
Age (years)	67.1 ± 9.4	67.3 ± 9.6
Male	210 (78.9%)	99 (73.9%)
Body mass index (kg/m^2)	24.0 ± 3.0	24.3 ± 3.0
Current smoker	53 (19.9%)	29 (21.6%)
Hypertension	208 (78.2%)	107 (79.9%)
Dyslipidaemia	218 (82.0%)	110 (82.1%)
Diabetes mellitus	96 (36.1%)	48 (35.8%)
Treated with insulin	24 (9.0%)	11 (8.2%)
HbA1c (%)	6.2 ± 1.1	6.2 ± 0.8
Prior intervention to target vessel	9 (3.4%)	7 (5.2%)
Prior myocardial infarction	42/262 (16.0%)	32 (23.9%)
Family history of premature CAD	16/246 (6.5%)	10/124 (8.1%)
Current evidence of ischaemia		
Stable angina	170 (63.9%)	88 (65.7%)
Unstable angina	26 (9.8%)	22 (16.4%)
Silent ischaemia	70 (26.3%)	24 (17.9%)
Number of target lesions		
One	257 (96.6%)	131 (97.8%)
Two	9 (3.4%)	3 (2.2%)
Non-study lesion treated	20 (7.5%)	10 (7.5%)
Target lesions[a]		
Total number of target lesions	275	137
Left anterior descending	127 (46.2%)	58 (42.3%)
Left circumflex/ramus	63 (22.9%)	36 (26.3%)
Right coronary artery	85 (30.9%)	43 (31.4%)
Calcification (moderate/severe)	76/274 (27.7%)	45 (32.8%)
Calcification (severe)	19/274 (6.9%)	15 (10.9%)
Tortuosity (moderate/severe)	23/274 (8.5%)	11 (8.0%)
Eccentric lesion	223/273 (81.7%)	113 (82.5%)
ACC/AHA lesion classification		
A	11 (4.0%)	5 (3.6%)
B1	55 (20.0%)	28 (20.4%)
B2	154 (56.0%)	68 (49.6%)
C	55 (20.0%)	36 (26.3%)

There were no significant differences between groups. ACC/AHA, American College of Cardiology/American Heart Association; BVS, bioresorbable vascular scaffold; CAD, coronary artery disease; CoCr-EES, cobalt-chromium everolimus-eluting stent.
[a]Core laboratory assessed.

Table 2 Procedural results

	BVS (*P* = 266, *L* = 275, *D* = 280)	CoCr-EES (*P* = 134, *L* = 137, *D* = 138)	*P*-value
Post OCT/IVUS assigned	183 (68.8%)	92 (68.7%)	1.00
Procedure duration (min)	49.8 ± 24.8	44.9 ± 21.7	0.04
Procedural information (per lesion)			
Assigned device implanted	272 (98.9%)	137 (100%)	0.55
Bailout device used	5 (1.8%)	1 (0.7%)	0.67
Total device length per lesion (mm)	20.2 ± 5.8	19.5 ± 5.8	0.22
Pre-dilatation (per lesion)			
Pre-dilatation performed	275 (100%)	137 (100%)	1.00
Semi-compliant balloon	143 (52.0%)	64 (46.7%)	0.31
Non-compliant balloon	97 (35.3%)	54 (39.4%)	0.41
Scoring or cutting balloon	54 (19.6%)	26 (19.0%)	1.00
Nominal balloon diameter (mm)	2.80 ± 0.37	2.86 ± 0.36	0.15
Pre-dilatation balloon pressure (atm)	11.6 ± 3.8	11.9 ± 3.7	0.52
Device deployment (per device)			
Nominal device diameter (mm)	3.09 ± 0.37	3.13 ± 0.38	0.30
Deployment pressure (atm)	10.4 ± 3.0	11.2 ± 2.7	0.003
Expected device diameter at deployment (mm)	3.30 ± 0.43	3.19 ± 0.42	0.01
Post-dilatation (per lesion)			
Post-dilatation performed	226 (82.2%)	106 (77.4%)	0.25
Nominal balloon diameter (mm)	3.18 ± 0.44	3.29 ± 0.51	0.0495
Balloon pressure (atm)	15.5 ± 4.2	16.0 ± 3.9	0.24
Expected post-dilatation balloon diameter (mm)	3.32 ± 0.44	3.45 ± 0.49	0.02
>0.5 mm larger than the BVS diameter	9 (4.0%)	–	–
Final balloon (per lesion)			
Balloon pressure (atm)	14.7 ± 4.1	15.1 ± 4.1	0.36
Expected final balloon diameter (mm)	3.34 ± 0.45	3.41 ± 0.48	0.15
Acute success			
Device success (per lesion)	271 (98.9%)*	136 (99.3%)	1.00
Procedural success (per patient)	259 (97.7%)**	132 (98.5%)	0.72

One patient in the BVS arm had CoCr-EES implantation without attempt of assigned BVS due to lack of BVS inventory and was excluded from the acute success analysis. *P* is for patient number, *L* is for lesion number, and *D* is for device number. Expected balloon/device diameter was determined from the compliance chart according to the maximum inflation pressure. BVS, bioresorbable vascular scaffold; DS, diameter stenosis; CoCr-EES, cobalt-chromium everolimus-eluting stent; ITT, intention-to-treat; IVUS, intravascular ultrasound; OCT, optical coherence tomography; QCA, quantitative coronary angiography; TLF, target lesion failure.
*$N = 274$.
**$N = 265$.

Clinical outcomes

Within 12 months, the primary endpoint of TLF occurred in 11/265 BVS patients (4.2%) and in 5/133 CoCr-EES patients (3.8%) (relative risk 1.10, 95% CI 0.39–3.11). The upper one-sided 95% confidence limit of the 0.4% difference in the rate of TLF (BVS minus CoCr-EES) was 3.95%, less than the pre-defined non-inferiority margin of 8.6%, demonstrating non-inferiority of BVSs to CoCr-EESs ($P_{\text{non-inferiority}} < 0.0001$). Comprehensive clinical outcomes with standard two-sided superiority tests are shown in *Table 4* and *Figure 2*. There were no significant differences in any of the endpoints at 12 months between BVSs and CoCr-EESs. Of note, peri-procedural MI rates were similar with the two devices (1.1 and 1.5%), as were the rates of definite/probable ST (1.5% in each group). At 12 months, 97.0 and 93.3% of the patients in the BVS and CoCr-EES arms, respectively, were taking dual antiplatelet therapy ($P = 0.08$) (Supplementary material online, Appendix). The reasons for discontinuation of dual antiplatelet therapy were adverse events ($n = 7$) and unknown ($n = 1$) in the BVS arm and adverse events ($n = 5$), non-compliance ($n = 2$), physician's judgement ($n = 1$), and unknown ($n = 1$) in the CoCr-EES arm. A detailed description of the patients with ST appears in the Supplementary material online, Appendix.

Table 3 QCA results (full-analysis-set)

	BVS	CoCr-EES	*P*-value
Baseline			
Number of lesions	272	137	
Lesion length (mm)	13.5 ± 5.28	13.3 ± 5.52	0.78
Reference vessel diameter (mm)	2.72 ± 0.44	2.79 ± 0.46	0.11
MLD (mm)	0.96 ± 0.33	0.99 ± 0.36	0.42
DS (%)	64.6 ± 11.2	64.7 ± 10.9	0.93
Post-procedure			
Number of lesions	272	137	
Reference vessel diameter (mm)	2.76 ± 0.42	2.85 ± 0.43	0.04
In-segment MLD (mm)	2.21 ± 0.39	2.26 ± 0.43	0.19
In-device MLD (mm)	2.42 ± 0.38	2.64 ± 0.40	<0.0001
In-segment DS (%)	19.9 ± 6.7	20.6 ± 8.7	0.44
In-device DS (%)	11.8 ± 7.4	7.1 ± 8.0	<0.0001
In-segment acute gain (mm)	1.25 ± 0.41	1.28 ± 0.45	0.56
In-device acute gain (mm)	1.46 ± 0.40	1.65 ± 0.40	<0.0001
Follow-up at 13 months			
Number of lesions	260	129	
Reference vessel diameter (mm)	2.70 ± 0.42	2.80 ± 0.44	0.046
In-segment MLD (mm)	2.08 ± 0.45	2.15 ± 0.50	0.18
In-device MLD (mm)	2.23 ± 0.47	2.48 ± 0.53	<0.0001
In-segment DS (%)	23.4 ± 11.3	23.7 ± 12.3	0.87
In-device DS (%)	17.4 ± 12.8	11.7 ± 12.3	<0.0001
In-segment binary restenosis	5 (1.9%)	5 (3.9%)	0.31
In-device binary restenosis	4 (1.5%)	2 (1.6%)*	1.0
In-segment late lumen loss (mm)	0.13 ± 0.30	0.12 ± 0.32	0.74
In-device late lumen loss (mm)	0.19 ± 0.31	0.16 ± 0.33	0.35
In-segment net gain (mm)	1.12 ± 0.47	1.15 ± 0.47	0.56
In-device net gain (mm)	1.28 ± 0.49	1.48 ± 0.48	0.0001

BVS, bioresorbable vascular scaffold; CoCr-EES, cobalt-chromium everolimus-eluting stent; DS, diameter stenosis; MLD, minimal lumen diameter.
*$N = 128$.

Angiographic outcomes

Angiographic follow-up at 13 months was performed in 262/270 (95.6%) target lesions in the BVS arm and in 129/137 (94.2%) target lesions in the CoCr-EES arm at 395 ± 28 days after device implantation (*Figure 1*). The major secondary endpoint of 13-month angiographic in-segment LLL was 0.13 ± 0.30 mm in the BVS arm and 0.12 ± 0.32 mm in the CoCr-EES arm (*Table 3* and *Figure 3*). The upper one-sided 95% confidence limit of the difference in in-segment LLL was 0.07 mm, less than the pre-defined non-inferiority margin of 0.195 mm, demonstrating non-inferiority of BVSs to CoCr-EESs ($P_{\text{non-inferiority}} < 0.0001$). In-device LLL was also not significantly different between the two arms, although in-device MLD and DS at 13 months were slightly smaller in the BVS arm. However, in-segment MLD, DS, and binary restenosis were similar in the two arms (*Table 3* and *Figure 3*). Isolated edge restenosis was numerically lower in the BVS arm than in the CoCr-EES arm [1/254 (0.4%) vs. 3/124 (2.3%), respectively, $P = 0.11$]. There were no significant differences in clinical or angiographic outcomes according to the performance of post-procedural intravascular imaging (Supplementary material online, Appendix).

Discussion

In the ABSORB Japan randomized trial, the Absorb BVS was comparable to CoCr-EES for the primary clinical endpoint of 12-month TLF. Safety measures with BVS, including the rates of death, MI (all and peri-procedural), and ST, occurred with similar frequency as with CoCr-EES, a DES with an excellent safety record.[10] BVS was also demonstrated to be comparable for the major secondary angiographic endpoint of in-segment LLL at 13 months. Other important findings included the low incidence of ID-TLR at 12 months and angiographic in-segment DS and binary restenosis at 13 months with BVS, similar to that with CoCr-EES, despite smaller in-device MLD and DS immediately after the BVS procedure.

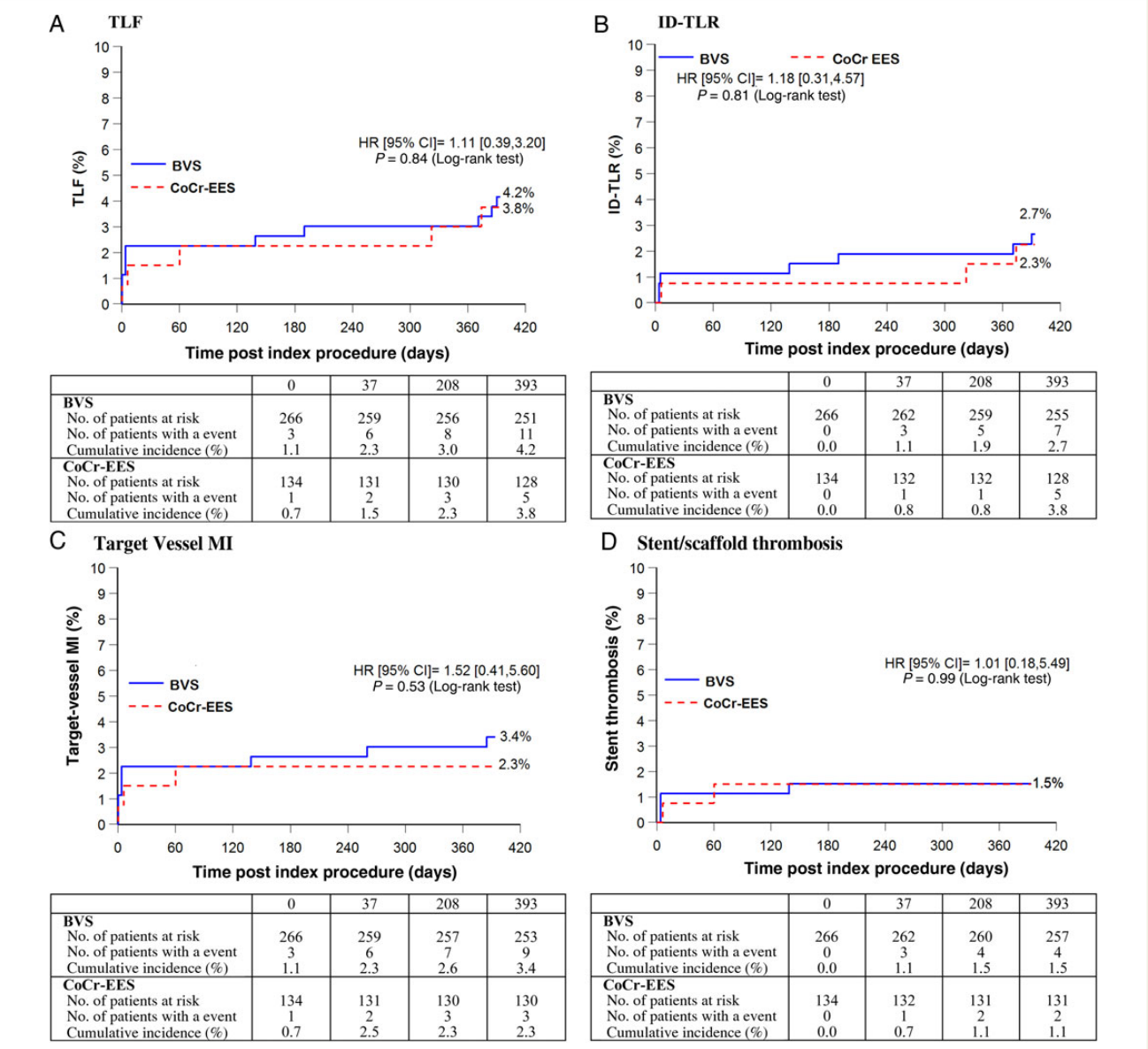
Absorb BVS, a first-generation drug-eluting bioresorbable scaffold, is composed of a poly-L-lactic acid frame with a strut thickness

Table 4 Clinical outcomes—composite and non-hierarchical events (ITT)

	BVS (*n* = 265)	CoCr-EES (*n* = 133)	Relative risk (95% CI)	*P*-value
Composite endpoints at 12 months				
TLF (cardiac death, target-vessel MI, ID-TLR)	11 (4.2%)	5 (3.8%)	1.10 (0.39, 3.11)	0.85
TVF (cardiac death, MI, ID-TVR)	16 (6.0%)	7 (5.3%)	1.15 (0.48, 2.72)	0.75
POCE (death, MI, revascularization)	26 (9.8%)	11 (8.3%)	1.19 (0.60, 2.33)	0.62
Cardiac death or myocardial infarction	9 (3.4%)	3 (2.3%)	1.51 (0.41, 5.47)	0.76
Individual endpoints at 12 months				
All-cause death	2 (0.8%)	0 (0.0%)	–	0.55
Cardiac death	0 (0.0%)	0 (0.0%)	–	1.00
All myocardial infarction	9 (3.4%)	3 (2.3%)	1.51 (0.41, 5.47)	0.76
Target-vessel myocardial infarction	9 (3.4%)	3 (2.3%)	1.51 (0.41, 5.47)	0.76
Target-vessel QMI	3 (1.1%)	0 (0.0%)	–	0.55
Target-vessel NQMI	6 (2.3%)	3 (2.3%)	1.00 (0.26, 3.95)	1.00
All revascularization	21 (7.9%)	9 (6.8%)	–	1.00
All TVR	13 (4.9%)	6 (4.5%)	1.09 (0.42, 2.80)	0.86
ID-TVR	13 (4.9%)	5 (3.8%)	1.30 (0.48, 3.58)	0.60
All TLR	7 (2.6%)	5 (3.8%)	0.70 (0.23, 2.17)	0.55
ID-TLR	7 (2.6%)	3 (2.3%)	1.17 (0.31, 4.46)	1.00
Type of MI				
Spontaneous QMI	3 (1.1%)	0 (0.0%)	–	0.55
Spontaneous NQMI	3 (1.1%)	2[a] (1.5%)	0.75 (0.13, 4.45)	1.00
Peri-procedure QMI	0 (0.0%)	0 (0.0%)	–	1.00
Peri-procedure NQMI	3 (1.1%)	2 (1.5%)	0.75 (0.13, 4.45)	1.00
At index procedure	3 (1.1%)	1 (0.8%)	1.51 (0.16, 14.34)	1.00
At revasularization	0 (0.0%)	1[a] (0.8%)	–	0.33
Scaffold/stent thrombosis				
Definite	4 (1.5%)*	1 (0.8%)	2.03 (0.23, 17.99)	0.67
Acute	0 (0.0%)**	0 (0.0%)	–	1.00
Subacute	3 (1.1%)	1 (0.8%)	1.51 (0.16, 14.34)	1.00
Late	1 (0.4%)*	0 (0.0%)	–	1.00
Definite/probable	4 (1.5%)*	2 (1.5%)	1.02 (0.19, 5.47)	1.00
Acute	0 (0.0%)**	0 (0.0%)	–	1.00
Subacute	3 (1.1%)	1 (0.8%)	1.51 (0.16, 14.34)	1.00
Late	1 (0.4%)*	1 (0.8%)	0.51 (0.03, 8.05)	1.00

BVS, bioresorbable vascular scaffold; CoCr-EES, cobalt-chromium everolimus-eluting stent; ID, ischaemia-driven; NQMI, non-Q-wave myocardial infarction; POCE, patient-oriented composite endpoint; QMI, Q-wave myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVF, target-vessel failure; TVR, target-vessel revascularization.
[a]This patient had spontaneous NQMI at day 4 and peri-procedural NQMI at day 6.
*$N = 262$.
**$N = 266$.

of 150 μm, with a poly-DL-lactic acid coating ~7 μm thick that elutes everolimus. The resulting crossing profile of BVS is larger than that of CoCr-EES (1.4 vs. 1.1 mm), raising concerns about the deliverability of BVS. However, the device and procedural success rates with BVS were similar to those of CoCr-EES in the ABSORB Japan and ABSORB II trials,[5] mitigating concerns about the deliverability of BVS in the relatively non-complex lesions enrolled in these studies. The acute recoil of BVS was reported to be similar to that of metallic DES in previous studies based on the QCA measurement of mean balloon diameter during balloon inflation.[3,5,11] However, in the current trial, as well as in previously reported studies,[5,6] the in-device MLD post-BVS implantation was significantly less than that after CoCr-EES implantation. The frequency and sizing of post-dilatation were comparable between the two groups, although post-dilatation pressure was lower in the BVS group. Thus, the smaller final in-device MLD associated with BVS may be attributed in part to technique, as well as to possible differences in the mechanical properties of the device compared with metallic DES, suggesting that acute performance of BVS remains inferior to contemporary metallic DES.[12] Nonetheless,



	0	37	208	393
BVS				
No. of patients at risk	266	259	256	251
No. of patients with a event	3	6	8	11
Cumulative incidence (%)	1.1	2.3	3.0	4.2
CoCr-EES				
No. of patients at risk	134	131	130	128
No. of patients with a event	1	2	3	5
Cumulative incidence (%)	0.7	1.5	2.3	3.8

	0	37	208	393
BVS				
No. of patients at risk	266	262	259	255
No. of patients with a event	0	3	5	7
Cumulative incidence (%)	0.0	1.1	1.9	2.7
CoCr-EES				
No. of patients at risk	134	132	132	128
No. of patients with a event	0	1	1	5
Cumulative incidence (%)	0.0	0.8	0.8	3.8

	0	37	208	393
BVS				
No. of patients at risk	266	259	257	253
No. of patients with a event	3	6	7	9
Cumulative incidence (%)	1.1	2.3	2.6	3.4
CoCr-EES				
No. of patients at risk	134	131	130	130
No. of patients with a event	1	2	3	3
Cumulative incidence (%)	0.7	2.5	2.3	2.3

	0	37	208	393
BVS				
No. of patients at risk	266	262	260	257
No. of patients with a event	0	3	4	4
Cumulative incidence (%)	0.0	1.1	1.5	1.5
CoCr-EES				
No. of patients at risk	134	132	131	131
No. of patients with a event	0	1	2	2
Cumulative incidence (%)	0.0	0.7	1.1	1.1

Figure 2 Cumulative incidence of TLF (*A*), ID-TLR (*B*), TV-MI (*C*), and stent/ST (*D*) through 393 days. TLF, target lesion failure; BVS, bioresorbable vascular scaffold; CoCr-EES, cobalt-chromium everolimus-eluting stent; ID-TLR, ischaemia-driven target lesion revascularization; MI, myocardial infarction.

BVS resulted in a similar in-device LLL, as well as in-segment MLD, DS, and binary restenosis at 13 months, which are more powerful angiographic surrogates of ID-TLR than in-device measures.[13] The low rates of ID-TLR noted with BVS in the present and prior randomized trials[5,6] suggest that the slightly smaller final in-device MLD post-BVS implantation may not adversely impact the mid-term rates of restenosis in non-complex lesions. The influence of smaller in-device MLD post-BVS implantation on mid-term effectiveness might have been minimized by the comparable post-procedural in-segment MLD between groups and small LLL with the drug-eluting capability.

In the current study, the 12-month rate of definite/probable ST was 1.5% with both BVSs and CoCr-EESs. The observed ST rate in the BVS arm in this study is consistent with recently published BVS studies, whereas the ST rate in the CoCr-EES arm was somewhat higher than expected, given enrolment of mostly non-complex lesions.[4,14–16] This observation was likely due to chance, given the low rates of ST with wide CIs (0.4–3.9% for BVS and 0.2–5.3% for CoCr-EES). Large-scale studies are required to evaluate the relative incidence of ST between these two devices. Nonetheless, as is evident from the descriptive data in the Supplementary material online, Appendix, patients with ST tended to have device implants in small vessels (<2.5 mm in diameter) and had small post-procedural in-device MLDs (all <2.5 mm). Although BVS did not have a greater rate of ST than CoCr-EES in small vessels in this study, smaller final in-device MLD in concert with the larger strut thickness of BVS

compared with newer generation metallic DES might contribute to a greater propensity for ST. Therefore, improving BVS implantation strategy and technique to ensure a 1:1 ratio of BVS to artery diameter and optimizing BVS expansion with aggressive pre- and post-dilatation to achieve optimal scaffold expansion may improve outcomes.[16,17] Furthermore, due to early concerns of strut fracture, investigators conservatively chose post-dilatation balloon diameters.[12] It has since been learned that strut fracture will not occur if the post-dilatation balloon is not sized >0.5 mm larger than the BVS scaffold diameter, regardless of pressure.[18] Use of intravascular imaging guidance to ensure optimal scaffold expansion, freedom from edge dissections, and residual disease may also improve device safety. Finally, development of a next generation BVS with thinner struts is underway and is expected to further improve outcomes.[19]

There are several limitations of the current study. First, the non-inferiority margin for the primary clinical endpoint was relatively large. The Japanese Regulatory Agency requested the sponsor to use the clinical endpoint (TLF) as the primary endpoint, but agreed to a relatively large non-inferiority margin to keep the sample size reasonable. Secondly, the observed event rate for TLF was 3.8% in the CoCr-EES arm, less than the 9.0% rate anticipated on which the non-inferiority margin of 8.6% was selected. Nonetheless, the one-sided upper 95% confidence limit for the 0.4% observed difference in event rates was 3.95%, suggesting that any absolute difference between the two devices is likely to be small. Thirdly, although the observed rates of death, ST, and MI were similar between BVS and CoCr-EES, the study was not powered to statistically evaluate differences in low frequency event rates. Fourth, the current study enrolled a highly selected patient population with mainly stable CAD and single *de novo* non-complex target lesions. As such, the study results should not be generalized to complex lesions, which are often encountered in clinical practice, such as bifurcations, heavily calcified lesions, diffuse disease, and thrombus. Fifth, the clinical profile of the CoCr-EES group might have been somewhat worse than the BVS group, although statistically not significant. Sixth, our definition for peri-procedural MI required CK-MB >5 × ULN rather than a lower threshold of CK-MB

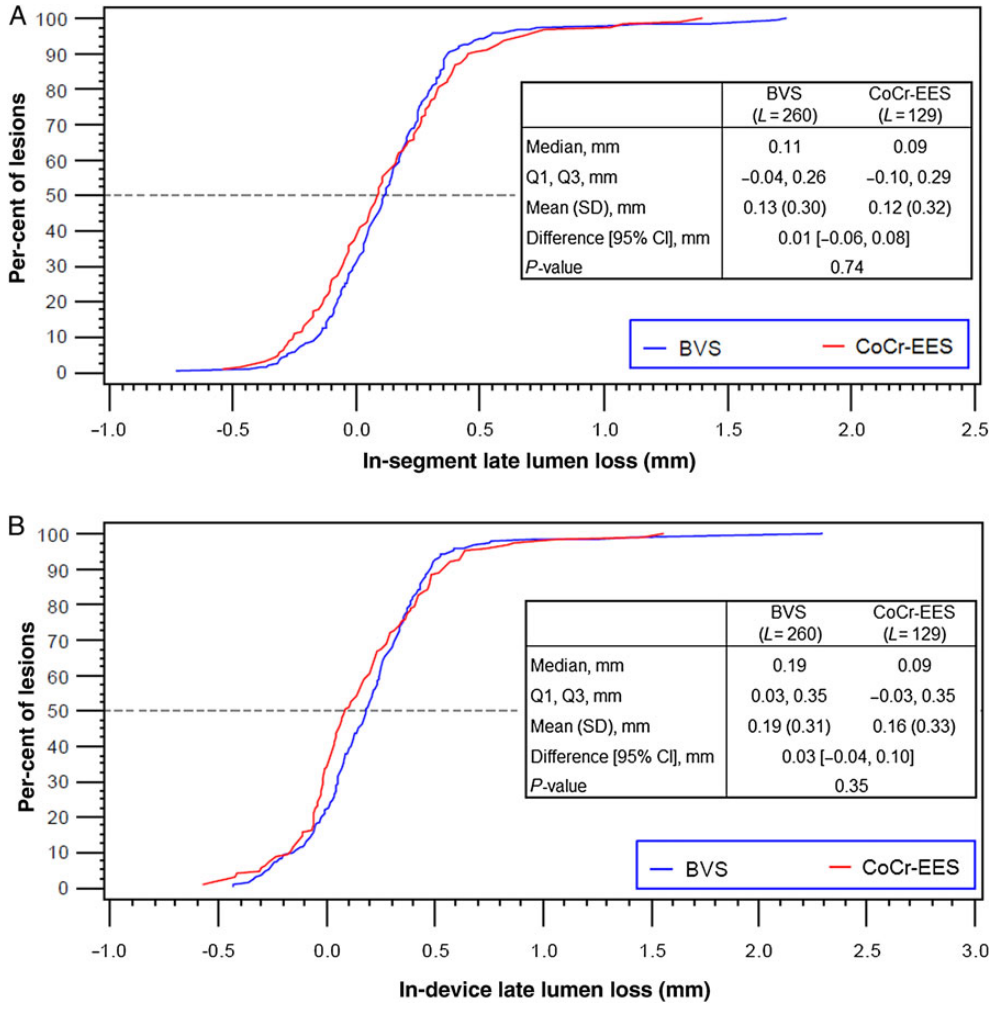
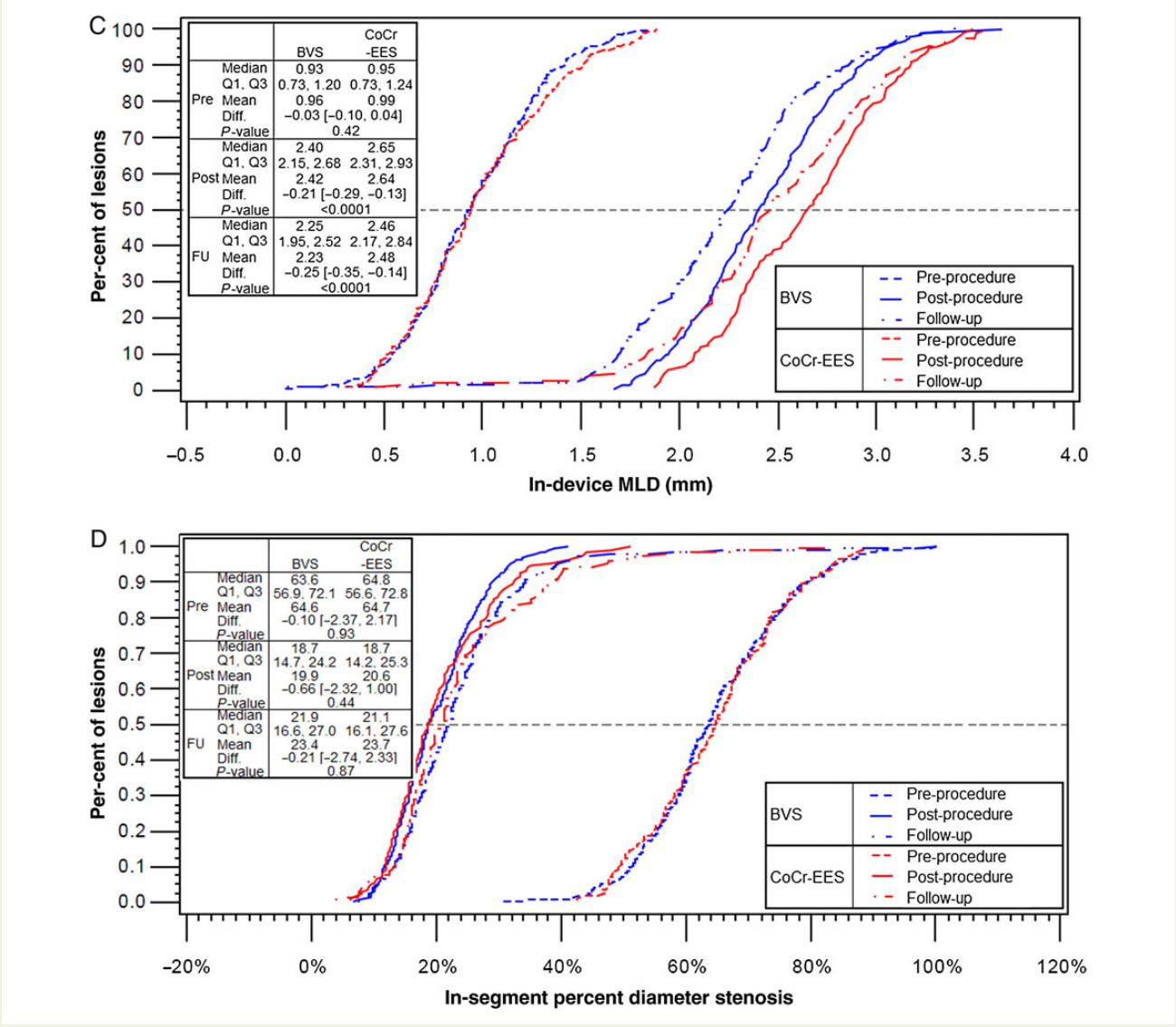


Figure 3 Cumulative distribution function curves for in-segment LLL (*A*), in-device LLL (*B*), in-device MLD (*C*), and in-segment per cent DS (*D*). BVS, bioresorbable vascular scaffold; CoCr-EES, cobalt-chromium everolimus-eluting stent; MLD, minimal lumen diameter; TLR, target lesion revascularization.



		BVS	CoCr-EES
Pre	Median	0.93	0.95
	Q1, Q3	0.73, 1.20	0.73, 1.24
	Mean	0.96	0.99
	Diff.	−0.03 [−0.10, 0.04]	
	P-value	0.42	
Post	Median	2.40	2.65
	Q1, Q3	2.15, 2.68	2.31, 2.93
	Mean	2.42	2.64
	Diff.	−0.21 [−0.29, −0.13]	
	P-value	<0.0001	
FU	Median	2.25	2.46
	Q1, Q3	1.95, 2.52	2.17, 2.84
	Mean	2.23	2.48
	Diff.	−0.25 [−0.35, −0.14]	
	P-value	<0.0001	

		BVS	CoCr-EES
Pre	Median	63.6	64.8
	Q1, Q3	56.9, 72.1	56.6, 72.8
	Mean	64.6	64.7
	Diff.	−0.10 [−2.37, 2.17]	
	P-value	0.93	
Post	Median	18.7	18.7
	Q1, Q3	14.7, 24.2	14.2, 25.3
	Mean	19.9	20.6
	Diff.	−0.66 [−2.32, 1.00]	
	P-value	0.44	
FU	Median	21.9	21.1
	Q1, Q3	16.6, 27.0	16.1, 27.6
	Mean	23.4	23.7
	Diff.	−0.21 [−2.74, 2.33]	
	P-value	0.87	

Figure 3 Continued.

>3 × ULN, which has been used in past studies. However, low levels of peri-procedural myonecrosis have not been associated with long-term mortality, justifying this progression.[20] Finally, long-term follow-up (in the present and larger trials) is required to determine whether the temporary scaffolding properties of BVSs are associated with similar or improved outcomes compared with a permanent metallic DES.

In conclusion, in the ABSORB Japan trial, Absorb BVS demonstrated a similar mid-term (12-month) clinical safety and efficacy profile as CoCr-EES, with comparable 13-month angiographic outcomes. These results support the feasibility of BVS use to potentially improve the long-term outcomes of patients undergoing percutaneous coronary intervention.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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Conflict of interest: T.K., J.J.P., and P.W.S. are members of Advisory Board of Abbott Vascular; T.K., K.K., S.N., K.T., and Y.O. are members of Advisory Board of Abbott Vascular Japan; S.Y., S.C., P.S., W.-F.C., and H.K. are employees of Abbott Vascular; G.W.S. is a consultant to Reva Corp.; and the other authors report no conflicts of interest with regard to this manuscript.

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