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Bioresorbable Vascular Scaffold Versus Metallic Drug-Eluting Stent in Patients at High Risk of Restenosis: The COMPARE-ABSORB Randomized Clinical Trial

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Brief title: Bioresorbable scaffolds in high-risk patients

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Abbreviations

BVS = bioresorbable vascular scaffold

EES = everolimus-eluting stents

PCI = percutaneous coronary intervention

TLF = target lesion failure

TVMI = target vessel myocardial infarction

Condensed abstract

The aim of this study was to investigate clinical outcomes of patients at high-risk for restenosis after implantation of bioresorbable vascular scaffold (BVS). Among 1,670 patients, [BVS 848 and everolimus-eluting stent (EES) 822], the rate of target lesion failure, a composite of cardiac death, target vessel myocardial infarction or clinically-indicated target lesion revascularization, was 5.1% in the BVS group and 4.2% in the EES group at 1 year. Although non-inferiority of BVS compared with EES in terms of target lesion failure at 1 year was met, BVS still carried a higher risk of device thrombosis and target vessel myocardial infarction than EES.

Aims

The aim of this study was to investigate clinical outcomes of patients at high risk of restenosis after implantation of bioresorbable vascular scaffold (BVS).

Methods and results:

The COMPARE-ABSORB trial was an investigator-initiated, prospective randomized study. Patients at high risk of restenosis were randomly assigned to receive either BVS or everolimus-eluting stent (EES). A dedicated implantation technique was recommended for BVS. The primary endpoint was target lesion failure (TLF), defined as the composite of cardiac death, target vessel myocardial infarction (TVMI) or clinically-indicated target lesion revascularization at 1 year.

The enrolment was discontinued prematurely because of a high thrombosis and TVMI rate in the BVS arm. A total of 1,670 patients were recruited (BVS 848 patients and EES 822 patients). TLF occurred in 43 patients (5.1 %) of the BVS group and 34 patients (4.2%) of the EES group (absolute difference 0.9%, 95% confidence interval (CI) -1.2%-3.0%, P non-inferiority < 0.001). Definite or probable device thrombosis (2.0% vs. 0.6%, hazard ratio 3.32, 95% CI 1.22 to 8.99, P=0.012) and TVMI (4.0% vs. 2.1%, hazard ratio 1.96, 95% CI 1.10 to 3.51, P=0.02) were significantly higher in the BVS group than the EES group.

Conclusions

In patients at high risk of restenosis, non-inferiority of BVS compared with EES in terms of TLF was met at 1 year. BVS carried a higher risk of device thrombosis and TVMI than EES.

Keywords: bioresorbable scaffold, drug-eluting stent, stent thrombosis

Introduction

The bioresorbable vascular scaffold (BVS) is designed for treatment of obstructive coronary artery disease providing temporary mechanical support and anti-proliferative drug delivery, but without perceived disadvantages of permanent metallic implants.[1] In a series of randomized trials, BVS met the criteria of non-inferiority compared with metallic drug-eluting stent (DES) for composite endpoints in relatively low-risk coronary lesions and patients at 1 year.[2, 3] However, BVS resulted in higher rates of target lesion failure (TLF) and device thrombosis compared with metallic DES at 3 years' follow-up.[4] These disappointing outcomes have been shown to be at least partially attributed to suboptimal implantation technique of this thick strut device.[5]

In previous randomized trials, the "BVS-specific" implantation technique was neither fully developed nor employed as part of the study design; whether using optimal implantation techniques with BVS could reduce the risk of device thrombosis requires further examination. In the era of DES, prevention of in-stent restenosis and neoatherosclerosis remain an unmet need, especially for patients at high risk of restenosis, such as long lesions and patients with diabetes mellitus.[6] We hypothesize that the use of BVS in a high risk population might demonstrate better long-term outcomes compared with DES after full BVS resorption. Therefore, we conducted the COMPARE-ABSORB trial to investigate the concept of short-term equivalence and long-term benefit of BVS over metallic DES in patients at high risk of restenosis with complex lesion(s).

Methods

The study design has been previously published.[7] In summary, the COMPARE-ABSORB trial is a prospective, randomized, controlled, single-blind, multi-center study across 45 centers in Europe (**Supplementary Table 1**). Patients aged 18-75 years with symptomatic ischemic heart disease and presence of high risk features for restenosis due to clinical profile or coronary lesion complexity and who were scheduled to undergo elective or emergent percutaneous coronary intervention (PCI) were eligible. Subjects participating in the trial met at least one of the inclusion criteria: medically treated diabetes, or multivessel disease with more than one de-novo target lesions and/or presence of at least one complex target lesion (long lesion, small vessel, total occlusion or bifurcation). Key exclusion criteria included target lesion not suitable for BVS implantation, patients with cardiogenic shock, severe renal failure, severe impaired ejection fraction, left main disease or on oral anticoagulants. Detailed criteria are listed in **Supplementary Table 2**. Patients were 1:1 randomly assigned to receive either BVS (Absorb, Abbott Vascular, Santa Clara, CA, USA) or EES (Xience, Abbott Vascular, Santa Clara, CA, USA). Blocked randomization was performed with randomly selected block sizes. A dedicated implantation technique was defined in the protocol: pre-dilatation using non-compliant balloons of the same diameter as the reference vessel diameter (RVD) and post-scaffold high-pressure (≥16 atm) dilatation were mandatory in the BVS group. Scaffold to vessel sizing was based on the instructions for use. The primary endpoint was TLF (a composite of cardiac death, myocardial infarction in target vessel territory and clinically-indicated target lesion revascularization) at 1 year. An extended Methods section is provided in **Supplement**, including study organizations (**Supplementary Table 3**), study procedures, hypotheses, endpoints (**Supplementary Table 4**), five definitions of optimal implantation technique (OIT) (**Supplementary Table 5**), and protocol revisions. Follow-up

is planned for all patients up to 7 years. Consideration will be given to extending follow-up to 10 years.

Statistical analysis

All clinical data were analyzed according to the intention-to-treat principle. For time-to-event endpoints, Kaplan-Meier plots were constructed and compared by the log-rank test. Binomial variables were evaluated with Fisher's exact probability test, continuous variables tested with a two-sample t-test or with the Mann-Whitney U test when data were not normally-distributed, and a P value for interaction was calculated for the sub-group analyses. The device implantation was evaluated in a combination of different parameters of pre-dilatation, central core lab quantitative coronary angiography (QCA) sizing and post-dilatation. A two-sided P value of less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed using SAS software version 9.3. This trial was registered at ClinicalTrials.gov (NCT 02486068).

Results

Baseline patient characteristics and follow-up

Between September 28, 2015 and August 31, 2017, 1,670 of the intended 2,100 patients with 2,457 lesions were randomly assigned to receive either BVS (848 patients with 1,243 lesions) or EES (822 patients with 1,214 lesions). The trial was prematurely stopped on recommendation of the Data and Safety Monitoring Board based on safety concerns seen in interim analyses. Follow-up at 12 months was complete in 824/848 patients treated with BVS versus 804/822 patients in the EES group (p=0.43). In the 24 BVS patients with incomplete follow-up the median duration of follow-up was 74 days versus 160 days in the 18 EES patients (p=0.36), (**Figure 1**). Baseline clinical characteristics are shown in **Table 1**. Of the 1,670

patients, 293 (34.6%) in the BVS group and 296 (36.1%) in the EES group had a history of diabetes, and 442 (52.1%) in the BVS group and 400 (48.7%) in the EES group presented with acute coronary syndrome.

Lesion and procedural characteristics

A total of 1,650 BVS and 1,554 EES were implanted in the two groups, respectively. **Table 2** shows a significant higher performance of optical coherence tomography in the BVS group, as well as higher incidences of both long lesions (>28 mm) and small-vessel lesions (between 2.25 and 2.75 mm) in the EES group. In the BVS group, pre-dilatation was performed in 96.8% of lesions and post-dilatation in 92.8% of lesions. The percentages of pre-dilatation and post-dilatation were significantly higher in the BVS group than in the EES group. According to angiographic analysis performed by the core lab, 21.9% (255/1,166) of lesions in the BVS group had a post-procedural in-scaffold RVD of less than 2.25 mm and 40.9% (477/1,166) less than 2.5 mm. Main failure with respect to the sizing recommendation were related to difference between visual estimated diameters and QCA, followed by mismatch between proximal and distal reference diameter. The proportions of lesions in the BVS group meeting the definition of OIT-0 to OIT-4 were as follows: OIT-0: 33.7% (383/1,137), OIT-1: 24.1% (274/1,137), OIT-2: 17.1% (194/1,137), OIT-3: 16.3% (185/1,137), and OIT-4: 11.1% (126/1,137). In addition, the device success rate was significantly lower in the BVS group than in the EES group (BVS 92.4% vs. EES 96.8%, p<0.001), driven by a lower rate of successful device delivery.

Clinical outcomes

The primary endpoint of TLF at 1 year occurred in 43 patients (5.1%) in the BVS group and in 34 patients (4.2%) in the EES group (**Table 3** and **Figure 2**). The primary hypothesis, non-

inferiority of BVS compared to EES, was met with an absolute difference of 0.9% and two-sided 95% confidence interval (CI) of -1.2% was demonstrated (difference 0.9% [two-sided 95% CI -1.2-3.0%], P non-inferiority < 0.001). For individual components of TLF, the frequencies of cardiac death (5 [0.6%] vs 1 [0.1%]; hazard ratio (HR), 4.87; 95% CI, 0.57 to 41.7; p=0.11) and clinically-indicated target lesion revascularization (20 [2.4%] vs 22 [2.7%]; HR, 0.89; 95% CI, 0.48 to 1.62; p=0.69) did not differ significantly between groups. However, target vessel myocardial infarction was significantly higher in the BVS group at 30 days than in the EES group (27 [3.2%] vs 10 [1.2%]; HR, 2.64; 95% CI, 1.28 to 5.45; p=0.006), while no significant difference between groups beyond 30 days to 1 year (7 [0.9%] vs 7 [0.9%]; HR, 0.99; 95% CI, 0.35 to 2.83; p=0.99) was observed. (**Table 3 and Figure 3)**. Similarly, definite or probable device thrombosis was significantly higher in the BVS group than in the EES group (13 [1.5%] vs 4 [0.5%]; HR, 3.16; 95% CI, 1.03 to 9.69; p=0.033) at 30 days and was not significantly different between 30 days and 1 year (4 [0.5%] vs 1 [0.1%]; HR, 3.94; 95% CI, 0.44 to 35.2; p=0.18). The majority of the BVS thromboses (13/17, 76%) occurred within 30 days of the index procedure and only 1 event was related to the cessation of antiplatelet agents. At 1-year follow-up, 80.0% of patients in the BVS group and 70.8% of patients in EES group remained on dual-antiplatelet treatment **(Supplementary Table 6)**. The 1-year TLF rates were comparable across all pre-specified subgroups (**Figure 4**).

Additional post-hoc analyses with respect to the TLF and definite and probable device thrombosis rates stratified by OIT did not show significant treatment-by-subgroup interactions **(Supplementary Figure 1A** and **1B)**. The definite device thrombosis rates did not differ significantly between lesions with or without a correct vessel sizing, though a combined proximal and distal oversizing of the scaffold showed a high event rate **(Supplementary Figure 2)**. Results of quality of life reported at follow-up are shown in **Supplementary Table 7**.

Discussion

In the present large-scale, randomized trial, the BVS was non-inferior to the EES in terms of TLF at 1 year in a population at high risk of restenosis. Moreover, the treatment effect on TLF was similar across different subgroups, including risk groups defined according to lesion complexity or baseline characteristics. Although non-inferiority of the primary endpoint was met, definite or probable device thrombosis and target vessel myocardial infarction rates were significantly higher in the BVS group compared with the EES group which resulted in premature cessation in recruitment of the study.

Compared with the 1-year results of the ABSORB III trial, the device thrombosis rate in the BVS group was slightly higher in the present study (2.0% vs. 1.5%), whilst it was similar in the EES group (0.6% vs. 0.7%). The observed higher device thrombosis rate in this trial is likely attributed to the complexity of patients and lesions included. Furthermore, device thrombosis events predominantly occurred during the early phase after implantation, implicating procedure-related causes. According to lessons learned from previous studies, a mismatch between vessel size and device size is a predictor of early and late scaffold thrombosis.[8] Furthermore, the meta-analysis on ABSORB trials incriminated BVS for vessels with a diameter less than 2.5 mm.[9] Theoretically, these problems might be reduced by implementing an optimal implantation technique. The COMPARE-ABSORB study excluded vessels smaller than 2.25 mm in the original study design, then amended the exclusion criterion of minimal vessel size to 2.5 mm during enrolment because of these safety concerns. Investigators were also advised to estimate the vessel size by *quantitative coronary analysis* or intravascular imaging if the vessel size was less than 2.75 mm by visual assessment. Nevertheless, the post-hoc angiographic analysis performed by the core lab showed 40.9% of lesions in the BVS group had a post-procedural RVD smaller than 2.5 mm. These findings emphasize the importance of appropriate vessel sizing, which could not be truly achieved by

visual assessment alone. Because underestimation of vessel size by QCA is a limitation of angiography,[10] mandatory intravascular imaging guidance should be explored in future when implanting BVS in order to enhance safety. On the other hand, only a minority of lesions (33.7%) fit the OIT criteria due to sizing mismatch (the lesion segment not fitting any scaffold diameter due to incompatibility of proximal and distal reference requirements in sizing for a specific scaffold diameter). In the BVS group, 11.5% of lesions had both proximal and distal reference diameter within the range of correct sizing which was defined as device size ± 0.25 mm, 27.1% had either proximal or distal reference diameter within the range but not both, 61.4% had both reference diameters out of the range (**Supplementary Table 8**). This demonstrates that correct sizing with BVS according to the OIT criteria is difficult to be achieved in the majority of lesions with one BVS. Further improvements to the device such as thinner and smaller struts, better conformability and radial strength are therefore indispensable.

In the COMPARE-ABSORB trial, high pressure post-dilatation with a non-compliant balloon was mandated by protocol. Nevertheless, based on angiographic analysis, acute gain and established post-procedural minimal lumen diameter in the BVS arm did not match those of the EES arm, although the absolute differences between both arms appear to be smaller than or similar to the differences observed in previous trials (**Supplementary Table 9**). This unclosed gap in acute performance between both devices could be a contributing factor for early scaffold thrombosis with BVS compared with EES.

Recently, the 5-year results of the ABSORB II trial[11] showed significant difference in TLF in favor of EES compared to BVS. This significant difference in TLF was driven by events that had occurred within the first 3 years. No scaffold thrombosis was observed between 3 and 5 years. Therefore, extension of follow-up duration from 5 to 7 years in this study is necessary to determine whether more normalized coronary function and physiology

after complete scaffold bioresorption will provide a clinical advantage for BVS over metallic DES.

Limitations

First of all, despite the fact that optimal implantation technique was incorporated in the study design, on-line QCA or intravascular imaging were suggested, but not mandatory for vessel sizing. Secondly, the 1-year TLF rates for both devices were remarkably lower than anticipated and therefore the noninferiority margin of 4.5% was relatively wide. However, the non-inferiority margin was in line with the ABSORB III study, in which the U.S. *Food and Drug Administration* was consulted. In the study design of ABSORB III,[12] the assumed rate of the primary endpoint was 7.0%. The ratio of noninferiority margin to assumed event rate was 64%. In our study, the assumed event rate was 8.5% and the ratio of noninferiority margin to assumed event rate was 53%, which was slightly stricter than that in the ABSORB III. Thirdly, because of significant differences in pre-and post-dilatation rates between both stent arms, we cannot exclude influence on outcomes solely caused by differences in implantation techniques. Fourthly, bleeding event was not a prespecified endpoint and thus not reported in this paper. Lastly, the study results only apply to the BVS, which is no longer commercially available for use in clinical practice. Nevertheless, the COMPARE-ABSORB study was the first trial to investigate the performance of BVS in complex lesions and high-risk patients.

Conclusion

In the present large-scale randomized trial of patients at high risk of restenosis, BVS was non-inferior to EES for the primary endpoint, TLF at 1 year. BVS carried a higher risk for device thrombosis and TVMI, especially in the early stages after implantation.

Impact on daily practice

This trial showed that using an optimal implantation technique did not prevent an increase of device thrombosis with BVS at 1 year. Further exploration of long-term benefit after BVS implantation and device modification is warranted.

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Conflict of interest statement

Dr. Smits received institutional research grants and speaker fees from Abbott Vascular, St. Jude Medical and Terumo.

Dr. Chevalier received grants and personal fees from Abbott Vascular during the conduct of the study; personal fees from Medtronic, Terumo, and Biotronik, outside the submitted work.

Dr. West received speaker fees from Abbott Vascular.

Dr. Gori received speaker fees from Abbott Vascular.

Dr. Barbato received personal fees from Boston scientific, Abbott Vascular, Opsens Medical, and GE Healthcare, outside the submitted work.

Dr. Kočka received personal fees from Abbott Vascular, Medtronic, B Braun, and Terumo, outside the submitted work.

Prof. Tijssen received grants and personal fees from Abbott Vascular during the conduct of the study.

Dr. Morice is the CEO of CERC, the CRO who conducted the trial.

Dr. Onuma was an advisor board member of Abbott Vascular.

Dr. van Geuns reports grants and personal fees from Abbott Vascular, outside the submitted work.

Table 1. Baseline characteristics

Characteristic	**BVS** (n=848)	**EES** (n=822)	p value
Patient measures			
Age	62 (56,69)	63 (56,69)	0.61
Male	674/848 (79.5%)	627/822 (76.3%)	0.13
Body mass index	27 (25,31)	27 (25,30)	0.43
Current smoker	241/837 (28.8%)	217/807 (26.9%)	0.41
Diabetes mellitus	293/846 (34.6%)	296/821 (36.1%)	0.57
Hypertension	601/839 (71.6%)	567/819 (69.2%)	0.31
Hypercholesterolemia	546/824 (66.3%)	531/801 (66.3%)	0.88
Family history of coronary artery disease	278/767 (36.2%)	241/760 (31.7%)	0.07
Previous MI	154/847 (18.2%)	166/820 (20.2%)	0.29
Established Peripheral Vascular Disease	59/842 (7.0%)	56/819 (6.8%)	0.92
Previous PCI	229/847 (27.0%)	238/822 (29.0%)	0.38
Previous CABG	16/848 (1.9%)	21/822 (2.6%)	0.41
Previous stroke	29/845 (3.4%)	39/820 (4.8%)	0.18
Renal Insufficiency[a]	33/845 (3.9%)	49/817 (6.0%)	0.054
Left ventricular ejection fraction			0.84
Good (> 60%)	492/661 (74.4%)	486/647 (75.1%)	
Reduced (30 to 60%)	155/661 (23.4%)	143/647 (22.1%)	
Poor (<30%)	14/661 (2.1%)	18/647 (2.8%)	
Clinical presentation			0.17
Stable coronary artery disease	406/848 (47.9%)	422/822 (51.3%)	
Silent ischemia	63/848 (7.4%)	73/822 (8.9%)	
Stable angina	343/848 (40.4%)	349/822 (42.5%)	
ACS	442/848 (52.1%)	400/822 (48.7%)	0.17
Unstable angina	149/848 (17.6%)	141/822 (17.2%)	
Non-ST elevation MI	183/848 (21.6%)	156/822 (19.0%)	
ST elevation MI	110/848 (12.9%)	103/822 (12.5%)	

Data are median (interquartile range) or counts (percentage).

a. Renal insufficiency is defined as MDRD estimated glomerular filtration rate less than 60ml/min or serum creatinine above 130 micromol/l.

ACS = acute coronary syndrome, BVS = bioresorbable vascular scaffold, EES = everolimus-eluting stent, CABG = coronary artery bypass graft, CAD = coronary artery disease, MDRD = modification of diet in renal disease, MI = myocardial infarction, PCI =percutaneous coronary intervention.

Table 2. Angiographic and procedural characteristics

	BVS (n=1,243 lesions)	EES (n=1,214 lesions)	p value
Patients measures			
Number of target lesions attempted to be treated	1 (1, 2) (n=848)	1 (1, 2) (822)	0.64
Multi-vessel treatment	441/848 (52.0%)	433/822 (52.7%)	0.81
IVUS performed post procedure	126/848 (14.9%)	122/822 (14.8%)	1.00
OCT performed post procedure	84/848 (9.9%)	24/822 (2.9%)	<0.001
Target lesion measures			
LAD	569/1,243 (45.8%)	503/1,214 (41.4%)	0.031
LCX	281/1,243 (22.6%)	310/1,214 (25.5%)	0.10
RCA	392/1,243 (31.5%)	400/1,214 (32.9%)	0.46
Left main	1/1,243 (0.1%)	1/1,214 (0.1%)	1.00
Bifurcation lesions	254/1,243 (20.4%)	269/1,214 (22.2%)	0.30
Pre-existing total occlusions	181/1,243 (14.6%)	159/1,214 (13.1%)	0.32
Long lesions (>28 mm)	312/1,243 (25.1%)	382/1,214 (31.5%)	<0.001
Small vessel lesions (>2.25, ≤ 2.75mm)	302/1,243 (24.3%)	404/1,214 (33.3%)	<0.001
SYNTAX score	11 (7,17)	11 (7,16)	0.88
Number of study devices implanted per lesion	1 (1,2)	1 (1,1)	0.06
Total device length per lesion	28 (18, 36)	28 (18, 38)	0.29
Average device diameter per lesion	3.0 (2.8, 3.5)	3.0 (2.8, 3.5)	<0.001
Overlapping devices implantation	194/1,243 (15.6%)	256/1,214 (21.1%)	<0.001
Bifurcation lesions	254/1,243 (20.4%)	269/1,214 (22.2%)	0.30
Two or more devices used in bifurcation lesions	82/254 (32.3%)	68/269 (25.3%)	0.08
Lesions without study device	44/1,243 (3.5%)	9/1,214 (0.7%)	<0.001
Pre-dilatation	1199/1,243 (96.5%)	954/1,214 (78.6%)	<0.001
Largest balloon (mm)	3.0 (2.5, 3.0)	3.0 (2.5, 3.0)	0.95
Non-compliant balloon used	815/1,199 (68.0%)	504/954 (52.8%)	<0.001
Maximum pressure used (atm)	16 (12, 18)	14 (12, 16)	0.002
Cutting/ scoring balloon used	72/1,243 (5.8%)	28/1,214 (2.3%)	<0.001
Post-dilatation	1113/1,199 (92.8%)	699/1,205 (58.0%)	<0.001
Largest balloon (mm)	3.5 (3.0, 3.5)	3.5 (3.0, 3.5)	0.53
Non-compliant balloon used	1039/1,199 (86.7%)	616/1,205 (51.1%)	<0.001
Maximum pressure used (atm)	18 (16, 20)	18 (16, 20)	0.80
Maximun pressure ≥ 16 atm	899/1,113 (80.8%)	561/699 (80.3%)	0.81
OIT-0	383/1,137 (33.7%)	226/1,139 (19.8%)	<0.001
Correct sizing by QCA	439/1,137 (38.6%)	527/1,139 (46.3%)	<0.001
Pre-dilatation performed	1161/1,199 (96.8%)	949/1,205 (78.8%)	<0.001
Any Post-dilatation	1071/1,199 (89.3%)	643/1,205 (53.4%)	<0.001
OIT-1	274/1,137 (24.1%)	161/1,139 (14.1%)	<0.001

Correct sizing by QCA	439/1,137 (38.6%)	527/1,139 (46.3%)	<0.001
Pre-dilatation performed	1161/1,199 (96.8%)	949/1,205 (78.8%)	<0.001
Post-dilatation with non-compliant balloon, maximum pressure≥ 16 atm	785/1,199 (65.5%)	442/1,205 (36.7%)	<0.001
OIT-2	194/1,137 (17.1%)	111/1,139 (9.7%)	<0.001
Correct sizing by QCA	439/1,137 (38.6%)	527/1,139 (46.3%)	<0.001
$RVD_a \geq 2.5$ mm by QCA	689/1,166 (59.1%)	733/1,183 (62.0%)	0.1636
Pre-dilatation performed	1161/1,199 (96.8%)	949/1,205 (78.8%)	<0.001
Post-dilatation with non-compliant balloon, maximum pressure ≥ 16 atm	785/1,199 (65.5%)	442/1,205 (36.7%)	<0.001
OIT-3	185/1,137 (16.3%)	100/1,139 (8.8%)	<0.001
Correct sizing by QCA	439/1,137 (38.6%)	527/1,139 (46.3%)	<0.001
$RVD_a \geq 2.5$mm by QCA	689/1,166 (59.1%)	733/1,183 (62.0%)	0.1636
Pre-dilatation performed	1161/1,199 (96.8%)	949/1,205 (78.8%)	<0.001
Post-dilatation with non-compliant balloon, pressure ≥16 atm, balloon diameter between device diameter and device diameter + 0.5 mm	744/1,199 (62.1%)	399/1,205 (33.1%)	<0.001
OIT-4	126/1,137 (11.1%)	75/1,139 (6.6%)	<0.001
Correct sizing by QCA	439/1,137 (38.6%)	527/1,139 (46.3%)	<0.001
$RVD_a \geq 2.5$mm by QCA	689/1,166 (59.1%)	733/1,183 (62.0%)	0.1636
Pre-dilatation performed	1161/1,199 (96.8%)	949/1,205 (78.8%)	<0.001
Post-dilatation with non-compliant balloon, maximum pressure ≥ 16 atm, balloon diameter ≥ device diameter + 0.25 mm	418/1,199 (34.9%)	270/1,205 (22.4%)	<0.001
Device success	1149/1,243 (92.4%)	1175/1,214 (96.8%)	<0.001
Successful delivery of device	1181/1,243 (95.0%)	1204/1,214 (99.2%)	<0.001
Residual stenosis < 30%	1204/1,243 (96.9%)	1183/1,214 (97.4%)	0.40
Procedure success	749/848 (88.3%)	772/820 (94.1%)	<0.001
TIMI flow post-procedure			0.80
Flow 0	2/1,243 (0.2%)	0/1,214 (0.0%)	
Flow 1	2/1,243 (0.2%)	1/1,214 (0.1%)	
Flow 2	8/1,243 (0.6%)	12/1,214 (1.0%)	
Flow 3	1231/1,243 (99.0%)	1201/1,214 (98.9%)	
Angiographic analysis (core laboratory)			
Pre-procedure			
Reference vessel diameter, mm	2.51 (0.50) (n=1,123)	2.49 (0.49) (n=1,109)	0.21
Minimum lumen diameter, mm	0.89 (0.49) (n=1,148)	0.89 (0.50) (n=1,129)	0.74
Diameter stenosis	64.3% (18.4) (n=1,148)	63.7% (18.7) (n=1,129)	0.41
Lesion length[b], mm	12.46 (6.96) (n=986)	12.46 (6.96) (n=973)	0.23
Post-procedure			
In-device measures			
Reference vessel diameter, mm	2.63 (0.45) (n=1,161)	2.66 (0.42) (n=1,159)	0.07
Minimum lumen diameter, mm	2.21 (0.41) (n=1,161)	2.32 (0.39) (n=1,159)	<0.001
Diameter stenosis	15.5% (8.6) (n=1,161)	12.10% (6.44) (n=1,159)	<0.001
Acute gain, mm	1.33 (0.57) (n=1,123)	1.42 (0.53) (n=1,111)	<0.001
In-segment measures			

Reference vessel diameter, mm	2.55 (0.46) (n=1,161)	2.57 (0.44) (n=1,159)	0.38
Minimum lumen diameter, mm	2.01 (0.42) (n=1,161)	2.02 (0.44) (n=1,159)	0.61
Diameter stenosis	21.0% (9.7) (n=1,161)	21.3% (10.3) (n=1,159)	0.52
Acute gain, mm	1.13 (0.56) (n=1,123)	1.13 (0.55) (n=1,111)	0.98

Data are median (interquartile range), mean (standard deviation) or counts (percentage).

a. in-device reference vessel diameter; b. ST elevation myocardial infarction and chronic total occlusion lesions were excluded.

BVS = bioresorbable vascular scaffold, EES = everolimus-eluting stent, IVUS = intravascular ultrasound, LAD = Left anterior descending artery, LCX = Left circumflex artery, OCT = optical coherence tomography, OIT = optimal implantation technique, PCI = percutaneous coronary intervention, QCA = *quantitative coronary analysis*, RCA = Right coronary artery, RVD = reference vessel diameter, SYNTAX = Synergy Between PCI With Taxus and Cardiac Surgery, TIMI=thrombolysis in myocardial infarction.

Table 3. Clinical outcomes at 1 year

	BVS (n=848)	EES (n=822)	Hazard ratio (95% CI)	p value
Primary outcome				
Target lesion failure[a]	5.1% (43)	4.2% (34)	1.24 (0.79-1.94)	0.35
Separate endpoints for the primary outcomes				
Cardiac death	0.6% (5)	0.1% (1)	4.87 (0.57-41.7)	0.11
Target-vessel myocardial infarction	4.0% (34)	2.1% (17)	1.96 (1.10-3.51)	0.020
Clinically indicated target-lesion revascularization	2.4% (20)	2.7% (22)	0.89 (0.48-1.62)	0.69
Secondary outcomes				
Target vessel failure[b]	6.3% (53)	4.8% (39)	1.33 (0.88-2.02)	0.17
Any death	0.7% (6)	0.6% (5)	1.17 (0.36-3.83)	0.80
Any myocardial infarction	4.0% (34)	2.4% (20)	1.67 (0.96-2.90)	0.07
Target-vessel myocardial infarction	4.0% (34)	2.1% (17)	1.96 (1.10-3.51)	0.020
Peri-procedural	2.0% (17)	1.2% (10)	1.65 (0.76-3.61)	0.20
Spontaneous	2.0% (17)	0.9% (7)	2.38 (0.99-5.73)	0.046
Non-target-vessel myocardial infarction	0.0% (0)	0.5% (4)	NA	0.043
Any revascularization	7.0% (59)	7.4% (60)	0.96 (0.67-1.37)	0.82
Target-lesion revascularization	3.7% (31)	3.6% (29)	1.05 (0.63-1.73)	0.86
Clinically indicated	2.4% (20)	2.7% (22)	0.89 (0.48-1.62)	0.69
Non-clinically indicated	1.8% (15)	1.5% (12)	1.22 (0.57-2.60)	0.61
Target-vessel revascularization	4.8% (40)	4.5% (37)	1.06 (0.68-1.65)	0.81
Clinically indicated	3.6% (30)	3.7% (30)	0.97 (0.59-1.61)	0.91
Non-clinically indicated	2.1% (18)	1.6% (13)	1.35 (0.66-2.76)	0.41
Non-Target Vessel revascularization	2.5% (21)	3.3% (27)	0.75 (0.43-1.34)	0.33
Thrombosis endpoints				
Definite device thrombosis	1.9% (16)	0.6% (5)	3.12 (1.14-8.51)	0.019
Probable device thrombosis	0.1% (1)	0.0% (0)	NA	0.32
Possible device thrombosis	0.2% (2)	0.1% (1)	1.95 (0.18-21.54)	0.58
Definite or probable device thrombosis	2.0% (17)	0.6% (5)	3.31 (1.22-8.98)	0.012
Acute (≤ 24 hour)	0.5% (4)	0.4% (3)	1.29 (0.29-5.77)	0.74
Sub-Acute (>24 hour to 30 days)	1.3% (11)	0.1% (1)	10.71 (1.38-82.99)	0.004
Late (30 days to 1 year)	0.5% (4)	0.1% (1)	3.91 (0.44-34.98)	0.19

Data are Kaplan-Meier estimates.

a. Cardiac death, target-vessel myocardial infarction, or clinically indicated target-lesion revascularization.

b. Cardiac death, target-vessel myocardial infarction, or clinically indicated target-vessel revascularization.

BVS = bioresorbable vascular scaffold, CI = confidence interval, EES = everolimus-eluting stent, NA = not applicable.

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Figure 1. Study flow chart

BVS = bioresorbable vascular scaffold, EES = everolimus-eluting stent

Figure 2. Kaplan–Meier plot for the primary endpoint

Kaplan–Meier curves show the cumulative incidence of target lesion failure.

BVS = bioresorbable vascular scaffold, CI = confidence interval, EES = everolimus-eluting stent, HR= hazard ratio, TLF = target lesion failure

Figure 3. Kaplan–Meier plots for the components of the primary endpoint and definite/probable device thrombosis

Cardiac death (Panel A); target vessel myocardial infarction (Panel B); clinically indicated target lesion revascularization (Panel C); definite/probable device thrombosis (Panel D)

BVS = bioresorbable vascular scaffold, CI = confidence interval, EES = everolimus-eluting stent, HR= hazard ratio, NA = not applicable, ST= stent thrombosis, TLR = target lesion revascularization, TVMI = target vessel myocardial infarction.

Figure 4. Stratified analyses of the primary endpoint across subgroups.

Hazard ratio with 95% CI and p-value results were from Cox-proportional hazards analysis.

BVS = bioresorbable vascular scaffold, EES = everolimus-eluting stent, HR= hazard ratio, N= number of patients, STEMI = ST elevation myocardial infarction.

Figure 1

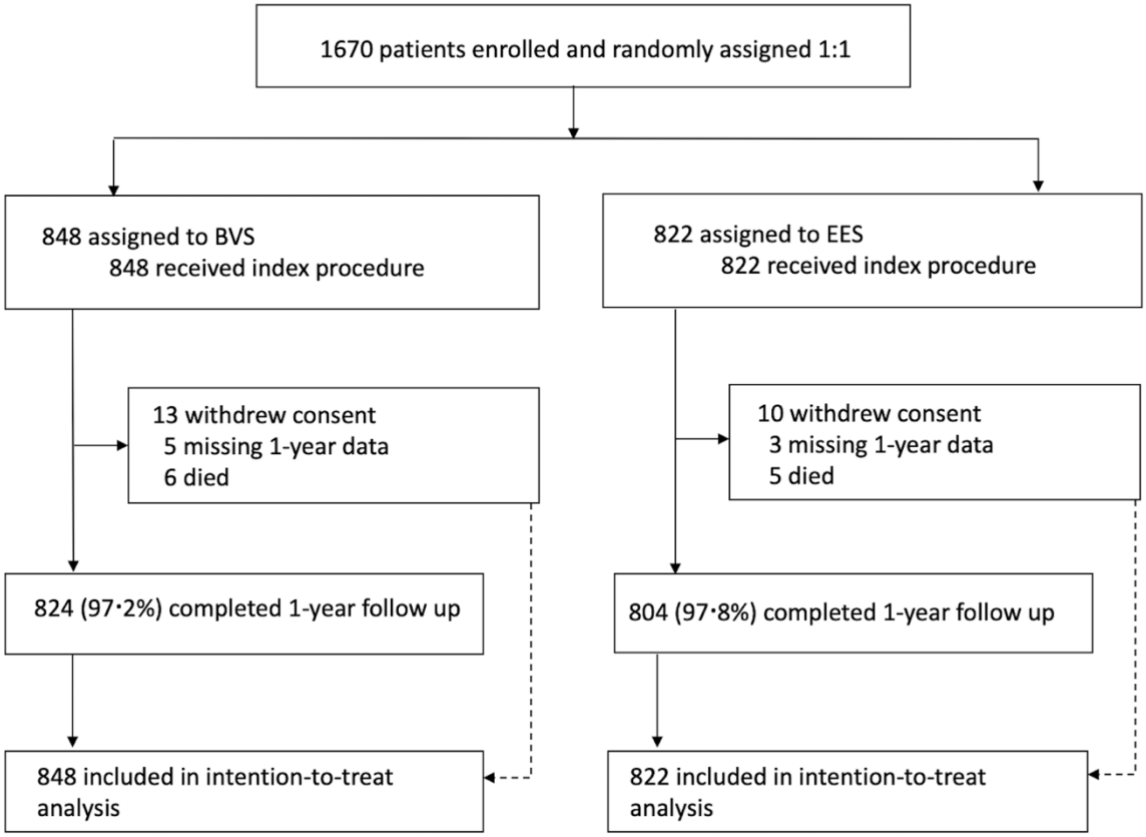
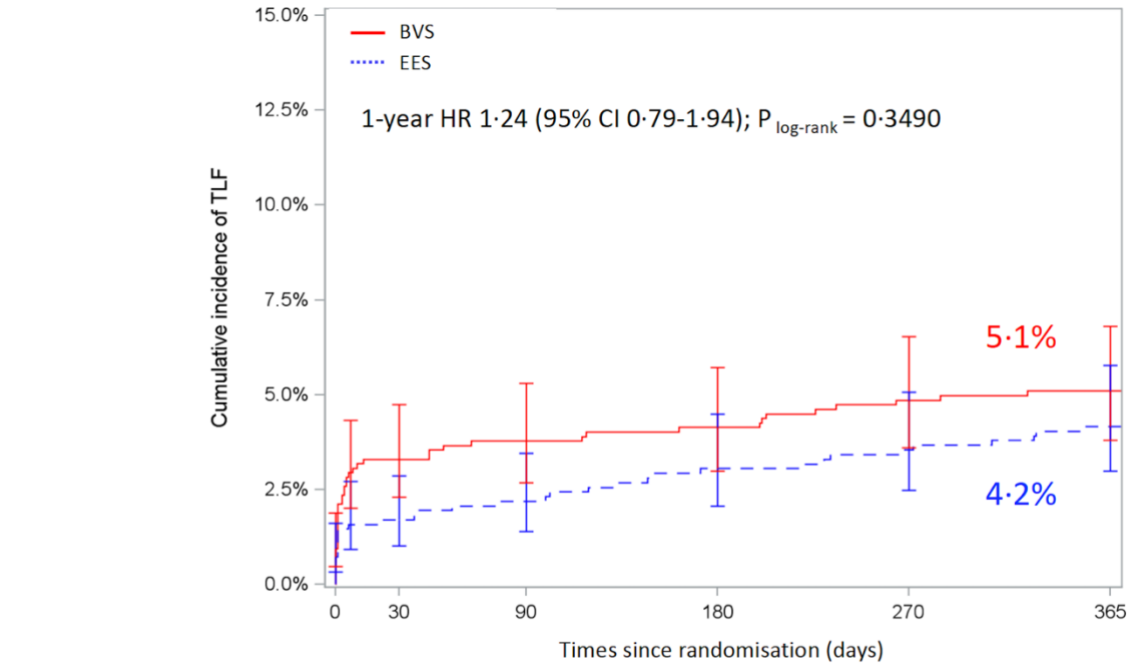


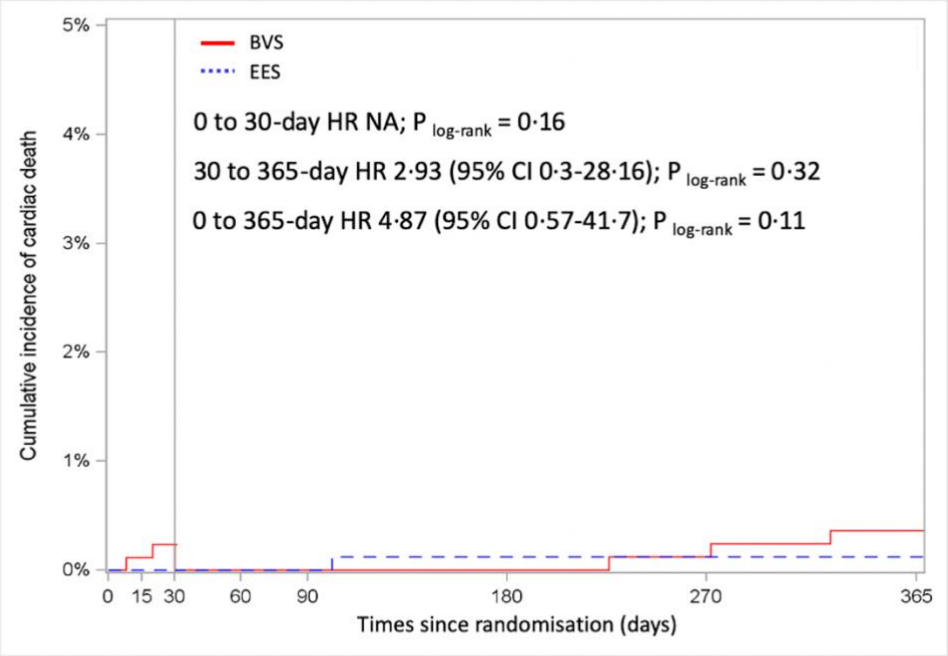
Figure 2



Number at risk	BVS	848	806	801	792	752
	EES	822	798	788	781	736

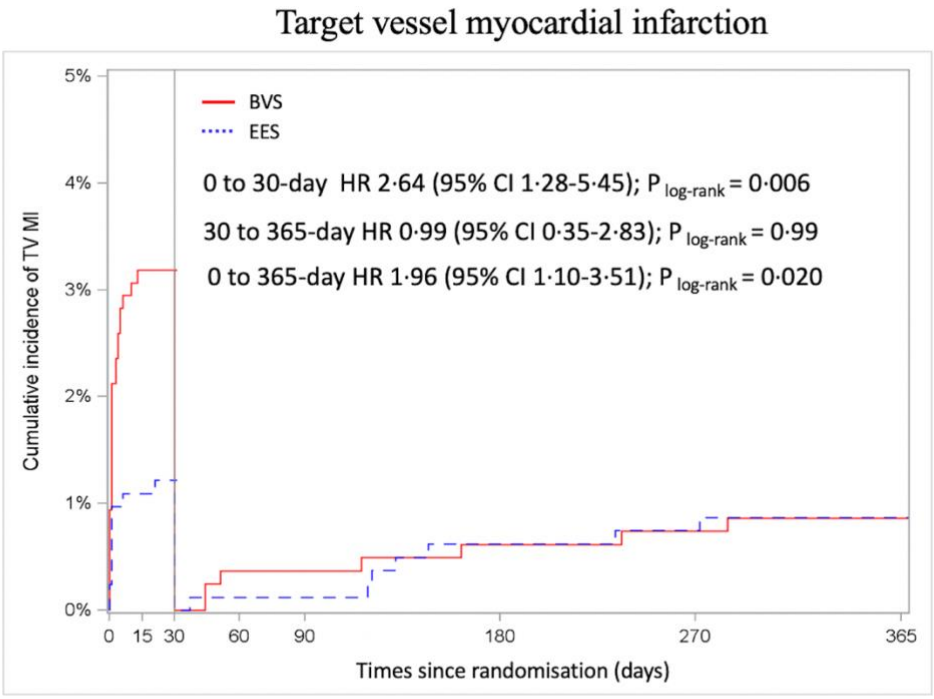
Figure 3a

Cardiac death



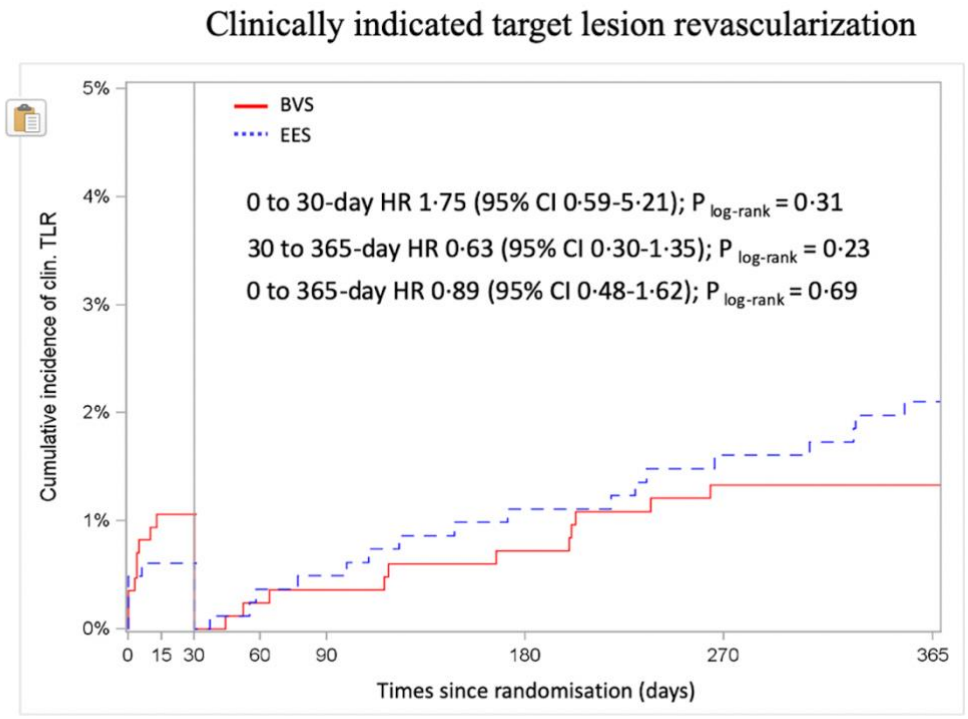
Number at risk	BVS	848	842	835	833	829	789
	EES	822	819	816	812	809	768

Figure 3b



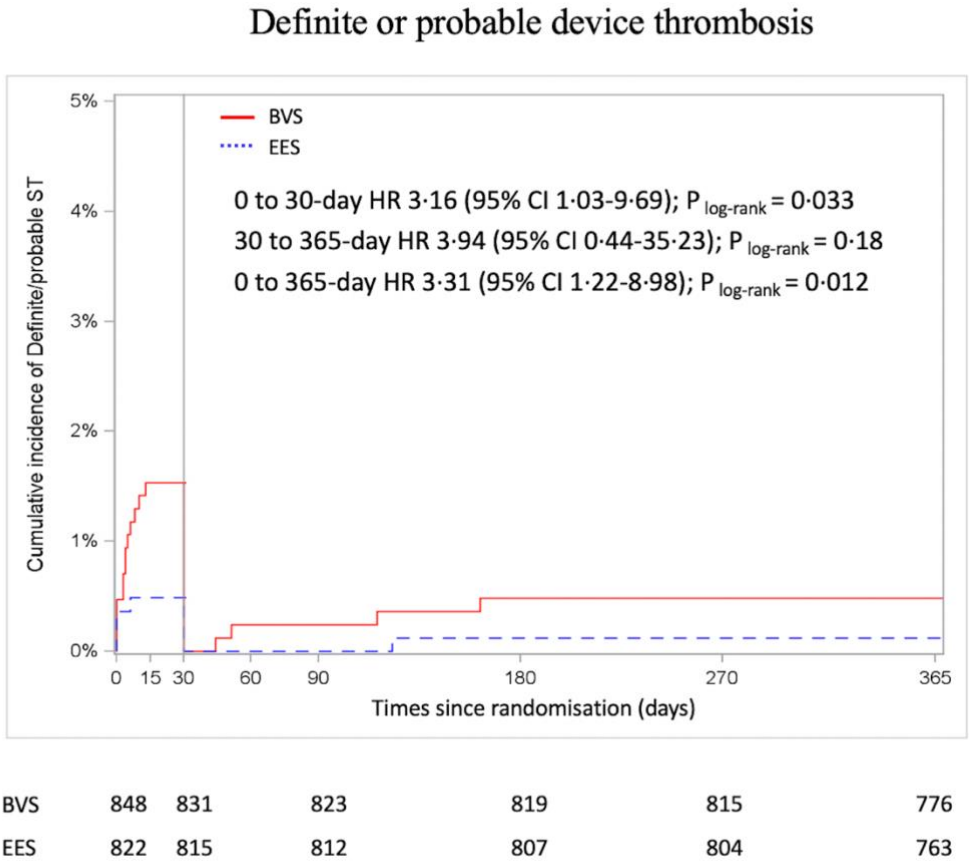
Number at risk	BVS	848	816	807	803	798	758
	EES	822	809	805	797	793	751

Figure 3c



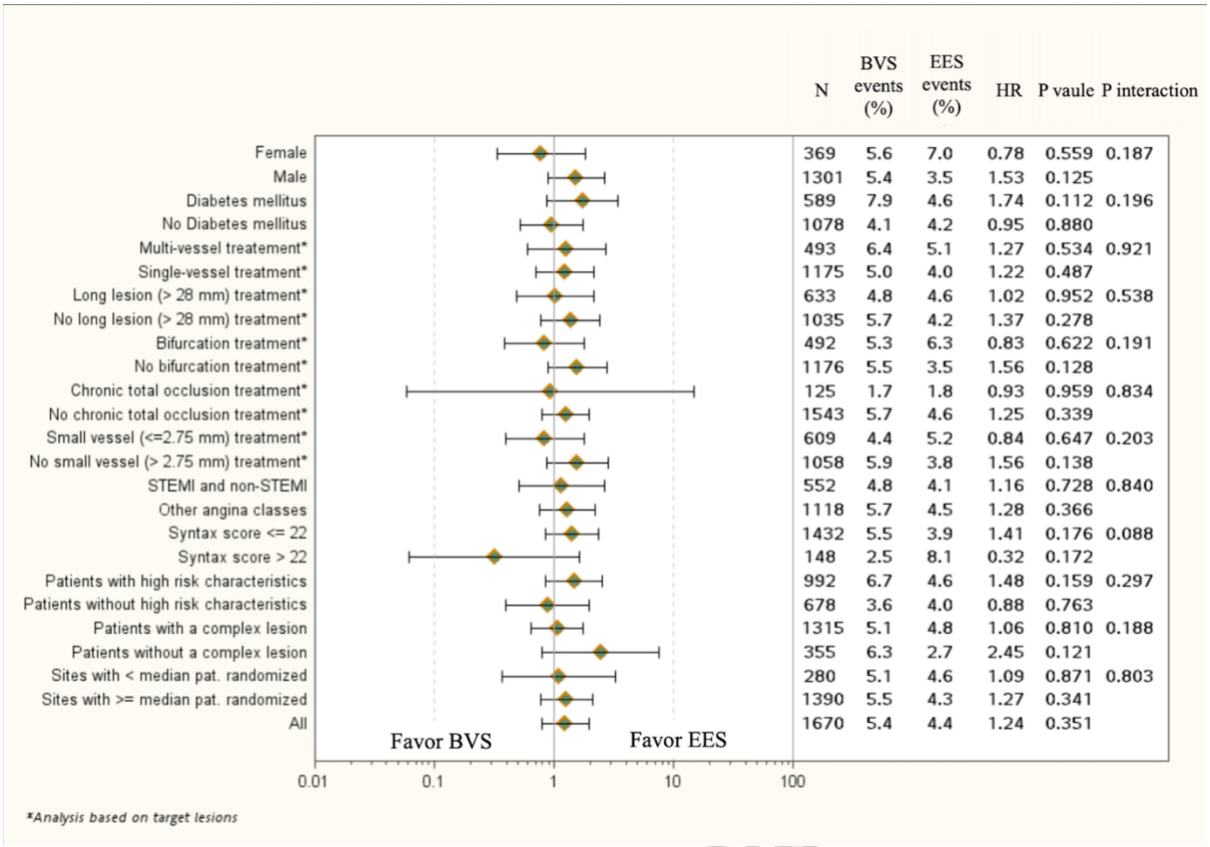
Number at risk	BVS	848	834	825	820	811	772
	EES	822	814	807	798	791	747

Figure 3d



Number at risk	BVS	848	831	823	819	815	776
	EES	822	815	812	807	804	763

Figure 4



*Analysis based on target lesions

Bioresorbable Vascular Scaffold Versus Metallic Drug-Eluting Stent in Patients at High Risk of Restenosis: The COMPARE-ABSORB Randomized Clinical Trial

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Supplementary Online Content

- **Supplementary Table 1.** Number of patients randomized per site.
- **Supplementary Table 2.** Inclusion and exclusion criteria.
- **Supplementary Methods section**
- **Supplementary Table 3**. Study Organization.
- **Supplementary Table 4.** Study endpoints and definitions.
- **Supplementary Table 5.** Definition of optimal Implantation techniques.
- **Supplementary Table 6**. Dual-antiplatelet treatment.
- **Supplementary Table 7.** Quality of life reported at 1-year follow up
- **Supplementary Table 8.** Correct sizing according to post-procedural quantitative angiographic analysis.
- **Supplementary Table 9**. Angiographic analysis in bioresorbable vascular scaffold trials.
- **Supplementary Figure 1.** Stratified analyses according to optimal implantation techniques.
- **Supplementary Figure 2.** Distribution of correct sizing and definite device thrombosis in the BVS group.

Supplementary Table 1. Number of patients randomized per site (Total number of patients: 1,670)

Site name	PI	Location	Number of patients enrolled
MAASSTADZIEKENHUIS	P. SMITS	ROTTERDAM	201
MIEDZIOWE CENTRUM ZDROWIA SA	A. WLODARCZAK	LUBIN	178
HÔPITAL PRIVÉ JACQUES CARTIER	B. CHEVALIER	MASSY	99
PAPWORTH HOSPITAL	S. HOOLE	CAMBRIDGE	89
UNIVERSITATSMEDIZIN MAINZ	T. GORI	MAINZ	72
SEGEBERGER KLINIKEN	M. ABDEL-WAHAB	BAD SEGEBERG	67
CARDIOVASCULAR CENTER AALST OLV HOSPITAL	E. BARBATO	AALST	66
UNIVERSITA DEGLI STUDI DI NAPOLI FEDERICO	G. ESPOSITO	NAPLES	62
ERASMUS MEDISCH CENTRUM	R. VAN GEUNS	ROTTERDAM	55
FREEMAN HOSPITAL	M. EGRED	NEWCASTLE	50
AZIENDA OSPEDALIERA DI PADOVA	G. TARANTINI	PADOVA	47
HOSPITAL DEL MAR	B. VAQUERIZO MONTILLA	BARCELONA	47
CARDIOCENTRE, UNIVERSITY HOSPITAL KRALOVS	V. KOCKA	PRAGUE	43
ROYAL BOURNEMOUTH HOSPITAL	P. O'KANE	BOURNEMOUTH	39
AMERICAN HEART OF POLAND	P. BUSZMAN	CHRZANOW	36
UNIVERSITY HOSPITAL BRNO	P. KALA	BRNO	34
UNIVERSITATSKLINIKUM ERLANGEN	S. ACHENBACH	ERLANGEN	33
CENTRAL MILITARY HOSPITAL	M. MALY	PRAGUE	30
AMERICAN HEART OF POLAND	K. MILEWSKI	TYCHY	30
CHARITÉ CAMPUS BENJAMIN FRANKIN	U. LANDMESSER	BERLIN	29
ALBERT SCHWEITZER HOSPITAL	S. IJSSELMUIDEN	DORDRECHT	29
ELISABETHKRANKENHAUS ESSEN	C. NABER	ESSEN	28
CATHERINA ZIENKENHUIS	P. TONINO	EINDHOVEN	26
CHU CLERMONT-FERRAND	P. MOTREFF	CLERMONT FERRAND	25
UNIVERSITATSKLINIKUM GIESSEN	H. NEF	GIESSEN	25
UNIVERSITY HOSPITAL KRAKOW	D. DUDEK	KRAKOW	25

CLINIQUE RHÔNE DURANCE	J. SAINSOUS	AVIGNON	24
HOSPITAL CLINIC	S. BRUGALETTA	BARCELONA	21
CHR DE LA CITADELLE	G. SAAD	LIEGE	19
KERCKHOFF KLINIK	C. LIEBETRAU	BAD NAUHEIM	19
UNIVERSITARIA DI PARMA	A. MENOZZI	PARMA	17
CLINIQUE PASTEUR	J. FAJADET	TOULOUSE	15
OSPEDALE SAN GIACOMO	C. CERNETTI	CASTELFRANCO VENETO	13
OSPEDALE PAPA GIOVANNI XXIII	O. VALSECCHI	BERGAMO	12
UNIVERSITATSKLINIKUM KOLN	T. RUDOLPH	KOLN	11
AMPHIA ZIEKENHUIS	M. MEUWISSEN	BREDA	11
HOSPITAL CLINICO SAN CARLOS	J. ESCANED	MADRID	11
UNIVERSITA DEGLI STUDI MAGNA GRAECIA	C. INDOLFI	CATANZARO	6
AZIENDA OSPEDALIERA BROTZU	B. LOI	CAGLIARI	6
UZ LEUVEN	W. DESMET	LEUVEN	4
CLINIQUE SAINT HILAIRE	R. KONING	ROUEN	4
KLINIKUM DER UNIVERSITÄT MÜNCHEN	J. MEHILLI	MUNCHEN	3
UNIVERSITÄTSKLINIKUM LEIPZIG	P. LURZ	LEIPZIG	3
ARNAS CIVICO PALERMO	M. CARUSO	PALERMO	3
HOSPITAL UNIVERSITARIO MARQUES DE VALD	J.M. DE LA TORRE HERNANDEZ	SANTANDER	3

Supplementary Table 2. Inclusion and exclusion criteria (latest protocol version)

Inclusion criteria

Patients aged 18-75 years with at least one of the following:

1. High-risk characteristics for restenosis

- Medically treated diabetes (oral medication or insulin) and/or multivessel disease of which more than one *de-novo* target lesion to be treated with the study scaffold/stent.

2. Complex target lesion

Single *de-novo* target lesion satisfying at least one of the following:

- Lesion length >28 mm
- Small vessels: Target lesion reference vessel diameter ≥2.5mm and ≤2.75mm
- Lesion with pre-existing total occlusion (pre-procedural TIMI = 0)
- Bifurcation with single stent strategy

Exclusion criteria

1. Age <18 years, or >75 years
2. Patients incapable of giving informed consent
3. Patients under judicial protection, tutorship or curatorship
4. Known comorbidities which make patients unable to complete 7 years of follow-up
5. Female of childbearing potential (and last menstruation within the last 12 months), who did not undergo tubal ligation, ovariectomy or hysterectomy
6. Pregnant woman
7. Breastfeeding woman
8. Known intolerance to aspirin, heparin, PLLA, everolimus, contrast material
9. Cardiogenic Shock (Killip >2)
10. PCI with implantation of stents/scaffolds within previous 30 days
11. Active bleeding or coagulopathy
12. Subject is currently participating in another clinical trial that has not yet completed its primary endpoint
13. Renal insufficiency (GFR <45 ml/min)
14. Life expectancy < 7 years
15. Known non-adherence to dual antiplatelet therapy
16. Patients on oral anticoagulation therapy (including novel oral anticoagulant such as dabigatran, rivaroxaban, apixaban and edoxaban)
17. Known Impaired left ventricular function (left ventricular ejection fraction <30%)
18. Patients at high bleeding risk who are not suitable for long-term DAPT
19. Following lesion characteristics:
    - Target lesion with reference vessel diameter (RVD) < 2.50 mm and > 4.0 mm
    - STEMI with RVD of >3.5mm of the culprit target lesion
    - Target lesion with in-stent/scaffold thrombosis
    - Graft lesions as target lesions
    - Lesion involving left main trunk
    - Severe tortuosity of target vessel
    - Aorto-ostial lesion(s)
    - In-scaffold/in-stent restenosis
    - Bifurcation target lesion with intended 2 stent/scaffold strategy
20. Non-target lesion and target lesion in the same epicardial coronary artery (right coronary artery, left circumflex artery or left anterior descending artery)

Supplementary Methods

Randomization

Patients were 1:1 randomly assigned to receive either BVS (Absorb, Abbott Vascular, Santa Clara, CA, USA) or EES (Xience, Abbott Vascular, Santa Clara, CA, USA). Randomization was performed after successful passage of the guidewire across the first target lesion. Randomization was stratified by study sites and study arm. Each site had its own dedicated randomization lists for both arms, respecting the 1:1 ratio. Each randomization list was built dynamically by the Electronic Data Capture (EDC) System whenever a new study site was declared within the system. The algorithm used when building a randomization list was based on the standard algorithm of Blocked Randomization with Randomly Selected Block Sizes.

Procedures

A dedicated implantation technique was defined in the protocol: pre-dilatation using non-compliant balloons of the same diameter as the reference vessel diameter and post-scaffold high-pressure (≥16 atm) dilatation were mandatory in the BVS group. Scaffold to vessel sizing was based on the instructions for use allowing a margin of plus or minus 0.25 between nominal device diameter and visual vessel reference diameter as established by the operator.

Study hypotheses and endpoints

The short-term primary hypothesis of the study was non-inferiority of the BVS group compared with the EES group in terms of the primary endpoint, TLF (a composite of cardiac death, myocardial infarction in target vessel territory and clinically-indicated target lesion revascularization) at 1 year. Additional study endpoints and definitions are presented in **Supplementary Table 4**.

Protocol revisions

In the original protocol, the long-term hypothesis was the superiority of BVS over EES in TLF between 1 and 5 years. During enrolment of the study, follow-up results of early randomized trials suggested that the potential benefits of BVS might only become apparent beyond 3 years, after completion of bioresorption. Therefore, the timing of landmark analysis of the long-term hypothesis was adjusted to between 3 and 7 years. The other change in the protocol was the inclusion criteria for small vessels. The initial protocol allowed inclusion of target vessels with reference diameter equal to 2.25 mm on visual estimation. However, because of evolving safety concerns regarding use of BVS in small vessels, the Steering Committee decided to exclude lesions with reference vessel diameter less than 2.5 mm and recommended additional quantitative sizing tools for vessels below 2.75mm.[7] Owing to an observed second phase of increased risk of scaffold thrombosis between 2 and 3 years[8], the Steering Committee advised prolongation of the duration of dual-antiplatelet treatment from the original 12 months to 36 months in the BVS group and the timing of landmark analysis of the long-term hypothesis was adjusted to between 3 and 7 years. On 31 August 2017, the Steering Committee prematurely stopped enrolment based on recommendation of the DSMB.

Supplementary Table 3. Study Organization

Principal investigator
Pieter C. Smits
Co-Principal investigator
Robert-Jan van Geuns
Executive Committee
Pieter C. Smits Robert-Jan van Geuns Marie-Claude Morice Yoshinobu Onuma
Steering Committee members
Pieter C. Smits Robert-Jan van Geuns Jan Tijssen Victor Kocka Dariusz Dudek Bernard Chevalier Tommaso Gori Stephan Achenbach Giuseppe Tarantini Emanuele Barbato Nick West Javier Escaned Marie-Claude Morice Yoshinobu Onuma
Data Safety Monitoring Board (DSMB)
Stefan James (chairman) Eric Boersma Michel Bertrand
Safety Reporting
The CRO CERC (7 rue du Théâtre, 91300 Massy, France) is responsible for entering all Serious Adverse Events (SAEs) including the assessment regarding relationship to the device (SADEs) or to the procedure from the eCRF in a safety database and for reporting these SAEs and SADEs according to the MEDDEV 2.7/3 guidelines and national requirements.
Data Management, Site Management and Monitoring
Data management, site management and monitoring were conducted by the Clinical Research Organisation (CRO) CERC (7, rue du theatre, 91300 Massy, France).
Clinical Event Adjudication Committee
Eugene McFadden Pascal Vranckx Joanna Wykrzykowska Ernest Spitzer
Core Laboratories
The independent angiography and intravascular ultrasound imaging Core Lab at Cardialysis (Cardialysis B.V., PO Box 2125, 3000 CC Rotterdam, The Netherlands) analyzed angiograms obtained during and/or before procedure. Members of the Angiographic/IVUS Core Lab were not involved as investigators or co-investigators in this study.
Statistical Analysis
The Cardialysis (Cardialysis B.V., PO Box 2125, 3000 CC Rotterdam, The Netherlands) is responsible for the statistical analysis.

Supplementary Table 4. Study endpoints and definitions

Primary Endpoints

Target lesion failure (TLF) as defined as a composite of

- Cardiac death
- Myocardial infarction (MI) in target vessel territory
- Clinically Indicated Target lesion revascularization

Secondary Endpoints

- Components of primary endpoints
- Target vessel failure and its components
- All-cause mortality
- Periprocedural MI and spontaneous MI
- All revascularization
- Definite or Probable Stent/Scaffold thrombosis (per the ARC definition)
- Cumulative recurrent or worsening angina at 12 months, excluding the angina episodes that occurred during index hospitalization or in the 7 days post index procedure, whichever comes first
- Health care cost related to diagnostic workup of presumed coronary ischemia and therapies in the first 12 months
- Health care costs related to target vessel failure up to 7 years
- Angina status at 1, 6, 12 months and at the time of any recurrent event assessed by Seattle angina questionnaire
- Quality of life at 1, 6, 12 months and at the time of any recurrent event assessed by EQ5D
- For STEMI patients, TIMI flow, myocardial blush and ST-segment resolution on ECG

Definitions of endpoints

Death

The deaths were adjudicated per the ARC definition. All deaths are considered cardiac unless an unequivocal non-cardiac cause can be established. Specifically, any unexpected death even in patients with coexisting potentially fatal non-cardiac disease (e.g. cancer, infection) should be classified as cardiac.

- **Cardiac death**: Any death due to proximate cardiac cause (e.g. MI, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, all study procedure related deaths including those related to concomitant treatment.
- **Vascular death**: Death due to non-coronary vascular causes such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular cause.
- **Non-cardiovascular death**: Any death not covered by the above definitions such as death caused by infection, malignancy, sepsis, pulmonary causes, accident, suicide or trauma.

Myocardial Infarction

Spontaneous myocardial infarction (MI) is defined based on the third universal definition of myocardial infarction, while periprocedural MI is defined according to the SCAI definition.

- **Spontaneous MI (>48 hours after intervention, MI type I):** Symptoms suggestive of ischemia/infarction in association with ECG, cardiac biomarker or pathologic evidence of infarction as follows: Detection of a rise and/or fall of cardiac biomarker values (preferably cardiac troponin T or I) with at least one value above the 99$_{th}$ percentile upper reference limit and with at least one of the following:
    - Symptoms of ischemia
    - New or presumed new significant ST segment-T wave (ST-T) changes or new LBBB
    - Development of new Q waves in the ECG
    - Evidence of new loss of viable myocardium or new regional wall motion abnormality
    - Identification of an intracoronary thrombus by angiography or autopsy

  Spontaneous MI typically occurs after the periprocedural period and may be secondary to late stent complications or progression of native disease (e.g., non-culprit lesion plaque rupture). Performance of ECG and angiography supports adjudication to either a target or non-target vessel or lesion in most cases.

- **Periprocedural** MI after PCI (within 48 hours after PCI, MI type 4a [post PCI] and 5 [post CABG])

  Periprocedural MI is defined based on the SCAI definitions as follows:

In patients with normal baseline CK-MB: The peak CK-MB measured within 48 hours of the procedure rises to ≥10x the local laboratory ULN, or to ≥5x ULN with new pathologic Q-waves in ≥2 contiguous leads or new persistent LBBB, *OR* in the absence of CK-MB measurements and a normal baseline cTn, a cTn (I or T) level measured within 48 hours of the PCI rises to ≥70x the local laboratory ULN, or ≥35x ULN with new pathologic Q-waves in ≥2 contiguous leads or new persistent LBBB.
In patients with elevated baseline CK-MB (or cTn) in whom the biomarker levels are stable or falling: The CK-MB (or cTn) rises by an absolute increment equal to those levels recommended above from the most recent pre-procedure level.
In patients with elevated CK-MB (or cTn) in whom the biomarker levels have not been shown to be stable or falling: The CK-MB (or cTn) rises by an absolute increment equal to those levels recommended above plus new ST-segment elevation or depression plus signs consistent with a clinically relevant MI, such as new onset or worsening heart failure or sustained hypotension.

- **Target**-vessel vs. non-target-vessel MI: Any MI not clearly attributable to a non-target vessel will be considered as target-vessel MI.

[Revascularization]

The revascularizations were adjudicated per the ARC definition.

- **Target Lesion Revascularization (TLR)**

  TLR is defined as any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion. All TLR should be classified prospectively as clinically indicated [CI] or not clinically indicated by the investigator prior to repeat angiography. The target lesion is defined as the treated segment from 5 mm proximal to the stent and to 5 mm distal to the stent/scaffold.

- **Target Vessel Revascularization (TVR)**

  TVR is defined as any repeat percutaneous intervention or surgical bypass of any segment of the target vessel. The target vessel is defined as the entire major coronary vessel proximal and distal to the target lesion which includes upstream and downstream branches and the target lesion itself

- **Non Target Lesion Revascularization (Non-TLR)**

  Any revascularization in the target vessel for a lesion other than the target lesion is considered a non-TLR.

- **Non Target Vessel Revascularization (Non-TVR)**

  Revascularization of the vessel identified and treated as the non-target vessel at the time of the index procedure.

  Note: TLR and TVR were adjudicated by the angiographic core laboratory.

- **Ischemia-driven Revascularization (CI-TLR/TVR)**

  A revascularization is considered clinically indicated if associated with any of the following:
  Positive functional ischemia study including positive FFR
  Ischemic symptoms and angiographic diameter stenosis ≥ 50% by core laboratory QCA
  Angiographic diameter stenosis ≥ 70% by core laboratory QCA without angina or positive functional study

Supplementary Table 5. Definition of Optimal Implantation techniques (OIT)

OIT-0

- Correct sizing by post-procedural QCA defined as the mean diameter of the distal or proximal segment within the range of the implanted device size ± 0.25 mm.
- Pre-dilatation performed.
- Any Post-dilatation.

OIT-1

- Correct sizing by post-procedural QCA defined as the mean diameter of the distal or proximal segment within the range of the implanted device size ± 0.25 mm.
- Pre-dilatation performed.
- Post-dilatation with non-compliant balloon, maximum pressure ≥ 16 atm.

OIT-2

- Correct sizing by post-procedural QCA defined as the mean diameter of the distal or proximal segment within the range of the implanted device size ± 0.25 mm.
- Minimal reference vessel diameter 2.5 mm by QCA.
- Pre-dilatation performed.
- Post-dilatation with non-compliant balloon, maximum pressure ≥ 16 atm.

OIT-3

- Correct sizing by post-procedural QCA defined as the mean diameter of the distal or proximal segment within the range of the implanted device size ± 0.25 mm.
- Minimal reference vessel diameter 2.5 mm by QCA.
- Pre-dilatation performed.
- Post-dilatation with non-compliant balloon, pressure ≥16 atm, balloon diameter between device diameter and device diameter + 0.5 mm

OIT-4

- Correct sizing by post-procedural QCA defined as the mean diameter of the distal or proximal segment within the range of the implanted device size ± 0.25 mm.
- Minimal reference vessel diameter 2.5 mm by QCA.
- Pre-dilatation performed.
- Post-dilatation with non-compliant balloon, maximum pressure ≥ 16 atm, balloon diameter ≥ device diameter + 0.25 mm.

*If multiple devices were used, the largest device should be correlated to the mean diameter of the proximal segment whereas the smallest device should be correlated to the mean diameter of the distal segment as defined above.

Supplementary Table 6. Dual-antiplatelet treatment

Characteristic	BVS (N = 848)	EES (N = 822)	Difference (95% CI)	P value
Discharge				
ASA	98.0% (831/848)	98.7% (811/822)	-0.7% [-1.9%, 0.6%]	0.3425
Clopidogrel	50.8% (431/848)	58.6% (482/822)	-7.8% [-12.6%, -3.1%]	0.0014
Prasugrel	12.6% (107/848)	9.0% (74/822)	3.6% [0.6%, 6.6%]	0.0182
Ticagrelor	38.3% (325/848)	34.2% (281/822)	4.1% [-0.5%, 8.7%]	0.0836
DAPT (ASA + Clopi)	49.9% (423/848)	57.9% (476/822)	-8.0% [-12.8%, -3.3%]	0.0012
DAPT (ASA + Tica or Prasu)	50.2% (426/848)	42.6% (350/822)	7.7% [2.9%, 12.4%]	0.0020
DAPT (ASA + Clopi or Tica or Prasu)	97.2% (824/848)	97.9% (805/822)	-0.8% [-2.2%, 0.7%]	0.3453
OAC alone	2.1% (18/848)	2.6% (21/822)	-0.4% [-1.9%, 1.0%]	0.6281
OAC and (ASA or Clopi or Tica or Prasu)	2.1% (18/848)	2.6% (21/822)	-0.4% [-1.9%, 1.0%]	0.6281
1 Month				
ASA	98.1% (806/822)	98.5% (790/802)	-0.5% [-1.7%, 0.8%]	0.5690
Clopidogrel	51.6% (424/822)	58.2% (467/802)	-6.6% [-11.5%, -1.8%]	0.0082
Prasugrel	12.8% (105/822)	9.2% (74/802)	3.5% [0.5%, 6.6%]	0.0263
Ticagrelor	38.0% (312/822)	33.5% (269/802)	4.4% [-0.2%, 9.1%]	0.0699
DAPT (ASA + Clopi)	50.1% (412/822)	57.4% (460/802)	-7.2% [-12.1%, -2.4%]	0.0039
DAPT (ASA + Tica or Prasu)	50.0% (411/822)	41.9% (336/802)	8.1% [3.3%, 12.9%]	0.0012
DAPT (ASA + Clopi or Tica or Prasu)	97.6% (802/822)	97.4% (781/802)	0.2% [-1.3%, 1.7%]	0.8749
OAC alone	2.8% (23/822)	2.6% (21/802)	0.2% [-1.4%, 1.8%]	0.8792
OAC and (ASA or Clopi or Tica or Prasu)	2.8% (23/822)	2.6% (21/802)	0.2% [-1.4%, 1.8%]	0.8792
6 Months				
ASA	97.4% (790/811)	98.1% (768/783)	-0.7% [-2.1%, 0.8%]	0.4023
Clopidogrel	53.4% (433/811)	57.7% (452/783)	-4.3% [-9.2%, 0.5%]	0.0866
Prasugrel	11.8% (96/811)	8.3% (65/783)	3.5% [0.6%, 6.5%]	0.0200
Ticagrelor	36.4% (295/811)	31.8% (249/783)	4.6% [-0.1%, 9.2%]	0.0572
DAPT (ASA + Clopi)	51.3% (416/811)	56.6% (443/783)	-5.3% [-10.2%, -0.4%]	0.0350
DAPT (ASA + Tica or Prasu)	47.6% (386/811)	39.6% (310/783)	8.0% [3.2%, 12.9%]	0.0015
DAPT (ASA + Clopi or Tica or Prasu)	96.4% (782/811)	94.6% (741/783)	1.8% [-0.2%, 3.8%]	0.0898
OAC alone	3.2% (26/811)	2.8% (22/783)	0.4% [-1.3%, 2.1%]	0.6630
OAC and (ASA or Clopi or Tica or Prasu)	3.0% (24/811)	2.8% (22/783)	0.1% [-1.5%, 1.8%]	0.8821
12 Months				
ASA	96.6% (785/813)	96.5% (766/794)	0.1% [-1.7%, 1.9%]	1.0000
Clopidogrel	49.2% (400/813)	43.8% (348/794)	5.4% [0.5%, 10.2%]	0.0316
Prasugrel	7.7% (63/813)	5.9% (47/794)	1.8% [-0.6%, 4.3%]	0.1666
Ticagrelor	29.0% (236/813)	24.2% (192/794)	4.8% [0.5%, 9.2%]	0.0319
DAPT (ASA + Clopi)	47.2% (384/813)	41.9% (333/794)	5.3% [0.4%, 10.1%]	0.0351
DAPT (ASA + Tica or Prasu)	36.2% (294/813)	29.8% (237/794)	6.3% [1.7%, 10.9%]	0.0080
DAPT (ASA + Clopi or Tica or Prasu)	80.0% (650/813)	70.8% (562/794)	9.2% [5.0%, 13.4%]	< 0.0001

Characteristic	BVS (N = 848)	EES (N = 822)	Difference (95% CI)	P value
OAC alone	4.1% (33/813)	3.0% (24/794)	1.0% [-0.8%, 2.8%]	0.2825
OAC and (ASA or Clopi or Tica or Prasu)	3.4% (28/813)	2.3% (18/794)	1.2% [-0.4%, 2.8%]	0.1790

ASA = aspirin, BVS = bioresorbable vascular scaffold, Clopi = Clopidogrel, DAPT = dual antiplatelet therapy, EES = everolimus-eluting stent, OAC = oral anticoagulants, Prasu = Prasugrel, Tica = Ticagrelor

Supplementary Table 7. Quality of life reported at 1-year follow-up

Characteristic	BVS (N = 848)	EES (N = 822)	p-Value
Seattle Angina Questionnaire			
Physical Limitation	84.9±19.5 (742)	85.0±19.7 (718)	0.93
Anginal Stability	55.3±17.8 (776)	54.6±16.8 (755)	0.40
Angina Frequency	93.8±13.0 (776)	93.4±14.0 (756)	0.57
Treatment Satisfaction	89.1±18.7 (761)	88.6±19.1 (739)	0.60
Disease Perception	78.9±20.2 (753)	78.0±20.9 (728)	0.40
Euro Qol			
Mobility			0.89
No problem in walking about	71.8% (562/783)	71.2% (541/760)	
Slight problems in walking about	15.8% (124/783)	17.0% (129/760)	
Moderate problems in walking about	8.2% (64/783)	7.9% (60/760)	
Severe problems in walking about	3.2% (25/783)	3.4% (26/760)	
Not able to walk about	1.0% (8/783)	0.5% (4/760)	
			0.82
No problem in walking about	71.8% (562/783)	71.2% (541/760)	
At least slight problems in walking about	28.2% (221/783)	28.8% (219/760)	
Self-care			0.95
No problems washing or dressing myself	89.1% (701/787)	88.9% (684/769)	
Slight problems washing or dressing myself	7.4% (58/787)	7.7% (59/769)	
Moderate problems washing or dressing myself	2.9% (23/787)	2.7% (21/769)	
Severe problems washing or dressing myself	0.6% (5/787)	0.5% (4/769)	
Unable to wash or dress myself	0.0% (0/787)	0.1% (1/769)	
			1.00
No problems washing or dressing myself	89.1% (701/787)	88.9% (684/769)	
At least slight problems washing or dressing myself	10.9% (86/787)	11.1% (85/769)	
Usual activity			0.73
No problems doing my usual activity	74.5% (587/788)	73.7% (566/768)	
Slight problems doing my usual activity	15.4% (121/788)	15.6% (120/768)	
Moderate problems doing my usual activity	6.9% (54/788)	7.9% (61/768)	
Severe problems doing my usual activity	2.9% (23/788)	2.5% (19/768)	
Unable to do my usual activities	0.4% (3/788)	0.3% (2/768)	
			0.73
No problems doing my usual activity	74.5% (587/788)	73.7% (566/768)	
At least slight problems doing my usual activity	25.5% (201/788)	26.3% (202/768)	
Pain/discomfort			0.14
No pain or discomfort	60.2% (473/786)	64.2% (493/768)	
Slight pain or discomfort	25.2% (198/786)	22.0% (169/768)	
Moderate pain or discomfort	11.2% (88/786)	10.7% (82/768)	
Severe pain or discomfort	2.7% (21/786)	2.6% (20/768)	
Extreme pain or discomfort	0.8% (6/786)	0.5% (4/768)	

			0.11
No pain or discomfort	60.2% (473/786)	64.2% (493/768)	
At least slight pain or discomfort	39.8% (313/786)	35.8% (275/768)	
Anxiety/depression			0.79
Not anxious or depressed	64.8% (508/784)	65.7% (504/767)	
Slightly anxious or depressed	25.0% (196/784)	23.5% (180/767)	
Moderately anxious or depressed	7.4% (58/784)	8.2% (63/767)	
Severely anxious or depressed	1.8% (14/784)	2.3% (18/767)	
Extremely anxious or depressed	1.0% (8/784)	0.3% (2/767)	
			0.71
Not anxious or depressed	64.8% (508/784)	65.7% (504/767)	
At least slightly anxious or depressed	35.2% (276/784)	34.3% (263/767)	
Health state (0-100)	77.9±15.6 (782)	77.8±15.2 (762)	0.91

BVS = bioresorbable vascular scaffold, EES = everolimus-eluting stent

Supplementary Table 8. Correct sizing according to post-procedural quantitative angiographic analysis

Correct sizing*	**BVS** N=1,137 lesions	**EES** N=1,139 lesions
Proximal segment +, Distal segment +	11.5% (131/1,137)	17.3% (197/1,139)
Proximal segment +, Distal segment -	20.6% (862/1,137)	21.7% (743/1,139)
Proximal segment -, Distal segment +	6.5% (74/1,137)	7.3% (83/1,139)
Proximal segment -, Distal segment -	61.4% (698/1,137)	53.7% (612/1,139)

*Please refer to the definition of correct sizing (Online Table 5).

"+": meet the criteria of correct sizing, "- ": not meet the criteria of correct sizing,

BVS = bioresorbable vascular scaffold, EES = everolimus-eluting stent, OIT = optimal implantation technique.

Supplementary Table 9. Angiographic analysis in bioresorbable vascular scaffold trials

Study	COMPARE ABSORB		ABSORB IV		ABSORB III	
Device	**BVS**	**EES**	**BVS**	**EES**	**BVS**	**EES**
Reference vessel diameter (mm)	2.51 ± 0.50	2.49 ± 0.49	NA	NA	NA	NA
Pre-procedure MLD (mm)	0.89 ± 0.49	0.89 ± 0.50	NA	NA	NA	NA
Post-procedure MLD (mm)	2.21 ± 0.41	2.32 ± 0.39*	2.66 ± 0.39	2.74 ± 0.41*	2.37 ± 0.40	2.49 ± 0.40*
Acute gain (mm)	1.33 ± 0.57	1.42 ± 0.53*	1.85 ± 0.46	1.92 ± 0.46*	1.45 ± 0.45	1.59 ± 0.44*

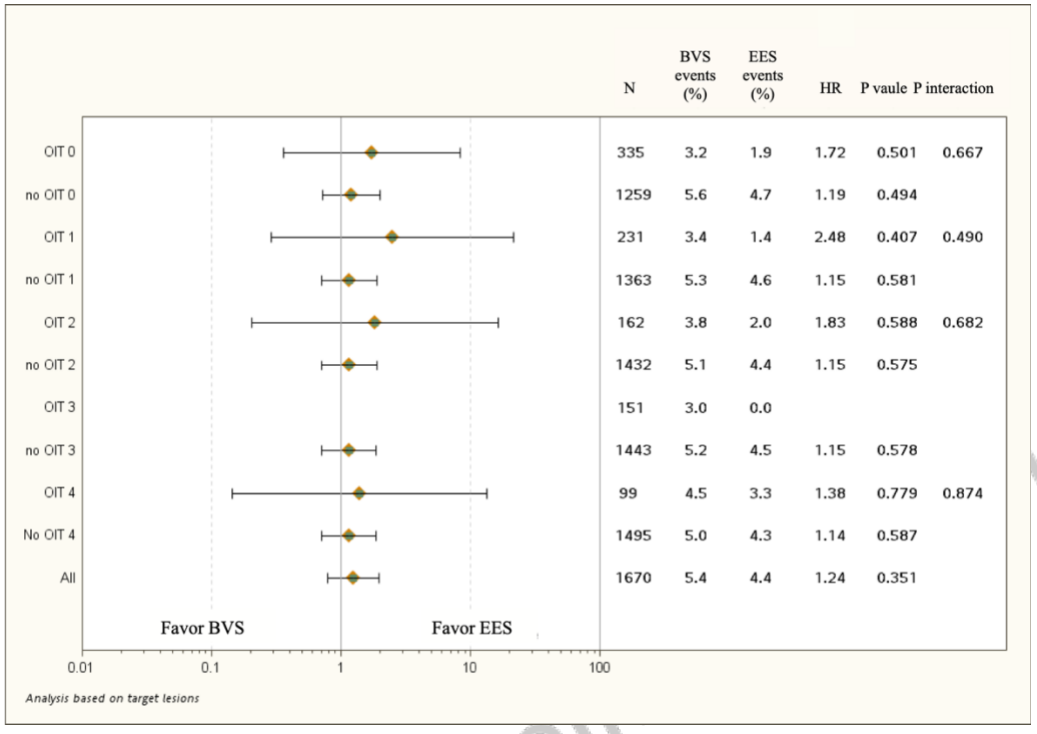
Study	ABSORB II		ABSORB Japan		ABSORB China	
Device	**BVS**	**EES**	**BVS**	**EES**	**BVS**	**EES**
Reference vessel diameter (mm)	2.59 ± 0.38	2.63 ± 0.40	2.72 ± 0.44	2.79 ± 0.46	2.81 ± 0.03	2.82 ± 0.03
Pre-procedure MLD (mm)	1.07 ± 0.32	1.05 ± 0.32	0.96 ± 0.33	0.99 ± 0.36	0.98 ± 0.03	1.01 ± 0.03
Post-procedure MLD (mm)	2.22 ± 0.33	2.50 ± 0.33*	2.42 ± 0.38	2.64 ± 0.40*	2.48 ± 0.02	2.59 ± 0.03*
Acute gain (mm)	1.15 ± 0.38	1.46 ± 0.38*	1.46 ± 0.40	1.65 ± 0.40*	1.51 ± 0.03	1.59 ± 0.03*

*P <0.05 (BVS vs. EES)

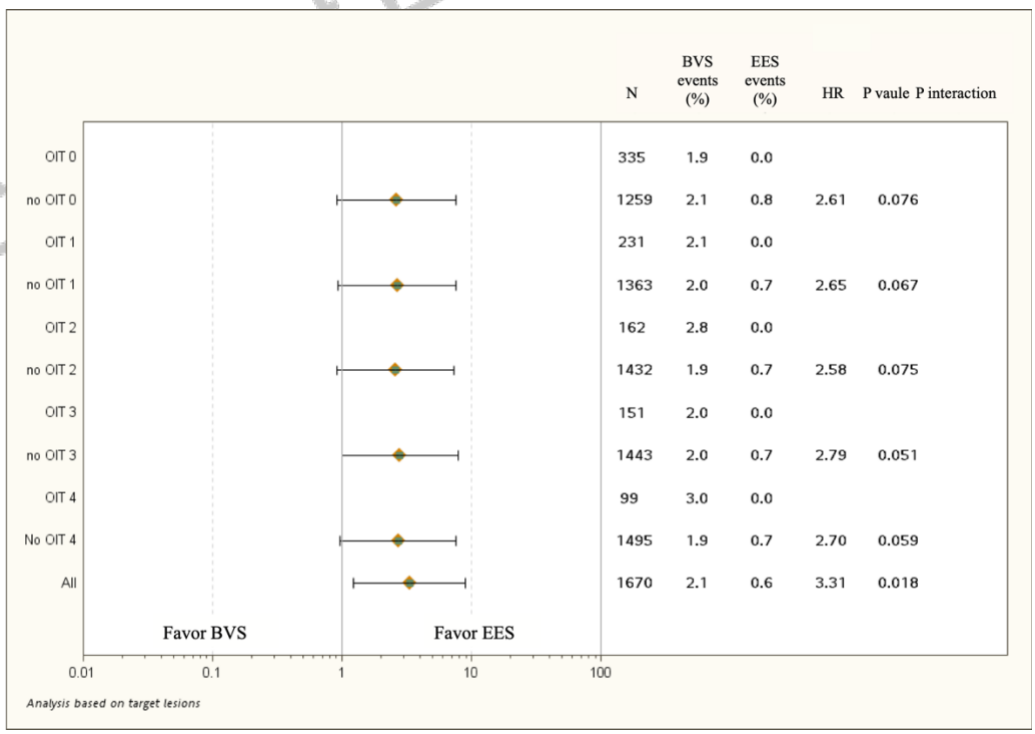
BVS = bioresorbable vascular scaffold, EES = everolimus-eluting stent, MLD = minimal lumen diameter, NA = not applicable

Supplementary Figure 1. Stratified analyses according to optimal implantation techniques

1A. Target lesion failure

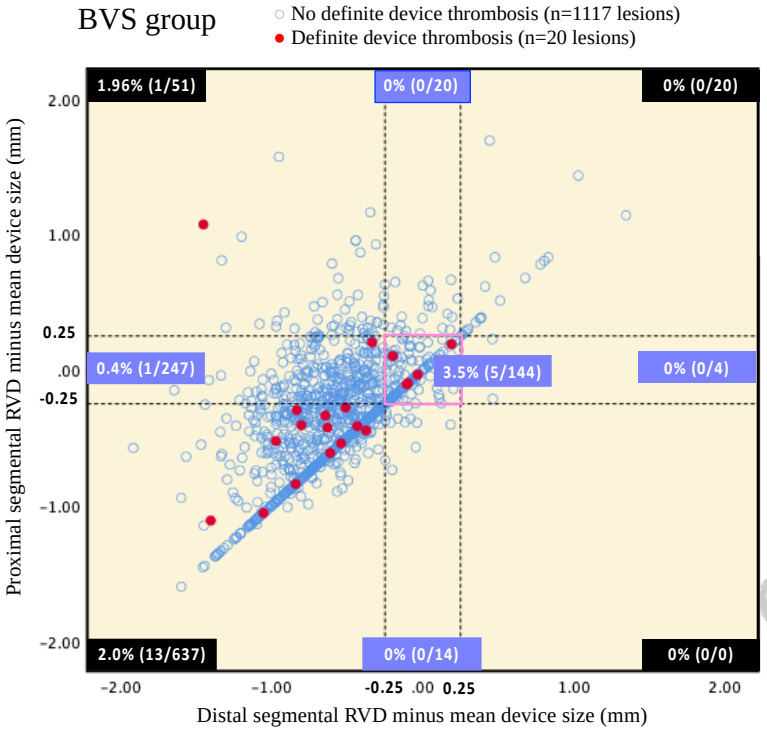


1B. Definite/Probable device thrombosis



BVS = bioresorbable vascular scaffold, EES = everolimus-eluting stent, HR = hazard ratio, N= number of patients, OIT = optimal implantation techniques

Supplementary Figure 2. Distribution of correct sizing and definite device thrombosis in the BVS group



Distribution of proximal and distal segment reference vessel diameters minus the device size in lesions with or without definite device thrombosis is shown. Correct sizing is the mean diameter of the distal or proximal segment within the range of the device size ± 0.25 mm. The differences between the proximal/distal segment and device size are plotted on the y-axis and x-axis, respectively. The definite device thrombosis rates of different quadrants/rectangles are shown. The definite device thrombosis rates had no significant differences between lesions with or without a correct vessel sizing [1.36% (6/439) vs. 2.0% (14/698), p = 0.494).

BVS = bioresorbable vascular scaffold, RVD = reference vessel diameter