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Everolimus-Eluting Bioresorbable Scaffolds for Coronary Artery Disease

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ABSTRACT

BACKGROUND

In patients with coronary artery disease who receive metallic drug-eluting coronary stents, adverse events such as late target-lesion failure may be related in part to the persistent presence of the metallic stent frame in the coronary-vessel wall. Bioresorbable vascular scaffolds have been developed to attempt to improve long-term outcomes.

METHODS

In this large, multicenter, randomized trial, 2008 patients with stable or unstable angina were randomly assigned in a 2:1 ratio to receive an everolimus-eluting bioresorbable vascular (Absorb) scaffold (1322 patients) or an everolimus-eluting cobalt–chromium (Xience) stent (686 patients). The primary end point, which was tested for both noninferiority (margin, 4.5 percentage points for the risk difference) and superiority, was target-lesion failure (cardiac death, target-vessel myocardial infarction, or ischemia-driven target-lesion revascularization) at 1 year.

RESULTS

Target-lesion failure at 1 year occurred in 7.8% of patients in the Absorb group and in 6.1% of patients in the Xience group (difference, 1.7 percentage points; 95% confidence interval, −0.5 to 3.9; P=0.007 for noninferiority and P=0.16 for superiority). There was no significant difference between the Absorb group and the Xience group in rates of cardiac death (0.6% and 0.1%, respectively; P=0.29), target-vessel myocardial infarction (6.0% and 4.6%, respectively; P=0.18), or ischemia-driven target-lesion revascularization (3.0% and 2.5%, respectively; P=0.50). Device thrombosis within 1 year occurred in 1.5% of patients in the Absorb group and in 0.7% of patients in the Xience group (P=0.13).

CONCLUSIONS

In this large-scale, randomized trial, treatment of noncomplex obstructive coronary artery disease with an everolimus-eluting bioresorbable vascular scaffold, as compared with an everolimus-eluting cobalt–chromium stent, was within the prespecified margin for noninferiority with respect to target-lesion failure at 1 year. (Funded by Abbott Vascular; ABSORB III ClinicalTrials.gov number, NCT01751906.)

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Contemporary drug-eluting coronary stents have been associated with better clinical outcomes than have either bare-metal stents or first-generation drug-eluting stents, but ongoing risks of stent thrombosis and restenosis limit their long-term safety and efficacy.[1-4] The development of late adverse events with permanent metallic stents may be related to persistent inflammation, loss of normal vessel curvature, impaired vasomotion, strut fracture, ongoing tissue growth within the stent frame, and neoatherosclerosis.[5,6] Furthermore, 20 to 30% of patients have recurrent angina during the first year after implantation of a drug-eluting stent.[7-9]

In this context, stents that are fully bioresorbable have been developed to provide mechanical support and drug-delivery functions similar to those of drug-eluting stents for approximately 1 year, followed by complete bioresorption over several years.[10-12] Because these novel devices are not metallic stents and are expected to leave no permanent material within the vessel over the long term, they have been termed "bioresorbable vascular scaffolds."

The Absorb bioresorbable vascular scaffold (Abbott Vascular) consists of a 150-μm-thick bioresorbable poly(L-lactide) scaffold with a 7-μm-thick bioresorbable poly(D,L-lactide) coating, which elutes everolimus. This bioresorbable vascular scaffold has been studied in registries[13-15] and in three modest-sized randomized trials.[16-18] In these trials, there was no significant difference in the rate of adverse events between the Absorb bioresorbable scaffold and the Xience cobalt–chromium stent (Abbott Vascular) within 1 year. However, these studies were not adequately powered for clinical end points, and therefore the safety and effectiveness of the bioresorbable scaffold, as compared with drug-eluting stents, have not yet been established. We therefore performed a large-scale, multicenter, randomized trial to determine the relative safety and effectiveness of the Absorb scaffold as compared with the Xience stent in patients with coronary artery disease.

Methods

Study Design and Oversight

The design of the ABSORB III trial has been described previously.[19] In summary, ABSORB III was a multicenter, single-blind, active-treatment, controlled clinical trial. The study organization and participating centers are listed in the Supplementary Appendix, available with the full text of this article at NEJM.org. The trial was designed by the principal investigators, study chair, and sponsor (Abbott Vascular), in concert with representatives of the Food and Drug Administration (FDA). The study protocol, which is available at NEJM.org, was approved by the institutional review board at each participating center. The sponsor funded the study and participated in site selection and management and in data collection and analysis. The principal investigators and study chair had unrestricted access to the data, prepared the manuscript, and vouch for the accuracy and completeness of the reported data and for the fidelity of this report to the trial protocol.

Study Patients

Patients 18 years of age or older with myocardial ischemia who were undergoing percutaneous coronary intervention (PCI) for one or two new native coronary artery lesions in separate epicardial coronary vessels were eligible for enrollment. Each lesion was required to be no more than 24 mm in length with a reference-vessel diameter of 2.5 to 3.75 mm on visual assessment. Patients with acute myocardial infarction and specific complex lesion features were excluded. A complete list of trial inclusion and exclusion criteria is provided in the Supplementary Appendix. All the patients provided written informed consent.

Treatments and Randomization

All the study patients received a loading dose of at least 300 mg of aspirin within 24 hours before the procedure. A loading dose of a $P2Y_{12}$ receptor antagonist was administered before the procedure or within 1 hour after the procedure. Other medications were administered according to standard practice.

Predilatation of the target lesion was required. After successful predilatation, patients were randomly assigned in a 2:1 ratio to receive one of the two study devices (the Absorb everolimus-eluting bioresorbable scaffold or the Xience everolimus-eluting cobalt–chromium stent). Randomization was performed with the use of an interactive voice–response system in random

block sizes of 3 or 6, stratified according to the presence or absence of diabetes, the number of target lesions, and clinical site. The investigator and staff members in the catheterization laboratory were aware of which device was implanted, but the patients and follow-up personnel were unaware of study-group assignments.

After implantation, high-pressure postdilatation was recommended to achieve 10% residual stenosis or less for both devices. Expansion of the bioresorbable scaffold to more than 0.5 mm larger than the nominal scaffold diameter was not permitted in order to avoid strut fracture. Dual antiplatelet therapy was continued for at least 1 year, and aspirin (at a dose of at least 81 mg daily) was continued indefinitely.

Clinical follow-up is to be performed through 5 years and is still ongoing. At each follow-up visit, patients are asked about interim clinical events, the presence and severity of anginal symptoms, and the use of cardiovascular medications. The Seattle Angina Questionnaire and other quality-of-life instruments were used to perform assessments at baseline, at 1 month, and at 12 months.

DATA MANAGEMENT

Independent study monitors verified all data from case-report forms. An independent clinical-events committee whose members were unaware of study-group assignments adjudicated major adverse cardiac events. With respect to the end point of thrombosis in the scaffold or stent, adjudication was also blinded, although identification of the device on angiography may have been possible in some instances. Independent angiographic analyses at a core laboratory were performed as described previously.[19] A data and safety monitoring committee reviewed outcome data periodically and recommended that the study continue without modification.

STUDY END POINTS

The primary end point was target-lesion failure (a composite of cardiac death, target-vessel myocardial infarction, or ischemia-driven target-lesion revascularization) at 1 year. Major secondary end points were the 1-year rates of angina (excluding symptoms through the time of hospital discharge), all revascularization, and ischemia-driven target-vessel revascularization.[19] Results of procedural quantitative coronary angiography were reported in-device (within the stent or scaffold, measured edge-to-edge) and in-segment (within the device plus the 5-mm proximal and distal margins). Detailed end-point definitions and additional prespecified secondary end points are listed in the Supplementary Appendix.

STATISTICAL ANALYSIS

We performed a noninferiority analysis for the primary end point. On the basis of FDA guidance, we selected a noninferiority margin of 4.5 percentage points for the risk difference, representing 50% of the lower boundary of the 90% confidence interval of the treatment effect for the everolimus-eluting cobalt–chromium stent as compared with a bare-metal stent.[20] We estimated that the assignment of 2000 patients in a 2:1 ratio to the Absorb group versus the Xience group would provide a power of 96% to demonstrate noninferiority, assuming a rate of target-lesion failure of 7.0% with both devices with a one-sided alpha level of 0.025 and a 5% loss to follow-up.

Noninferiority for the primary end point was tested by means of the likelihood-score method by Farrington and Manning at a one-sided 0.025 level (equivalent to the upper boundary of the two-sided 95% confidence interval).[21] The consistency of the primary end point in nine clinically relevant subgroups was examined with formal interaction testing.

We used Pearson's chi-square test or Fisher's exact test to compare categorical variables and the t-test to compare continuous variables. All principal analyses were performed in the intention-to-treat population, which consisted of all the patients who underwent randomization, regardless of the treatment received. Patients who were lost to follow-up in whom no known event had occurred were not included in the denominator for calculations of binary end points. A post hoc sensitivity analysis was also performed in the as-treated cohort. We used Kaplan–Meier estimates to construct survival curves for time-to-event variables, which were compared by means of the log-rank test. A two-sided P value of less than 0.05 was considered to indicate statistical significance for superiority testing. All statistical analyses were performed with the use of SAS software, version 9.2 (SAS Institute).

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Absorb Scaffold (N=1322)	Xience Stent (N=686)
Age — yr	63.5±10.6	63.6±10.3
Male sex — no. (%)	934 (70.7)	481 (70.1)
White race — no. (%)†	1152 (87.1)	606 (88.3)
Body-mass index‡	30.6±6.2	30.5±6.3
Medical condition — no./total no. (%)		
Hypertension	1122/1322 (84.9)	583/686 (85.0)
Hyperlipidemia	1140/1322 (86.2)	592/686 (86.3)
Diabetes mellitus		
Any	416/1320 (31.5)	224/686 (32.7)
Insulin-treated	138/1320 (10.5)	77/686 (11.2)
Previous myocardial infarction	282/1311 (21.5)	150/681 (22.0)
Renal insufficiency§	143/1319 (10.8)	76/685 (11.1)
Current tobacco use — no. (%)	281 (21.3)	142 (20.7)
Clinical presentation — no./total no. (%)		
Silent ischemia	132/1321 (10.0)	70/686 (10.2)
Angina		
Stable	757/1321 (57.3)	417/686 (60.8)
Unstable	355/1321 (26.9)	168/686 (24.5)
Target-lesion measures		
Coronary-artery location — no./total no. of target lesions (%)		
Left anterior descending	617/1385 (44.5)	301/713 (42.2)
Left circumflex	363/1385 (26.2)	218/713 (30.6)
Right	404/1385 (29.2)	194/713 (27.2)
ACC–AHA lesion class B2 or C — no./total no. of target lesions (%)	949/1381 (68.7)	513/708 (72.5)
Reference vessel diameter — mm	2.67±0.45	2.65±0.46
Minimum luminal diameter — mm	0.92±0.37	0.90±0.34
Diameter stenosis — %	65.3±12.5	65.9±11.7
Lesion length — mm	12.6±5.4	13.1±5.8

* Plus–minus values are means ±SD. Shown are data for patients who were assigned to receive an everolimus-eluting bioresorbable vascular (Absorb) scaffold or an everolimus-eluting cobalt–chromium (Xience) stent. There were no significant differences between groups except for the presence of a lesion in the left circumflex artery (P=0.03) and lesion length (P=0.05). ACC–AHA denotes American College of Cardiology–American Heart Association.
† Race was self-reported.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.
§ Renal insufficiency was defined as an estimated glomerular filtration rate of less than 30 ml per minute per 1.73 m^2 of body-surface area or the need for dialysis.

RESULTS

PATIENTS AND PROCEDURES

From March 19, 2013, to April 3, 2014, we assessed 13,789 patients for eligibility at 202 clinical sites in the United States and Australia. Of the 2008 patients at 193 sites who underwent randomization, 1322 were assigned to receive the Absorb scaffold, and 686 to receive the Xience stent (Fig. S1 in the Supplementary Appendix). The baseline characteristics of the groups were well matched (Table 1).

Despite nominally larger device diameters and more frequent postdilatation, the mean acute gain in minimum lumen diameter and the absolute minimum lumen diameter within the device were less with the Absorb scaffold than with the Xience stent (Table 2). However, there was no significant between-group difference in the in-segment angiographic measures. The use of an unassigned device to complete the procedure was also more frequent in the Absorb group than in the Xience group, and as a result device success rates (as defined in the Supplementary Appendix) were lower in the Absorb group than in the Xience group (Table 2). However, there was no significant difference in the procedural success rates with the two devices (as defined in the Supplementary Appendix).

CLINICAL OUTCOMES

Data regarding 1-year follow-up were complete for 1989 patients (99.1%) (Fig. S1 in the Supplementary Appendix). The use of cardiovascular medications is shown in Tables S1 and S2 in the Supplementary Appendix. There was no significant between-group difference in the use of dual antiplatelet therapy during hospitalization or at 30 days. At 1 year, the use of clopidogrel was less common and the use of prasugrel was more common in the Absorb group than in the Xience group.

The primary end point of target-lesion failure at 1 year occurred in 7.8% of patients in the Absorb group and in 6.1% of patients in the Xience group (risk difference, 1.7 percentage points; 95% confidence interval [CI], −0.5 to 3.9; P=0.007 for noninferiority and P=0.16 for superiority) (Table 3). A time-to-event analysis for the primary end point showed similar results (Fig. 1). At 1 year, the relative rates of target-lesion failure were consistent across subgroups (Fig. 2). In the post hoc as-treated analysis, target-lesion failure at 1 year occurred in 99 of 1245 patients (8.0%) in the Absorb group and in 44 of 726 patients (6.1%) in the Xience group (risk difference, 1.9 percentage points; 95% CI, −0.4 to 4.1; P=0.01 for noninferiority and P=0.12 for superiority) (Table S3 in the Supplementary Appendix).

Individual components of target-lesion failure and other ischemic end points did not differ significantly between the two groups (Table 3). Rates of periprocedural myocardial infarction were not significantly different in the two groups on the basis of either the protocol definition (creatine kinase MB isoform of more than five times the upper limit of the normal range) or criteria that are more or less sensitive than the protocol definition (Table 3, and Table S4 in the Supplementary Appendix). Rates of angina, all revascularization, and ischemia-driven target-vessel revascularization were not significantly different between devices at 1 year (Table 3).

Within 1 year, device thrombosis had occurred in 1.5% of patients in the Absorb group and in 0.7% of those in the Xience group (P=0.13) (Table 3). The rate of subacute device thrombosis (occurring from >24 hours to 30 days after the procedure) was nominally significantly higher in the Absorb group than in the Xience group, whereas the rates of acute device thrombosis (occurring ≤24 hours after the procedure) and late device thrombosis (occurring from >30 days to 1 year after the procedure) were not significantly higher. In the as-treated cohort, thrombosis rates did not differ significantly between the devices during any interval (Table S3 in the Supplementary Appendix). No significant interactions between device type and subgroup with respect to device thrombosis were observed at 1 year (Fig. S2 in the Supplementary Appendix).

DISCUSSION

In our study, the Absorb everolimus-eluting bioresorbable vascular scaffold was within the prespecified noninferiority margin in comparison with the Xience everolimus-eluting cobalt–chromium stent for the primary end point of target-lesion failure at 1 year. In addition, there were no significant differences between the Absorb scaffold and the Xience stent in 1-year rates of angina, total revascularization, and ischemia-driven target-vessel revascularization, the major secondary end points of the trial. At 1 year, the rates of death, myocardial infarction (including periprocedural myocardial infarction), and device thrombosis also did not vary significantly between the two devices, although rates of subacute thrombosis were higher after implantation of the Absorb scaffold.

Conventional metallic stents are associated with an ongoing long-term risk of target-lesion failure.[3,22,23] Such failure may be caused by the presence of a permanent metallic implant that interferes with vasoregulation and chronic adap-

Table 2. Procedural Outcomes.*

Outcome	Absorb Scaffold	Xience Stent	P Value
During procedure			
Patients			
Total no.	1322	686	
Bivalirudin use — no. (%)	803 (60.7)	403 (58.7)	0.39
Glycoprotein IIb/IIIa inhibitor use — no. (%)	133 (10.1)	85 (12.4)	0.11
Treated lesions			
Any lesion†	1.2±0.4	1.2±0.4	0.45
Target lesion	1.0±0.2	1.0±0.2	0.38
Device implantation — no./total no. (%)‡			
Any assigned study device	1262/1322 (95.5)	681/686 (99.3)	<0.001
Only assigned study devices	1240/1322 (93.8)	680/686 (99.1)	<0.001
Any unassigned device	79/1322 (6.0)	4/686 (0.6)	<0.001
Only unassigned devices	58/1322 (4.4)	4/686 (0.6)	<0.001
Unplanned overlapping devices	82/1322 (6.2)	58/686 (8.5)	0.06
Postdilatation performed — no./total no. (%)	866/1322 (65.5)	351/686 (51.2)	<0.001
Intravascular imaging guidance — no./total no. (%)	146/1302 (11.2)	73/673 (10.8)	0.81
Procedure duration — min	42.2±23.1	38.3±20.9	<0.001
Treated lesions			
Total no.	1385	713	
Total study device length — mm	20.5±7.2	20.7±9.0	0.56
Maximum device diameter — mm§	3.18±0.43	3.12±0.45	0.007
Ratio of maximum device diameter to vessel diameter§	1.21±0.15	1.19±0.14	0.054
Maximum device pressure — atm§	15.4±3.0	15.4±3.2	0.83
Device success — no./total no. (%)	1278/1355 (94.3)	699/704 (99.3)	<0.001
After procedure			
Patients			
Total no.	1322	686	
Procedure success — no./total no. (%)	1240/1311 (94.6)	652/678 (96.2)	0.12
Treated lesions			
Total no.	1385	713	
In-device measures			
Acute gain — mm	1.45±0.45	1.59±0.44	<0.001
Minimum luminal diameter — mm	2.37±0.40	2.49±0.40	<0.001
Diameter stenosis — %	11.6±8.8	6.4±8.9	<0.001
In-segment measures			
Acute gain — mm	1.23±0.46	1.24±0.44	0.50
Minimum luminal diameter — mm	2.15±0.41	2.14±0.43	0.58
Diameter stenosis — %	20.0±7.9	19.8±8.2	0.55

* Plus–minus values are means ±SD.
† The lesions include target lesions according to random study-group assignment and nontarget lesions that were not included in the randomization.
‡ Patients who received "only" the assigned study device received the randomly assigned device and no other type of device. Patients who received "any" assigned device received the assigned study device but may also have received other, unassigned devices. Patients who received "any" unassigned device received an unassigned device but may have received an assigned study device. Patients who received "only" unassigned devices did not receive the assigned study device but received other, unassigned devices.
§ Listed is the maximum diameter or pressure of the predilatation balloon, the stent or scaffold delivery-system balloon, or the postdilatation balloon.

Table 3. Safety and Efficacy Outcomes at 1 Year.*

Adverse Event	Absorb Scaffold (N=1322)	Xience Stent (N=686)	Relative Risk (95% CI)	P Value
	no./total no. (%)			
Target-lesion failure	102/1313 (7.8)	41/677 (6.1)	1.28 (0.90–1.82)	0.16
Cardiac death	8/1313 (0.6)	1/677 (0.1)	4.12 (0.52–32.91)	0.29
Target-vessel myocardial infarction	79/1313 (6.0)	31/677 (4.6)	1.31 (0.88–1.97)	0.18
Ischemia-driven target-lesion revascularization	40/1313 (3.0)	17/677 (2.5)	1.21 (0.69–2.12)	0.50
Death from any cause	15/1313 (1.1)	3/677 (0.4)	2.58 (0.75–8.87)	0.12
Any myocardial infarction	90/1313 (6.9)	38/677 (5.6)	1.22 (0.85–1.76)	0.28
Q-wave	10/1313 (0.8)	3/677 (0.4)	1.72 (0.47–6.22)	0.56
Non–Q-wave	80/1313 (6.1)	35/677 (5.2)	1.18 (0.80–1.73)	0.40
During procedure	41/1313 (3.1)	22/677 (3.2)	0.96 (0.58–1.60)	0.88
Not during procedure	49/1313 (3.7)	16/677 (2.4)	1.58 (0.90–2.76)	0.10
Any revascularization	120/1313 (9.1)	55/677 (8.1)	1.12 (0.83–1.53)	0.45
Ischemia-driven	115/1313 (8.8)	54/677 (8.0)	1.10 (0.81–1.50)	0.55
Target vessel	66/1313 (5.0)	25/677 (3.7)	1.36 (0.87–2.14)	0.18
Nontarget vessel	71/1313 (5.4)	39/677 (5.8)	0.94 (0.64–1.37)	0.74
Not ischemia-driven	8/1313 (0.6)	5/677 (0.7)	0.82 (0.27–2.51)	0.77
Target lesion	2/1313 (0.2)	2/677 (0.3)	0.52 (0.07–3.65)	0.61
Target vessel	3/1313 (0.2)	3/677 (0.4)	0.52 (0.10–2.55)	0.42
Nontarget vessel	5/1313 (0.4)	2/677 (0.3)	1.29 (0.25–6.63)	1.00
Patient-reported angina	238/1302 (18.3)	125/678 (18.4)	0.99 (0.82–1.21)	0.93
Definite or probable device thrombosis	20/1301 (1.5)	5/675 (0.7)	2.08 (0.78–5.51)	0.13
Early: 0 to 30 days	14/1315 (1.1)	5/686 (0.7)	1.46 (0.53–4.04)	0.46
Acute: ≤24 hr	2/1320 (0.2)	4/686 (0.6)	0.26 (0.05–1.42)	0.19
Subacute: >24 hr to 30 days	12/1315 (0.9)	1/686 (0.1)	6.26 (0.82–48.04)	0.04
Late: 31 days to 1 yr	6/1299 (0.5)	0/675	NA	0.10
Definite	18/1301 (1.4)	5/675 (0.7)	1.87 (0.70–5.01)	0.21
Probable	2/1301 (0.2)	0/675	NA	0.55

* One-year follow-up includes a window of ±28 days. NA denotes not applicable.

tive vascular responses, which may result in chronic inflammation, neoatherosclerosis, or device fracture.[5,6,10-12] Thus, bioresorbable vascular scaffolds were developed to improve long-term outcomes with contemporary metallic drug-eluting stents. Imaging studies support the novel attributes of bioresorbable scaffolds, with restoration of cyclic pulsatility at the device site 6 months after implantation, restored vasomotion by 12 months, and late lumen gain with plaque regression between 2 and 5 years, benefits that are not possible with permanent metallic stents.[11-14,16,24,25] However, if there are benefits from these attributes, they are likely to become evident only in the longer term. The ongoing ABSORB IV trial (ClinicalTrials.gov number, NCT02173379), which will enroll approximately 5000 patients, has a powered primary end point of improved rates of target-lesion failure at 1 to 5 years after implantation, an outcome that is designed to address this question.

Rates of target-lesion failure at 1 year were 1.7 percentage points higher in the Absorb group than in the Xience group, a nonsignificant difference that met the study criteria for noninferiority. According to the 95% confidence inter-

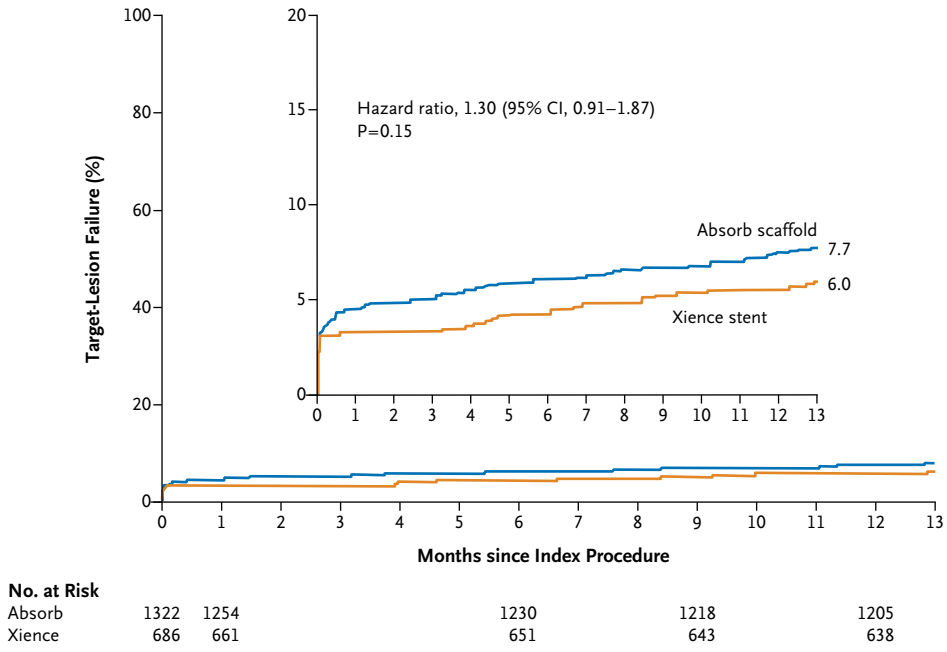

Figure 1. Target-Lesion Failure at 1 Year.

Data for the primary outcome are shown through 13 months, the outside limit of the 1-year follow-up window, for patients who received an everolimus-eluting bioresorbable vascular (Absorb) scaffold or an everolimus-eluting cobalt–chromium (Xience) stent. Shown are Kaplan–Meier estimates, which may differ from the binary event rates reported in the text and in Table 3. The inset graph shows the same data on an enlarged y axis.

val, the rate of failure in the target lesion for the Absorb scaffold at 1 year could range from 0.5 percentage points lower to 3.9 percentage points higher than that of the Xience stent. The difference in rates was somewhat greater in the post hoc analysis of the as-treated cohort, although the criteria for noninferiority were still met. The observed between-group difference in our study is similar to the 1-year difference of 1.8 percentage points in the rate of target-lesion failure between the Absorb scaffold and the Xience stent in the ongoing ABSORB II trial[16] (NCT01425281) but higher than the difference of 0.4 percentage points in the ongoing ABSORB Japan trial[18] (NCT01844284). In the Comparison of Everolimus- and Biolimus-Eluting Stents with Everolimus-Eluting Bioresorbable Vascular Scaffold Stents (EVERBIO II) trial, the 9-month rate of the device-oriented composite end point of cardiac death, myocardial infarction, or target-lesion revascularization was 2.1 percentage points higher with the bioresorbable scaffold than with metallic drug-eluting stents (including the everolimus-eluting cobalt–chromium stent).[17] In each of these cases, event rates were higher with the bioresorbable scaffold than with the metallic stent, although none of the differences were significant. Larger trials (e.g., ABSORB IV) are required to more precisely determine whether there are clinically meaningful differences in the 1-year rates of target-lesion failure between these two devices.

Although 1-year thrombosis rates were not significantly different between the Absorb scaffold and the Xience stent, subacute thrombosis between 1 day and 30 days was more common with the Absorb scaffold in the intention-to-treat analysis (although not in the as-treated cohort). This concern, which was first raised by the early Gauging Coronary Healing with Bioresorbable Scaffolding Platforms in Europe (GHOST-EU) registry,[15] has not been uniformly observed in other registries or randomized trials.[16-18,26] Increased rates of subacute thrombosis with the Absorb scaffold in our study may be attributable to the higher rate of in-device postprocedural residual stenosis than in the Xience stent,[27] possibly because of greater strut thickness or recoil.

Subgroup	Absorb (N=1322)	Xience (N=686)	Risk Ratio (95% CI)	P Value for Interaction
	no. of events/total no. (%)			
All patients	102/1313 (7.8)	41/677 (6.1)	1.28 (0.90–1.82)	
Age				0.69
≥64 yr	54/665 (8.1)	21/355 (5.9)	1.37 (0.84–2.23)	
<64 yr	48/648 (7.4)	20/322 (6.2)	1.19 (0.72–1.97)	
Sex				0.68
Female	33/386 (8.5)	15/203 (7.4)	1.16 (0.64–2.08)	
Male	69/927 (7.4)	26/474 (5.5)	1.36 (0.88–2.10)	
Diabetes mellitus				0.68
Yes	44/411 (10.7)	20/220 (9.1)	1.18 (0.71–1.95)	
No	57/900 (6.3)	21/457 (4.6)	1.38 (0.85–2.24)	
Diagnosis				0.35
Unstable angina or recent myocardial infarction	25/386 (6.5)	12/181 (6.6)	0.98 (0.50–1.90)	
Stable coronary artery disease	77/926 (8.3)	29/496 (5.8)	1.42 (0.94–2.15)	
Target lesion treated				0.50
Single	96/1249 (7.7)	38/651 (5.8)	1.32 (0.92–1.89)	
Dual	6/64 (9.4)	3/26 (11.5)	0.81 (0.22–3.01)	
$P2Y_{12}$ receptor antagonist				0.43
Clopidogrel	66/821 (8.0)	30/438 (6.8)	1.17 (0.77–1.78)	
Prasugrel or ticagrelor	34/479 (7.1)	10/230 (4.3)	1.63 (0.82–3.25)	
Median vessel diameter				0.90
<2.63 mm	65/660 (9.8)	27/347 (7.8)	1.27 (0.82–1.94)	
≥2.63 mm	37/649 (5.7)	14/329 (4.3)	1.34 (0.73–2.44)	
Median lesion length				0.23
<11.75 mm	50/635 (7.9)	16/333 (4.8)	1.64 (0.95–2.83)	
≥11.75 mm	52/673 (7.7)	25/342 (7.3)	1.06 (0.67–1.67)	
ACC–AHA lesion class				0.07
B2 or C	75/914 (8.2)	37/496 (7.5)	1.10 (0.75–1.61)	
A or B1	27/398 (6.8)	4/180 (2.2)	3.05 (1.08–8.60)	

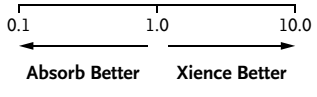

Figure 2. Subgroup Analyses of Target-Lesion Failure at 1 Year.

The P value for interaction represents the likelihood of interaction between the variable and the relative treatment effect. The proportions of patients who received $P2Y_{12}$ receptor antagonists as a procedural loading dose are shown. Patients with multiple target lesions were classified as having a vessel diameter of less than 2.63 mm, a lesion length of 11.75 mm or greater, or a class B2 or C lesion according to the criteria of the American College of Cardiology–American Heart Association (ACC–AHA) if one or more of the treated lesions met these criteria.

The thicker strut dimensions of the bioresorbable scaffold did not translate into greater rates of periprocedural myonecrosis, regardless of biomarker threshold.

In our study at 1 year, there was no significant between-group difference in the rates of ischemia-driven target-lesion revascularization, a finding that was consistent with the results of previous trials.[16-18] The 1-year rates of patient-reported angina were also nearly identical with the two devices. In contrast, during follow-up in the earlier ABSORB II trial, site-reported recurrent angina and severe exercise-induced ischemia were less common with the bioresorbable scaffold than with the cobalt–chromium stent.[16] The reasons for this discordance are unclear. The causes of chest pain after stenting are multifactorial and in addition to ischemia from incomplete revascularization or restenosis may include microcirculatory dysfunction, impaired vasomotion, and strut-fracture–related events.[10-12,28] Neurogenic pain from endoluminal penetration by thin stent struts and nonanginal chest pain may be mistaken as cardiac in origin.[29,30] Although the presence and severity of angina were queried at each follow-up visit in our study, central adjudication was not performed. Further insight may be gleaned from the assessment of data from the Seattle Angina Questionnaire, which is not yet complete. Recurrent angina after interven-

tion with the Absorb scaffold versus the Xience stent is being prospectively examined with greater rigor in the ongoing ABSORB IV trial.

Several limitations of our study should be noted. First, enrollment in ABSORB III was restricted to patients with relatively stable symptoms and noncomplex coronary lesions. Our findings may not be generalizable to patients with acute coronary syndromes and more complex disease. Second, the study was underpowered to examine low-frequency events such as cardiac death and stent or scaffold thrombosis, and interpretation of these rates deserves caution, especially when differences between devices are not significant. For example, the 0.6% cardiac death rate for the Absorb scaffold is within the range of 0.4 to 0.8% observed with the everolimus-eluting cobalt–chromium stent in the previous U.S.-based Clinical Evaluation of the XIENCE V Everolimus-Eluting Coronary Stent System in the Treatment of Subjects with de Novo Native Coronary Artery Lesions (SPIRIT) III and IV trials.[31,32] In contrast, the 0.1% cardiac death rate with the Xience stent in our study was lower than that observed previously. Similarly, the subgroup testing in our study was inherently underpowered. Finally, long-term follow-up from our study and other large-scale clinical trials is required to determine whether there are meaningful late clinical differences between the two devices studied.

In conclusion, in this large-scale randomized trial, treatment of noncomplex coronary lesions with the Absorb everolimus-eluting bioresorbable vascular scaffold was within the prespecified range for noninferiority to the Xience everolimus-eluting cobalt–chromium stent with regard to target-lesion failure at 1 year.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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