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1-Year Outcomes of Everolimus-Eluting Bioresorbable Scaffolds Versus Everolimus-Eluting Stents

A Propensity-Matched Comparison of the GHOST-EU and XIENCE V USA Registries

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ABSTRACT

OBJECTIVES The purpose of this study was to compare the 1-year outcomes of the ABSORB everolimus-eluting bioresorbable scaffold (BRS) (Abbott Vascular, Santa Clara, California) and the XIENCE everolimus-eluting stent (EES) (Abbott Vascular) in patients undergoing percutaneous coronary intervention.

BACKGROUND Randomized studies of the ABSORB BRS have been performed in selected patient and lesion scenarios. The available registries of the ABSORB BRS reflect real-world practice more closely compared with randomized studies, but most of them are limited by the small sample size and the lack of comparative outcomes versus second-generation drug-eluting stents.

METHODS A total of 1,189 consecutive patients treated with ABSORB BRS from the GHOST-EU (Gauging coronary Healing with bioresorbable Scaffolding plaTforms in EUrope) registry and 5,034 patients treated with XIENCE EES from the XIENCE V USA registry were analyzed. Clinical outcomes were compared with the use of propensity-score matching techniques and reported as Kaplan-Meier estimates and absolute risk difference (D) with 95% confidence intervals (CIs). The primary endpoint was a device-oriented composite endpoint, including cardiac death, target vessel myocardial infarction, and ischemia-driven target lesion revascularization at 1-year follow-up.

RESULTS After propensity score matching was performed for the entire population (N = 6,223), there were 905 matched pairs of patients. In the matched cohort (N = 1,810), there was no significant difference between ABSORB BRS and XIENCE EES in the risk of device-oriented composite endpoint at 1 year (5.8% vs. 7.6%, D = −1.8 [95% CI: −4.1 to 0.5]; p = 0.12). Cardiac death was less likely to occur in the ABSORB BRS group (0.7% vs. 1.9%, D = −1.2 [95% CI: −2.2 to 0.2]; p = 0.03), and a trend toward a reduction in myocardial infarction was noted with ABSORB BRS compared with XIENCE EES (2.4% vs. 4.0%, D = −1.6 [95% CI: −3.2 to 0.0]; p = 0.07). Conversely, no differences in ischemia-driven target lesion revascularization (4.6% vs. 3.5%, D = 1.1 [95% CI: −0.7 to 2.9]; p = 0.22) and definite or probable device thrombosis (1.8% vs. 1.1%, D = 0.7 [95% CI: −0.4 to 1.8]; p = 0.23) were detected between ABSORB BRS and XIENCE EES.

CONCLUSIONS In a contemporary large cohort of patients undergoing percutaneous coronary intervention with ABSORB BRS, the combined rate of ischemic events at 1 year was low and nonsignificantly different compared with matched patients treated with XIENCE EES. (J Am Coll Cardiol Intv 2016;9:440–9) © 2016 by the American College of Cardiology Foundation.

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Current-generation drug-eluting stents (DES) have significantly improved the outcomes of percutaneous coronary intervention (PCI) compared with earlier-generation devices (1). In particular, a network meta-analysis of randomized clinical trials identified everolimus-eluting stents (EES) as the benchmark for future studies of upcoming devices in the field due to their lowest rate of thrombosis within 2 years of implantation compared with other DES and bare-metal stents (2). Despite the undeniable advantages of DES, however, permanent vessel caging by metallic struts remains the trigger of numerous potential PCI shortcomings, including vascular inflammation, restenosis, thrombosis, and neoatherosclerosis (1,3).

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Bioresorbable scaffolds (BRS) are emerging as a promising technology to address some of the pending concerns of metallic DES. BRS provide early temporary scaffolding and then disappear, thus liberating the treated vessel from a metallic cage and enabling restoration of important coronary functions that include vasomotion, adaptive shear stress, and expansive remodeling (4). In view of these attributes, the benefits of BRS over current-generation DES are expected to accrue in the long term. Conversely, in the early phase (where the bioresorption process has not started yet), BRS are demanded to exert their scaffolding function analogously to conventional metallic stents. Reassuringly low event rates up to 12 months have been reported so far in early experiences with the ABSORB BRS (Abbott Vascular, Santa Clara, California) mostly conducted in Europe (5–9). By lacking a contemporary control group, however, most of these registries failed in providing important information on the comparative efficacy and safety of ABSORB BRS and current-generation DES. In contrast, the few ABSORB BRS studies where a control group was available were typically limited by the small sample size and/or patients' selection (10–17).

In the GHOST-EU (Gauging coronary Healing with bioresorbable Scaffolding plaTforms in EUrope) registry, the largest series of ABSORB BRS published so far, follow-up information was available in 76% of patients at 6 months and no comparison versus contemporary DES was available (5). These issues complicate the interpretation of the study, which showed acceptable rates of target lesion failure at 6 months but unexpectedly high rates of scaffold thrombosis mainly clustered within 30 days after implantation. To meaningfully reappraise the safety and efficacy of the ABSORB BRS in the GHOST-EU registry, with extended follow-up information now available, and to put these results into perspective of contemporary PCI outcomes with second-generation DES in the real world, we conducted a 1-year comparison of ABSORB BRS versus matched patients from the XIENCE V USA (XIENCE V Everolimus Eluting Coronary Stent System Condition-of-Approval Post-Market; IDE G050050) study, a large, multicenter, post-marketing registry of EES (XIENCE V, Abbott Vascular) (18).

ABBREVIATIONS AND ACRONYMS

BRS = bioresorbable scaffold(s)

DES = drug-eluting stent(s)

DOCE = device-oriented composite endpoint

EES = everolimus-eluting stent(s)

PCI = percutaneous coronary intervention

METHODS

STUDY POPULATION AND DESIGN. Details of the GHOST-EU and XIENCE V USA registries have been published elsewhere (5,18). Briefly, the GHOST-EU registry was an investigator-initiated, retrospective, multicenter, observational, single-arm registry with site-reported data collection and adjudication. The registry included patients undergoing single or multivessel percutaneous coronary intervention with the current generation of the everolimus-eluting ABSORB BRS device at 10 European centers in Germany, Italy, Poland, and the United Kingdom. The XIENCE V USA study was a sponsored, post-marketing, prospective, multicenter, observational, single-arm registry with centrally adjudicated events and 30% random monitoring, including patients treated with the XIENCE EES from 162 sites in 37 states across the United States.

STUDY OUTCOMES. The primary outcome of interest was the 1-year incidence of the Academic Research

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Consortium-defined device-oriented composite endpoint (DOCE), defined as the combination of cardiovascular death, target vessel myocardial infarction, or clinically driven target lesion revascularization, either percutaneous or surgical (19). Secondary outcomes of interest included the components of DOCE and Academic Research Consortium-defined definite or probable device thrombosis. Target vessel myocardial infarction was adjudicated in both groups based on the Third Universal Definition of Myocardial Infarction (20).

STATISTICAL ANALYSIS. Continuous variables are presented as mean ± SD and were compared using a Student unpaired *t* test. Categorical variables are presented as counts and percentages, and were compared using chi-square or Fisher exact tests.

Control of confounders between the GHOST EU and XIENCE V USA datasets was undertaken by propensity score matching. The propensity score is the conditional probability of being part of a group according to a set of measured covariates. A nonparsimonious logistic regression model encompassing 26 baseline demographics, clinical, angiographic, and procedural risk factors was used to calculate the propensity score for each patient (Online Table 1 for the list of variables used to construct the propensity score). A multiple imputation strategy assuming multivariate normality (Markov Chain Monte Carlo method) was used to account for missing values, avoid loss of matchable patients, and reflect uncertainties about the correct value to impute. The average propensity score from multiple imputed datasets was used in patient matching. A Greedy match algorithm with a 1:1 ratio was used to select an equal number of ABSORB BRS patients from the GHOST-EU registry and XIENCE EES patients from the XIENCE V USA registry on the basis of similar propensity scores. A matching distance (i.e., the difference in propensity scores between 2 patients) <0.1 was used as matching criterion. If a subject of the ABSORB BRS group could not be matched to any subject of the XIENCE EES group, that subject was discarded from the matched analysis. Finally, of 1,189 ABSORB BRS patients from GHOST-EU, 905 (76%) patients were matched with XIENCE EES patients from XIENCE V USA.

After all of the propensity-score matches were performed, the baseline covariates were recompared between the 2 groups with statistical tests for matched data. The primary analysis of 12-month outcomes using the raw counts of the 2 groups was deemed invalid because the exposure to the 2 treatment options was unequal due to a lower 1-year follow up retention in the ABSORB BRS group (87% vs. 94%; $p < 0.01$). Therefore, time-to-endpoint event Kaplan-Meier methods were used to provide an exposure-stratified comparison, and survival curves at 12 months were constructed with differences between groups analyzed by a log-rank test. Patients were considered at risk until the date of last contact or at day 365 of follow-up, whichever came first, at which point they were censored. The risks of each outcome were compared with the use of Cox regression models and presented as absolute risk difference (D), hazard ratio (HR) and corresponding 95% confidence interval (CI). All reported p values are 2-sided, and p values <0.05 were considered to indicate statistical significance. All data were processed using the Statistical Package for Social Sciences, version 20.0 (SPSS, IBM, Chicago, Illinois) and SAS/STAT (SAS Institute Inc., Cary, North Carolina).

RESULTS

CHARACTERISTICS OF THE STUDY POPULATION. Characteristics of patients included in the GHOST-EU and XIENCE V USA registries have been previously reported in detail (5,18). Briefly, a total of 1,189 patients undergoing PCI with ABSORB BRS between November 2011 and January 2014 were entered in GHOST-EU and 5,034 patients undergoing stenting with XIENCE EES between July 2008 and December 2008 were entered in XIENCE V USA. The 2 cohorts differed significantly in terms of many potential confounders (**Table 1**). In particular, patients who received ABSORB BRS were younger; more likely to be male; and less likely to present with diabetes, hyperlipidemia, hypertension, renal disease, and history of prior revascularization. Conversely, ABSORB BRS patients were more frequently treated in the context of an acute coronary syndrome, including ST-segment elevation myocardial infarction.

The 2 groups did not differ significantly in terms of the proportion of patients with multivessel coronary artery disease and those with American College of Cardiology (ACC)/American Heart Association (AHA) lesion class B2/C, but ABSORB BRS were more likely to be used in coronary bifurcations and chronic total occlusions, and less likely to be used for ostial and restenotic lesions compared with XIENCE EES. The mean reference vessel diameter of treated lesions was similar between groups, but lesions in the ABSORB BRS group were on average longer (**Table 1**). Clinical outcomes of the 2 unmatched cohorts have been reported previously (5,18).

CHARACTERISTICS OF PATIENTS MATCHED FOR PROPENSITY SCORE. After propensity score matching was performed

TABLE 1 Baseline Characteristics in GHOST-EU Versus XV USA (Analysis Before Match)

	GHOST-EU (n = 1,189)	XV USA (n = 5,034)	Total (N = 6,223)	Difference (95 CI%)	p Value
Age, yrs	62.15 ± 10.99 (1,189)	64.75 ± 11.06 (5,034)	64.26 ± 11.09 (6,223)	−2.60 (−3.30 to −1.91)	<0.0001
Male	79.4 (944/1,189)	68.8 (3,464/5,034)	70.8 (4,408/6,223)	10.58 (7.88 to 13.14)	<0.0001
Current smoker	29.5 (351/1,189)	22.8 (1,082/4,756)	24.1 (1,433/5,945)	6.77 (3.97 to 9.67)	<0.0001
Diabetes	24.8 (295/1,189)	35.7 (1,777/4,977)	33.6 (2,072/6,166)	−10.89 (−13.62 to −8.04)	<0.0001
Diabetes treated with insulin	8.9 (106/1,189)	12.0 (595/4,977)	11.4 (701/6,166)	−3.04 (−4.80 to −1.08)	0.0030
Hyperlipidemia	52.9 (629/1,189)	91.1 (4,443/4,878)	83.6 (5,072/6,067)	−38.18 (−41.12 to −35.24)	<0.0001
Hypertension	73.5 (874/1,189)	88.6 (4,407/4,976)	85.7 (5,281/6,165)	−15.06 (−17.78 to −12.46)	<0.0001
Family history of CAD	32.9 (391/1,189)	54.7 (2,242/4,101)	49.8 (2,633/5,290)	−21.78 (−24.81 to −18.66)	<0.0001
History of PCI	33.6 (399/1,189)	40.1 (1,946/4,851)	38.8 (2,345/6,040)	−6.56 (−9.53 to −3.50)	<0.0001
History of CABG	4.6 (55/1,189)	15.5 (753/4,851)	13.4 (808/6,040)	−10.90 (−12.38 to −9.22)	<0.0001
History of renal disease	14.9 (111/743)	24.1 (1,129/4,689)	22.8 (1,240/5,432)	−9.14 (−11.83 to −6.14)	<0.0001
AMI	34.1 (406/1,189)	10.0 (501/5,034)	14.6 (907/6,223)	24.19 (21.42 to 27.05)	<0.0001
ACS	47.4 (563/1,189)	32.6 (1,643/5,034)	35.4 (2,206/6,223)	14.71 (11.60 to 17.83)	<0.0001
Multiple vessel disease	59.1 (701/1,186)	59.2 (2,978/5,034)	59.1 (3,679/6,220)	−0.05 (−3.18 to 3.03)	0.9741
NSTEMI	18.0 (214/1,189)	7.3 (369/5,034)	9.4 (583/6,223)	10.67 (8.46 to 13.06)	<0.0001
STEMI	16.1 (192/1,189)	2.6 (132/5,034)	5.2 (324/6,223)	13.53 (11.49 to 15.76)	<0.0001
Left main vessel	1.4 (16/1,176)	2.2 (111/5,033)	2.0 (127/6,209)	−0.84 (−1.53 to 0.07)	0.0653
ACC/AHA lesion class (B2/C)	53.8 (599/1,113)	52.4 (2,203/4,205)	52.7 (2,802/5,318)	1.43 (−1.87 to 4.71)	0.3960
De novo lesions	96.1 (1,143/1,189)	88.6 (4,460/5,032)	90.1 (5,603/6,221)	7.50 (5.99 to 8.82)	<0.0001
Chronic total occlusion	7.9 (94/1,189)	2.9 (140/4,824)	3.9 (234/6,013)	5.00 (3.51 to 6.73)	<0.0001
Ostial lesion	7.8 (82/1,046)	15.5 (727/4,691)	14.1 (809/5,737)	−7.66 (−9.48 to −5.61)	<0.0001
Bifurcated lesion	26.7 (317/1,189)	10.7 (538/5,026)	13.8 (855/6,215)	15.96 (13.37 to 18.67)	<0.0001
Post-dilation	51.1 (607/1,189)	57.5 (2,897/5,034)	56.3 (3,504/6,223)	−6.50 (−9.65 to −3.35)	<0.0001
Target lesion length, mm	20.42 ± 15.18 (850)	17.48 ± 10.61 (4,760)	17.92 ± 11.47 (5,610)	2.94 (1.88 to 4.01)	<0.0001
Lesion RVD, mm	2.96 ± 0.52 (861)	2.97 ± 0.52 (4,811)	2.96 ± 0.52 (5,672)	−0.00 (−0.04 to 0.03)	0.8520
Pre-procedure DS	85.19 ± 13.27 (988)	86.02 ± 10.17 (5,010)	85.88 ± 10.75 (5,998)	−0.83 (−1.70 to 0.05)	0.0630

Values are mean ± SD (N) or % (n/N). p Values are from *t* test for continuous variables and chi-square or Fisher tests for binary variables.

ACC = American College of Cardiology; ACS = acute coronary syndrome; AHA = American Heart Association; AMI = acute myocardial infarction; CABG = coronary artery bypass graft; CAD = coronary artery disease; CI = confidence interval; DS = diameter stenosis; NSTEMI = non-ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; RVD = reference vessel diameter; STEMI = ST-segment elevation myocardial infarction.

for the entire population (N = 6,223), there were 905 matched pairs of patients (Table 2). In this matched cohort, the mean age was 63 years, men accounted for 78% of patients, and diabetes mellitus was recorded in 27%. A total of 42% of patients presented with an acute coronary syndrome, 59% had multivessel disease, and 55% had 1 or more ACC/AHA B2/C lesion(s). The mean lesion reference vessel diameter and length were 3 and 18 mm, respectively. In the matched cohorts, there was no longer any significant difference between the ABSORB BRS and the XIENCE EES group for any covariate (Table 2).

1-YEAR OUTCOMES OF THE MATCHED COHORTS. Table 3 reports Kaplan-Meier estimates of the matched ABSORB BRS and XIENCE EES cohorts, along with absolute and relative risk estimates at 1 year. Corresponding Kaplan-Meier curves are shown in Figures 1 and 2. There was no significant difference between matched ABSORB BRS and XIENCE EES in the Kaplan-Meier estimates of DOCE during the 1-year follow-up period (5.8% ABSORB BRS vs. 7.6% XIENCE EES, D = −1.8 [95% CI: −4.1 to 0.5]; p = 0.12). Among DOCE components, there was no observable difference between ABSORB BRS and XIENCE EES in terms of clinically driven target lesion revascularization (4.6% ABSORB BRS vs. 3.5% XIENCE EES, D = 1.1 [95% CI: −0.7 to 2.9]; p = 0.22). However, at 1 year, the rate of cardiovascular death was significantly lower in patients with ABSORB BRS compared with XIENCE EES (0.7% ABSORB BRS vs. 1.9% XIENCE EES, D = −1.2 [95% CI: −2.2 to 0.2]; p = 0.03) and there was a trend towards a reduction in target vessel myocardial infarction with ABSORB BRS (2.4% ABSORB BRS vs. 4.0% XIENCE EES, D = −1.6 [95% CI: −3.2 to 0.0]; p = 0.07). Finally, there was no observable difference between ABSORB BRS and XIENCE EES in terms of definite or probable device thrombosis (1.8% ABSORB BRS vs. 1.1% XIENCE EES, D = 0.7 [95% CI: −0.4 to 1.8]; p = 0.23).

DISCUSSION

The main findings of this observational study can be summarized as follows. First, patients who were implanted with ABSORB BRS in the GHOST-EU registry had very different characteristics compared with

TABLE 2 Baseline Characteristics in GHOST-EU Versus XV USA (Analysis After Match)

	GHOST-EU (n = 905)	XV USA (n = 905)	Total (N = 1,810)	Difference (95% CI)	p Value
Age, yrs	62.75 ± 10.65 (905)	63.04 ± 11.02 (905)	62.89 ± 10.83 (1,810)	−0.29 (−1.28 to 0.71)	0.5745
Male	77.9 (705/905)	77.9 (705/905)	77.9 (1,410/1,810)	0.00 (−3.82 to 3.82)	1.0000
Current smoker	28.4 (257/905)	27.8 (240/862)	28.1 (497/1,767)	0.56 (−3.64 to 4.74)	0.7952
Diabetes	27.5 (249/905)	27.1 (240/887)	27.3 (489/1,792)	0.46 (−3.67 to 4.57)	0.8284
Diabetes treated with insulin	9.8 (89/905)	9.0 (80/887)	9.4 (169/1,792)	0.82 (−1.91 to 3.54)	0.5550
Hyperlipidemia	67.2 (608/905)	67.8 (582/858)	67.5 (1,190/1,763)	−0.65 (−5.01 to 3.72)	0.7709
Hypertension	78.9 (714/905)	78.9 (699/886)	78.9 (1,413/1,791)	0.00 (−3.78 to 3.78)	0.9995
Family history of CAD	37.3 (338/905)	37.7 (276/733)	37.5 (614/1,638)	−0.31 (−5.02 to 4.39)	0.8990
History of PCI	35.5 (321/905)	35.3 (309/875)	35.4 (630/1,780)	0.16 (−4.28 to 4.59)	0.9454
History of CABG	5.9 (53/905)	5.1 (45/875)	5.5 (98/1,780)	0.71 (−1.43 to 2.86)	0.5094
History of renal disease	16.0 (94/588)	19.3 (164/848)	18.0 (258/1,436)	−3.35 (−7.27 to 0.70)	0.1036
AMI	26.2 (237/905)	27.2 (246/905)	26.7 (483/1,810)	−0.99 (−5.06 to 3.08)	0.6325
ACS	42.3 (383/905)	42.5 (385/905)	42.4 (768/1,810)	−0.22 (−4.76 to 4.32)	0.9242
Multiple vessel disease	57.9 (522/902)	59.8 (541/905)	58.8 (1,063/1,807)	−1.91 (−6.43 to 2.63)	0.4100
NSTEMI	15.5 (140/905)	16.7 (151/905)	16.1 (291/1,810)	−1.22 (−4.60 to 2.17)	0.4815
STEMI	10.7 (97/905)	10.5 (95/905)	10.6 (192/1,810)	0.22 (−2.63 to 3.07)	0.8787
Left main vessel	1.3 (12/895)	1.0 (9/905)	1.2 (21/1,800)	0.35 (−0.71 to 1.44)	0.4939
ACC/AHA lesion class (B2/C)	54.6 (454/832)	54.7 (415/759)	54.6 (869/1,591)	−0.11 (−4.99 to 4.78)	0.9649
De novo lesions	95.4 (863/905)	95.1 (861/905)	95.2 (1,724/1,810)	0.22 (−1.77 to 2.22)	0.8251
Chronic total occlusion	7.7 (70/905)	7.5 (65/865)	7.6 (135/1,770)	0.22 (−2.28 to 2.71)	0.8614
Ostial lesion	8.2 (65/797)	10.9 (93/853)	9.6 (158/1,650)	−2.75 (−5.59 to 0.10)	0.0581
Bifurcated lesion	22.0 (199/905)	22.5 (203/902)	22.2 (402/1,807)	−0.52 (−4.35 to 3.32)	0.7918
Post-dilation	51.9 (470/905)	50.8 (460/905)	51.4 (930/1,810)	1.10 (−3.49 to 5.70)	0.6382
Target lesion length, mm	20.05 ± 14.86 (654)	19.72 ± 12.94 (850)	19.86 ± 13.80 (1,504)	0.33 (−1.10 to 1.77)	0.6486
Lesion RVD, mm	2.97 ± 0.53 (663)	2.95 ± 0.54 (868)	2.96 ± 0.53 (1,531)	0.02 (−0.03 to 0.07)	0.4898
Pre-procedure DS	85.49 ± 12.75 (742)	85.38 ± 10.61 (900)	85.43 ± 11.62 (1,642)	0.11 (−1.04 to 1.26)	0.8556

Values are mean ± SD (N) or % (n/N). p Values are from tests for matched data.
Abbreviations as in Table 1.

those who received XIENCE EES in the XIENCE V USA registry: they were typically younger, presented with less coronary risk factors and comorbidities, and were more likely to be treated in the context of acute coronary syndromes and long lesions. Second, after accounting for these multiple confounders by propensity score matching, there were no differences between ABSORB BRS and XIENCE EES at 1 year in terms of a patient-oriented composite endpoint of cardiovascular death, target vessel myocardial infarction, and ischemia-driven target lesion revascularization. In aggregate, these findings suggest a substantial degree of patient and lesion selection in contemporary daily use of ABSORB BRS, translating into midterm outcomes that resemble those of matched second-generation XIENCE EES.

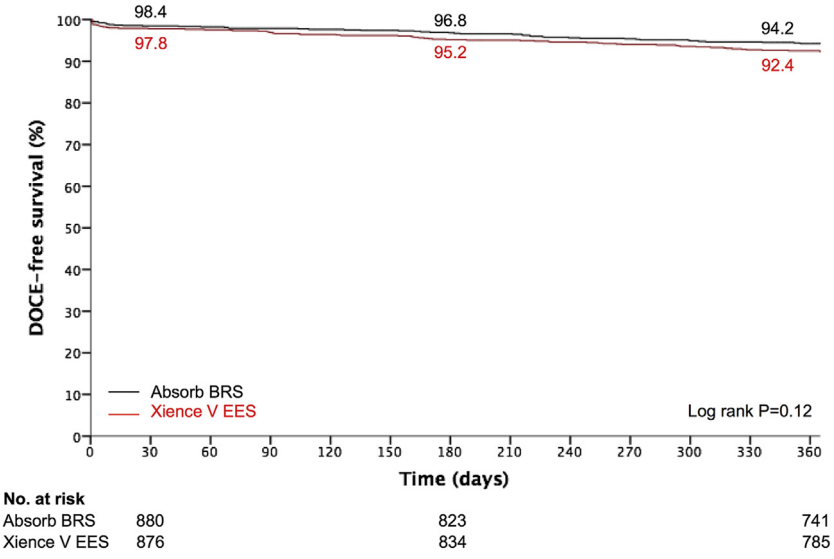
CHARACTERISTICS OF ABSORB BRS AND EES PATIENTS IN THE PRESENT STUDY. Our cross-sectional comparison of 2 large multicenter registries of ABSORB BRS and XIENCE EES enables a number of considerations on the contemporary use of coronary scaffolds across

TABLE 3 Kaplan-Meier Estimates and Treatment Effects of ABSORB BRS Versus EES at 1 Year

	ABSORB BRS (%)	XIENCE EES (%)	Difference (95% CI)	Hazard Ratio (95% CI)	p Value
Device-oriented composite endpoint	5.8	7.6	−1.8 (−4.1 to 0.5)	0.75 (0.52 to 1.08)	0.12
Cardiovascular death	0.7	1.9	−1.2 (−2.2 to −0.2)	0.36 (0.14 to 0.92)	0.025
Target vessel myocardial infarction	2.4	4.0	−1.6 (−3.2 to 0.0)	0.61 (0.36 to 1.05)	0.07
Clinically driven target lesion revascularization	4.6	3.5	+1.1 (−0.7 to 2.9)	1.35 (0.84 to 2.17)	0.22
Definite or probable device thrombosis	1.8	1.1	+0.7 (−0.4 to 1.8)	1.62 (0.73 to 3.57)	0.23

Percentages are reported as 12-month Kaplan-Meier estimates.
BRS = bioresorbable scaffold(s); CI = confidence interval; EES = everolimus-eluting stent(s).

FIGURE 1 Kaplan-Meier–Free Survival From the DOCE

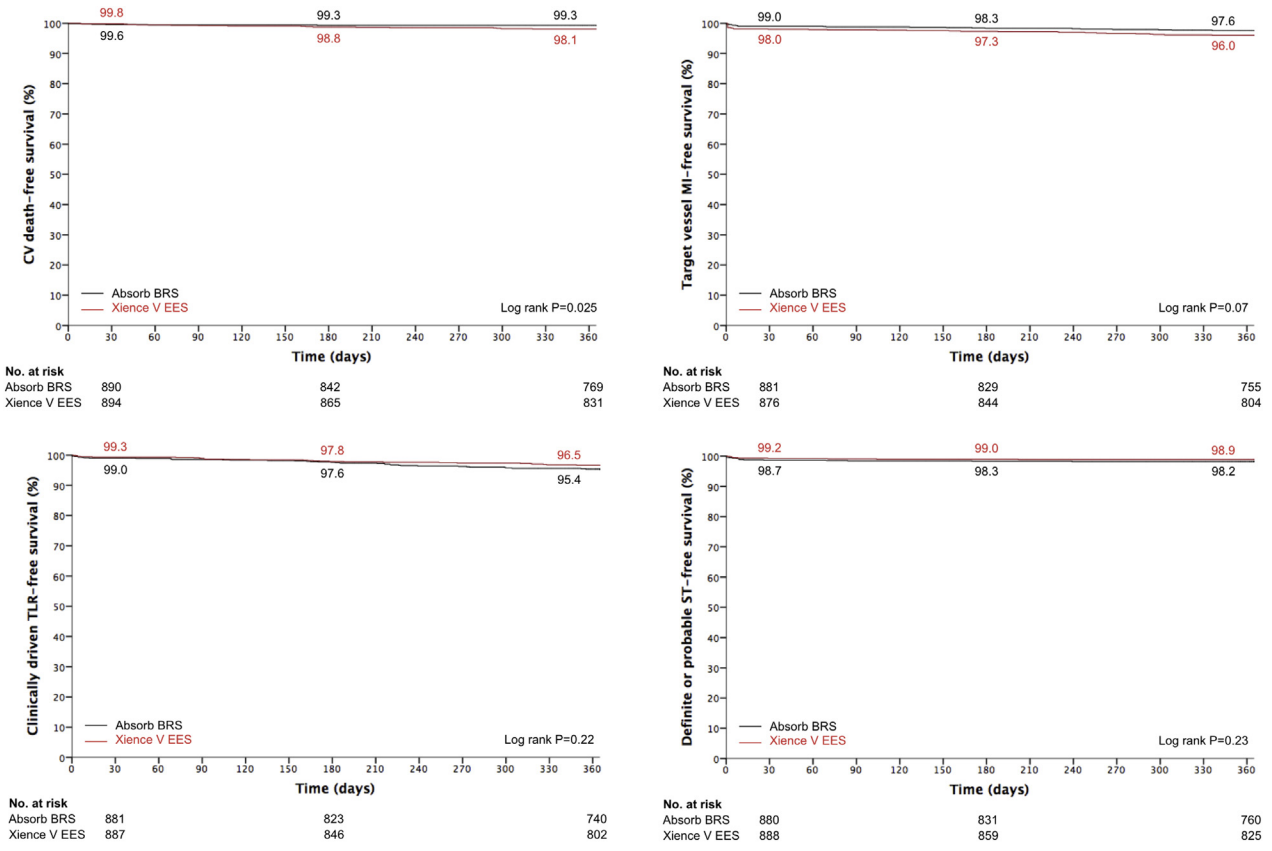


BRS = bioresorbable scaffold(s); DOCE = device-oriented composite endpoint; EES = everolimus-eluting stent(s).

different countries and local practices. First, patients who received scaffolds were younger than their XIENCE EES counterparts and were more likely to present with acute coronary syndromes. Indeed, clinical, intracoronary imaging, and vasomotion data appear to provide a rationale for the use of ABSORB BRS in the setting of acute coronary syndromes (7). Second, compared with XIENCE EES, ABSORB BRS were more likely to be implanted in bifurcation lesions, long lesions, and chronic total occlusions and less likely to be used in ostial and restenotic lesions. This is consistent with a recent European survey (21), and is not surprising because 1 common perception about scaffolds is their potential role where complex coronary reconstructions are needed, which otherwise would require long chains of metallic stents to be placed, or permanent layering of struts. Conversely, in GHOST-EU, scaffolds were less likely to be placed in lesions where high radial strength is necessary (i.e., ostial, in-stent restenosis), in keeping with observational data from bench testing (22).

PREVIOUS STUDIES OF ABSORB BRS VERSUS DES. Six randomized studies have reported comparative data of ABSORB BRS versus DES so far. In the ABSORB II trial, ABSORB BRS were compared 2:1 to XIENCE EES in 501 patients with mostly ACC/AHA class B lesions (13). At 1 year, there were no differences between the ABSORB BRS and XIENCE EES groups in terms of clinical endpoints, with the notable exception of a trend toward more protocol-defined myocardial infarctions in the ABSORB BRS group. DOCE occurred in 5% of patients in the ABSORB BRS group and 3% of patients in the XIENCE EES group (D = 1.80, 95% CI: −2.48 to 5.16; p = 0.35). Another trial, EVERBIO II (Comparison of Everolimus- and Biolimus-Eluting Stents With Everolimus-Eluting Bioresorbable Vascular Scaffold Stents II), randomly assigned 240 patients with ~30% of ACC/AHA class B2/C lesions in a 1:1:1 fashion to PROMUS ELEMENT EES (Boston Scientific, Natick, Massachusetts), biolimus-eluting stents, or ABSORB BRS (n = 78) (12). At 9 months, DOCE were 12% in ABSORB BRS and 9% in the DES combined group (p = 0.6). In TROFI II (Thrombus Aspiration on Flow Area in Patients With ST-Elevation Myocardial Infarction II) (n = 191), a trial of ABSORB BRS and XIENCE XPEDITION EES conducted in patients with ST-segment elevation myocardial infarction, the device-oriented composite endpoint was comparably low between groups (1.1% ABSORB BRS vs. 0% XIENCE XPEDITION EES) at 6 months, with only 1 patient in the ABSORB BRS group experiencing a subacute definite stent thrombosis (15). In ABSORB-Japan, 400 patients were enrolled and 2:1 randomly assigned to ABSORB BRS (n = 266) or XIENCE EES (n = 134). DOCE through 12 months was 4.2% with ABSORB BRS and 3.8% with XIENCE EES (p for noninferiority = 0.0001) (14). ABSORB-CHINA randomized 480 patients 1:1 to ABSORB BRS (n = 241) or XIENCE EES (n = 239), with DOCE at 12 months being 2.4% and 4.2%,

FIGURE 2 Kaplan-Meier–Free Survival From Cardiac Death, Target Vessel MI, TLR, and Definite or Probable ST



MI = myocardial infarction; ST = stent thrombosis; TLR = target lesion revascularization; other abbreviations as in Figure 1.

respectively (p = 0.62) (16). Finally, the pivotal U.S. trial ABSORB III randomized 2:1 a total of 1,322 patients to ABSORB BRS and 686 patients to XIENCE EES (17). DOCE rates at 1 year were 7.8% in the ABSORB BRS group and 6.1% in the XIENCE EES group (p for non-inferiority = 0.007 and p for superiority = 0.16). Two registries have also compared ABSORB BRS and XIENCE EES with the use of propensity score matching techniques. Brugaletta et al. (10) matched 290 ABSORB BRS patients undergoing primary PCI in the context of ST-segment elevation myocardial infarction with a corresponding cohort of patients who received XIENCE EES in the same setting. The cumulative incidence of DOCE did not differ between ABSORB BRS and XIENCE EES at 1 year (4.1% vs. 4.1%; p = 0.994), but the definite or probable ABSORB BRS thrombosis rate was 1% higher compared with XIENCE EES thrombosis (2.4% vs. 1.4%; p = 0.948). In a matched comparison of diabetic patients from the ABSORB EXTEND and SPIRIT (Clinical Evaluation of the Xience V Everolimus Eluting Coronary Stent System in the Treatment of Patients with de novo Native Coronary Artery Lesions) I to IV studies, those treated with ABSORB BRS (n = 102) had a similar incidence of 1-year DOCE compared with those treated with XIENCE EES (3.9% vs. 6.4%; p = 0.38) (11). In aggregate, the ability of most of these studies to detect differences in clinical endpoints is hampered by the low number of ABSORB BRS patients included. In addition, all of the randomized comparisons applied a number of clinical and angiographic exclusion criteria.

COMPARATIVE OUTCOMES OF ABSORB BRS AND XIENCE EES IN THE MATCHED COHORTS. At 1 year, the rate of DOCE in our matched cohort of ABSORB BRS (n = 905) was found to be 5.8%. In a previous report of the unmatched GHOST-EU population, the rate of DOCE at 6 months was 4.4%. In the present study, the observed rate of DOCE was not statistically different

compared with matched XIENCE EES patients from the XIENCE V USA registry ($p = 0.12$) and is in the range of composite events reported in ABSORB II (5%), ABSORB-JAPAN (4.2%), and ABSORB III (6.1%), although more complex patient and lesion characteristics were included in our registry. Notably, the upper 95% confidence limit of the absolute risk reduction with ABSORB BRS versus XIENCE EES excluded differences in DOCE >0.5%. This is important, because the benefits of ABSORB BRS are expected to be apparent at long term, when bioresorption liberates the vessel from permanent caging and vessel functions are restored (4). Therefore, the finding that ABSORB BRS show a comparable performance to that of XIENCE EES at 1 year (the timeframe where restenosis may be more likely to occur) is promising.

We found a statistically significant reduction in cardiac mortality and a trend toward a reduction in target vessel myocardial infarction with BRS. These findings are difficult to explain, particularly in view of the numerically higher, yet not statistically different rate of device thrombosis observed in the BRS compared with the EES group. Notably, propensity matching did not account for the differential use of newer $P2Y_{12}$ inhibitors in the ABSORB BRS and XIENCE EES groups, with patients in GHOST-EU being on prasugrel or ticagrelor in about 25% of cases, and patients in XIENCE V USA being almost invariably on clopidogrel. Also, dual antiplatelet therapy was prescribed for 12 months in 94% of patients in GHOST-EU, whereas ~25% of patients in XIENCE V USA were not on clopidogrel at 1 year. Whether these different antiplatelet regimens may have played a role in the observed reductions in cardiac mortality and myocardial infarction with ABSORB BRS compared with XIENCE EES remains speculative. In addition, alternative arguments can be advocated that do not actually support the conclusion of BRS reducing cardiac mortality compared with EES, including biological implausibility, the presence of unidentified confounders, differences in follow-up availability between 6 months and 1 year, and, ultimately, the play of chance. That being said, it is notable that in this propensity score matched study, BRS were at least not found to significantly increase cardiovascular mortality and myocardial infarction compared with EES, which provides reassurance on the post-marketing performance of the device at 1 year.

Scaffold thrombosis occurred in 1.8% of matched ABSORB BRS patients at 1 year versus 1.1% of stent thrombosis in the EES group. In an earlier publication of the GHOST-EU registry (overall cohort), the Kaplan-Meier estimate of scaffold thrombosis was 2.1% at 6 months, when follow-up was available in 76% of patients (5). The profile of the event-free survival curve for the ABSORB BRS (**Figure 2**) clearly indicates that most of the events occurred in the first 6 months after scaffold implantation, and particularly within the first 30 days, with relatively fewer events between 6 and 12 months. Clustering of events in the first month may suggest a role for procedural factors, which underscores the need for optimal patient selection and implantation techniques (21,23). Indeed, GHOST-EU represents the initial experience of the participating centers with the ABSORB BRS technology, and new iterations of the device along with better patient selection and implantation techniques are expected to ameliorate the rates of early scaffold thrombosis in the future. With all of these points taken into consideration, it is encouraging that the rate of thrombosis with ABSORB BRS in our study was not statistically different to that observed with matched XIENCE EES in the same time period, although the 95% CI for the true absolute risk reduction with ABSORB BRS was quite large and did not exclude potentially relevant differences up to 1.8%. Head-to-head studies of ABSORB BRS and XIENCE EES and meta-analyses in larger populations are, therefore, necessary to clarify this issue.

STUDY STRENGTHS AND LIMITATIONS. Our study collected more complex patients and lesions than those included in the randomized ABSORB II, EVERBIO II, TROFI II, ABSORB-JAPAN, ABSORB-CHINA, and ABSORB III trials, where multiple restrictions applied. Thanks to the availability of the large XIENCE V USA cohort for this analysis, we were able to match three-fourths of the 1,189 patients included in the original GHOST-EU publication (Online Table 2 for a comparison of matched versus unmatched patients in GHOST-EU).

On the other hand, this study carries a number of limitations. The most important limitation is the lack of a random assignment to the treatment groups. Evaluating the effect of a specific treatment using a registry can lead to incorrect conclusions because of the influence of unidentified confounding variables. To partly compensate for the baseline and angiographic imbalance between the ABSORB BRS and XIENCE EES groups, we performed adjustment with propensity score matching, minimizing residual selection biases. It is impossible to know if these adjustments are appropriate or if the relevant characteristics have been correctly identified, because only randomization can provide an unbiased estimation of the effects of a treatment. On this background, the study showed comparable outcomes between ABSORB BRS and XIENCE EES at 1 year, which partly

addresses the important and urgent questions regarding the midterm safety and efficacy of ABSORB BRS in contemporary practice. Another caveat is the 7% difference in the loss at follow-up between the ABSORB BRS and the XIENCE EES group, resulting in unequal duration of exposure to the risk of events, which complicates the interpretation of the results. Loss of more patients in the ABSORB BRS than in the XIENCE EES group depends on the different nature and quality of the 2 registries (GHOST-EU was an investigator-initiated, retrospective study; XIENCE V USA was a sponsored, post-marketing, prospective study). We sought to partly address this limitation by using Kaplan-Meier methods. Finally, our results need to be interpreted with caution because of the theoretical bias arising from potential under-reporting in GHOST-EU (where all events were site-reported), whereas 30% random monitoring with 100% source verification was undertaken in XIENCE V USA.

CONCLUSIONS

In a contemporary large cohort of patients undergoing PCI with ABSORB BRS, the combined rate of ischemic events at 1 year was low and nonsignificantly different compared with matched patients treated with XIENCE EES.

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PERSPECTIVES

WHAT IS KNOWN? BRS have shown promising outcomes in early registries and randomized studies, but their comparative efficacy and safety versus second-generation DES in the real world remains uncertain.

WHAT IS NEW? At 1 year, BRS showed comparable results to those of matched second-generation DES, with low event rates.

WHAT IS NEXT? Large randomized trials with long follow-up in relatively unselected patients and lesions are needed to clarify the pending efficacy and safety questions surrounding BRS.

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KEY WORDS bioresorbable scaffolds, drug-eluting stent(s), propensity score

APPENDIX For supplemental tables, please see the online version of this article.