THREE-YEAR CLINICAL OUTCOMES OF THE ABSORB BIORESORBABLE VASCULAR SCAFFOLD COMPARED TO XIENCE EVEROLIMUS-ELUTING STENT IN ROUTINE PCI IN PATIENTS WITH DIABETES MELLITUS—AIDA SUB-STUDY

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Abstract

Background: In this prespecified AIDA-trial sub-study we investigate the clinical performance of absorb bioresorbable vascular scaffold (BVS) compared to Xience everolimus-eluting stent (EES) in routine percutaneous coronary intervention (PCI) in patients with diabetes mellitus (DM) at complete 3-year follow-up.

Methods and results: All 1,845 randomized patients were subdivided by medical history with DM or without DM. Of the 924 Absorb BVS patients, 171 (18.5%) patients had DM, of which 65 (38.0%) were treated with insulin (iTDM). Of the 921 Xience EES patients, 153 (16.6%) patients had DM, of which 45 (29.4%) were insulin-treated diabetes mellitus (iTDM). Target vessel failure (TVF), composite of cardiac death, target vessel myocardial infarction, and target vessel revascularization, occurred in 18.7% of diabetic patients treated with Absorb patients versus in 18.0% patients treated with Xience EES (p = .840). In nondiabetics the rates of TVF were 12.3% in Absorb BVS versus 11.0% in Xience EES (p = .391). Definite/probable device thrombosis occurred more frequently in Absorb BVS compared to Xience EES.

Abbreviations: Absorb BVS, absorb bioresorbable vascular scaffold; DM, diabetes mellitus; iTDM, insulin-treated diabetes mellitus; oTDM, oral-treated diabetes mellitus; PCI, percutaneous coronary intervention; TLF, target lesion failure; TLR, target lesion revascularization; TVF, target vessel failure; TV-MI, target vessel myocardial infarction; Xience EES, Xience everolimus-eluting stent.

The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation. Any author unable to make this statement must instead state their specific contribution to the manuscript.

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1 | INTRODUCTION

Diabetic patients represent a major challenge for the interventional cardiologists as they have more rapidly progressing coronary artery disease, and more often have long coronary lesions, when compared to nondiabetic patients. Despite advances in pharmacotherapy, revascularization techniques, and advances in-stent technology, diabetes mellitus (DM) still remains a significant predictor of adverse clinical and angiographic outcomes after percutaneous coronary intervention (PCI).1,2 This higher risk of adverse events may be due to their pronounced chronic coronary inflammation and abnormal vessel healing.3,4

The design of the absorb bioresorbable vascular scaffolds (BVS) is pinnacled around the concept of providing temporary coronary vessel scaffolding after PCI, and allowing for complete coronary vessel healing after the scaffold has been resorbed.5 Given the increased peri-strut inflammation in patients with DM, absorb BVS implantation might be associated with favorable clinical outcomes after PCI in diabetic patients, since the inflammation induced by the foreign body of the implant might be transient.8,9 The Amsterdam Investigator-Initiated Absorb Strategy All-Comers (AIDA) trial is a randomized (1:1) clinical trial that compared the absorb BVS with the Xience everolimus-eluting stent (EES) in a population that reflects routine clinical PCI practice. At 2-year follow-up, Absorb BVS was noninferior to Xience EES for the primary endpoint of target vessel failure (TVF).10 Absorb BVS was, however, associated with increased risk of device thrombosis that continued to accrue until 3-year follow-up.11 The goal of the current AIDA-trial sub-study is to provide insights in the clinical outcomes in diabetic versus nondiabetic patients at complete 3-year follow-up; a significant landmark in the resorption progress of the absorb BVS.

2 | MATERIALS AND METHODS

2.1 | Study design AIDA trial

The AIDA trial was a multicenter, investigator-initiated, randomized controlled trial. The study design,12 the preliminary safety report,13 2-year10 and 3-year11 results have been published previously. Briefly, in both diabetic and nondiabetic patients (4.8% versus 0.7%; p = .028 and 3.2% vs. 0.5%; p < .001, respectively).

Conclusions: In routine PCI practice, both Absorb BVS and Xience EES have worse clinical outcomes in diabetic patients as compared to nondiabetic patients. Throughout all clinical presentations, Absorb BVS was associated with higher rates of device thrombosis at 3-year follow-up.

KEYWORDS
bioresorbable scaffolds, diabetes mellitus, drug eluting stents
based predictors of LOCE in diabetic patients were calculated by univariate and multivariate logistic regression. All statistical analyses were performed with use of SPSS software, version 23 (IBM Corp., Armonk NY).

4 | RESULTS

4.1 Baseline, procedural, and QCA characteristics

In the absorb BVS group, 171 (18.5%) patients had DM, of which 95 (55.6%) patients were treated with oral medication (oTDM) and 65 (38.0%) patients were treated with insulin (iTDM). In the Xience EES group, 153 (16.6%) patients had DM, of which 97 (63.4%) patients were oTDM and 45 (29.4%) iTDM.

Compared with patients without DM, patients with DM were older and more frequently had coexisting cardiovascular risk factors including history of smoking, hypertension, and hyperlipidemia. Diabetic patients presented less frequently with ST-segment elevation myocardial infarction (17.6 vs. 26.8%, \( p < .001 \)) and more often with stable angina (48.5 vs. 37.7%, \( p < .001 \)). The baseline demographic and clinical characteristics of the randomized absorb BVS- and Xience EES-treated groups were well matched in patients with and without DM (Table 1).

In diabetic patients, the implantation rate of any assigned study device was lower compared to nondiabetics (96.0 vs. 98.8%, \( p < .001 \)). Patients with DM had more often moderate/severe calcified lesions compared with patients without DM (37.8 vs. 24.8%, \( p < .001 \)). Procedural and QCA characteristics are described in Table 2. In diabetic patients, post-dilatation was more frequently performed in Absorb BVS compared to Xience EES (Table 2). Among non-DM, lesions were less frequently moderate/severe calcified in Xience EES compared to Absorb BVS (Table 2). Other procedural and QCA characteristics did not differ among DM and non-DM patients treated with Absorb BVS and Xience EES. Multivariate analysis

### TABLE 1 Baseline characteristics

|                          | Diabetic patients | Nondiabetic patients | \( p \)-value | Diabetic patients | Nondiabetic patients | \( p \)-value |
|--------------------------|------------------|----------------------|--------------|------------------|----------------------|--------------|
| Age                      | 66.14 ± 10.13    | 66.48 ± 9.43         | .753         | 63.86 ± 10.70    | 64.46 ± 10.68        | -            |
| Male sex                 | 112 (65.5%)      | 106 (69.3%)          | .479         | 558 (74.1%)      | 594 (77.3%)          | .151         |
| Diabetic treatment       |                  |                      |              |                  |                      |              |
| Oral medication          | 95 (55.6%)       | 97 (63.4%)           | .174         | n/a              | n/a                  | n/a          |
| Insulin                  | 65 (38.0%)       | 45 (29.4%)           | .126         | n/a              | n/a                  | n/a          |
| None                     | 8 (4.7%)         | 10 (6.5%)            | .479         | n/a              | n/a                  | n/a          |
| Unknown                  | 3 (1.8%)         | 1 (0.7%)             | .625         | n/a              | n/a                  | n/a          |
| Risk factors             |                  |                      |              |                  |                      |              |
| Hypertension             | 123 (71.9%)      | 107 (70.4%)          | .806         | 345 (46.1%)      | 357 (46.5%)          | .877         |
| Hypercholesterolemia     | 98 (57.6%)       | 78 (51.3%)           | .264         | 246 (33.0%)      | 272 (35.7%)          | .279         |
| Family history of CAD    | 72 (42.1%)       | 74 (52.5%)           | .169         | 379 (52.3%)      | 395 (51.4%)          | .834         |
| Current smoker           | 38 (23.9%)       | 28 (19.9%)           | .698         | 210 (29.7%)      | 245 (34.0%)          | .176         |
| History                  |                  |                      |              |                  |                      |              |
| Chronic renal failure    | 29 (17.0%)       | 31 (20.3%)           | .476         | 41 (5.4%)        | 60 (7.8%)            | .065         |
| Ejection fraction <30%   | 9 (5.3%)         | 31 (20.3%)           | .150         | 13 (1.8%)        | 14 (1.9%)            | 1.000        |
| Previous myocardial infarction | 44 (25.7%) | 42 (27.5%) | .801 | 122 (16.2%) | 130 (16.9%) | .730 |
| Previous PCI             | 60 (35.1%)       | 48 (31.4%)           | .555         | 142 (18.9%)      | 136 (17.7%)          | .596         |
| Previous CABG            | 6 (3.5%)         | 7 (4.6%)             | .779         | 32 (4.2%)        | 19 (2.5%)            | .064         |
| Presentation             |                  |                      |              |                  |                      |              |
| STEMI                    | 38 (22.2%)       | 19 (12.4%)           | .028         | 202 (26.8%)      | 206 (26.8%)          | 1.000        |
| NSTEMI                   | 31 (18.1%)       | 28 (18.3%)           | 1.000        | 154 (20.5%)      | 164 (21.4%)          | .705         |
| Unstable angina          | 10 (5.8%)        | 18 (11.8%)           | .074         | 60 (8.0%)        | 69 (9.0%)            | .520         |
| Stable angina            | 76 (44.4%)       | 81 (52.9%)           | .148         | 285 (37.8%)      | 289 (37.6%)          | .958         |
| Angiography driven       | 11 (6.4%)        | 7 (4.6%)             | .682         | 40 (5.3%)        | 29 (3.8%)            | .175         |
| Other                    | 5 (2.9%)         | 0 (0%)               | .062         | 12 (1.6%)        | 11 (1.4%)            | .836         |
| Syntax score             |                  |                      |              |                  |                      |              |
| Mean                     | 13.63 ± 8.95     | 12.94 ± 8.79         | .506         | 13.06 ± 8.57     | 12.50 ± 8.35         | .219         |
| Median (interquartile range) | 11.5 (8.00–17.62) | 11.0 (7.00–17.00) | .322 | 11.0 (7.00–18.00) | 11.0 (7.00–17.00) | .219 |

Note: Table 1 shows the baseline characteristics of the two study arms within both diabetic and nondiabetic patients. Data are n (%) or mean ± SD. Abbreviations: BVS, bioresorbable vascular scaffold; CABG, coronary artery bypass graft; CAD, coronary artery disease; EES, everolimus eluting stent; NSTEMI, non-ST-elevated myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.
suggests that the procedural and QCA differences have no impact on the occurrence of LOCE (Supplementary Table 1).

### 4.2 Clinical outcomes

Overall rates of TVF at 3-years were higher among DM compared to non-DM patients when pooled across Absorb BVS and Xience EES (18.3 vs. 11.6%; \( p = .002 \)). Compared with patients without DM, patients with DM had higher rates of all-cause death (7.8 vs. 4.7%, \( p = .024 \)), any revascularization (21.1 vs. 13.1%, \( p < .001 \)) and TLR at 3 years (9.9 vs. 6.2%, \( p = .020 \)).

The 3-year rates of TVF (Figure 1) and its individual endpoints were not significantly different between Absorb BVS and Xience EES in either DM or non-DM (Table 3). Results were similar in per protocol analysis (Supplementary Table 2). Figure 1b demonstrates that diabetic patients have similar results in the first year, but higher incidence of TVF between 1 and 3 years. No difference between the two devices for TVF was found. Definite or probable device thrombosis occurred more frequently in Absorb BVS compared to Xience EES in DM (4.8 vs. 0.7%, \( p = .028 \)) and in non-DM (3.5 vs. 0.9%, \( p = .001 \)). No significant interactions were found between DM status and treatment in any of the study outcomes.

### 4.3 Outcomes in ITDM and OTDM patients

The baseline demographic, procedural and QCA characteristics of oTDM and iTMD patients were not different between Absorb BVS and Xience EES, except for higher prevalence of presentation with STEMI in Absorb BVS compared to Xience EES in oTDM patients (Supplementary Table 3). In addition, post-dilatation was significantly more often performed in Absorb BVS compared to Xience EES among oTDM patients (Supplementary Table 4).

The clinical outcomes of oTDM patients and iTDM patients per randomized treatment strategy are shown in Supplementary Table 5. Within the oTDM patients, TVF occurred in 14.1% of Absorb BVS patients and in 17.8% Xience EES patients (\( p = .531 \)). Definite or probable scaffold thrombosis occurred in 6.2% of the Absorb BVS iTDM patients whereas definite stent thrombosis did not occur in Xience EES iTDM patients (\( p = .949 \)).

### 5 DISCUSSION

In the AIDA trial, Absorb BVS was associated with higher rates of target vessel myocardial infarction (TV-MI) and device thrombosis at 3 years compared to Xience EES.\(^{11}\) In this sub-study, we found that (1) DM is associated with higher rates of all-cause death, revascularization and TLR, (2) TVF and its individual components were not different between absorb BVS and Xience EES in both DM and non-DM, (3) Absorb BVS implantation lead to higher rates of device thrombosis in patients both with and without DM, and (4) rates of TVF were
highest in iTDM patients, both for absorb BVS versus Xience EES (25.2 vs. 20.5%, respectively).

This study is the first to report the clinical outcomes of Absorb BVS and Xience EES treatment strategies in diabetic or nondiabetic patients at complete three-year follow-up. Previously, in low to medium risk patients, absorb BVS showed acceptable safety and efficacy in patients with DM at 1-year follow-up. We showed that diabetics have increased risk of adverse events after the first year compared with nondiabetics. In addition, the AIDA population is a more complex population that reflects routine PCI practice. At complete 3-year follow-up, among diabetic patients, similar rates of TVF in absorb BVS compared to Xience EES were observed. However, rates of device thrombosis were significantly higher in the absorb BVS group compared to the Xience EES, regardless of diabetic status. It can be concluded that safety concerns that were previously put forward by the unpredictable occurrence of very late scaffold thrombosis, are also seen in diabetic patients within AIDA. The exact cause of the increased rates of scaffold thrombosis remains party

**Figure 1** Figure 1 shows the Kaplan–Meier curves of target vessel failure among diabetic and nondiabetic patients randomly assigned to Absorb BVS or Xience EES throughout (a) 3 years and (b) with landmark at 1 year. Target vessel failure is defined as a composite of cardiac death, target vessel myocardial infarction or target vessel revascularization. BVS, bioresorbable vascular scaffold; EES, everolimus-eluting stent [Color figure can be viewed at wileyonlinelibrary.com]
understood. It has been hypothesized that implantation techniques might mitigate the risk of increased occurrence of stent thrombosis, however, results and definition of these strategies have been varying.

The availability of second-generation DES improved safety and efficacy compared with first-generation DES. However, this improvement in clinical outcomes does not extend to diabetic patients. A patient-pooled analysis of data from four randomized trials—SPIRIT II, III, IV and COMPARE—found that in nondiabetic patients, the use of Xience EES significantly reduced the rates of cardiac death, MI and TLR at 2 years compared to paclitaxel-eluting stent (6.2 vs. 11.4%; Odds Ratio 0.53; 95% CI [0.43–0.65]). However, in diabetic patients, there was no difference between the two stents (10.1 vs. 10.3%; Odds Ratio 0.94; 95% CI [0.68–1.30]). And still nowadays, diabetic patients seem to benefit less from the improvements in technology and stent technique. In the present trial, both the absorb BVS and the Xience EES have worse clinical outcomes after PCI in diabetic patients compared to nondiabetic patients.

This AIDA-trial sub-study, as other sub-studies, highlights the unmet need of clinical outcome improvements with current-generation DES technology, as well as the Absorb BVS, in diabetic patients. Two hypotheses have emerged for the relative ineffectiveness of -imus drug. One reason is the direct resistance of vascular smooth muscle cells to mammalian target of rapamycin (mTOR) inhibition in diabetic patients. Another reason is the effect of leptin.

The body mass index strongly correlates with risk of DM. Obesity is associated with elevated levels of the hormone leptin, which has been found to promote vascular remodeling and neointimal growth in animal studies. Increased leptin levels have been associated with in-stent restenosis. DM has reached pandemic proportions; as the worldwide prevalence of DM has increased over the last decades from 108 million people in 1980 to 422 million people in 2014. Due to this increased prevalence and the undesirable PCI outcomes in diabetic-patients, there is an urgent need to enhance stent technology tailored to the needs of the diabetic patients.

### LIMITATIONS

The current study has limitations. As any subgroup analysis, this study might be subject to under powering (especially in the low number of insulin-treated diabetic patients). Based on the TVF rate in this study, and a noninferiority boundary of 5%, this study needed a sample size of 1,003 patients per group to have at least 80% power. Second, the AIDA population reflects routine PCI. In routine PCI, intracoronary imaging is not mandatory, and therefore it is not possible to quantify successful lesion preparation and/or device implantation. Third, inflammatory and immunologic markers, in order to understand the role of both inflammation and cell proliferation in restenosis, have not been collected. Fourth, as a post-hoc analysis, information on HbA1C

| TABLE 3 Outcomes at 3 years |
|-----------------------------|
|                            | Diabetic patients | Nondiabetic patients |
|                            | Absorb BVS (n = 171) | Xiense EES (n = 153) | p-value | Absorb BVS (n = 753) | Xiense EES (n = 768) | p-value | pInteraction |
| All-cause death             | 7.8% (13)          | 7.9% (12)            | .971     | 4.1% (31)           | 5.3% (40)            | .309     | 0.621        |
| Cardiac death              | 3.1% (5)           | 4.7% (7)             | .463     | 2.4% (18)           | 2.5% (19)            | .904     | 0.562        |
| Any myocardial infarction  | 8.6% (14)          | 5.4% (8)             | .273     | 8.1% (60)           | 5.5% (41)            | .042     | 0.897        |
| Target vessel myocardial infarction | 6.1% (10) | 4.1% (6) | .398 | 5.9% (44) | 3.9% (29) | .062 | 0.971 |
| Any revascularization      | 22.7% (37)         | 19.4% (29)           | .538     | 14.0% (103)         | 12.2% (91)           | .309     | 0.987        |
| Target vessel revascularization | 14.1% (23) | 12.8% (19) | .744 | 9.1% (67) | 7.8% (58) | .351 | 0.849 |
| Target lesion revascularization | 11.1% (18) | 8.7% (13) | .527 | 7.2% (53) | 5.2% (39) | .114 | 0.804 |
| Device thrombosis related  | 3.7% (6)           | 0.7% (1)             | .076     | 3.1% (23)           | 0.5% (4)             | <.001    | 0.947        |
| Device stenosis related    | 7.4% (12)          | 8.1% (12)            | .794     | 4.2% (31)           | 4.7% (35)            | .660     | 0.992        |
| Target vessel failure      | 18.7% (31)         | 18.0% (27)           | .840     | 12.3% (92)          | 11.0% (83)           | .391     | 0.790        |
| Target lesion failure      | 15.7% (26)         | 15.3% (23)           | .915     | 10.9% (81)          | 9.1% (69)            | .248     | 0.623        |
| Patient-oriented composite endpoint | 30.3% (51) | 27.0% (41) | .522 | 19.2% (144) | 17.8% (136) | .472 | 0.854 |
| Device thrombosis          |                  |                    |          |                    |                    |          |              |
| Definite                   | 3.7% (6)           | 0.7% (1)             | .076     | 3.2% (24)           | 0.5% (4)             | <.001    | 0.918        |
| Probable                   | 1.2% (2)           | 0 (0%)              | .181     | 0.3% (2)            | 0.4% (3)             | .669     | 0.914        |
| Definite/probable          | 4.8% (8)           | 0.7% (1)             | .028     | 3.5% (26)           | 0.9% (7)             | .001     | 0.575        |

Note: Table 3 shows the 3-year clinical outcomes by randomized device modality in both diabetic and nondiabetic patients. Data are presented in % (n). Abbreviations: BVS, bioresorbable vascular scaffold; EES, everolimus eluting stent.
is lacking which would have provide better insights. Fifth, restarting or prolonging DAPT through 3 years after scaffold implantation was recommended at the request of the DSMB. This recommendation might have influenced the occurrence of thrombosis-related outcomes in patients on prolonged or restarted DAPT. Exact information on the duration of DAPT in every patient would have given greater insights.

7 | CONCLUSIONS

In routine PCI practice, both absorb BVS and Xience EES have worse clinical outcomes in diabetic patients as compared to nondiabetics. Specifically insulin-treated diabetics are at higher risk of adverse clinical events. Throughout all clinical presentations, Absorb BVS was associated with higher rates of device thrombosis at 3-year follow-up.

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CONFLICT OF INTEREST

The Amsterdam UMC Heart Center received an unrestricted educational research grant from Abbott Vascular. The Research Department of the cardiology division of the Medical Center Leeuwarden received nonstudy related unrestricted educational research grants from Abbott Vascular. Joanna J. Wykrzykowska receives consultancy fees and research grants from Abbott Vascular. Jose P.S. Henriques receives research grants from Abbott Vascular. Jan G.P. Tijssen served on the DSMB of the early ABSORB trials, including ABSORB II. The other coauthors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data available at request

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REFERENCES

1. Ritsinger V, Saleh N, Lagerqvist B, Norhammar A. High event rate after a first percutaneous coronary intervention in patients with diabetes mellitus: results from the Swedish coronary angiography and angioplasty registry. Circ Cardiovasc Interv. 2015;8(6):e002328.
2. Stettler C, Allemann S, Wandel S, et al. Drug eluting and bare metal stents in people with and without diabetes: collaborative network meta-analysis. BMJ. 2008;337:a1331.
3. Koskinas KC, Siontis GC, Piccolo R, et al. Impact of diabetic status on outcomes after revascularization with drug-eluting stents in relation to coronary artery disease complexity: patient-level pooled analysis of 6081 patients. Circ Cardiovasc Interv. 2016;9(2):e003255.
4. Moreno PR, Murcia AM, Palacios IF, et al. Coronary composition and macrophage infiltration in atherectomy specimens from patients with diabetes mellitus. Circulation. 2000;102(18):2180-2184.
5. Serruys PW, Garcia-Garcia HM, Onuma Y. From metallic cages to transient bioresorbable scaffolds: change in paradigm of coronary revascularization in the upcoming decade? Eur Heart J. 2012;33(1):16-25b.
6. Hayden JM, Reaven PD. Cardiovascular disease in diabetes mellitus type 2: a potential role for novel cardiovascular risk factors. Curr Opin Lipidol. 2000;11(5):519-528.
7. Sato T, Jose J, El-Mawardy M, et al. Relationship between peri-strut low intensity areas and vascular healing response after everolimus-eluting bioresorbable scaffold implantation: an optical coherence tomography study. J Cardiol. 2017;69(4):606-612.
8. Hommels TM, Hermanides RS, Rasoul S, et al. The 1 year safety and efficacy outcomes of absorb bioresorbable vascular scaffolds for coronary artery disease treatment in diabetes mellitus patients: the ABSORB DM Benelux study. Neth Heart J. 2019;27:541-549.
9. Kerelakes DJ, Ellis SG, Kimura T, et al. Efficacy and safety of the absorb everolimus-eluting bioresorbable scaffold for treatment of patients with diabetes mellitus: results of the absorb diabetic substudy. JACC Cardiovasc Interv. 2017;10(1):42-49.
10. Tijssen RYG, Kraak RP, Hofma SH, et al. Complete two-year follow-up with formal non-inferiority testing on primary outcomes of the AIDA trial comparing the absorb bioresorbable scaffold with the XIENCE drug-eluting metallic stent in routine PCI. EuroIntervention. 2018;14:e426-e433.
11. Kerkmeijer LSM, Tijssen RYG, Hofma SH, et al. Comparison of an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent in routine PCI: three-year clinical outcomes from the AIDA trial. EuroIntervention. 2019;15(7):603-606.
12. Woudstra P, Grundekein MJ, Kraak RP, et al. Amsterdam investigator-initiated absorb strategy all-comers trial (AIDA trial): a clinical evaluation comparing the efficacy and performance of ABSORB everolimus-eluting bioresorbable vascular scaffold strategy vs the XIENCE family (XIENCE PRIME or XIENCE Xpedition) everolimus-eluting coronary stent strategy in the treatment of coronary lesions in consecutive all-comers: rationale and study design. Am Heart J. 2014;167(2):133-140.
13. Wykrzykowska JJ, Kraak RP, Hofma SH, et al. Bioresorbable scaffolds versus metallic stents in routine PCI. N Engl J Med. 2017;376(24):2319-2328.
14. Markovic S, Kugler C, Rottbauer W, Wohlr J. Long-term clinical results of bioresorbable absorb scaffolds using the PSP-technique in patients with and without diabetes. J Interv Cardiol. 2017;30(4):325-330.
15. Ishibashi Y, Nakatani S, Sotomi Y, et al. Relation between bioresorbable scaffold sizing using QCA-Dmax and clinical outcomes at 1 year in 1,232 patients from 3 study cohorts (ABSORB cohort B, ABSORB EXTEND, and ABSORB II). JACC Cardiovasc Interv. 2015;8(13):1715-1726.
16. Tijssen RYG, Kerkmeijer LSM, Katagiri Y, et al. The relationship of pre-procedural Dmax based sizing to lesion level outcomes in absorb BVS and Xience EES treated patients in the AIDA trial. Int J Cardiovasc Imaging. 2019;35(7):1189-1198.
17. Serruys PW, Onuma Y. Dmax for sizing, PSP-1, PSP-2, PSP-3 or OCT guidance: interventionlists’ jargon or indispensable implantation techniques for short- and long-term outcomes of absorb BRS? EuroIntervention. 2017;12(17):2047-2056.
18. Tijssen RYG, Kraak RP, Elias J, et al. Implantation techniques (predilatation, sizing, and post-dilatation) and the incidence of scaffold thrombosis and revascularisation in lesions treated with an everolimus-eluting bioresorbable vascular scaffold: insights from the AIDA trial. EuroIntervention. 2018;14(4):e434-e442.
19. Stone GW, Kedhi E, Kereiakes DJ, et al. Differential clinical responses to everolimus-eluting and paclitaxel-eluting coronary stents in patients with and without diabetes mellitus. Circulation. 2011;124(8):893-900.

20. Woods TC. Dysregulation of the mammalian target of rapamycin and p27Kip1 promotes intimal hyperplasia in diabetes mellitus. Pharmaceuticals (Basel). 2013;6(6):716-727.

21. Lightell DJ Jr, Woods TC. Relative resistance to mammalian target of rapamycin inhibition in vascular smooth muscle cells of diabetic donors. Ochsner J. 2013;13(1):56-60.

22. Schafer K, Halle M, Goeschen C, et al. Leptin promotes vascular remodeling and neointimal growth in mice. Arterioscler Thromb Vasc Biol. 2004;24(1):112-117.

23. Piatti P, Di Mario C, Monti LD, et al. Association of insulin resistance, hyperleptinemia, and impaired nitric oxide release with in-stent restenosis in patients undergoing coronary stenting. Circulation. 2003;108(17):2074-2081.

24. World Health Organization fact-sheet on diabetes 2018. [updated October 30, 2018].

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

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