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Bioresorbable Scaffolds versus Metallic Stents in Routine PCI

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ABSTRACT

BACKGROUND

Bioresorbable vascular scaffolds were developed to overcome the shortcomings of drug-eluting stents in percutaneous coronary intervention (PCI). We performed an investigator-initiated, randomized trial to compare an everolimus-eluting bioresorbable scaffold with an everolimus-eluting metallic stent in the context of routine clinical practice.

METHODS

We randomly assigned 1845 patients undergoing PCI to receive either a bioresorbable vascular scaffold (924 patients) or a metallic stent (921 patients). The primary end point was target-vessel failure (a composite of cardiac death, target-vessel myocardial infarction, or target-vessel revascularization). The data and safety monitoring board recommended early reporting of the study results because of safety concerns. This report provides descriptive information on end-point events.

RESULTS

The median follow-up was 707 days. Target-vessel failure occurred in 105 patients in the scaffold group and in 94 patients in the stent group (2-year cumulative event rates, 11.7% and 10.7%, respectively; hazard ratio, 1.12; 95% confidence interval [CI], 0.85 to 1.48; P=0.43); event rates were based on Kaplan–Meier estimates in time-to-event analyses. Cardiac death occurred in 18 patients in the scaffold group and in 23 patients in the stent group (2-year cumulative event rates, 2.0% and 2.7%, respectively), target-vessel myocardial infarction occurred in 48 patients in the scaffold group and in 30 patients in the stent group (2-year cumulative event rates, 5.5% and 3.2%), and target-vessel revascularization occurred in 76 patients in the scaffold group and in 65 patients in the stent group (2-year cumulative event rates, 8.7% and 7.5%). Definite or probable device thrombosis occurred in 31 patients in the scaffold group as compared with 8 patients in the stent group (2-year cumulative event rates, 3.5% vs. 0.9%; hazard ratio, 3.87; 95% CI, 1.78 to 8.42; P<0.001).

CONCLUSIONS

In this preliminary report of a trial involving patients undergoing PCI, there was no significant difference in the rate of target-vessel failure between the patients who received a bioresorbable scaffold and the patients who received a metallic stent. The bioresorbable scaffold was associated with a higher incidence of device thrombosis than the metallic stent through 2 years of follow-up. (Funded by Abbott Vascular; AIDA ClinicalTrials.gov number, NCT01858077.)

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Drug-eluting stents are the standard of care in percutaneous coronary intervention (PCI).[1,2] Nevertheless, their rigid metallic cages hamper vasomotion, and they are associated with the development of neoatherosclerosis, which results in an ongoing risk of stent thrombosis (rate of 0.1 to 0.2% per year) and repeat revascularization (rate of 2 to 3% per year).[3-6]

Bioresorbable vascular scaffolds theoretically leave no permanent implant and allow for restoration of vessel function.[7] The ABSORB III trial showed the noninferiority of the bioresorbable vascular scaffold (Absorb, Abbott Vascular) to the cobalt–chromium everolimus-eluting metallic stent (Xience, Abbott Vascular) with respect to target-lesion failure at 1 year.[8] However, subsequent studies have suggested that the risk of device thrombosis is higher with bioresorbable scaffolds than with metallic stents.[9-15]

The bioresorbable vascular scaffold was approved by the Food and Drug Administration (FDA) and obtained a Conformité Européenne mark in 2010, which indicates market approval throughout the European Union. Although this device has gained acceptance in ordinary interventional practice, data from adequately powered, randomized studies addressing safety and efficacy are lacking in this context. The Amsterdam Investigator-Initiated Absorb Strategy All-Comers Trial (AIDA) was designed to compare the bioresorbable vascular scaffold with the metallic stent in a patient population that reflects that seen in routine clinical practice. This article is an early report of the data, which the data and safety monitoring board recommended to be released owing to safety concerns.

Methods

Study Design and Oversight

AIDA was a single-blind, multicenter, investigator-initiated, noninferiority, randomized, clinical trial. The design has been published previously.[16] The study was financially supported by an unrestricted educational grant from Abbott Vascular. The funder had no role in the design of the study, the collection or management of the data, or the statistical analysis; the funder critically reviewed the first submitted version of the manuscript but was not involved in the writing or approval of the manuscript or the decision to submit the manuscript for publication. All final revisions were made and independently approved by the authors and the investigators. No stents, scaffolds, or other equipment were donated for the trial by Abbott Vascular or any other party.

Investigators affiliated with the Heart Center at the Academic Medical Center (AMC)–University of Amsterdam designed the study, collected and managed the data, and performed the statistical analyses. The study design was approved by the institutional review board at the AMC for all the participating centers. An independent data and safety monitoring board reviewed cumulative safety data at regular intervals to safeguard the well-being of the participants. The authors had unrestricted access to the data and vouch for the accuracy and completeness of the data and analyses and for the fidelity of the study to the protocol, which is available with the full text of this article at NEJM.org.

Study Population

We enrolled patients with coronary artery disease who were undergoing PCI and had one or more target lesions that were considered, on the basis of clinical judgment, to be suitable for drug-eluting stent implantation. Key exclusion criteria were target lesions more than 70 mm in length, a reference vessel diameter of less than 2.5 mm or more than 4.0 mm (as estimated visually), bifurcation lesions for which the use of two stents or scaffolds was planned, and in-stent restenosis. All inclusion and exclusion criteria are listed in Table S1 in the Supplementary Appendix, available at NEJM.org. All the patients provided written informed consent. Staged informed consent (oral followed by written consent) was allowed for urgent procedures.

Randomization and Treatment

After successful predilation of the first lesion, patients were randomly assigned, in a 1:1 ratio, to receive either an everolimus-eluting bioresorbable scaffold or an everolimus-eluting metallic stent. Randomization was performed with the use of a centralized Web-based system in random block sizes. Patients, but not operators or investigators, were unaware of study-group assignments.

During the first year of enrollment, scaffolds were implanted according to the manufacturer's instructions, which, at that time, did not include mandatory postdilation (i.e., dilation of the device after implantation); postdilation was per-

formed in 63% of the lesions in the scaffold group during the first year of enrollment. The steering committee recommended routine postdilation of the scaffold device from October 1, 2014, onward.

Dual antiplatelet therapy and other medications were administered before the procedure in accordance with the guidelines of the European Society of Cardiology and the device manufacturer's instructions for use. Dual antiplatelet therapy — preferably with ticagrelor or prasugrel in patients with acute coronary syndromes — was recommended for at least 1 year after the procedure in both study groups.

FOLLOW-UP

Clinical follow-up of the patients was conducted through telephone contact and was scheduled at 30 days, 180 days, and 1, 2, 3, 4, and 5 years after the procedure. Cross-sectional data were assessed in November and December 2016 to ascertain the event status of all patients who did not have their routine follow-up contact after September 1, 2016. Vital status was verified in all patients. Independent study monitors (Cordinamo) verified 15% of all data from case-report forms.

STUDY END POINTS

The primary end point of target-vessel failure was a composite of cardiac death, target-vessel myocardial infarction, or target-vessel revascularization. Major secondary end points were death from any cause, all myocardial infarctions, all revascularizations (including target-vessel revascularization, target-lesion revascularization, and non–target-vessel revascularization), and device thrombosis. Detailed definitions of end points and additional secondary end points are listed in Table S2 in the Supplementary Appendix. An independent clinical-events committee staffed by the contract research organization Cardialysis adjudicated events according to the definitions of the Academic Research Consortium[17] and the Third Universal Definition of Myocardial Infarction.[18]

ANGIOGRAPHIC ASSESSMENTS

Calculations of the angiographic SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) scores were performed by core laboratory staff at Cardialysis. The SYNTAX score reflects a comprehensive angiographic assessment of the coronary vasculature, with 0 as the lowest score and higher scores (no upper limit) indicating more complex coronary anatomy. Quantitative coronary angiography was performed with the use of dedicated software (Cardiovascular Angiography Analysis System [CAAS], version 5.11, Pie Medical) on the postprocedural angiograms obtained from the patients in the scaffold group; measurements were made in a single projection that had the best visibility of the scaffolded segment. Whenever multiple projections were available, a projection that showed the highest grade of stenosis, as assessed visually, was selected. All interpretations of the quantitative coronary angiographic findings were performed by seven analysts under the supervision of a cardiologist who is an expert in this method; the analysts were unaware of the clinical events in the patients.

STATISTICAL ANALYSIS

The primary analysis was designed to test whether the bioresorbable scaffold was noninferior to the metallic stent, as determined by the rates of target-vessel failure at 2 years. To satisfy the noninferiority hypothesis, the upper limit of the (two-sided) 95% confidence interval for the rate difference (equivalent to noninferiority testing at a one-sided alpha level of 2.5%) had to fall below a prespecified margin of 4.5 percentage points. Under the assumption of a 7.3% event rate for the primary end point at 2 years and a rate of loss-to-follow-up of 3.0%, we estimated that we would need to enroll 1790 patients for the study to have at least 95% power. The first version of the protocol included a noninferiority margin of 3.3 percentage points, which required enrollment of 2690 patients for 90% power. After publication of the results of the ABSORB III trial,[8] we amended the protocol, on the basis of FDA guidance, to adopt the noninferiority margin of 4.5 percentage points used in that trial.[19] At the time that the protocol change was approved by the institutional review board in December 2015, a total of 1845 patients had been enrolled, and enrollment was complete.

After a safety review on November 11, 2016, the data and safety monitoring board recommended early reporting of the results because of safety concerns. The data and safety monitoring board also recommended that the benefits and risks of extended dual antiplatelet therapy should be considered in patients treated with a bioresorbable scaffold, including those participating in AIDA. This report provides descriptive infor-

mation — without formal hypothesis testing — on all end-point events that occurred before December 16, 2016.

Analyses were performed according to the intention-to-treat principle. Event rates were based on Kaplan–Meier estimates in time-to-event analyses. Follow-up of the patients was censored on December 16, 2016, or at the last known event-free time point, whichever came first. For time-to-event analysis, hazard ratios with 95% confidence intervals were determined, and Kaplan–Meier curves were compared by means of the log-rank test. The 95% confidence interval for the rate difference (the rate in the scaffold group minus the rate in the stent group) of the primary end point was calculated according to the method of Com-Nougue et al.,[20] with the use of Kaplan–Meier estimates and Greenwood estimators of the standard error. We used the chi-square test or Fisher's exact test to com-

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Scaffold Group (N=924)	Stent Group (N=921)
Age — yr	64.3±10.6	64.0±10.5
Male sex — no. (%)	670 (72.5)	700 (76.0)
Risk factors — no./total no. (%)		
Diabetes mellitus	171/924 (18.5)	153/921 (16.6)
Treated with oral medication	95/171 (55.6)	97/153 (63.4)
Treated with insulin	65/171 (38.0)	45/153 (29.4)
Hypertension	468/920 (50.9)	464/919 (50.5)
Hypercholesterolemia	344/915 (37.6)	350/914 (38.3)
Family history of coronary artery disease	451/886 (50.9)	469/886 (52.9)
Current smoker	248/867 (28.6)	273/861 (31.7)
History — no./total no. (%)		
Chronic renal failure	70/924 (7.6)	91/921 (9.9)
Ejection fraction <30%	22/910 (2.4)	17/900 (1.9)
Previous stroke or transient ischemic attack	46/923 (5.0)	58/921 (6.3)
Peripheral vascular disease	65/924 (7.0)	56/918 (6.1)
Previous myocardial infarction	166/924 (18.0)	172/921 (18.7)
Previous percutaneous coronary intervention	202/924 (21.9)	184/921 (20.0)
Previous bypass surgery	38/924 (4.1)	26/921 (2.8)
Clinical presentation — no. (%)		
ST-segment elevation myocardial infarction	240 (26.0)	225 (24.4)
Non–ST-segment elevation myocardial infarction	185 (20.0)	192 (20.8)
Unstable angina	70 (7.6)	87 (9.4)
Stable angina, documented ischemia, or both	361 (39.1)	370 (40.2)
Angiographically driven indication for PCI†	51 (5.5)	36 (3.9)
Other	17 (1.8)	11 (1.2)
SYNTAX score‡		
Mean	13.2±8.6	12.6±8.4
Median (interquartile range)	11 (7–18)	11 (7–17)

* Plus–minus values are means ±SD. Shown are data for patients who were assigned to receive an everolimus-eluting bioresorbable vascular scaffold or an everolimus-eluting cobalt–chromium stent. There were no significant between-group differences in the characteristics evaluated at baseline.

† The indication for percutaneous coronary intervention (PCI) was considered to be angiographically driven if PCI was performed on an angiographically significant lesion — that is, a lesion that was detected on angiography in a patient who did not have symptoms or evidence of myocardial ischemia.

‡ The SYNTAX score reflects a comprehensive angiographic assessment of the coronary vasculature, with 0 as the lowest score and higher scores (no upper limit) indicating more complex coronary anatomy. Information on SYNTAX score was available for 831 patients in the scaffold group and for 830 patients in the stent group.

pare categorical variables and the independent t-test to compare continuous variables. All statistical analyses were performed with SPSS software, version 23.0 (IBM).

RESULTS

PATIENTS AND PROCEDURES

A total of 1845 patients were enrolled between August 28, 2013, and December 27, 2015, at five high-volume PCI centers in the Netherlands. We randomly assigned 924 patients to receive a bioresorbable vascular scaffold and 921 patients to receive a metallic stent. During this period, 9653 patients underwent implantation of a drug-eluting stent at the five centers (Fig. S1 in the Supplementary Appendix). The baseline characteristics of the two study groups were well balanced (Table 1). Patients with acute coronary syndrome represented 54% of the population. A SYNTAX score was available for 1661 patients (90.0%) and ranged from 1 to 57, with a median of 11.

A total of 2446 lesions were treated. At least one assigned study device was implanted successfully in 895 of the 924 patients in the scaffold group (96.9%) and in 919 of the 921 patients in the stent group (99.8%) (Table 2). Only assigned study devices were implanted in 859 of

Table 2. Procedural Characteristics.*

Outcome	Scaffold Group	Stent Group	P Value
Patients			
Total no.	924	921	
Treated lesions per patient	1.34±0.63	1.31±0.59	0.36
No. of devices per patient	1.54±0.84	1.45±0.79	0.01
Total device length per patient — mm	31.1±19.6	29.7±19.2	0.11
Minimum device diameter per patient — mm	2.73±0.27	2.88±0.35	0.05
Device implantation — no. (%)			
Any assigned study device	895 (96.9)	919 (99.8)	<0.001
Only assigned study devices	859 (93.0)	910 (98.8)	<0.001
Any unassigned device	65 (7.0)	11 (1.2)	<0.001
Only unassigned devices	29 (3.1)	2 (0.2)	<0.001
After failure of assigned device	20	1	
Unassigned device first choice	9	1	
Procedure time — min†	49±26	44±23	<0.001
Contrast material used — ml‡	160±74	151±72	0.02
Predilation of first treated lesion — no. (%)	911 (98.6)	892 (96.9)	0.01
Procedural success — no. (%)§	833 (90.2)	887 (96.3)	<0.001
Treated lesions¶			
Total no.	1237	1209	
Rotational atherectomy — no./total no. of target lesions (%)	24/1232 (1.9)	26/1208 (2.2)	0.78
Predilation performed — no. (%)	1199 (96.9)	1103 (91.2)	<0.001
Total number of devices implanted	1425	1336	
Number of devices per lesion	1.15±0.40	1.11±0.34	0.001
Postdilation performed — no. (%)‖	915 (74.0)	594 (49.1)	<0.001

* Plus–minus values are means ±SD.
† Data on procedure time were available for 919 patients in the scaffold group and 918 patients in the stent group.
‡ Data on contrast material used were available for 902 patients in the scaffold group and for 897 patients in the stent group.
§ Procedural success was defined as a final in-scaffold or in-stent residual stenosis of less than 20% (as estimated visually), with Thrombolysis in Myocardial Infarction (TIMI) grade 3 (complete) flow in the treated vessel and no clinical events during the hospital stay.
¶ Treated lesions included all treated lesions at the time of randomization and scheduled staged procedures.
‖ Rates of postdilation in the scaffold group increased from 63% in the first year to 83% in the last year.

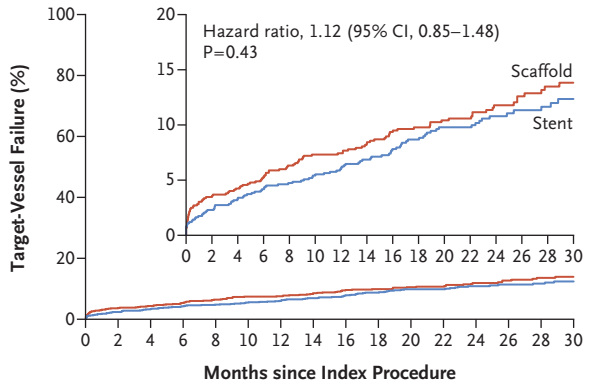

Figure 1. Kaplan–Meier Curves for Target-Vessel Failure.

Shown is the event rate of target-vessel failure (the primary end point) through 30 months among the patients randomly assigned to receive bioresorbable vascular scaffolds or metallic stents. We defined target-vessel failure as a composite of cardiac death, target-vessel myocardial infarction, or target-vessel revascularization. The inset shows the same data on an enlarged y axis.

the 924 patients in the scaffold group (93.0%), as compared with 910 of the 921 patients in the stent group (98.8%) (Table 2). Scaffold implantation was associated with, on average, a 5-minute longer procedure time and a 9-ml greater use of contrast material than stent implantation. In the scaffold group, the mean (±SD) residual percent diameter stenosis was 17.0±9.5%, with 9% of the patients having a residual percent diameter stenosis greater than 30%. (Detailed characteristics of the lesions at baseline, procedural characteristics, and quantitative coronary angiography data for the patients in the scaffold group are presented in Tables S3 through S5 in the Supplementary Appendix.)

FOLLOW-UP DATA

The median duration of clinical follow-up was 707 days. At the time of the cross-sectional data assessment, clinical follow-up had been completed in 899 patients in the scaffold group (97.3%) and in 894 patients in the stent group (97.1%). Dual antiplatelet therapy was used through 1 year after implantation in 789 of 882 patients in the scaffold group (89.5%) and in 785 of 881 patients in the stent group (89.1%) (Table S6 in the Supplementary Appendix).

CLINICAL OUTCOMES

The primary end point of target-vessel failure occurred in 105 patients in the scaffold group and in 94 patients in the stent group (hazard ratio with bioresorbable scaffolds, 1.12; 95% confidence interval [CI], 0.85 to 1.48; P=0.43) (Fig. 1 and Table 3). Kaplan–Meier estimates of target-vessel failure rates at 2 years were 11.7% in the scaffold group and 10.7% in the stent group (difference in rates, 1.0 percentage point; 95% CI, –2.1 to 4.2). The results of per-protocol and as-treated analyses were similar to those of the main analysis (Tables S7 through S10 in the Supplementary Appendix).

Cardiac death by 2 years occurred in 18 patients in the scaffold group and in 23 patients in the stent group (2.0% and 2.7%, respectively; hazard ratio, 0.78; 95% CI, 0.42 to 1.44; P=0.43). Rates of target-vessel myocardial infarction were 5.5% in the scaffold group and 3.2% in the stent group (hazard ratio, 1.60; 95% CI, 1.01 to 2.53; P=0.04). Rates of target-vessel revascularization were 8.7% in the scaffold group and 7.5% in the stent group (hazard ratio, 1.16; 95% CI, 0.84 to 1.62; P=0.37). Rates of target-lesion revascularization were 7.0% in the scaffold group and 5.2% in the stent group (hazard ratio, 1.33; 95% CI, 0.90 to 1.96; P=0.15) (Table 3). Details of all cases of target-lesion revascularization are provided in Table S11 in the Supplementary Appendix.

Definite or probable device thrombosis occurred in 31 patients in the scaffold group, with cardiac death as the worst outcome in 6 patients and nonfatal myocardial infarction in 25 patients. Definite or probable device thrombosis occurred in 8 patients in the stent group, of whom 2 died from cardiac causes and 6 had nonfatal myocardial infarctions. The 2-year Kaplan–Meier event rates of definite or probable device thrombosis were 3.5% in the scaffold group and 0.9% in the stent group (hazard ratio, 3.87; 95% CI, 1.78 to 8.42; P<0.001). The numbers of patients with definite or probable device thrombosis were higher in the scaffold group than in the stent group over all postimplantation periods (acute [≤24 hours] or subacute [>24 hours to 30 days], 13 patients vs. 5 patients; late [31 days to 1 year], 8 patients vs. 1 patient; and very late [>1 to 3 years], 10 patients vs. 2 patients) (Table 3 and Fig. 2, and Fig. S2 in the Supplementary Appendix).

No interaction with respect to device thrombosis was seen between the study groups and

Table 3. Safety and Efficacy Outcomes.

Outcome	Patients with an Event		2-Year Cumulative Event Rate*		Hazard Ratio (95% CI)	P Value†
	Scaffold Group (N=924)	Stent Group (N=921)	Scaffold Group (N=924)	Stent Group (N=921)		
	number		*percent*			
Clinical events						
Death from any cause	32	43	3.5	4.3	0.74 (0.47–1.17)	0.19
Cardiac	18	23	2.0	2.7	0.78 (0.42–1.44)	0.43
Cardiovascular	22	25	2.6	2.9	0.88 (0.49–1.55)	0.65
Noncardiovascular	10	18	0.9	1.5	0.55 (0.25–1.19)	0.13
All myocardial infarction	62	41	7.1	4.2	1.52 (1.02–2.25)	0.04
Target vessel	48	30	5.5	3.2	1.60 (1.01–2.53)	0.04
During index procedure	9	6	1.0	0.7	1.50 (0.53–4.20)	0.44
Not during index procedure	39	24	4.5	2.6	1.62 (0.98–2.70)	0.06
Nontarget vessel	15	11	1.7	1.0	1.36 (0.62–2.96)	0.44
Death or myocardial infarction	88	80	9.6	8.1	1.10 (0.82–1.49)	0.52
Any revascularization	115	103	13.2	11.6	1.11 (0.85–1.45)	0.43
Target vessel	76	65	8.7	7.5	1.16 (0.84–1.62)	0.37
Target lesion	60	45	7.0	5.2	1.33 (0.90–1.96)	0.15
Device thrombosis–related	26	5	3.0	0.6	5.19 (1.99–13.50)	<0.001
Device stenosis–related	35	40	4.1	4.6	0.87 (0.55–1.36)	0.53
Nontarget lesion	21	22	2.5	2.5	0.94 (0.52–1.71)	0.84
Nontarget vessel	55	50	6.8	5.5	1.09 (0.74–1.60)	0.66
Composite end points						
Target-vessel failure‡	105	94	11.7	10.7	1.12 (0.85–1.48)	0.43
Target-lesion failure§	91	78	10.3	8.9	1.17 (0.86–1.58)	0.31
Patient-oriented end point¶	161	149	17.8	16.1	1.08 (0.87–1.35)	0.49
Device thrombosis						
Definite	27	5	3.1	0.6	5.39 (2.08–14.00)	<0.001
Probable	4	3	0.4	0.4	1.32 (0.30–5.91)	0.71
Possible	6	12	0.6	1.5	0.50 (0.19–1.33)	0.15
Definite or probable	31	8	3.5	0.9	3.87 (1.78–8.42)	<0.001
Acute (≤24 hr)	3	3				
Subacute (>24 hr to 30 days)	10	2				
Late (31 days to 1 yr)	8	1				
Very late (>1 to 2 yr)	9	2				
Very late (>2 to 3 yr)	1	0				
Any device thrombosis	37	20	4.1	2.5	1.85 (1.08–3.19)	0.02

* Event rates were based on Kaplan–Meier estimates in time-to-event analyses.
† P values were calculated with the use of the log-rank test.
‡ Target-vessel failure was a composite of cardiac death, target-vessel myocardial infarction, or target-vessel revascularization (primary end point).
§ Target-lesion failure was a composite of cardiac death, target-vessel myocardial infarction, or target-lesion revascularization (equivalent to device-oriented end point).
¶ Patient-oriented end point was a composite of death from any cause, all myocardial infarction, or all revascularization.

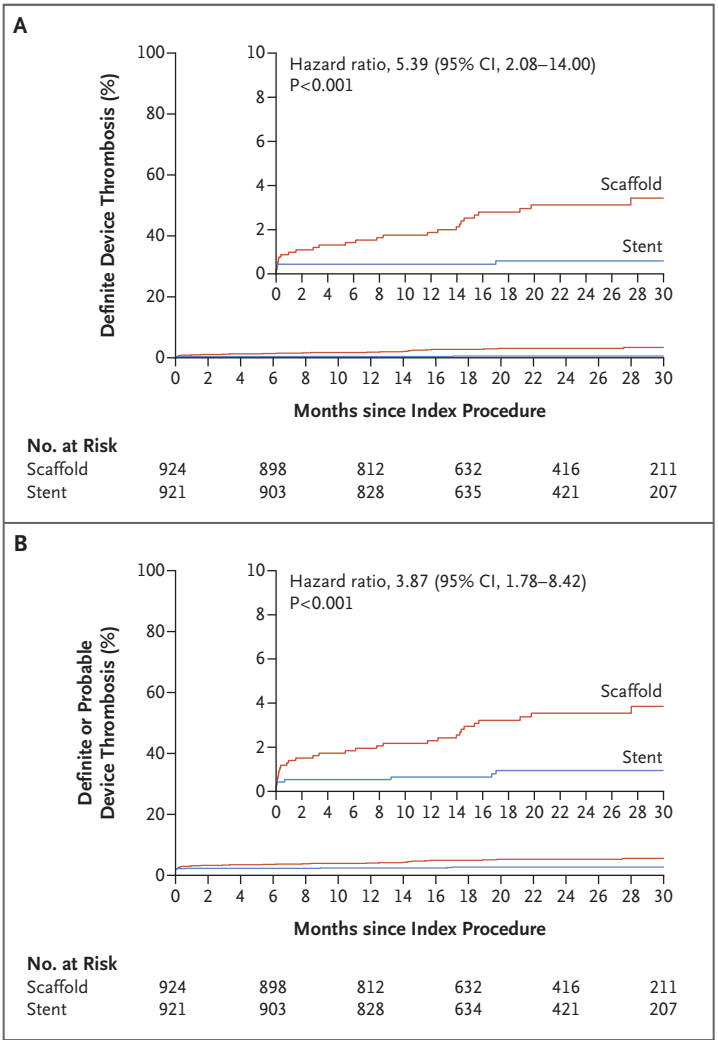

Figure 2. Kaplan–Meier Curves for Definite or Probable Device Thrombosis.
Shown are the event rates of definite device thrombosis (Panel A) and definite or probable device thrombosis (Panel B) through 30 months among the patients randomly assigned to receive bioresorbable vascular scaffolds or metallic stents. In each panel, the inset shows the same data on an enlarged y axis.

presenting symptoms, age, cardiovascular risk factors, lesion characteristics, or time of randomization. Vessel size of 2.25 mm or smaller, adequate device sizing, and postdilation were not associated with the occurrence of scaffold thrombosis. Among the patients in the scaffold group who had definite or probable device thrombosis, 19% had a residual diameter stenosis of 30% or greater; among the patients who did not have device thrombosis, 9% had a residual percent diameter stenosis of 30% or greater (P=0.05) (Fig. S3 and Tables S5 and S12 in the Supplementary Appendix).

DISCUSSION

In AIDA, we compared an everolimus-eluting bioresorbable vascular scaffold with an everolimus-eluting metallic stent in routine PCI. In this preliminary analysis from the trial, we found that the rate of definite or probable device thrombosis in the scaffold group was approximately 3.5 times as high as that in the stent group over the course of 2 years. The higher incidence of scaffold thrombosis was associated with a significantly higher incidence of myocardial infarction, although this finding was not corrected for multiple testing. The rate of the primary composite end point of target-vessel failure, as well as the rates of death from any cause, cardiac death, and revascularizations, did not differ significantly between the two study groups.

Concern about an increased rate of scaffold thrombosis was first raised by investigators who examined data from the GHOST-EU (Gauging Coronary Healing with Bioresorbable Scaffolding Platforms in Europe) registry and reported a 2.1% rate of scaffold thrombosis at 6 months.[11] A recent meta-analysis of 16,830 patients showed an overall rate of scaffold thrombosis of 1.8% at a median follow-up of 1 year.[21] Furthermore, in the ABSORB Japan trial, four cases of definite scaffold thromboses (in 1.6% of the patients) occurred between the first and second year after implantation.[13] Cases of scaffold thrombosis have been reported as late as 44 months after implantation.[22] The ABSORB II trial showed ongoing scaffold thrombosis events at 3 years.[15] Our findings confirm and extend these concerns to the use of the scaffold device in routine clinical practice.

Scaffold implantation was associated with a longer procedure time, more use of contrast material, and a lower likelihood of receiving the assigned device than was stent implantation. These findings attest to delivery challenges associated with scaffold implantation. An observational study showed that the 1-year rate of scaffold thrombosis was lower when a scaffold-specific implantation strategy (consisting of predilation, adequate sizing, and postdilation) was used.[23] In our trial, scaffold thrombosis occurred regardless of implantation technique.

The causes of the higher rate of device thrombosis with scaffolds than with stents are only partly understood. Incomplete lesion coverage, underdeployment, and malapposition have been observed with the use of optical coherence tomography in acute and subacute cases of scaffold thrombosis.[24] Thick stent struts, such as the 150-μm struts in the Absorb scaffold, are associated with blood-flow alterations and thrombogenicity, especially when they are left malapposed.[25,26] Late events might be related to a combination of nonembedded and nonabsorbed scaffold struts in complex lesions and late structural discontinuity or device dismantling.[27-29] Newer generations of bioresorbable scaffolds, with thinner struts, increased radial strength, different composition, and faster resorption, may overcome these issues. Given the lack of putative benefit in the ABSORB Japan and ABSORB II trials, the advantage of bioresorbable technology over metallic stents remains to be established.

Because of the finding of an increased incidence of very late scaffold thrombosis, the data and safety monitoring board recommended early reporting of the study findings (i.e., after enrollment of all patients but before follow-up was completed). On the basis of the considerations noted below, the data and safety monitoring board also recommended that extended dual antiplatelet therapy should be considered for recipients of the bioresorbable scaffold. The AIDA investigators are implementing this recommendation among the patients in the scaffold group. As a result of this decision, the trial participants were informed of their treatment assignment in December 2016. A final analysis of the primary end point is planned when all the patients in the trial have reached 2 years of follow-up.

The recommendation for use of extended dual antiplatelet therapy in recipients of the bioresorbable scaffold to reduce the risk of device thrombosis was made on the basis of information from previous studies. In the Dual Antiplatelet Therapy (DAPT) study, prolongation of dual antiplatelet therapy in patients who received first-generation drug-eluting stents was associated with a lower rate of stent thrombosis than aspirin therapy alone and was not harmful.[30] The ABSORB II investigators did not observe any case of very late scaffold thrombosis among 63 patients who did not interrupt dual antiplatelet therapy for up to 3 years.[15] Further research is necessary to establish whether long-term dual antiplatelet therapy would prevent very late scaffold thrombosis.

Several limitations of our study should be noted. First, routine intravascular imaging at the time of implantation and device thrombosis was not performed, which limited our insights into the mechanisms of device thrombosis. Second, we measured postprocedure cardiac enzymes only when clinically indicated. Myocardial infarctions were adjudicated according to the Third Universal Definition of Myocardial Infarction,[18] and the results could have been different if we had performed systematic blood sampling or had used another definition of myocardial infarction. Third, not all case-report forms were monitored. However, monitoring of 15% of case-report forms did not reveal any additional events that required adjudication. Finally, our study provides a median follow-up of 2 years. Longer follow-up from our trial and other clinical trials will provide information about possible ongoing risk of scaffold thrombosis beyond the second year.

In conclusion, in AIDA, we compared an everolimus-eluting bioresorbable vascular scaffold with an everolimus-eluting metallic stent in the context of routine PCI. In this preliminary report, there was no significant difference between the two study groups with respect to the primary outcome of target-vessel failure. However, treatment with the bioresorbable scaffold was associated with a significantly higher incidence of overall and very late device thrombosis than was the metallic stent through 2 years of follow-up.

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