EuroIntervention 2020;16:e904-e912 published online May 2019 ■ published online e-edition December 2020

Mini focus on bioresorbable scaffolds

Outcomes of bioresorbable vascular scaffolds versus everolimus-eluting stents by coronary complexity: a sub-analysis of the AIDA trial

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This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-18-00884

KEYWORDS

- bioresorbable scaffolds
- drug-eluting stent
- miscellaneous (clinic presentation)
- stent thrombosis

Abstract

Aims: We aimed to evaluate the impact of the complexity of coronary disease as assessed by the SYNTAX score (SXscore) on the clinical outcomes in the AIDA trial.

Methods and results: In the AIDA trial, we compared Absorb versus XIENCE in routine clinical practice. Clinical outcomes were stratified by SXscore tertiles: SXlow (SXscore ≤8), SXmid (SXscore >8 and ≤15) and SXhigh (>15). The SXscore was available in 1,661 of the 1,845 (90%) patients. The event rate of TVF was numerically lower in Absorb compared to XIENCE (3.7% versus 5.6%; p=0.257) in the SXlow tertile, numerically higher in Absorb in the SXmid tertile (11.4% versus 9.3%, p=0.421) and similar in the SXhigh tertile (15.5% versus 15.6%; p=0.960). The rates of definite/probable device thrombosis in Absorb versus XIENCE were significantly higher in the SXmid tertile (3.3% versus 0.8%, p=0.043) and in the SXhigh tertile (3.7% versus 0.8%, p=0.006).

Conclusions: We found no significantly different rates of TVF between Absorb and XIENCE patients. Absorb-treated patients in the SXmid and SXhigh tertiles had an increased risk of device thrombosis when compared to XIENCE-treated patients. The rates of device thrombosis in the SXlow tertile, while still higher for Absorb, are more acceptable than in the SXmid and SXhigh score tertiles.

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SUBMITTED ON 02/09/2018 - REVISION RECEIVED ON 1st 01/02/2019 / 2nd 11/03/2019 / 3rd 16/04/2019 - ACCEPTED ON 03/05/2019

DOI: 10.4244/EIJ-D-18-00884

Abbreviations

AIDA	Amsterdam Investigator-Initiated Absorb Strategy All-Comers Trial
CI	confidence interval
DES	drug-eluting stent
MI	myocardial infarction
PCI	percutaneous coronary intervention
ScT	scaffold thrombosis
STEMI	ST-segment elevation myocardial infarction
SXscore	SYNTAX score
TLF	target lesion failure
TLR	target lesion revascularisation
TVF	target vessel failure
TV-MI	target vessel myocardial infarction
TVR	target vessel revascularisation

Introduction

Despite encouraging initial short-term and long-term safety and efficacy in the ABSORB studies[1-3], increased scaffold thrombosis rates in randomised controlled trials and in registries have been reported[4-6]. The Amsterdam Investigator-Initiated Absorb Strategy All-Comers Trial (AIDA trial) confirmed these concerns about the increased risk of scaffold thrombosis (ScT)[7]. However, its primary endpoint of non-inferiority on target vessel failure (TVF) at two-year follow-up was met[8]. The extent of coronary artery disease may affect outcomes after percutaneous coronary intervention (PCI). The SYNTAX score (SXscore) is an angiographic score of the coronary anatomy and lesion characteristics, which can be used as a measure of coronary artery disease complexity[9]. The SXscore has prognostic value in patients with *de novo* coronary artery disease undergoing revascularisation, and is associated with the burden of atherosclerotic plaque(s)[10,11]. Furthermore, it has been used to compare clinical outcomes after PCI with first- and second-generation drug-eluting stents (DES) in a variety of clinical and interventional settings[12-14]. In this pre-specified subgroup analysis of the AIDA trial, we evaluated the impact of SXscore on clinical outcomes.

Methods

The detailed study outline, the preliminary results, and the full two-year results of the AIDA trial were published previously[7,8,15]. SXscore was assessed using baseline diagnostic angiograms. All lesions were combined to provide the overall SXscore. Each coronary lesion with a diameter stenosis ≥50% in vessels ≥1.5 mm was scored. SXscore calculations were performed by core laboratory analysts blinded for clinical events (Cardialysis B.V., Rotterdam, the Netherlands). Occluded infarct-related arteries were scored as occlusions of unknown duration in a similar manner to any chronically occluded artery. Patients with in-stent restenosis lesions (non-target lesions) were scored in the same manner as a *de novo* lesion (www.syntaxscore.com).

STUDY ENDPOINTS

The primary endpoint of this substudy was TVF, defined as a composite of cardiac death, target vessel-related myocardial infarction (TV-MI) and target vessel revascularisation (TVR).

Secondary endpoints were TLF (a composite of cardiac death, TV-MI and target lesion revascularisation [TLR]), any revascularisation, all death, all myocardial infarction and device thrombosis. An independent clinical events committee (Cardialysis B.V., Rotterdam, the Netherlands) assessed all clinical endpoints according to the definitions of the Academic Research Consortium or the third universal definition of myocardial infarction.

STATISTICAL ANALYSIS

A pre-specified subgroup analysis, stratified by the tertiles of the SXscore, of clinical outcomes was performed. Analyses were performed according to the intention-to-treat principle. Event rates were based on Kaplan-Meier estimates, and Kaplan-Meier curves were compared by means of the log-rank test. Cox regressions were used to determine hazard ratios with 95% confidence intervals (CI) to compare the outcomes between the stent types across SXscore tertiles. Normally distributed continuous variables were presented as the mean with standard deviation (SD), variables with a skewed distribution as the median with interquartile range (IQR). These variables were compared with the ANOVA and the Kruskal-Wallis test, respectively. Categorical variables were presented as numbers and percentages and were compared with the chi-square test for trends. All statistical analyses were performed using SPSS software, Version 24.0 (IBM Corp., Armonk, NY, USA).

Results

SYNTAX SCORE AND BASELINE CHARACTERISTICS

In the overall AIDA study population, 924 patients were randomised to Absorb™ and 921 patients were randomised to XIENCE (both Abbott Vascular, Santa Clara, CA, USA). The SXscore was prospectively calculated in 1,661 of the 1,845 patients (90%). The predominant reason for not being able to calculate the SXscore was the unavailability of baseline angiograms with visualisation of both coronary arteries. The SXscore ranged from 1 to 57, with a mean±SD of 12.9±8.5. The SXscore tertiles were defined as SXlow (SXscore ≤8) (n=589), SXmid (SXscore >8 and ≤15) (n=538), and SXhigh (>15) (n=534). Full patient characteristics, target lesion characteristics, and procedural characteristics according to the three SXscore tertiles are summarised in **Table 1**, **Supplementary Table 1** and **Supplementary Table 2**.

OVERALL CLINICAL OUTCOMES

At two-year follow-up, the Kaplan-Meier estimates of the TVF rate for the overall AIDA study population were 15.5% in the SXhigh tertile, 10.4% in the SXmid tertile and 4.7% in the SXlow tertile (p<0.001). The occurrence of definite or probable device thrombosis was significantly higher in the SXhigh tertile (SXhigh 2.9% versus SXmid 2.5% versus SXlow 0.7%; p=0.023) **(Table 2)**.

ABSORB CLINICAL OUTCOMES

Within the Absorb group, Kaplan-Meier estimates for TVF were significantly higher in the SXhigh tertile (15.5%; p<0.001) and

Table 1. Baseline characteristics.

	Low SYNTAX score (N=589)		Middle SYNTAX score (N=538)		High SYNTAX score (N=534)		*p*-value
Age, years	62.3	±10.5	64.7	±10.0	65.3	±10.9	<0.001
Male sex, n (%)	419	(71%)	401	(75%)	410	(77%)	0.09
Risk factors, n/total n (%)							
Diabetes mellitus	94/589	(16%)	107/538	(20%)	92/442	(17%)	0.21
Requiring oral medication	59/94	(63%)	59/107	(55%)	53/92	(58%)	
Requiring insulin	28/94	(30%)	40/107	(37%)	35/91	(38%)	
Hypertension	294/589	(50%)	286/536	(53%)	274/533	(51%)	0.56
Hypercholesterolaemia	239/584	(41%)	218/533	(41%)	180/531	(34%)	0.02
Family history of coronary artery disease	300/578	(52%)	281/524	(54%)	278/534	(53%)	0.83
Current smoker	187/558	(34%)	146/516	(28%)	143/516	(28%)	0.14
History, n/total n (%)							
Chronic renal failure	33/589	(6%)	48/538	(9%)	70/534	(13%)	<0.001
Ejection fraction <30%	11/583	(2%)	5/528	(0.9%)	18/520	(4%)	0.02
Previous stroke or transient ischaemic attack	27/588	(5%)	37/538	(7%)	31/534	(6%)	0.26
Peripheral vascular disease	34/588	(6%)	40/538	(7%)	36/533	(7%)	0.53
Previous myocardial infarction	74/515	(13%)	107/538	(20%)	123/534	(23%)	<0.001
Previous percutaneous coronary intervention	84/589	(14%)	121/538	(23%)	132/534	(25%)	<0.001
Previous bypass surgery	0/589	(0%)	3/538	(0.6%)	53/534	(10%)	<0.001
Clinical presentation, n (%)							
ST-segment elevation myocardial infarction	155	(26%)	127	(24%)	171	(32%)	0.01
Non-ST-segment elevation myocardial infarction	111	(19%)	113	(21%)	98	(18%)	0.50
Unstable angina	62	(11%)	42	(8%)	25	(5%)	0.001
Stable angina and/or documented ischaemia	236	(40%)	217	(40%)	206	(39%)	0.82
Angiographically driven	17	(3%)	32	(6%)	30	(6%)	0.03
Other	8	(1%)	7	(1%)	4	(0.7%)	0.58
SYNTAX score#							
SYNTAX score, mean±SD	5.2	±2.1	11.4	±1.9	22.8	±7.3	<0.001
SYNTAX score, median [Q1–Q3]	5	[4-7]	11	[10-13]	20.5	[17.5-25.5]	

Plus-minus variables are means±SD. # SYNTAX score was available in 831 patients assigned to Absorb and 830 to XIENCE.

in the SXmid tertile (11.4%; p=0.001) as compared with the SXlow tertile (3.7%). No statistically significant difference was observed between the SXmid and SXhigh tertiles (p=0.160) **(Figure 1)**. Cardiac death rates did not differ significantly among the three tertiles **(Figure 2A)**. Rates of TV-MI were significantly higher in the SXhigh tertile (7.4%; p=0.004) and in the SXmid tertile (5.5%; p=0.016), as compared to the SXlow tertile (1.5%). No difference was observed between the SXmid and SXhigh tertiles (p=0.366) **(Figure 2B)**. The same observation was found for the rates of TVR and TLR, with statistically significant higher revascularisation rates for the SXhigh and SXmid tertiles as compared to the SXlow tertile **(Figure 2C, Figure 2D)**. The rates of definite ScT were numerically, but not statistically significantly higher for the SXhigh tertile (3.7%; p=0.060) and the SXmid tertile (3.3%; p=0.094) versus the SXlow tertile (1.1%).

XIENCE CLINICAL OUTCOMES

Within the XIENCE group, Kaplan-Meier estimates for TVF were 15.6% (SXhigh), 9.3% (SXmid) and 5.6% (SXlow) (p-value for trend p<0.001). Rates were significantly different between the SXhigh and SXlow tertiles (p<0.001) and between the SXhigh and SXmid tertiles (p=0.04), while no statistically significant difference was observed between SXmid and SXlow (p=0.10) **(Figure 3A)**. There were no statistically significant differences for the rates of TV-MI **(Figure 3B)**.

There was a significant difference between the SXlow and SXhigh tertiles for the rates of TVR (p=0.01) and TLR (p=0.07). No statistically significant difference was observed between SXlow and SXmid, or between SXmid and SXhigh tertiles for TLR and TVR **(Figure 3C, Figure 3D)**. The rates of definite ScT were not different across the three SXgroup tertiles

Table 2. Safety and efficacy outcomes in all patients.

	Low SYNTAX score		Middle SYNTAX score		High SYNTAX score		Hazard ratio (CI)[β]		*p*-value[¶]
Clinical events									
All-cause death	12	2.1%	19	3.6%	26	4.9%	2.40	[1.21-4.75]	0.04
Cardiac	3	0.5%	9	1.7%	17	3.2%	6.27	[1.84-21.40]	0.00
Cardiovascular	5	0.9%	11	2.1%	19	3.6%	4.20	[1.57-11.25]	0.01
Non-cardiovascular	7	1.2%	8	1.5%	7	1.2%	1.11	[0.39-3.16]	0.91
All myocardial infarction	15	2.6%	29	5.5%	42	8.0%	3.18	[1.77-5.74]	<0.001
Target vessel	11	1.9%	23	4.3%	31	5.9%	3.17	[1.59-6.31]	0.00
Non-target vessel	4	0.7%	6	1.1%	12	2.3%	3.36	[1.09-10.42]	0.06
Death or myocardial infarction	27	4.7%	44	8.3%	62	11.7%	2.62	[1.67-4.21]	<0.001
Any revascularisation	39	6.8%	59	11.2%	93	17.8%	2.81	[1.93-4.09]	<0.001
Target vessel	20	3.5%	44	8.3%	57	11.0%	3.28	[1.97-5.46]	<0.001
Target lesion	15	2.6%	34	6.4%	42	8.1%	3.18	[1.76-5.73]	<0.001
Non-target lesion	5	0.9%	14	2.7%	16	3.1%	3.60	[1.32-9.82]	0.03
Non-target vessel	22	3.8%	23	4.4%	51	9.8%	2.66	[1.62-4.39]	<0.001
Composite endpoints									
Target vessel failure*	27	4.7%	55	10.4%	82	15.5%	3.53	[2.28-5.45]	<0.001
Target lesion failure[#]	23	4.0%	48	9.1%	70	13.3%	3.49	[2.18-5.59]	<0.001
Patient-oriented composite endpoint[$]	55	9.5%	81	15.2%	125	23.5%	2.50	[1.87-3.33]	<0.001
Device thrombosis									
Definite	4	0.7%	11	2.1%	12	2.3%	3.33	[1.08-10.34]	0.08
Probable	0	0.0%	2	0.4%	3	0.6%	–	–	0.22
Possible	1	0.2%	4	0.8%	7	1.4%	7.77	[0.74-51.25]	0.08
Definite/probable device thrombosis	4	0.7%	13	2.5%	15	2.9%	4.17	[1.38-12.56]	0.02
≤24 hours (acute)	1		1		2				
>24 hours to 30 days (subacute)	2		4		6				
31 days to 1 year (late)	0		4		3				
1-2 years (very late)	1		4		4				
Any	5	0.9%	17	3.2%	22	4.2%	4.91	[1.86-12.96]	0.00

[β] Hazard ratio low versus high SYNTAX score. [¶] *p*-values were calculated by log-rank test. * Composite of cardiac death, target vessel myocardial infarction and target vessel revascularisation. [#] Composite of cardiac death, target vessel myocardial infarction and target lesion revascularisation. [$] Composite of all-cause death, all myocardial infarction and all revascularisation.

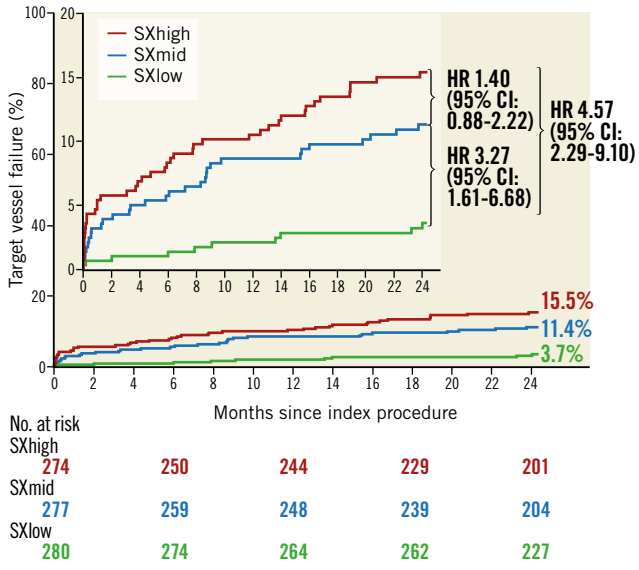

Figure 1. *Kaplan-Meier curves for target vessel failure within the Absorb arm.*

(p-value for trend: 0.726). The rates for definite ScT were 0.3% in the SXlow tertile, 0.8% in the SXmid tertile, and 0.8% in the SXhigh tertile.

ABSORB VERSUS XIENCE PER SYNTAX SCORE GROUP

Neither the primary endpoint of TVF nor the other combined endpoint of TLF differed significantly between Absorb and XIENCE in all three SXscore tertiles. Full results of Absorb versus XIENCE per SYNTAX score group are shown in **Table 3**. The rate of definite device thrombosis differed significantly between Absorb and XIENCE in both the SXmid group (3.3% vs 0.8; p=0.043) and the SXhigh group (3.7% vs 0.8%; p=0.026), while no difference in definite device thrombosis was observed in the SXlow group (1.1% vs 0.3%; p=0.272) **(Figure 4)**. Within the Absorb group, 859 patients were treated with Absorb only, and within the XIENCE group 910 patients were treated with XIENCE only. Analyses of the as-treated population are shown in **Supplementary Table 3**. Multivariate Cox proportional hazards analyses for the outcomes of TVF and

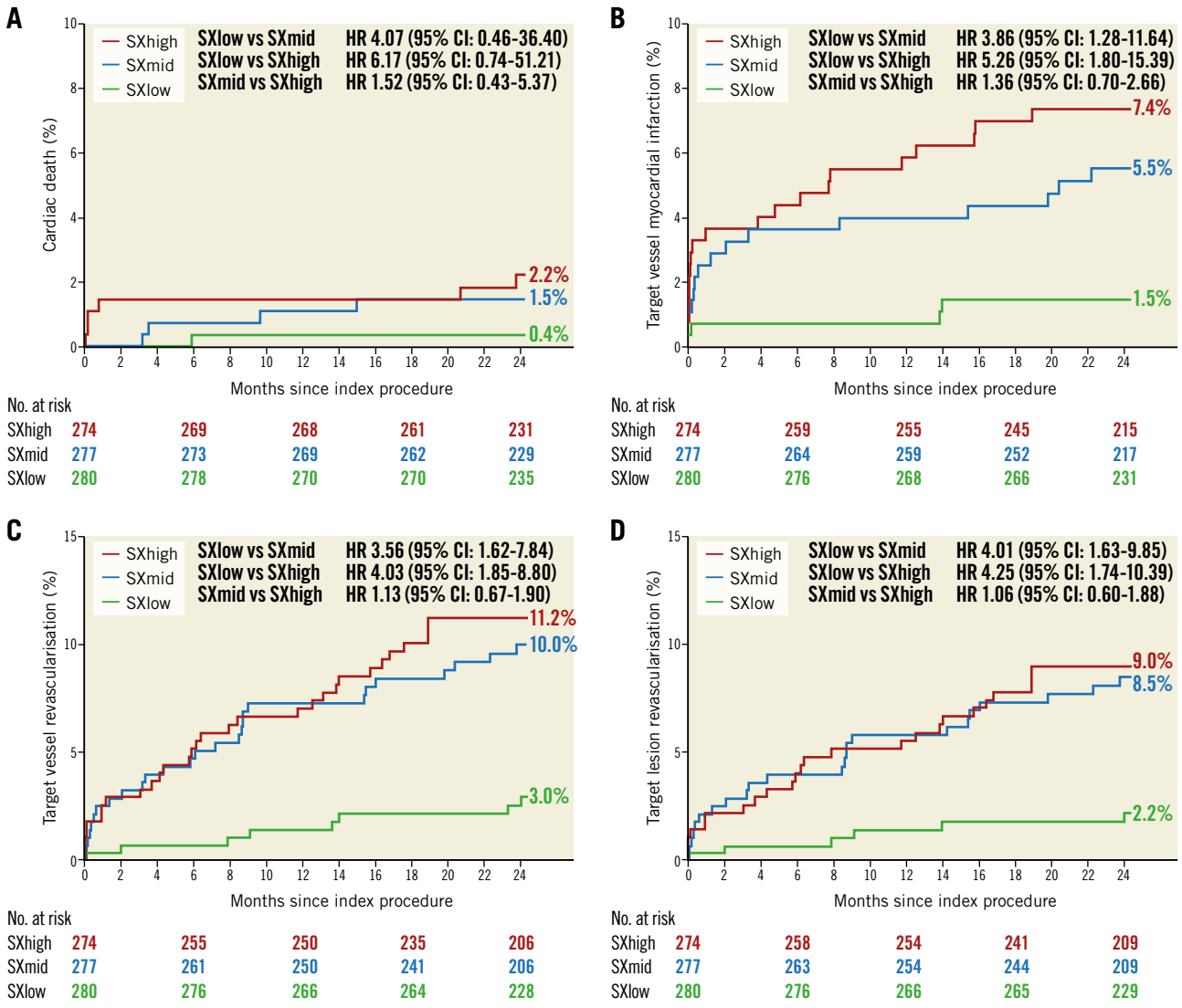

Figure 2. *Kaplan-Meier curves for cardiac death (A), target vessel MI (B), TVR (C), and TLR (D) within the Absorb arm.*

definite device thrombosis are shown in **Supplementary Table 4** and **Supplementary Table 5**, respectively.

Discussion

The major findings in this AIDA trial substudy are the following.

1) When compared to XIENCE, in the SXlow group, the event rate of TVF was numerically lower within the Absorb group, whereas in the SXmid group the event rate of TVF was numerically higher within the Absorb group. In the SXhigh group, TVF rates were similar between the randomised device modalities.

2) Patients treated with Absorb, and whose SXscore was ≤8 have an acceptable, albeit still threefold higher, thrombotic risk compared with XIENCE at a follow-up of two years.

The current analysis on SXscore identified a patient population (SXscore ≤8) in which Absorb implantation is associated with a lower TLR rate and tolerable ScT rate of 1.1%, which, however, still remains threefold higher compared to patients treated with the XIENCE stent (0.3%). The SXscore, divided into tertiles, proved to be an effective tool to discriminate between groups in routine PCI trials. Most importantly, in patients undergoing PCI with early and newer-generation DES, a higher anatomic angiographic complexity tertile is associated with a gradual increase in rates of clinical events[12-14,16,17]. We have demonstrated that this finding also applies for the overall patient population and the XIENCE group of the AIDA trial. Both analyses demonstrated a significant difference for MI and revascularisations between the SXlow and the SXhigh groups, while no difference was observed between the SXlow and SXmid groups and between the SXmid and SXhigh groups. In the Absorb group, however, no gradual but rather a more abrupt increase in the risk of clinical outcomes was observed. Patients treated with the Absorb in the medium SXscore group (i.e., >8 ≤15) demonstrated a similar rate of clinical events to patients with a high SXscore >15.

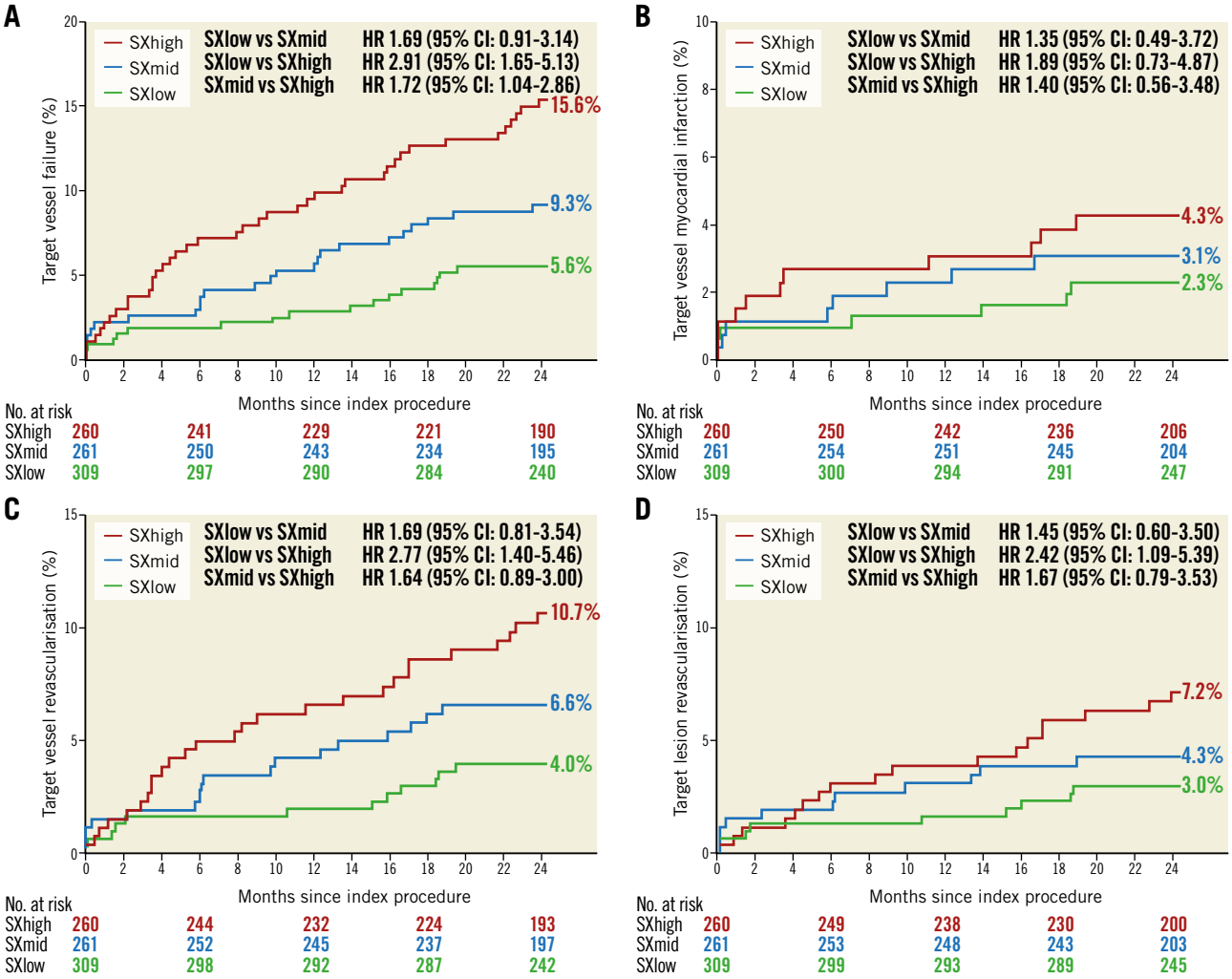

Figure 3. *Kaplan-Meier curves for target vessel failure (A), target vessel MI (B), TVR (C), and TLR (D) within the XIENCE arm.*

The results of this subgroup analysis of the AIDA trial suggest that implantation of the Absorb should only have been considered in patients with relatively simple coronary artery disease, as assessed by an SXscore ≤8. The abrupt increase in events in the Absorb arm observed in this analysis might be due to the insufficient mechanical strength of the device in order to counteract the force of the increased atherosclerotic plaque in patients with an SXscore >8[11]. The lack of mechanical strength could potentially lead to non-embedded, malapposed or even fractured struts, especially in more complex lesions, which can be a potential nidus for neoatherosclerosis, restenosis and/or ScT, MI and revascularisation[18]. Based on the findings of this subgroup analysis, we recommend not to use a bioresorbable coronary device in routine PCI before short- and long-term safety in low-risk patients and low-complex lesions has been thoroughly evaluated in randomised clinical trials.

Limitations

The present analysis has limitations. First, it is subject to statistical underpowering. Second, as the SXscore was evaluated on the diagnostic angiographic films prior to the procedure, no residual SXscores could be evaluated. Third, acute occlusions in STEMI have been evaluated as total occlusions of unknown duration; this could have led to a possible overestimation of the SXscore. Fourth, due to missing data on ejection fraction or kidney function, no clinical SXscore could be assessed. Fifth, mostly due to logistic reasons, the SXscore was collected in 90% of the patients. However, as the angiograms were collected by research staff blinded to clinical events, bias in collecting the baseline angiographic films is not expected. Sixth, the SYNTAX score showed a core lab reproducibility of <0.6; the reproducibility of this analysis might therefore be limited.

Conclusions

We found no significantly different rates of TVF between Absorb and XIENCE patients. Absorb-treated patients in the SXmid and SXhigh tertiles, however, had an increased risk of device thrombosis when compared to XIENCE-treated patients. The rates of device thrombosis in the SXlow tertile, while still higher for Absorb, are more acceptable than in SXmid and SXhigh score tertiles.

Table 3. Safety and efficacy outcomes in randomised groups.

	Low SYNTAX score				Hazard ratioβ (95% CI)		p-value¶	Middle SYNTAX score				Hazard ratioβ (95% CI)		p-value¶	High SYNTAX score				Hazard ratioβ (95% CI)		p-value¶
	Absorb (N=280)		XIENCE (N=309)					Absorb (N=277)		XIENCE (N=261)					Absorb (N=274)		XIENCE (N=260)				
Clinical events																					
All-cause death	6	2.2%	6	2.0%	1.10	[0.35-3.40]	0.87	9	3.3%	10	3.9%	0.86	[0.35-2.11]	0.74	9	3.3%	17	7.5%	0.91	[0.22-1.12]	0.09
Cardiac	1	0.4%	2	0.7%	0.55	[0.05-6.03]	0.62	4	1.5%	5	2.0%	0.76	[0.20-2.84]	0.68	6	2.2%	11	4.3%	0.52	[0.19-1.40]	0.18
Cardiovascular	3	1.1%	2	0.7%	1.65	[0.28-9.84]	0.58	5	1.8%	6	2.3%	0.79	[0.24-2.60]	0.70	7	2.6%	12	4.7%	0.55	[0.22-1.40]	0.21
Non-cardiovascular	3	1.1%	4	1.3%	0.82	[0.18-3.67]	0.80	4	1.5%	4	1.6%	0.95	[0.24-3.81]	0.95	2	0.8%	5	2.0%	0.38	[0.07-1.93]	0.22
All myocardial infarction	7	2.6%	8	2.6%	0.96	[0.35-2.65]	0.94	20	7.4%	9	3.5%	2.14	[0.97-4.69]	0.05	25	9.2%	17	6.6%	1.41	[0.76-2.62]	0.27
Target vessel	4	1.5%	7	2.3%	0.63	[0.18-2.14]	0.45	15	5.5%	8	3.1%	1.79	[0.76- 4.23]	0.18	20	7.4%	11	4.3%	1.74	[0.84-3.64]	0.13
Non-target vessel	3	1.1%	1	0.3%	3.31	[0.34-31.84]	0.27	5	1.9%	1	0.4%	4.77	[0.56-40.83]	0.12	6	2.2%	6	2.3%	0.95	[0.31-2.95]	0.70
Any revascularisation	19	7.0%	20	6.6%	1.04	[0.55-1.94]	0.92	35	12.9%	24	9.3%	1.39	[0.83-2.34]	0.21	51	19.1%	42	16.5%	1.17	[0.78-1.76]	0.45
Target vessel	8	3.0%	12	4.0%	0.73	[0.30-1.78]	0.48	27	10.0%	17	6.6%	1.53	[0.83-2.80]	0.17	30	11.2%	27	10.7%	1.06	[0.63-1.79]	0.82
Target lesion	6	2.2%	9	3.0%	0.73	[0.26-2.05]	0.55	23	8.5%	11	4.3%	2.00	[0.98-4.11]	0.05	24	9.0%	18	7.2%	1.28	[0.69-2.36]	0.43
Non-target lesion	2	0.7%	3	1.0%	0.73	[0.12-4.37]	0.73	7	2.6%	7	2.7%	0.95	[0.33-2.71]	0.93	7	2.6%	9	3.5%	0.74	[0.27-1.98]	0.54
Non-target vessel	12	4.4%	10	3.3%	1.32	[0.57-3.05]	0.52	13	4.9%	10	3.9%	1.23	[0.54-2.79]	0.63	29	10.8%	22	8.6%	1.25	[0.72-2.18]	0.43
Composite endpoints																					
Target vessel failure*	10	3.7%	17	5.6%	0.64	[0.29-1.40]	0.26	31	11.4%	24	9.3%	1.24	[0.73-2.12]	0.42	42	15.5%	40	15.6%	1.01	[0.66-1.56]	0.96
Target lesion failure#	9	3.3%	14	4.6%	0.70	[0.30-1.62]	0.40	28	10.3%	20	7.8%	1.34	[0.76-2.38]	0.31	37	13.7%	33	12.9%	1.08	[0.68-1.73]	0.75
Patient-oriented composite endpoint$	27	9.9%	28	10.2%	1.06	[0.66-1.69]	0.99	46	16.8%	35	13.6%	1.34	[0.90-2.00]	0.19	64	23.5%	61	23.5%	0.98	[0.71-1.36]	0.94
Device thrombosis																					
Definite	3	1.1%	1	0.3%	3.31	[0.34-31.79]	0.27	9	3.3%	2	0.8%	4.27	[0.92-19.75]	0.04	10	3.7%	2	0.8%	4.77	[1.05-21.78]	0.03
Probable	0	0.0%	0	0.0%				0	0.0%	2	0.8%	0.02	[<0.01->1,000]	0.15	3	1.1%	0	0.0%	62.32	[0.01->1,000]	0.09
Possible	0	0.0%	1	0.3%	0.02	[<0.01->1,000]	0.34	1	0.4%	3	1.2%	0.32	[0.03-3.07]	0.30	2	0.8%	5	2.0%	0.38	[0.07-1.93]	0.08
Definite/probable device thrombosis	3	1.1%	1	0.3%	3.31	[0.34-31.79]	0.27	9	3.3%	4	1.5%	2.14	[0.66-6.95]	0.20	13	4.8%	2	0.8%	6.21	[1.40-27.53]	0.01
≤24 hours (acute)	1							0							1						
>24 hours to 30 days (subacute)	1							3							6						
31 days to 1 year (late)	0							3							3						
1-2 years (very late)	1							3							3						
Any device thrombosis	3	1.1%	2	0.7%	1.65	[0.28-9.89]	0.58	10	3.7%	7	2.7%	1.36	[0.52-3.58]	0.53	15	5.6%	7	2.8%	2.05	[0.84-5.03]	0.11

β Hazard ratio low versus high SYNTAX score. ¶ *p*-values were calculated by log-rank test. * Composite of cardiac death, target vessel myocardial infarction and target vessel revascularisation. # Composite of cardiac death, target vessel myocardial infarction and target lesion revascularisation. $ Composite of all-cause death, all myocardial infarction and all revascularisation.

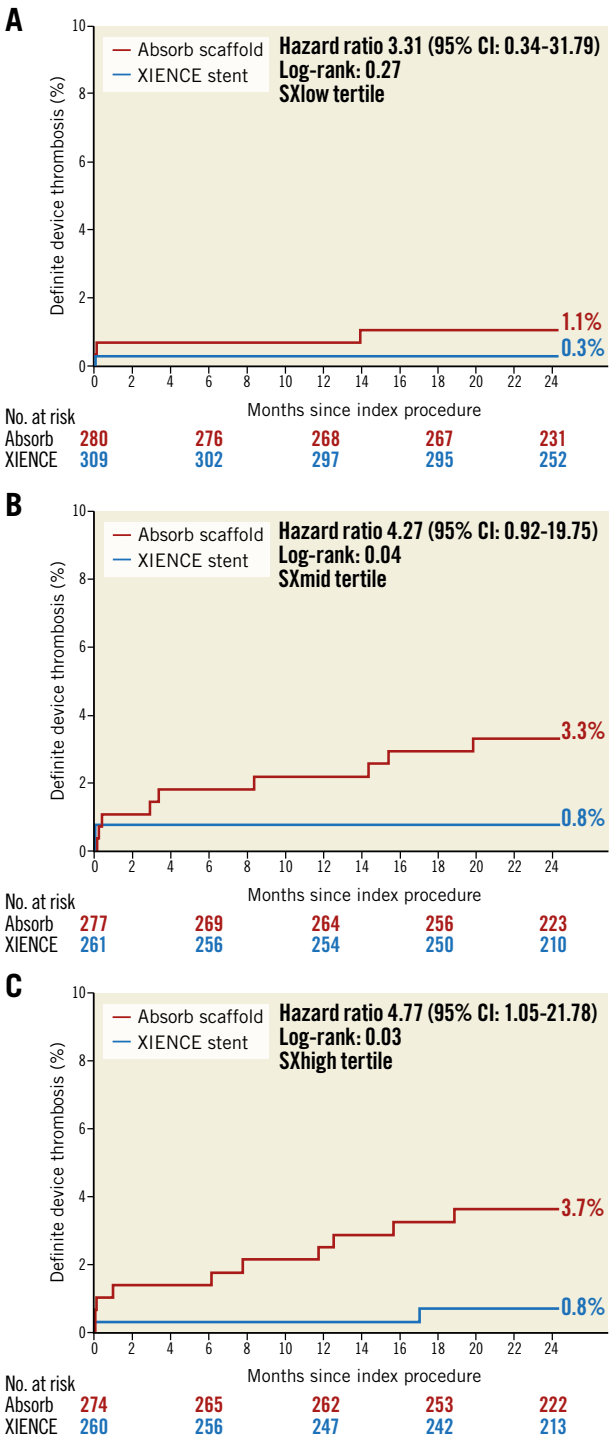

Figure 4. *Definite device thrombosis in the three SX tertile groups.*

Impact on daily practice

Implantation of any coronary bioresorbable scaffold in daily clinical care should be reserved for patients with a SYNTAX score ≤8, while implantation in more complex patients, at the moment, should be withheld until future clinical trials, or longer-term follow-up, demonstrate benefits for bioresorbable technology over conventional drug-eluting metallic stents.

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Funding

The AIDA trial is supported by an unrestricted educational grant from Abbott Vascular. The AMC Heart Center has received an educational research grant from Abbott Vascular for AIDA. The Research Departments of the Cardiology Division of the Medical Center Leeuwarden and of the Onze Lieve Vrouwe Gasthuis have received non-study-related unrestricted educational research grants from Abbott Vascular.

Conflict of interest statement

J.P.S. Henriques receives research grants from Abbott Vascular. J.G.P. Tijssen served on the DSMB of the early ABSORB trials, including ABSORB II. The other authors/study collaborators have no conflicts of interest to declare.

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Supplementary data

Supplementary Table 1. Target lesion measures.

Supplementary Table 2. Procedural characteristics.

Supplementary Table 3. Outcomes of the as-treated population.

Supplementary Table 4. Univariate and multivariate Cox proportional hazards analysis for target vessel failure.

Supplementary Table 5. Univariate and multivariate Cox proportional hazards analysis for definite device thrombosis.

The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-18-00884

Supplementary data

Supplementary Table 1. Target lesion measures[¥].

	Low SYNTAX score		Middle SYNTAX score		High SYNTAX score		*p*-value
	N=589		N=538		N=534		
Coronary artery location							
Left main	248	(36%)	318	(43%)	374	(48%)	<0.001
Left anterior descending	199	(29%)	171	(23%)	181	(23%)	0.029
Left circumflex	247	(36%)	239	(33%)	196	(25%)	<0.001
Right	0	(0.0%)	0	(0.0%)	2	(0.3%)	0.158
Arterial bypass graft	0	(0.0%)	0	(0.0%)	11	(1.4%)	<0.001
Venous bypass graft	0	(0.0%)	4	(0.5%)	9	(1.2%)	0.014
AHA/ACC lesion type							
A	99/692	(14%)	77/730	(11%)	44/770	(6%)	<0.001
B1	281/692	(41%)	271/730	(37%)	232/770	(30%)	<0.001
B2	236/692	(34%)	263/730	(36%)	295/770	(38%)	0.245
C	76/692	(11%)	119/730	(16%)	199/770	(26%)	<0.001
Bifurcation, n (%)	29	(4%)	45	(6%)	47	(6%)	0.181
Chronic total occlusion, n (%)	17	(2%)	30	(4%)	39	(5%)	0.100
Moderately or severely calcified, n (%)	146	(21%)	210	(29%)	285	(37%)	0.044
Thrombus present, n (%)	97	(14%)	85	(12%)	134	(17%)	0.006
Lesion length >20 mm[¶], n (%)	157	(23%)	206	(28%)	273	(35%)	0.021
Reference vessel diameter ≤2.75 mm, n (%)	193/692	(28%)	189/731	(26%)	186/770	(24%)	0.266
Lesion length, mm[¶]	17.6	±7.6	18.9	±9.7	20.0	±9.6	<0.001
Reference vessel diameter, mm[¶]	3.03	±0.43	3.03	±0.41	3.06	±0.40	0.387
Percentage stenosis[¶]	85.2	±11.8	84.8	±11.9	86.7	±12.0	0.007

[¥] All target lesion measures are as site-reported.

[¶] Visually estimated and as site-reported.

Supplementary Table 2. Procedural characteristics.

	Low SYNTAX score		Middle SYNTAX score		High SYNTAX score		*p*-value
Patients							
Total number	589		538		534		
Treated lesions per patient	1.18	±0.45	1.37	±0.62	1.45	±0.72	<0.001
Number of devices per patient	1.29	±0.61	1.53	±0.85	1.67	±0.95	<0.001
Procedure time, min mean (total no.) ±SD	39 (585)	±21	49 (535)	±27	53 (533)	±26	<0.001
Contrast use, ml mean (total no.) ±SD	141 (575)	±61	163 (523)	±75	176 (520)	±78	<0.001
Predilatation first treated lesion, no./total no. of target lesions (%)	572	(97%)	524	(97%)	526	(99%)	0.276
Treated lesions¶							
Total number	694		732		773		
Rotational atherectomy, no./total no. of target lesions (%)	4	(0.6%)	19	(2.6%)	19	(2.6%)	0.001
Thrombus aspiration, no./total no. of target lesions (%)	52	(7.5%)	38	(5.2%)	38	(5.2%)	0.665
Predilatation, no./total no. of target lesions (%)							
Predilatation performed	657	(94%)	682	(93%)	733	(95%)	0.323
Predilatation balloon diameter, mm mean (total no.) ±SD	2.66 (647)	±0.38	2.69 (665)	±0.37	2.69 (672)	±0.38	0.258
Predilatation balloon pressure, atm mean (total no.) ±SD	11.3 (646)	±2.8	11.5 (668)	±2.9	11.4 (725)	±3.1	0.505
Device implantation							
Total number	762		825		893		
Device diameter, mm mean±SD	3.05	±0.40	3.04	±0.38	3.07	±0.38	0.288
Device length, mm mean±SD	19.3	±6.2	20.3	±6.6	20.4	±6.6	0.001
Device pressure, atm mean±SD	13.1	±2.8	13.0	±2.6	13.4	±2.7	0.038
Number of devices per lesion	1.10	±0.43	1.13	±0.39	1.16	±0.40	0.014
Post-dilatation, no./total no. of target lesions (%)							
Post-dilatation performed	413	(60%)	461	(63%)	503	(65%)	0.087
Post-dilatation balloon diameter, mm mean (total no.) ±SD	3.31 (413)	±0.46	3.24 (459)	±0.46	3.28 (503)	±0.45	0.038
Post-dilatation balloon pressure, atm mean (total no.) ±SD	15.3 (410)	±3.4	15.4 (456)	±3.7	15.5 (500)	±3.7	0.764

Plus-minus variables are means±SD.

¶ All treated lesions at time of randomisation and staged procedures.

Supplementary Table 3. Outcomes of the as-treated population.

	Low SX score				HR	(95% CI)	*p*-value*	Middle SX score				HR	(95% CI)	*p*-value	High SX score				HR	(95% CI)	*p*-value
	Absorb (n=272)		XIENCE (n=305)					Absorb (n=253)		XIENCE (n=257)					Absorb (n=252)		XIENCE (n=257)				
Clinical events																					
All-cause death	6	2.3%	6	2.0%	1.16	[0.36–3.46]	0.850	9	3.6%	9	3.6%	1.03	[0.41–2.58]	0.975	8	3.2%	16	6.2%	0.51	0.22–1.19	0.113
Cardiac	1	0.4%	2	0.7%	0.56	[0.05–6.14]	0.627	4	1.6%	4	1.6%	1.03	[0.26–4.10]	0.972	6	2.4%	10	4.0%	0.61	0.22–1.69	0.339
Cardiovascular	3	1.2%	2	0.7%	1.67	[0.28–10.02]	0.568	5	2.0%	5	2.0%	1.03	[0.30–3.54]	0.968	7	2.8%	11	4.3%	0.65	0.25–1.68	0.370
Non-cardiovascular	2	1.1%	4	1.3%	0.84	[0.19–3.74]	0.815	4	1.6%	4	1.6%	1.03	[0.26–4.12]	0.966	1	0.4%	5	2.0%	0.20	0.02–1.74	0.106
All myocardial infarction					0.98	[0.35–2.69]	0.963	20	8.1%	8	3.1%	2.61	[1.15–5.92]	0.017	20	8.1%	16	6.3%	1.30	0.67–2.50	0.439
Target vessel					0.64	[0.19–2.18]	0.468	15	6.0%	7	2.8%	2.22	[0.91–5.44]	0.074	16	6.4%	10	4.0%	1.65	0.75–3.65	0.205
Non-target vessel					3.37	[0.35–32.43]	0.263	5	2.0%	1	0.4%	5.15	[0.60–44.06]	0.115	4	1.6%	6	2.4%	0.69	0.19–2.43	0.558
Any revascularisation	19	7.2%	20	6.7%	1.05	[0.56–1.97]	0.871	35	14.1%	24	9.5%	1.51	[0.90–2.53]	0.120	44	18.0%	41	16.3%	1.12	0.73–1.71	0.607
Target vessel	8	3.1%	12	4.0%	0.74	[0.31–1.81]	0.508	27	10.9%	17	6.7%	1.65	[0.90–3.04]	0.100	27	11.0%	27	10.8%	1.04	0.61–1.77	0.897
Target lesion	6	2.3%	9	3.0%	0.74	[0.26–2.08]	0.569	23	9.3%	11	4.3%	2.17	[1.06–4.45]	0.030	23	9.4%	18	7.2%	1.33	0.72–2.47	0.361
Non-target lesion	2	0.8%	3	1.0%	0.74	[0.12–4.45]	0.745	7	2.9%	7	2.8%	1.03	[0.36–2.93]	0.959	5	2.0%	9	3.6%	0.57	0.19–1.70	0.307
Non-target vessel	12	4.5%	10	3.3%	1.34	[0.58–3.10]	0.493	13	5.4%	10	4.0%	1.32	[0.58–3.02]	0.504	24	9.8%	21	8.3%	1.17	0.65–2.11	0.595
Composite endpoints																					
Target vessel failure[#]	10	3.8%	17	5.7%	0.65	[0.30–1.42]	0.227	13	12.4%	22	8.7%	1.47	[0.85–2.55]	0.161	37	14.8%	39	15.4%	0.98	0.63–1.54	0.931
Target lesion failure[$]	9	3.4%	14	4.7%	0.71	[0.31–1.65]	0.428	28	11.3%	18	7.1%	1.62	[0.90–2.93]	0.107	33	13.3%	32	12.6%	1.07	0.66–1.74	0.793
POCE[†]	27	10.2%	28	9.3%	1.08	[0.67–1.72]	0.804	46	18.3%	33	13.0%	1.48	[0.98–2.23]	0.097	56	22.4%	59	23.0%	0.95	0.67–1.33	0.933
Device thrombosis																					
Definite	3	1.1	1	0.3	3.36	[0.35–32.33]	0.264	9	3.6%	2	0.8%	4.61	[1.00–21.31]	0.032	9	3.6%	2	0.8%	4.64	1.00–21.52	0.030
Probable	0	0	0	0	-		-	0	0%	2	0.8%	0.02	[<0.01–>1,000]	0.163	3	1.2%	0	0%	67.23	[0.01–>1.00]	0.079
Possible	0	0	1	3.3	0.02	[<0.01– >1,000]	0.344	1	0.4%	3	1.2%	0.35	[0.04–3.31]	0.333	2	0.9%	4	1.6%	0.51	[0.09–2.77]	0.423
Definite/probable	3	1.1%	1	0.3%	3.36	[0.35–32.33]	0.264	9	3.6%	4	1.6%	2.31	[0.71–7.50]	0.152	12	4.8%	2	0.8%	6.21	[1.39–27.72]	0.006
<24 hr acute	1							0							1						
>24 hr to 30 d (subacute)	1							3							6						
31 d to 1 yr (late)	0							3							3						
1-2 yrs (very late)	1							3							3						
Any device thrombosis	3	1.1%	2	0.7%	1.68	[0.28–10.07]	0.564	10	4.0%	7	2.8%	1.47	[0.56–3.87]	0.430	14	5.7%	6	2.4%	2.42	[0.93–6.30]	0.062

[*] p-values were calculated by the log-rank test.

[#] Composite of cardiac death, target vessel myocardial infarction and target vessel revascularisation (primary endpoint).

[$] Composite of cardiac death, target vessel myocardial infarction and target vessel revascularisation.

[†] Composite of all-cause death, all myocardial infarction and all revascularisation.

CI: confidence interval; d: day; hr: hour(s); HR: hazard ratio; POCE: patient-oriented composite endpoint; SX: SYNTAX; yr: year

Supplementary Table 4. Univariate and multivariate Cox proportional hazards analysis for target vessel failure.

Target vessel failure*	Univariate Cox regression		*p*-value	Multivariate Cox regression		*p*-value
	Hazard ratio	(95% CI)		Hazard ratio	(95% CI)	
Patient-related factors						
Randomisation result	0.89	0.57–1.19	0.436			
Age	1.01	1.00–1.03	0.113			
Gender	0.74	0.52–1.05	0.088	0.86	0.59–1.25	0.420
Diabetes mellitus	0.66	0.47–0.92	0.013	0.68	0.47–0.97	0.032
Hypercholesterolaemia	1.17	0.87–1.59	0.296			
Hypertension	0.83	0.62–1.10	0.196			
Familial history of CAD	1.04	0.77–1.39	0.800			
Current smoker	1.33	1.10–1.61	0.004	1.24	1.01–1.53	0.044
Congestive heart failure	0.62	0.27–1.39	0.242			
Chronic renal insufficiency	0.45	0.31–0.65	<0.001	0.57	0.38–0.86	0.007
Peripheral vascular disease	0.94	0.54–1.66	0.837			
History of stroke	1.21	0.62–2.36	0.583			
Previous myocardial infarction	0.78	0.55–1.09	0.147			
Previous CABG	0.23	0.15–0.33	<0.001	0.49	0.29–0.85	0.011
Previous PCI	0.60	0.44–0.81	0.001	0.68	0.48–0.97	0.033
SYNTAX score	1.05	1.03–1.06	<0.001	1.03	1.01–1.04	0.003

* Composite of cardiac death, target vessel myocardial infarction and target vessel revascularisation (primary endpoint).

CABG: coronary artery bypass grafting; CAD: coronary artery disease; CI: confidence interval; PCI: percutaneous coronary intervention

Supplementary Table 5. Univariate and multivariate Cox proportional hazards analysis for definite device thrombosis.

Definite device thrombosis	Univariate Cox regression		*p*-value	Multivariate Cox regression		*p*-value
	Odds ratio	(95% CI)		Odds ratio	(95% CI)	
Patient-related factors						
Randomisation result	0.19	0.07–0.50	0.001	0.24	0.09–0.64	0.004
Age	1.01	0.98–1.05	0.468			
Gender	0.84	0.36–1.95	0.681			
Diabetes mellitus	1.11	0.43–2.88	0.837			
Hypercholesterolaemia	1.29	0.61–2.74	0.508			
Hypertension	0.64	0.31–1.33	0.233			
Familial history of CAD	1.89	0.90–3.97	0.093	1.66	0.77–3.57	0.200
Current smoker	1.13	0.72–1.78	0.608			
Congestive heart failure	0.19	0.06–0.63	0.007	0.29	0.07–1.24	0.095
Chronic renal insufficiency	0.87	0.27–2.87	0.821			
Peripheral vascular disease	0.64	0.20–2.11	0.463			
History of stroke	0.87	0.21–3.64	0.846			
Previous myocardial infarction	0.93	0.38–2.27	0.872			
Previous CABG	0.48	0.15–1.57	0.225			
Previous PCI	0.90	0.39–2.09	0.810			
SYNTAX score	1.04	1.01–1.08	0.027	1.04	1.00–1.07	0.044

CABG: coronary artery bypass grafting; CAD: coronary artery disease; CI: confidence interval; PCI: percutaneous coronary intervention