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First-in-man randomised comparison of the Angiolite durable fluoroacrylate polymer-based sirolimus-eluting stent versus a durable fluoropolymer-based everolimus-eluting stent in patients with coronary artery disease: the ANGIOLITE trial

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KEYWORDS

- clinical trials
- drug-eluting stent
- optical coherence tomography
- QCA

Abstract

Aims: The durable fluoroacrylate polymer-based sirolimus-eluting stent (Angiolite SES) has shown promising preclinical and clinical results regarding inflammatory vascular reaction and neointimal healing. We aimed to compare performance between the Angiolite SES and an everolimus-eluting stent (EES) in patients with coronary artery disease.

Methods and results: The ANGIOLITE trial, a prospective, randomised, multicentre trial, compared the restenosis parameters of both stents in *de novo* coronary lesions. The primary endpoint was late lumen loss at six-month angiographic follow-up. In-stent healing was assessed by optical coherence tomography (OCT). The main clinical endpoint was target lesion failure (TLF) evaluated up to 24 months. A total of 223 patients were randomised 1:1 to EES or SES. At six months, in-stent late lumen loss was 0.08 mm (±0.38) for EES vs 0.04 mm (±0.39) for SES (difference=−0.04 mm, 95% CI: –0.15, 0.07, p for non-inferiority=0.002). By OCT, the rate of uncovered to total number of struts score >30% was comparable between the groups whereas neointimal thickness was reduced in the SES arm (9.0% [7.6, 10.6] vs 9.9% [8.5, 11.3], p=0.41; and 86.4 [81.6, 91.2] µm vs 72.1 [68.2, 76.0] µm, p<0.01, respectively). At 24 months, TLF occurred in eight patients (7.6% [3.3, 14.5]) in the EES arm and in seven patients (7.1% [2.9, 14.0]) in the SES arm (p=0.88). The definite/probable stent thrombosis rate was comparable between the groups (1.9% [0.2, 6.7] vs 1.0% [0.0, 5.5] EES vs SES, respectively; p=0.59).

Conclusions: This trial demonstrates similar antirestenotic efficacy at midterm follow-up of the Angiolite SES vs an EES. Clinical endpoints were comparable between the groups at two-year follow-up.

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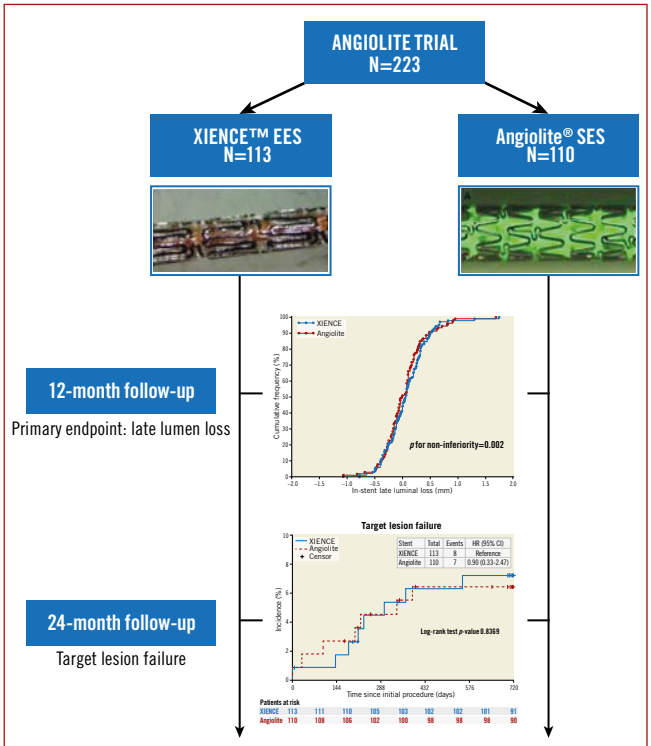

Visual summary. *Main results of the ANGIOLITE trial.*

Abbreviations

DAPT	dual antiplatelet therapy
DES	drug-eluting stent(s)
EES	everolimus-eluting stent(s)
LLL	late lumen loss
MACE	major adverse cardiac events
MI	myocardial infarction
MLD	minimum lumen diameter
OCT	optical coherence tomography
PCI	percutaneous coronary intervention
QCA	quantitative coronary angiography
RUTTS	rate of uncovered to total number of struts
SES	sirolimus-eluting stent(s)
TLF	target lesion failure
TLR	target lesion revascularisation

Introduction

The design of drug-eluting stents (DES) with an antiproliferative drug included in a polymer matrix was a breakthrough in the field of percutaneous coronary intervention (PCI), leading to a significant reduction of major adverse cardiac events (MACE) that was mainly driven by a lesser number of new revascularisations[1,2]. However, a higher than expected rate of stent thrombosis was observed with first-generation DES, which caused health alerts[3] and forced the medical community to recommend prolonging the dual antiplatelet regimen[4]. The permanent polymer used in those early stents was responsible for chronic inflammation, delayed endothelialisation, and stent thrombosis[5]. New-generation DES incorporated several modifications, such as the use of biocompatible polymers, different antiproliferative limus analogues and metallic alloys allowing the design of thinner struts, and modifications in stent architecture. As a result, they offered similar antirestenotic efficacy but a better safety profile, compared to their first-generation counterparts. Among second-generation DES, the cobalt-chromium everolimus-eluting stent (EES) has shown favourable efficacy and safety profiles and has been used as a workhorse in routine clinical practice and as a control arm in many randomised trials evaluating the performance of new DES[6].

The Angiolite® stent (iVascular, Barcelona, Spain) is a thin-strut cobalt-chromium sirolimus-eluting stent (SES) with an open-cell design containing a durable biostable coating composed of three layers - acrylate to ensure adhesion to the metal surface, fluoroacrylate that carries the sirolimus (1.4 microgr/mm^2), and a top layer of fluoroacrylate to control drug release (>75% elution within the first month). This composition demonstrated *in vitro* early endothelial cell growth and a reduction of smooth muscle cell proliferation **(Supplementary Appendix 1, Supplementary Table 1, Supplementary Table 2, Supplementary Figure 1-Supplementary Figure 5)**. Preclinical studies in animals have demonstrated a favourable healing process with a reduction in injury score and inflammation score that led to a reduction in neointimal area and an increase in the percentage of endothelialised surface as compared to the EES stent[7]. These preclinical results were later confirmed in the ANCHOR trial[8] that assessed strut healing after Angiolite SES implantation. As early as three months after implantation, the percentage of strut coverage was nearly 90%. For these reasons, we considered the design of a non-inferiority trial against the world's most commonly implanted DES. (www.clinicaltrials.gov NCT03049657).

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Methods

PATIENTS AND STUDY DESIGN

This prospective, randomised, multicentre, controlled trial was designed to test the non-inferiority of the Angiolite SES in comparison with EES in patients with coronary artery disease. Detailed inclusion and exclusion criteria are presented in **Supplementary Appendix 2**. Briefly, patients aged at least 18 years, with ischaemic heart disease (stable angina, silent ischaemia, or acute coronary syndrome) and scheduled for PCI of *de novo* epicardial coronary stenosis were eligible. Patients were enrolled at 11 academic medical centres in Spain between February 2016 and February 2017 **(Supplementary Table 3)**. Written informed consent was obtained from each patient prior to study enrolment. All participants were randomly allocated in a 1:1 ratio to either the SES or EES. To generate comparable groups regarding known and unknown risk factors, randomisation was independently conducted online via a web-based application. The randomisation was balanced and stratified by participating centre and allocated treatment group. All centres received the approval of their medical ethics committee. The study was conducted in compliance with the protocol, the Declaration of Helsinki, BS EN ISO 14155 Part 1 and Part 2, and

applicable local requirements. A description of the data and safety monitoring board and clinical events committee can be found in **Supplementary Table 4**.

STUDY ENDPOINTS AND DEFINITIONS

The primary endpoint of the trial was in-stent late lumen loss (LLL), defined as the angiographic minimum lumen diameter (MLD) immediately after PCI minus the MLD at angiographic follow-up at six months measured by off-line quantitative coronary angiography (QCA) within in-stent boundaries. Additionally, as an exploratory analysis, we aimed to compare the rate of target lesion failure (TLF) as a composite of cardiac death, target vessel-related MI or clinically driven target lesion revascularisation (TLR) at 12 months. Secondary clinical endpoints included device success, procedural success, MACE (a composite of all-cause death, any MI or any revascularisation) and stent thrombosis defined according to the Academic Research Consortium criteria[9]. The main secondary angiographic endpoints included acute gain, in-segment LLL, MLD, percentage diameter stenosis and binary restenosis **(Supplementary Appendix 3)**. An optical coherence tomography (OCT) study was performed at six-month follow-up in a cohort of patients in five predefined centres (OCT subgroup). The OCT parameters included the OCT-derived stent-level and strut-level neointimal proliferation, strut coverage measured by the % of uncovered stent struts and the number of cross-sections by rate of uncovered to total number of struts (RUTTS) score >30%, and rates of incomplete stent apposition **(Supplementary Appendix 4)**. Clinical follow-up was scheduled at 1, 6, 12 and 24 months.

CORONARY STENTING PROCEDURE

Coronary interventions were performed according to current standard techniques. All patients received aspirin (300 mg) and a loading dose of clopidogrel (600 mg) or ticagrelor (180 mg) prior to the procedure, unless already receiving these drugs. Heparin i.v. was given to maintain an activated clotting time at >250 sec with an additional bolus during the procedure if needed. After the procedure, aspirin was prescribed indefinitely (100 mg/day), and clopidogrel (75 mg/day) or ticagrelor (90 bid) or prasugrel (10 mg/day) was prescribed for a minimum of six months after the index procedure. Specific descriptions of the stents used in this trial are presented in **Supplementary Table 1** and **Supplementary Table 2**.

STATISTICAL ANALYSIS

To test the non-inferiority of the Angiolite SES versus the XIENCE EES (Abbott Vascular, Santa Clara, CA, USA) in terms of six-month in-stent LLL, a mean late loss of 0.10 mm (standard deviation [SD] 0.45 mm) was assumed for both stents, which was extrapolated from the QCA results for the EES in the SPIRIT I and SPIRIT II trials[10,11]. For non-inferiority testing, with a 0.2 mm non-inferiority margin, type I error at 0.05 (one-sided), 90% statistical power, and 1:1 sampling ratio (Angiolite SES: EES), a sample of 176 patients (88 per group) was needed. Assuming a 12% drop-out rate during follow-up, a total of 200 patients (100 per group) constituted the final calculated sample size. We finally decided to increase this sample size by 10% to ensure the inclusion of at least 80 patients in the OCT substudy.

For continuous variables, results are presented as mean±SD. Variables were compared using an independent t-test or the Mann-Whitney test when applicable. Categorical variables are presented as counts and percentages and compared using the chi-square test or Fisher's exact test. The null hypothesis was evaluated on a non-inferiority basis, using a mixed effects linear regression model of the mean in both groups. Angiographic and OCT outcomes were analysed at lesion level with mixed effects linear regression models (continuous variables) or mixed effects logistic regression models (categorical variables) that account for the non-independence of multiple lesions within patients. Clinical variables at 12 and at 24 months were compared with the χ^2 test. Time-to-event hazard curves, presented with Kaplan-Meier estimates, were compared using a log-rank test. Associations were considered statistically significant in the presence of a two-sided p-value <0.05.

Results

PATIENTS AND PROCEDURES

A total of 223 patients were enrolled in the trial: 110 were allocated to SES and 113 to EES **(Figure 1)**. The two groups were well balanced in terms of baseline clinical characteristics **(Supplementary Table 5)**. Mean age was 63.0 years, with a male preponderance (78.5%). More patients in the EES group had prior myocardial infarction (MI) (16.1% vs 7.3%; p=0.04) and prior revascularisation procedures (18.8% vs 9.1%; p=0.04). There were differences in lesion type distribution (p=0.02), with more type C lesions in the SES group (3.3% vs 9.5%). Device success was achieved in 99.3% of lesions in the SES group and 100% in the EES arm. Procedural success was achieved in 99.3% of lesions in both arms **(Table 1)**.

QUANTITATIVE CORONARY ANGIOGRAPHY RESULTS

Baseline and post-procedure QCA data were similar between the groups **(Table 2)**. The acute gain in the SES group was 1.65±0.48 mm versus 1.64±0.50 mm in the EES group (p=0.84). Follow-up angiography was performed in 90 patients (106 lesions) in the SES group (81.8% of those allocated) and in 90 patients (104 lesions) in the EES group (79.6%). The primary endpoint, in-stent LLL, was 0.04±0.39 mm in the SES group and 0.08±0.38 mm in the EES arm (difference=−0.04 mm, 95% CI: −0.15, 0.07, p for non-inferiority=0.002) **(Figure 2)**. Similarly, in-segment LLL was non-inferior between the groups (0.00±0.44 mm in the SES group vs 0.06±0.38 mm in the EES group; difference=−0.06 mm, 95% CI: −0.18, 0.06, p for non-inferiority=0.007). Cumulative frequency distributions of in-stent and in-segment LLL curves are presented in **Figure 2A** and **Figure 2B**. In-stent binary restenosis occurred in three patients, two in the EES group and one in the SES arm. Cumulative frequency distribution curves of MLD pre intervention, post intervention and at follow-up are presented in **Supplementary Figure 6**.

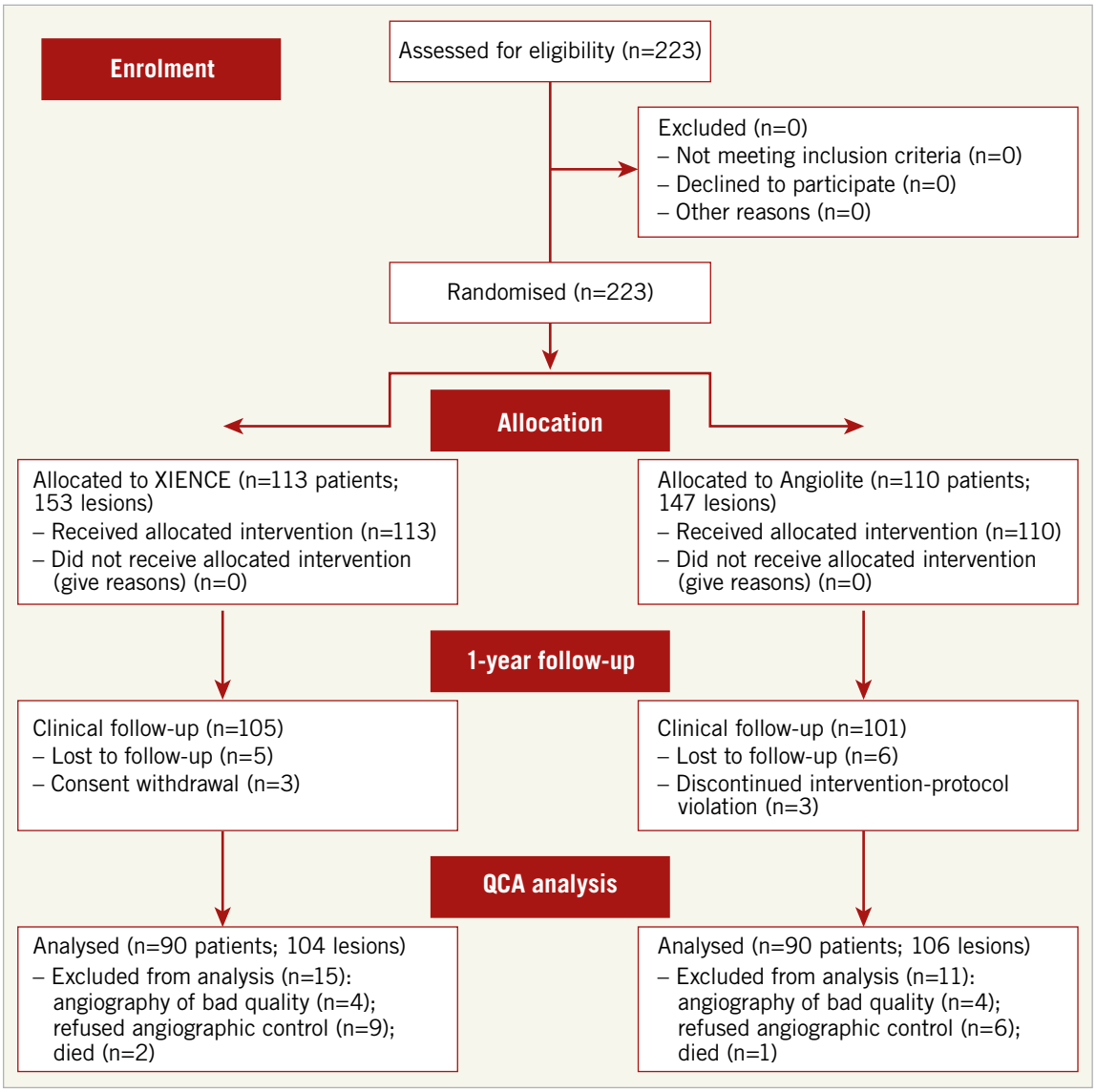

Figure 1. *Flow chart of the study according to CONSORT 2010 guidelines.*

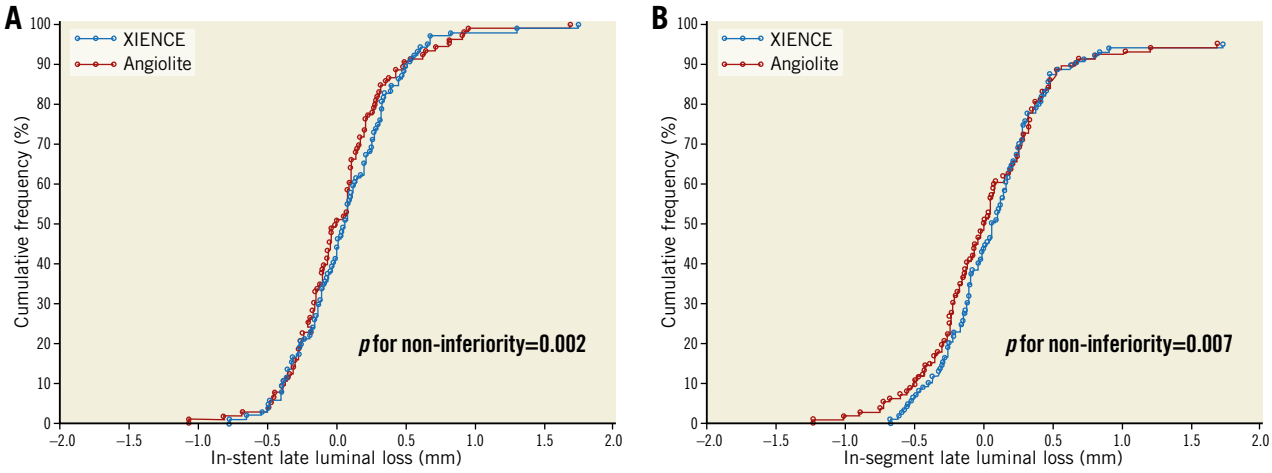

Figure 2. *Cumulative frequency distribution curves. A) In-stent LLL. B) In-segment LLL.*

Table 1. Angiographic characteristics.

	EES (N=113; L=153)	SES (N=110; L=147)	*p*-value
Numbers of lesions per patient	1.4±0.6	1.3±0.6	0.46
Number of stents per lesion	1.1±0.3	1.1±0.3	1.00
Culprit artery			
LAD	62 (40.5)	67 (45.6)	0.11
LCX	40 (26.1)	37 (25.2)	
RCA	51 (33.3)	43 (29.3)	
ACC/AHA classification			0.02
A	33 (21.6)	22 (15.0)	0.14
B1	68 (44.4)	79 (53.7)	0.10
B2	47 (30.7)	32 (21.8)	0.08
C	5 (3.3)	14 (9.5)	0.03
Pre-PCI TIMI flow grade			
0	6 (3.9)	6 (4.1)	0.11
1	6 (3.9)	0 (0.0)	
2	6 (3.9)	5 (3.4)	
3	135 (88.2)	136 (92.5)	
Intracoronary thrombus	9 (5.9)	15 (10.2)	0.17
Severe calcification	17 (11.1)	20 (13.6)	0.50
Ulcerated lesion	10 (6.5)	10 (6.8)	0.91
Bifurcation with side branch >2 mm	11 (7.2)	15 (10.2)	0.35
Lesion length, mm	17.7±8.1	17.5±6.7	0.81
Total stent length, mm	22.1±9.7	22.2±7.9	0.92
% diameter stenosis	84.7±9.9	85.6±8.7	0.50
Direct stenting	57 (37.2)	55 (37.4)	0.19
Thrombus aspiration	1 (0.7)	2 (1.4)	0.62
Lesion debulking	5 (3.3)	2 (1.4)	0.28
Predilatation	90 (58.8)	89 (60.5)	0.62
Stent diameter, mm	3.1±0.4	3.0±0.5	0.52
Stent length, mm	20.2±7.0	20.6±5.6	0.57
Post-dilatation	28 (18.3)	38 (25.9)	0.15
Need for a second stent	14 (9.2)	15 (10.2)	0.74
Device success*	153 (100.0)	146 (99.3)	0.98
Procedural success#	152 (99.3)	146 (99.3)	0.99

Data presented as n (%) or mean±SD. *One patient allocated to the SES group achieved a 30.5% residual diameter stenosis in a calcified vessel not completely predilated. #One patient allocated to the EES arm had recurrent chest pain during admission; subsequent angiography revealed significant stenosis remote from the target segment that was treated accordingly. EES: everolimus-eluting stent; LAD: left anterior descending artery; LCX: left circumflex; PCI: percutaneous coronary intervention; RCA: right coronary artery; SES: sirolimus-eluting stent

OPTICAL COHERENCE TOMOGRAPHY SUBSTUDY

A total of 88 patients were included in the OCT substudy (47 in the SES group and 41 in the EES group). There were no differences between the groups in baseline characteristics **(Supplementary Table 6)**. The main QCA parameters in this subgroup of patients mimicked those of the overall study population **(Supplementary Table 7)**.

The main OCT findings are displayed in **Table 3**. In the EES arm, 10,597 struts (90.9%) were fully covered, RUTTS score >30% was observed in 9.0% of the analysed cross-sections and 1.6% of struts were incompletely apposed. In the SES arm, 15,547 struts (89.6%) were fully covered, the RUTTS score >30% was observed in 9.9% of analysed cross-sections, and 2.4% of struts showed incomplete apposition. Mean neointimal thickness and neointimal area obstruction were lower in the SES group.

CLINICAL OUTCOMES

During hospitalisation, there were no differences in clinical outcomes between the groups. Three major complications prolonging hospital stay occurred – one acute definite stent thrombosis in the EES group and two bradyarrhythmia events not related to the device in the SES arm.

At one year, there were no differences in outcomes between the groups **(Figure 3, Supplementary Table 8)**. Eleven patients presented with TLF (seven in the EES group and four in the SES group). In the EES arm, this included one cardiac death at seven months due to cardiac arrest at home, two acute MI (one in the first 24 hours post PCI due to stent thrombosis and the other at 7.1 months), and four clinically driven TLRs. The SES arm had one MI secondary to definite stent thrombosis at 7.4 months and three clinically driven TLRs. Additionally, there were two non-cardiac deaths (one secondary to colonic necrosis in the EES arm and the other secondary to staphylococci meningitis in the SES group) and nine non-target vessel revascularisations (three in the EES arm and six in the SES group).

Final clinical follow-up at 24 months was obtained in 91.5% of patients. Most patients in both groups had discontinued dual antiplatelet therapy (DAPT) (21% remained on DAPT in the EES arm vs 21.1% in the SES arm; p=0.96) **(Supplementary Table 8)**. Overall, there were no differences in outcomes between the groups (TLF 7.6% [3.3, 14.5] in the EES arm vs 7.1% [2.9, 14.0] in the SES arm; p=0.88). Concomitant medication was also comparable between the groups during follow-up **(Supplementary Table 9)**.

Discussion

The ANGIOLITE study is the first prospective, multicentre, randomised controlled trial designed to assess the efficacy of the new second-generation Angiolite SES. As compared to the XIENCE EES, the SES appeared to be non-inferior in angiographic parameters of restenosis. From the clinical point of view, few events were observed in either group at two-year follow-up.

In-stent LLL is frequently used to quantify the degree of neointimal hyperplasia, as it reflects the biological activity occurring after stent implantation. It is a simple measure, easy to understand and rather intuitive, and has been used in several randomised controlled trials to compare the efficacy of different types of DES. Moreno et al[12] concluded, using meta-regression techniques, that the number of patients needed to treat to reduce one TLR compared with a bare metal stent is related to late loss. In a recent patient-level meta-analysis of seven randomised clinical trials involving

Table 2. Quantitative coronary angiography results.

		Total (N=180; L=210)	EES (N=90; L=104)	SES (N=90; L=106)	Difference [95% CI] *p*-value
Baseline					
MLD, mm		0.93±0.40	0.98±0.41	0.88±0.38	0.10 [–0.01, 0.21] 0.06
RVD, mm		2.78±0.58	2.76±0.59	2.81±0.57	–0.05 [–0.22, 0.12] 0.57
%DS		66.80±12.4	64.80±12.8	68.70±11.7	–3.90 [–7.51, –0.29] 0.02
Post PCI					
In-stent	MLD, mm	2.58±0.46	2.62±0.45	2.53±0.46	0.09 [–0.04, 0.22] 0.16
	RVD, mm	2.92±0.46	2.93±0.45	2.91±0.48	0.02 [–0.11, 0.16] 0.67
	%DS	11.80±6.4	10.60±6.3	12.90±6.4	–2.30 [–4.17, –0.43] 0.01
In-segment	MLD, mm	2.34±0.45	2.38±0.46	2.30±0.43	0.08 [–0.05, 0.21] 0.17
	RVD, mm	2.90±0.50	2.93±0.50	2.87±0.51	0.06 [–0.09, 0.21] 0.39
	%DS	19.40±6.8	18.80±6.8	19.90±6.8	–1.10 [–3.10, 0.90] 0.24
	In-stent acute gain, mm	1.65±0.49	1.64±0.50	1.65±0.48	–0.01 [–0.15, 0.13] 0.84
Follow-up					
In-stent	MLD, mm	2.52±0.50	2.54±0.53	2.49±0.47	0.05 [–0.10, 0.20] 0.48
	RVD, mm	2.86±0.47	2.87±0.46	2.85±0.47	0.02 [–0.12, 0.16] 0.72
	%DS	12.10±8.6	11.80±8.7	12.30±8.6	–0.50 [–3.05, 2.05] 0.68
In-segment	MLD, mm	2.31±0.51	2.32±0.53	2.29±0.50	0.03 [–0.12, 0.18] 0.71
	RVD, mm	2.86±0.51	2.87±0.52	2.84±0.51	0.03 [–0.12, 0.18] 0.73
	%DS	19.30±9.9	19.30±10.2	19.30±9.6	0.00 [–2.91, 2.91] 0.99
Late lumen loss	In-stent LLL, mm	0.06±0.39	0.08±0.38	0.04±0.39	0.04 [–0.07, 0.15] 0.45*
	In-segment LLL, mm	0.03±0.41	0.06±0.38	0.00±0.44	0.06 [–0.06, 0.18] 0.30*
	In-stent binary restenosis	3 (1.4%)	2 (1.9%)	1 (1.0%)	0.90 [–2.6, 4.8] 0.58
	In-segment binary restenosis	7 (3.3%)	4 (4.4%)	3 (3.3%)	1.10 [–4.5, 6.8] 0.70

Data are presented as mean±SD or n (%). * Difference (95% CI), *p*-value for non-inferiority: in-stent LLL: –0.04 [–0.15, 0.07], 0.002; in-segment LLL: –0.06 [–0.18, 0.06], 0.007. DS: diameter stenosis; EES: everolimus-eluting stent; LLL: late lumen loss; MLD: minimal lumen diameter; RVD: reference vessel diameter; SES: sirolimus-eluting stent

2,426 patients, Asano et al[13] reported an exponential relationship between in-stent LLL and the two-year incidence of TLR.

QCA provided very low mean values of LLL, especially in the measurements obtained in-segment that could be related to positive remodelling of the vessel after stent implantation. At the stented segment, mean LLL in the Angiolite SES group was similar to that obtained in the ANCHOR trial[8] (0.04±0.36 mm vs 0.07±0.37 mm). The mean LLL in the EES group was also very low, in concordance with values reported in other trials[14-16]. In general, reported LLL values in current-generation DES are below a 0.20 mm

Table 3. Optical coherence tomography results.

		Total	EES	SES	*p*-value
Patients analysed		88 (100.0)	41 (46.6)	47 (53.4)	
Stents analysed		96 (100.0)	44 (45.8)	52 (54.2)	
Cross-sections analysed		3,309 (100.0)	1,411 (42.6)	1,898 (57.4)	
Strut analysis	Analysable struts	29,008	11,660	17,348	
	Covered struts	26,144 (90.1)	10,597 (90.9)	15,547 (89.6)	<0.01
	Uncovered struts	2,266 (7.8)	877 (7.5)	1,389 (8.0)	0.13
	Incomplete strut apposition	598 (2.1)	186 (1.6)	412 (2.4)	<0.01
	Cross-section with RUTTS >30%	314 (9.5)	127 (9.0)	187 (9.9)	0.41
Stent analysis	Neointimal thickness, µm	78.2±88	86.4±91	72.1±86	<0.01
	Luminal area, mm^2	6.6±2.5	6.6±2.6	6.5±2.5	0.23
	Stent area, mm^2	7.1±2.4	7.3±2.4	6.9±2.3	<0.01
	Neointimal area obstruction, mm^2	0.5±1.0	0.7±0.9	0.4±1.0	<0.01

Data presented as n (%) or mean±SD. EES: everolimus-eluting stent; RUTTS: rate of uncovered to total number of struts; SES: sirolimus-eluting stent

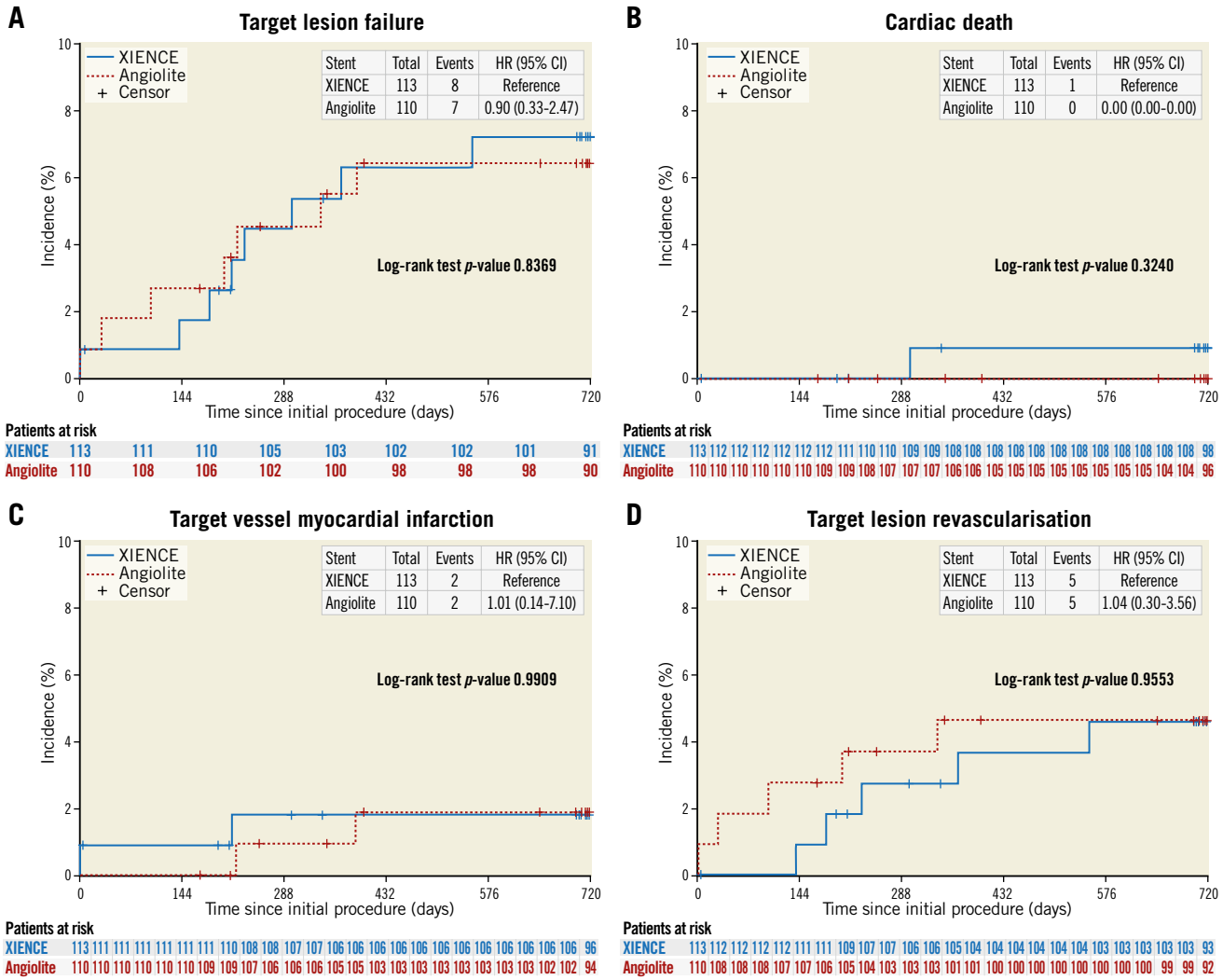

Figure 3. *Kaplan-Meier curves. A) TLF. B) Cardiac death. C) Target vessel myocardial infarction. D) TLR.*

threshold. The BIOFLOW-II trial[15] compared EES to SES with biodegradable polymer drug release, showing a similar in-stent LLL between groups (0.10±0.32 mm vs 0.11±0.29 mm, respectively). The PRISON IV trial also showed very low LLL in the XIENCE arm (0.07±0.46 mm)[16]. Finally, LLL of the Resolute™ stent (Medtronic, Minneapolis, MN, USA) was also very low (0.14±0.37 mm) in the PIONEER trial[17]. Variations in LLL values across trials can be related to variability of core lab analyses and different timing of the angiographic follow-up (6 vs 9 months). A broad SD of LLL is typically seen when using DES. The important suppression of neointimal proliferation (with values of LLL close to 0) leads to a wide SD induced for the few restenoses that may occur. Besides, LLL after bare metal stent implantation used to show normal distribution as opposed to that after DES implantation, which is usually non-normal[18]. In such a scenario, comparison of medians could be more accurate. However, for historical reasons and comparability with previous stent generations, current DES trials ultimately keep using mean±SD for LLL comparisons. Overall, LLL of metallic coronary stents reflected the capacity to prevent neointimal proliferation, with early and late constrictive remodelling being prevented by the metallic backbone of the device. However, in the era of first-generation DES, eradication of neointimal proliferation was related to late events such as stent thrombosis[5]. Therefore, the analysis of LLL represents a surrogate of the antirestenotic efficacy, but it may not be enough to discriminate the quality of the healing process as a parameter of device safety. To that end, the concomitant use of imaging techniques such as OCT can be helpful. Indeed, a very low LLL may reflect an incomplete healing process with uncovered and malapposed struts, only seen on OCT[19]. Therefore, the findings of the current OCT substudy are reassuring and support the good safety profile of the Angiolite SES. In the previous ANCHOR study[8], the healing process of the Angiolite SES stent was evaluated by OCT at three and six months after implantation. As early as three months, strut coverage was evident in 86.3% of struts and the incomplete apposition rate was 1.3%. In keeping with these data, the OCT substudy of the ANGIOLITE trial corroborated a high degree of SES strut coverage at six months (nearly 90%) with a low incomplete apposition rate.

From the clinical point of view, the number of events at two years was very low in both groups, reflecting good clinical performance without the occurrence of late catch-up events after discontinuation of DAPT.

Study limitations

Several caveats of the ANGIOLITE study warrant consideration. First, the study was designed to evaluate efficacy in terms of LLL, and therefore the sample size is too small to draw conclusions on clinical events. Second, we excluded patients with left main disease, ST-segment elevation MI Killip III-IV or total chronic occlusion, and therefore conclusions cannot be applicable to these specific groups. Third, OCT was performed in five pre-selected centres. However, baseline characteristics and outcomes of patients included in the OCT cohort were similar to those of the non-OCT cohort **(Supplementary Table 10)**. Besides, OCT was only performed at six-month angiographic follow-up. Therefore, we cannot discern whether the incomplete stent apposition observed at follow-up was also present at baseline. Finally, a large-scale trial powered for clinical events with longer follow-up is needed to confirm the results of this study.

Conclusions

In conclusion, this first randomised trial with a novel thin-strut, cobalt-chromium SES with a durable fluoroacrylate-based biostable polymer found it to be non-inferior to the gold standard second-generation EES in terms of the angiographic parameters of restenosis.

Impact on daily practice

The angiographic results and neointimal stent coverage of the novel Angiolite SES appeared to be comparable to those of the gold standard EES in a broad spectrum of coronary artery disease patients. The Angiolite SES can be incorporated as a good option in the armamentarium of the interventional cardiologist.

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Conflict of interest statement

J. Moreu has received honoraria from Biosensors, Boston, Cardiva, Edwards Lifesciences and Medtronic. R. Moreno-Gómez has received honoraria from Abbott, Astra, Amgen, Bayer, Biosensors, Biotronik, Boston, Cardiva, Daiichi Sankyo, and Medtronic. A. Pérez de Prado reports grants and personal fees from iVascular, personal fees from Boston Scientific, Cardiva, and Terumo, grants from Abbott, grants and personal fees from AstraZeneca, and grants from Medtronic, during the conduct of the study. The other authors have no conflicts of interest to declare.

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Supplementary data

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The supplementary data are published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-19-00206

Supplementary data

Supplementary Appendix 1. Description of the Angiolite SES

The Angiolite SES (iVascular, Barcelona, Spain; CE mark reference number: 2014 12 0833 ED) is made from a cobalt-chromium alloy backbone, with a strut thickness of 75 μm for stent diameters less than 2.75 mm and 85 μm for larger diameters. The stent is manufactured from a metal tube that is laser cut and subjected to various treatments, providing a smooth, glossy surface finish. The stent structure has been modified to consist of eight crowns linked by three rows of non-concatenated connectors in a non-continuous sinusoid fashion. It has been designed to protect the expansion and to ensure the integrity of the coating around all the stent structure. From a design point of view, the number of zig-zags of the Angiolite is greater than that of other drug-eluting stents. The idea is to reduce the deformation on the curved part of the strut. A schematic view of the impact of the number of zig-zags in the deformation of the material is seen in **Supplementary Figure 1**.

The coating of the Angiolite stent is composed of three layers - acrylate to ensure adhesion to the metal surface, fluoroacrylate that carries the sirolimus (1.4 microgr/mm²), and a top layer of fluoroacrylate to control drug release (>75% elution within the first month, followed by complete sirolimus elution by the end of the second month). The recoil is <4%; the degree of shortening during expansion is <3%. Fluoroacrylate is a proprietary formulation designed by iVascular that has selective cellular activity. This composition demonstrated in vitro early endothelial cell growth and reduction of smooth muscle cell proliferation **(Supplementary Figure 2)**.

The Angiolite coating has an excellent integrity. In comparison with other drug-eluting stents, the Angiolite coating has the capability for not being damaged, without delaminating, cracking or peeling. **Supplementary Figure 3** shows an example of this behaviour. The excellent integrity of the Angiolite is achieved by the adhesion capability of the polyacrylate primer and the flexibility and cohesion of the proprietary fluoroacrylate polymer.

As reference, **Supplementary Figure 4** shows some of the coating defects of other drug-eluting stents.

Supplementary Appendix 2. Eligibility criteria for the ANGIOLITE trial

INCLUSION CRITERIA:

● Patient age ≥18 years

● Ability to acknowledge verbally the risks, benefits and treatment ramifications of receiving the Angiolite or XIENCE Xpedition stent

● Written informed consent given by legally authorised agent prior to any study-related procedure

● Indication for use of drug-eluting stent based on ACC/AHA/SCAI and ESC/EACTS guidelines and/or clinical judgement of interventional cardiologist

● Target lesion(s) in coronary artery or graft vessel with estimated reference diameter ≥2 mm and ≤4.0 mm

● Target lesion(s) amenable to percutaneous coronary intervention

EXCLUSION CRITERIA:

● Known hypersensitivity or contraindication to any of the following agents: heparin, aspirin, clopidogrel, sirolimus, everolimus, cobalt-chromium or contrast media

● Inability to tolerate aspirin or clopidogrel for the six-month duration of the study

● Females with childbearing potential (unless providing a recent negative pregnancy test) or anticipating pregnancy following study enrolment

● Planned major non-cardiac surgery within designated study period

● Patients with acute myocardial infarction in Killip class III or IV or in cardiogenic shock

● Non-cardiac comorbid conditions limiting life expectancy (to <1 year) or potentially undermining protocol compliance

● Unwillingness or inability to comply with protocol procedures

● Target lesion located in the left main

- Total chronic occlusion as target lesion

Supplementary Appendix 3. Definitions of clinical and angiographic endpoints

All-cause death included cardiac death, vascular death and non-cardiovascular death. Cardiac death was defined according to ARC criteria as any death due to a proximate cardiac cause (e.g., MI, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, and all procedure-related deaths, including those related to concomitant treatment.

MI was defined according to the third universal definition (Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD; Writing Group on the Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. Third universal definition of myocardial infarction. Eur Heart J. 2012 Oct;33(20):2551-67).

TLR was considered clinically driven if associated with any of the following: non-invasive positive functional ischaemia study (e.g., exercise testing or equivalent tests) or invasive positive functional ischaemia study (e.g., fractional flow reserve or coronary flow reserve); ischaemic symptoms and an angiographic minimal lumen diameter stenosis ≥50% by on-line QCA; or diameter stenosis ≥70% by on-line QCA without either ischaemic symptoms or a positive functional study.

Device success was defined as the implantation of the allocated stent with the attainment of residual stenosis <30% and TIMI flow >2.

Procedural success was defined as device success with the absence of major adverse cardiac events.

In-stent acute gain was defined as minimal luminal diameter post stent implantation minus pre intervention.

In-segment LLL measured LLL within the segment encompassed by 5 mm both proximal and distal from the stent edge.

% diameter stenosis (%DS) was calculated as the ratio of minimal luminal diameter over the interpolated reference diameter in %.

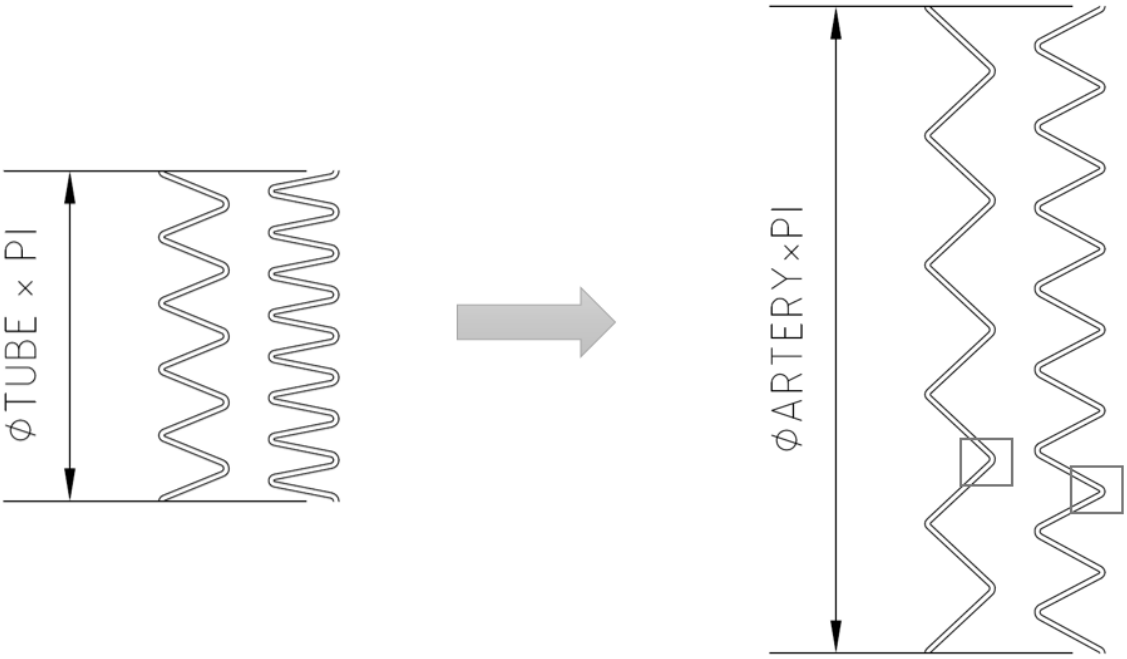
Binary restenosis was defined as %DS >50%.

Lesion debulking was defined as the need for debulking techniques prior to stent implantation (rotablation, cutting balloon, ….).

Need for a second stent was defined as the need for additional stent implantation to cover the entire diseased/predilated segment or to cover any distal/proximal iatrogenic dissection.

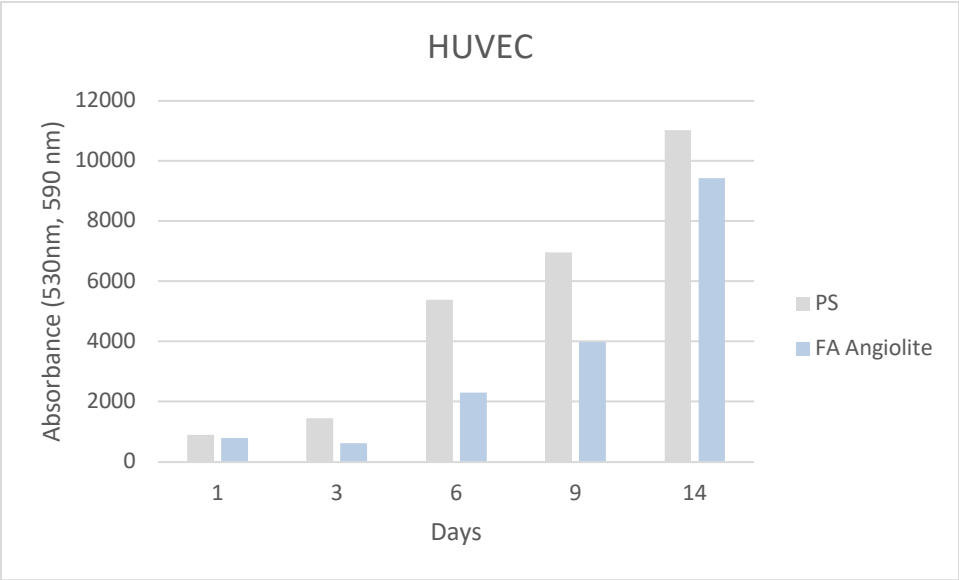
Supplementary Appendix 4. QCA and OCT evaluation

An independent core laboratory (iCORELab, Instituto Ciencias del Corazón, Escuela de Medicina de Valladolid, Valladolid, Spain) conducted the QCA and OCT analyses. Angiographies of the target segment were preceded by intracoronary injection of nitrates. The average of at least two orthogonal views per lesion separated by more than 30° was used, except for length. For length the maximum of all available orthogonal views was used. For variables that show the difference of values between phases (e.g., LLL, acute gain), only lesions with matching orthogonal views were used. The analysts were blinded to the type of stent implanted. Off-line QCA analysis was performed with the CAAS system (Pie Medical Imaging, Maastricht, the Netherlands) according to standard operational protocols (Serruys PW, Foley DP, de Feyter PJ. Quantitative coronary angiography in clinical practice. Dordrecht/Boston/London: Kluwer Academic Publishers; 1994). Intracoronary OCT was performed using the C7XR™ Fourier-Domain OCT system (St. Jude Medical, St. Paul, MN, USA) or the Lunawave® OCT system (Terumo Medical Corporation, Tokyo, Japan) at the time of scheduled angiographic follow-up. Intracoronary nitrates (100–200 mg) were administered prior to OCT catheter intubation. Automated OCT pullback was performed at a speed of 20 mm sec^{-1} at a frame rate of 100 frames sec^{-1}. Frequency-domain OCT images were calibrated by adjusting for the Z-offset. All OCT frames were digitally stored, and cross-sectional OCT images of stented segments were analysed at 0.4/0.6 mm alternate stepping intervals (yielding an average inter-slice distance of 0.5 mm).



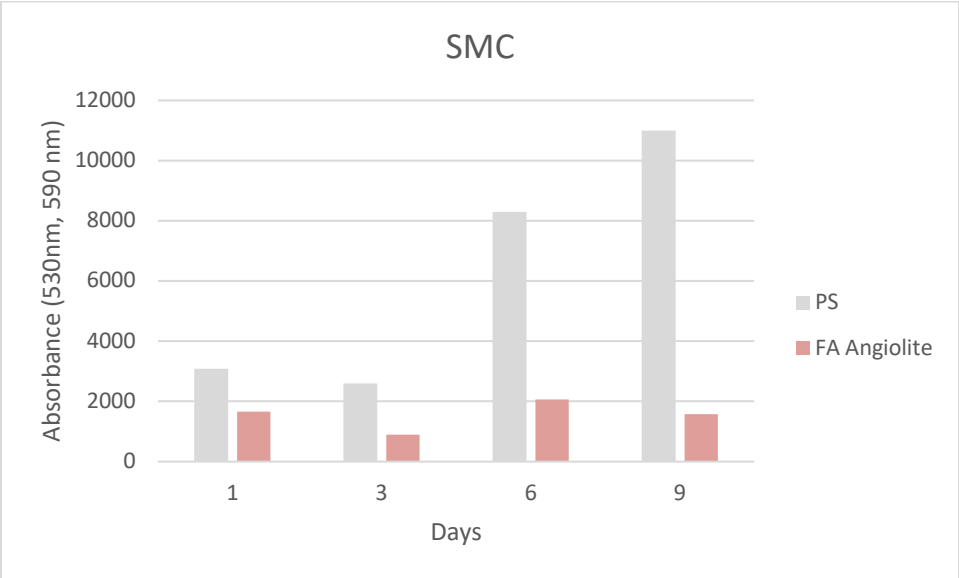
Supplementary Figure 1. Impact of the number of zig-zags on the deformation of the material.

A.



HUVEC: human umbilical vein endothelial cells; PS: polystyrene (control); FA Angiolite: fluoroacrylate polymer

B.



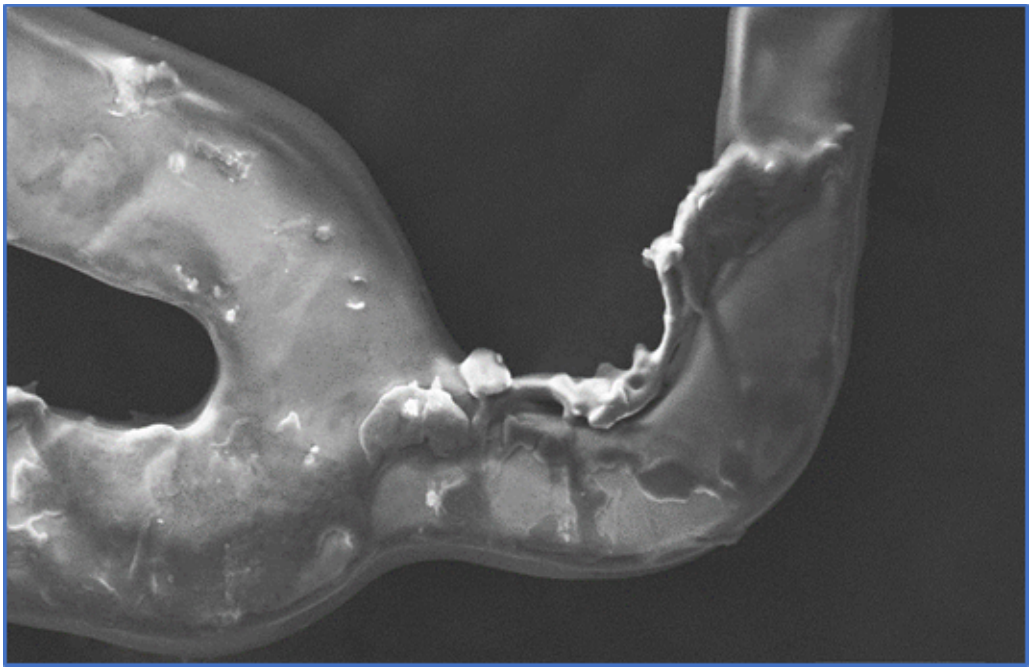
SMC: smooth muscle cells; PS: polystyrene (control); FA Angiolite: fluoroacrylate polymer

Supplementary Figure 2. Fluoroacrylate polymer-based Angiolite stent demonstrated similar increase in endothelial cells (A) and reduced smooth muscle cell proliferation (B).

Supplementary Figure 3. Integrity of the Angiolite® stent.

SEM image of Angiolite magnified 500 times.

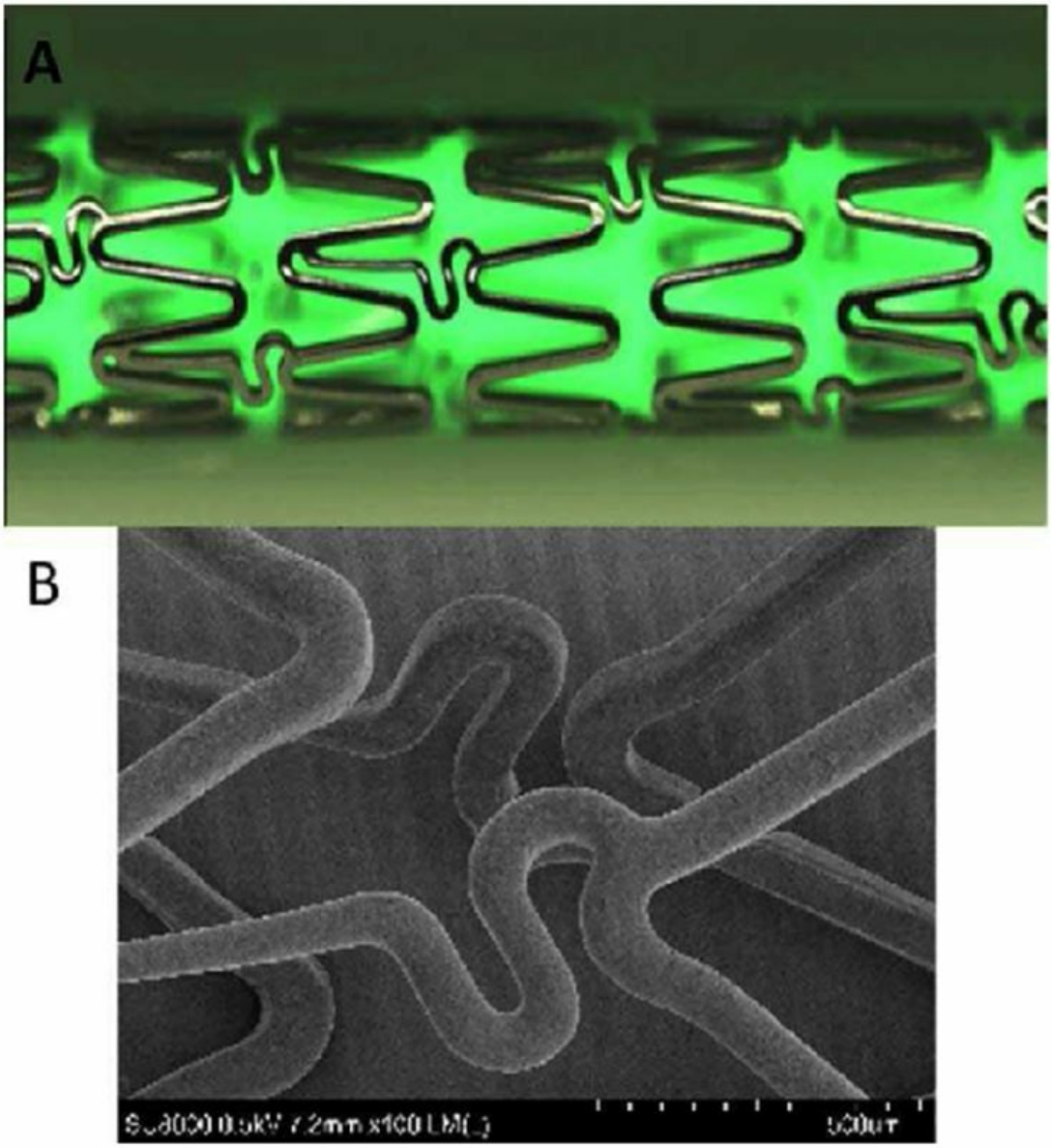
A.



SEM image of an example of a defect of XIENCE magnified 500 times.

SEM image of defects of Resolute Onyx magnified 500 times.

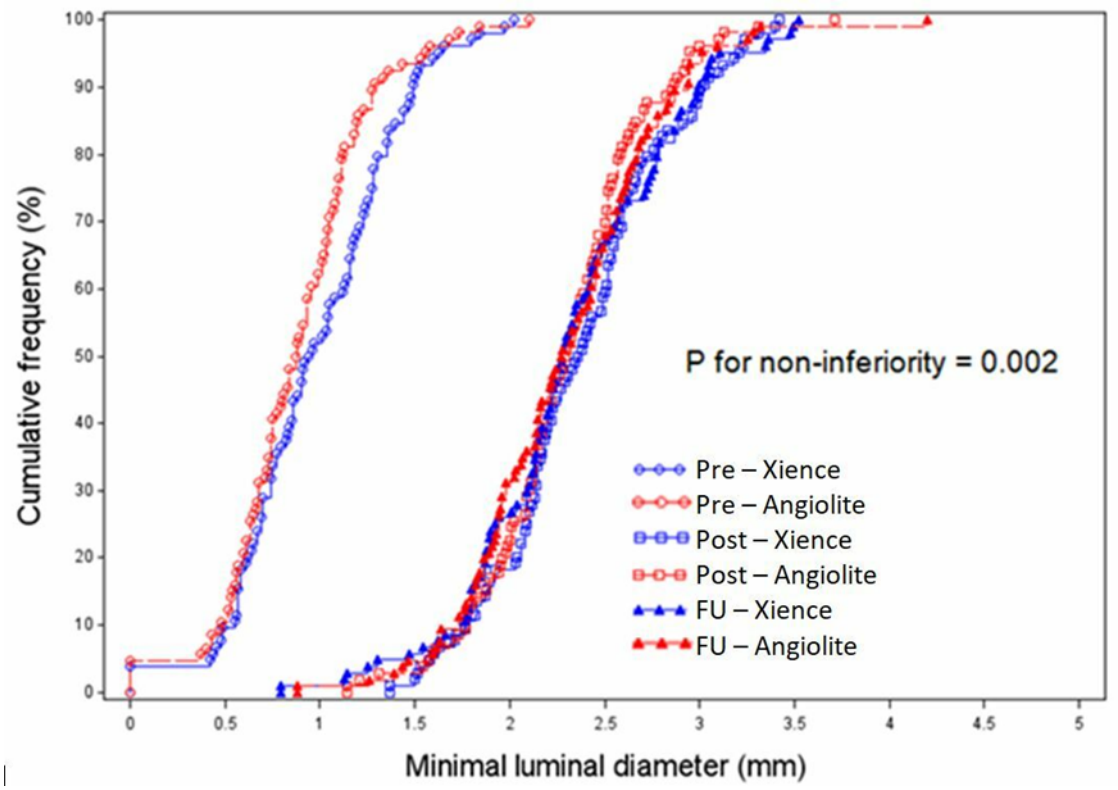
Supplementary Figure 4. Integrity of the XIENCE stent (A) and of the Onyx stent (B).



Supplementary Figure 5. Characteristic features of the Angiolite DES.

A) The Angiolite drug-eluting stent, comprising a laser-cut cobalt-chromium (L605), thin-strut (80 μm) backbone, featuring an open-cell design consisting of eight crowns linked by three rows on non-concatenated connectors in a non-continuous sinusoidal fashion.

B) Micro-CT of the Angiolite DES showing the result of an innovative coating technology that provides a smooth, glossy surface finish.



Supplementary Figure 6. Cumulative frequency distribution curves of minimal luminal diameter pre intervention, post intervention and at follow-up.

Supplementary Table 1. Technical features of Angiolite® stent system.

Characteristic	**Angiolite® stent system**
Available stent lengths (mm)	9, 14, 16, 19, 24, 29, 34, 39
Available stent diameters (mm)	2, 2.25, 2.50, 2.75, 3.00, 3.50, 4.00, 4.50*; *not available with length 9 mm
Stent material	Cobalt-chromium alloy
Drug product	Sirolimus 1.4 mg mm^2
Polymer	Biostable, durable fluoroacrylate-based polymer
Delivery system length	142 cm
Stent delivery balloon	Semi-compliant, with two radiopaque markers
Balloon inflation pressure	Nominal inflation pressure: 9–12 atm Rated burst pressure (RBP): 16 atm Average burst pressure (ABP): 22 atm
Recommended guidewire	0.014-inch
Catheter shaft outer diameter	Proximal: 2 Fr Mid: 2.6 Fr Distal: 2.4 Fr
Stent strut thickness	75–85 μm

Supplementary Table 2. Technical features of XIENCE stent system.

Characteristic	**XIENCE stent system**
Available stent lengths (mm)	8, 12, 15, 18, 23, 28, 33, 38
Available stent diameters (mm)	2.25, 2.50, 2.75, 3.00, 3.50, 4.00
Stent material	Cobalt-chromium alloy
Drug product	Everolimus
Polymer	Biostable, durable fluoropolymer
Delivery system length	145 cm
Stent delivery balloon	Semi-compliant, with two radiopaque markers
Balloon inflation pressure	Rated burst pressure (RBP): 16 atm
Recommended guidewire	0.014-inch
Catheter shaft outer diameter	Proximal: 2.1 Fr Mid: 2.7 Fr Distal: 2.2 Fr
Stent strut thickness	81 μm

Supplementary Table 3. Centres and investigators involved in the ANGIOLITE study.

Centre	Investigators	Number of patients included
HOSPITAL UNIVERSITARIO DE SANTIAGO, SANTIAGO DE COMPOSTELA	Ramiro Trillo Nouche Xoan Carlos Sanmartín Pena Ana Belén Cid Álvarez	20
HOSPITAL MARQUES DE VALDECILLA, SANTANDER	Javier Zueco Tamara García Camarero Lee Hwang DAE Hyun	20
HOSPITAL VALL D'HEBRON, BARCELONA	Bruno García Imanol Otaegui Bernat Serra	21
HOSPITAL VIRGEN DE LAS NIEVES, GRANADA	Eduardo Molina Joaquín Sánchez Gila Vicente Alcalde Martínez	20
HOSPITAL DE LA ARRIXACA, MURCIA	Eduardo Pinar Bermúdez José Antonio Hurtado Martínez Javier Lacunza Ruiz	20
HOSPITAL LA PAZ, MADRID	Raúl Moreno Gómez Guillermo Galeote García Angel Sánchez Recalde	20
HOSPITAL VIRGEN DE LA SALUD, TOLEDO	José Moreu Burgos Esther Lázaro Fernández Tomás Cantón Rubio	22
HOSPITAL UNIVERSITARIO DE VALLADOLID, VALLADOLID	Ignacio J. Amat-Santos Ana Serrador Roman J. Arnold Hipólito Gutiérrez	20
HOSPITAL UNIVERSITARIO DE LEON, LEON	Armando Pérez de Prado Carlos Cuellas Ramón Felipe Fernández Vázquez	20

HOSPITAL INFANTA CRISTINA, BADAJOZ	Antonio Merchán Herrera Reyes González Fernández José Ramón López Mínguez	20
HOSPITAL JUAN RAMÓN JIMÉNEZ, HUELVA	José Francisco Díaz Fernández Enrique Gómez Menchero Santiago Jesús Camacho Freire	20

Supplementary Table 4. List of the committees and members/institutions.

Committee	List of members
Steering Committee	Dr. José F. Diaz-Fernandez Dr. Ramiro Trillo Dr. Javier Zueco Dr. Bruno Garcia Dr. Eduardo Molina Dr. Eduardo Pinar Dr. Raúl Moreno Dr. Jose Moreu Dr. Roman J. Arnold Dr. Armando Perez de Prado Dr. Antonio Merchan
Data Safety Monitoring Board	Dr. Ignacio Sanchez Perez Dr. Javier Benecet Mazuecos Dra. Maria Teresa Velazquez Martin
Clinical Events Committee	Dra. María Thiscal Lopez LLuva Dr. Agustín Albarran Gonzalez Trevilla Dr. Arturo Garcia Touchard
QCA and OCT core lab	iCORELAB, Valladolid, Spain
CRO	Effice SL
Monitoring	Effice SL
Statistics	Effice SL

The Steering Committee was responsible for overseeing the scientific and operational aspects of the study.

The Data and Safety Monitoring Board, blinded (i.e., unaware of the patients' treatment allocation), not affiliated with any of the involved centres, and not participating in the trial, periodically reviewed and analysed all serious adverse events and made recommendations to the Steering Committee regarding endpoint analysis or potential safety concerns.

The Clinical Events Committee (CEC) consisted of cardiologists not participating in the trial and blinded to the patients' treatment allocation and trial results.

QCA and OCT analyses were performed at iCORELab (Instituto Ciencias del Corazón, Escuela de Medicina de Valladolid, Valladolid, Spain).

On-site monitoring and statistical analysis was performed by an independent CRO (Effice SL).

Supplementary Table 5. Baseline characteristics of the ANGIOLITE trial.

	EES N=113	SES N=110	*p*-value
Age, years, mean±SD	63.6±9.5	62.4±10.5	0.38
Male, n (%)	88 (77.9)	87 (79.1)	0.83
Coronary risk factor			
Diabetes, n (%)	34 (30.4)	28 (25.5)	0.42
Hypertension, n (%)	74 (66.1)	64 (58.2)	0.23
Dyslipidaemia, n (%)	57 (50.9)	62 (56.4)	0.41
Never smoker, n (%)	46 (41.1)	40 (36.4)	0.74
Familiar CVD, n (%)	15 (13.4)	16 (14.5)	0.80
CVD history	34 (30.4)	24 (21.8)	0.15
Prior MI, n (%)	18 (16.1)	8 (7.3)	0.04
Prior CABG-PCI, n (%)	21 (18.8)	10 (9.1)	0.04
Prior TIA, n (%)	2 (1.8)	1 (0.9)	1.00
PVD, n (%)	4 (3.6)	5 (4.5)	0.71
AF, n (%)	3 (2.7)	2 (1.8)	1.00
PCI indication			0.25
Silent ischaemia, n (%)	9 (8.0)	4 (3.6)	
Stable angina, n (%)	32 (28.3)	29 (26.4)	
Unstable angina, n (%)	29 (25.7)	21 (19.1)	
Non-ST ACS, n (%)	33 (29.2)	44 (40.0)	
ST ACS, n (%)	10 (8.8)	12 (10.9)	

ACS: acute coronary syndrome; AF: atrial fibrillation; CABG: coronary artery bypass grafting; CVD: cardiovascular disease; EES: everolimus-eluting stent; MI: myocardial infarction; PCI: percutaneous coronary intervention; PVD: peripheral vascular disease; SES: sirolimus-eluting stent; TIA: transient ischaemic attack

Supplementary Table 6. OCT subgroup: clinical characteristics.

	EES N=41	Angiolite SES N=47	*p*-value
Age, years, mean±SD	64.05 (8.6)	60.98 (11.2)	0.15
Male, n (%)	34 (82.9)	37 (78.7)	0.62
Coronary risk factor			
Diabetes, n (%)	12 (29.3)	10 (21.3)	0.39
Hypertension, n (%)	25 (61.0)	26 (55.3)	0.59
Dyslipidaemia, n (%)	22 (53.7)	26 (55.3)	0.88
Never smoker, n (%)	20 (48.8)	15 (31.9)	0.23
Familiar CVD, n (%)	4 (9.8)	12 (25.5)	0.06
CVD history			
Prior MI, n (%)	4 (9.8)	1 (2.1)	0.18
Prior CABG-PCI, n (%)	8 (19.5)	1 (2.1)	0.00
Prior TIA, n (%)	0 (0.0)	1 (2.1)	1.00
PVD, n (%)	2 (4.9)	2 (4.3)	1.00
AF, n (%)	0 (0.0)	1 (2.1)	1.00
PCI indication			0.15
Silent ischaemia, n (%)	3 (7.3)	1 (2.1)	
Stable angina, n (%)	18 (43.9)	12 (25.5)	
Unstable angina, n (%)	9 (22.0)	10 (21.3)	
Non-ST ACS, n (%)	9 (22.0)	19 (40.4)	
ST ACS, n (%)	2 (4.9)	5 (10.6)	

AF: atrial fibrillation; CABG: coronary artery bypass grafting; CVD: cardiovascular disease; EES: everolimus-eluting stent; MI: myocardial infarction; Non-ST ACS: non-ST-elevation acute coronary syndrome; PCI: percutaneous coronary intervention; PVD: peripheral vascular disease. SES: sirolimus-eluting stent; ST ACS: ST-elevation acute coronary syndrome; TIA: transient ischaemic attack

Supplementary Table 7. OCT subgroup: QCA results.

	Total (N=88; L=99)	EES (N=41; L=47)	Angiolite SES (N=47; L=52)	*p*-value
Post PCI				
In-stent				
MLD, mm	2.61±0.47	2.70±0.47	2.53±0.46	0.07
RVD, mm	2.96±0.48	3.03±0.48	2.89±0.48	0.17
% DS	11.7±6.1	10.8±6.3	12.5±5.8	0.10
In-segment				
MLD, mm	2.36±0.49	2.41±0.50	2.31±0.47	0.33
RVD, mm	2.92±0.54	2.98±0.55	2.85±0.52	0.24
% DS	19.2±6.7	19.4± 6.5	19.1±7.0	0.78
In-stent AG, mm	1.61±0.45	1.65±0.50	1.58±0.41	0.07
Follow-up				
In-stent				
MLD, mm	2.55±0.50	2.62±0.57	2.48±0.42	0.16
RVD, mm	2.86±0.49	2.90±0.54	2.83±0.45	0.45
% DS	11.3±6.3	10.2±6.0	12.3±6.5	0.09
In-segment				
MLD, mm	2.32±0.51	2.40±0.57	2.24±0.45	0.12
RVD, mm	2.88±0.56	2.94±0.57	2.83±0.54	0.32
% DS	19.7±9.3	18.6±10.0	20.6±8.6	0.29
Late lumen loss				
In-stent LLL, mm	0.07±0.34	0.08±0.36	0.05±0.32	0.71*
In-segment LLL, mm	0.04±0.37	0.01±0.36	0.07±0.38	0.38*

*p-values for non-inferiority: in-stent LLL: 0.007; in-segment LLL: 0.001.
AG: acute gain; EES: everolimus-eluting stent; LLL: late lumen loss; MLD: minimal lumen diameter; % DS: % diameter stenosis; RVD: reference vessel diameter; SES: sirolimus-eluting stent

Supplementary Table 8. Clinical outcomes at 12 and 24 months.

12-month outcomes	Total (N=206)	EES (N=105)	SES (N=101)	*p*-value
Target lesion failure	11 (5.3)	7 (6.7)	4 (4.0)	0.387
Cardiac death	1 (0.5)	1 (1.0)	0 (0.0)	0.978
Myocardial infarction	3 (1.5)	2 (1.9)	1 (1.0)	0.584
Target lesion revascularisation	7 (3.4)	4 (3.8)	3 (3.0)	0.739
Major adverse cardiac events	22 (10.7)	11 (10.5)	11 (10.5)	0.967
All-cause death	3 (1.5)	2(1.9)	1 (1)	0.584
Any myocardial infarction	3 (1.5)	2 (1.9)	1 (1.0)	0.584
Any revascularisation	16 (7.8)	7 (6.7)	9 (9.0)	0.958
Definite or probable stent thrombosis*	3 (1.5)	2 (1.9)	1 (1.0)	0.584
24-month outcomes	**Total (N=204)**	**EES (N=105)**	**SES (N=99)**	***p*-value**
Target lesion failure	15 (7.4)	8 (7.6)	7 (7.1)	0.881
Cardiac death	1 (0.5)	1 (1.0)	0 (0.0)	1.000
Myocardial infarction	4 (2.0)	2 (1.9)	2 (2.0)	0.953
Target lesion revascularisation	10 (4.9)	5 (4.8)	5 (5.1)	0.924
Major adverse cardiac events	26 (12.7)	12 (11.4)	14 (14.1)	0.561
All-cause death	3 (1.5)	2 (1.9)	1 (1.0)	0.596
Any myocardial infarction	4 (2.0)	2 (1.9)	2 (2.0)	0.953
Any revascularisation	19 (9.3)	8 (7.6)	11 (11.1)	0.391
Definite or probable stent thrombosis*	3 (1.5)	2 (1.9)	1 (1.0)	0.596

Data are presented as n (%).
*ARC definition. EES: everolimus-eluting stent; SES: sirolimus-eluting stent

Supplementary Table 9. Concomitant medication during the study.

	Total (N=223)	EES (N=113)	Angiolite SES (N=110)	*p*-value
Hospital discharge, n (%)	**N=223**	**N=113**	**N=110**	
Aspirin	217 (97.3)	108 (95.6)	109 (99.1)	0.105
Clopidogrel	133 (59.6)	70 (61.9)	63 (57.3)	0.477
Prasugrel	19 (8.5)	10 (8.8)	9 (8.2)	0.858
Ticagrelor	70 (31.4)	32 (28.3)	38 (34.5)	0.316
Oral anticoagulant	5 (2.2)	3 (2.7)	2 (1.8)	0.673
Statin	191 (85.7)	95 (84.1)	96 (87.3)	0.495
Lipid-lowering agent	10 (4.5)	5 (4.4)	5 (4.5)	0.965
Beta-blocker	146 (65.5)	78 (69.0)	68 (61.8)	0.258
Calcium channel blocker	29 (13.0)	18 (15.9)	11 (10.0)	0.188
ACE inhibitor	132 (59.2)	65 (57.5)	67 (60.9)	0.607
Month 12, n (%)	**N=206**	**N=105**	**N=101**	
Aspirin	204 (99.0)	102 (97.1)	101 (100.0)	0.332
Clopidogrel	119 (57.8)	66 (62.9)	53 (52.5)	0.132
Prasugrel	15 (7.3)	6 (5.7)	9 (8.9)	0.377
Ticagrelor	63 (30.6)	28 (26.7)	35 (34.7)	0.214
Oral anticoagulant	10 (4.9)	6 (5.7)	4 (4.0)	0.558
Statin	186 (90.3)	94 (89.5)	92 (91.1)	0.704
Lipid-lowering agent	13 (6.3)	3 (2.9)	10 (9.9)	0.038
Beta-blocker	143 (69.4)	68 (64.8)	75 (74.3)	0.139
Calcium channel blocker	22 (10.7)	10 (9.5)	12 (11.9)	0.584
ACE inhibitor	120 (58.3)	61 (58.1)	59 (58.4)	0.963
Month 24, n (%)	**N=204**	**N=105**	**N=99**	
Aspirin	191 (93.6)	99 (94.3)	92 (92.9)	0.692
Clopidogrel	27 (13.2)	12 (11.4)	15 (15.2)	0.433
Prasugrel	4 (2.0)	1 (1.0)	3 (3.0)	0.285
Ticagrelor	13 (6.4)	8 (7.6)	5 (5.1)	0.453
Oral anticoagulant	15 (7.4)	6 (5.7)	9 (9.1)	0.356
Statin	174 (85.3)	90 (85.7)	84 (84.8)	0.861
Lipid-lowering agent	34 (16.7)	17 (16.2)	17 (17.2)	0.851

Beta-blocker	136 (66.7)	68 (64.8)	68 (68.7)	0.552
Calcium channel blocker	27 (13.2)	16 (15.2)	11 (11.1)	0.385
ACE inhibitor	129 (63.2)	64 (61.0)	65 (65.7)	0.486

EES: everolimus-eluting stent; SES: sirolimus-eluting stent

Supplementary Table 10. Clinical characteristics between the OCT and non-OCT groups.

	OCT N=88	Non-OCT N=135	*p*-value
Age, years, mean±SD	62.41 (10.10)	63.38 (9.89)	0.479
Male, n (%)	71 (80.7)	104 (77.0)	0.517
Coronary risk factor			
Diabetes, n (%)	22 (25.0)	40 (29.6)	0.431
Hypertension, n (%)	51 (58.0)	87 (64.4)	0.295
Dyslipidaemia, n (%)	48 (54.5)	71 (52.6)	0.820
Never smoker, n (%)	35 (39.8)	51 (37.8)	0.927
Familiar CVD, n (%)	16 (18.2)	15 (11.1)	0.142
CVD history			
Prior MI, n (%)	5 (5.7)	21 (15.6)	0.024
Prior CABG-PCI, n (%)	9 (10.2)	22 (16.3)	0.193
Prior TIA, n (%)	1 (1.1)	2 (1.5)	1.000
PVD, n (%)	4 (4.5)	5 (3.7)	0.764
AF, n (%)	1 (1.1)	4 (3.0)	0.651
PCI indication			0.460
Silent ischaemia, n (%)	4 (4.5)	9 (6.7)	
Stable angina, n (%)	30 (34.1)	31 (23.0)	
Unstable angina, n (%)	19 (21.6)	31 (23.0)	
Non-ST ACS, n (%)	28 (31.8)	49 (36.3)	
ST ACS, n (%)	7 (8.0)	15 (11.0)	

ACS: acute coronary syndrome; AF: atrial fibrillation; CABG: coronary artery bypass grafting; CVD: cardiovascular disease; MI: myocardial infarction; OCT: optical coherence tomography; PCI: percutaneous coronary intervention; PVD: peripheral vascular disease; TIA: transient ischaemic attack