Comparison of the Absorbable Polymer Sirolimus-Eluting Stent (MiStent) to the Durable Polymer Everolimus-Eluting Stent (Xience) (from the DESSOLVE I/II and ISAR-TEST-4 Studies)

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We compared the outcomes of a novel, thin-strut, cobalt-chromium, absorbable, polymer sirolimus-eluting stent (APSES; MiStent) to the durable polymer cobalt-chromium everolimus-eluting stent (EES; Xience). A propensity-matched analysis was performed comparing data from the DES With Sirolimus and a Bioabsorbable Polymer for the Treatment of Patients With De Novo Lesions in the Native Coronary Arteries (DESSOLVE) I and II studies, evaluating the APSES to the EES arm of the Intracoronary Stenting and Angiographic Results: Test Efficacy of 3 Limus-Eluting Stents-4 study. Target lesion failure (TLF) and its components were evaluated at 12 months and annually to 3 years; 805 patients (APSES = 153; EES = 652) were included with propensity matching in 204 patients (APSES = 102; EES = 102). APSES compared with EES had lower TLF at 1 year (3.0% vs 8.0%, p = 0.12) driven by a difference in target lesion revascularization (TLR; 1% vs 6%, p = 0.05), with no difference in target vessel myocardial infarction (p = 0.56) or stent thrombosis (p = 0.31). At 3 years, TLF (5.0% vs 12.5%, p = 0.07) and TLR (2.0% vs 8.4%, p = 0.04) remained lower with APSES. By landmark analysis, there was no significant difference in TLF between 1 and 3 years (p = 0.36). In conclusion, in a propensity-matched analysis, the APSES demonstrated reduced clinically indicated TLR rates at 1 and 3 years compared with the durable polymer EES, with minimal accrual of events between 1 and 3 years. **(Am J Cardiol 2016;117:532−538)**

Drug-eluting stents (DES) have markedly reduced revascularization rates after percutaneous coronary interventions compared with bare metal stents.[1] Despite these benefits, durable polymer DES exhibit delayed vessel healing, hypersensitivity reactions, and neoatheroma formation, resulting in delayed restenosis and repeat revascularization and late and very late stent thrombosis.[2,3] Bioabsorbable polymer coatings degrade over months to years and allow delivery of an antiproliferative drug until the polymer disappears leaving behind a bare metal stent. Limiting the duration of polymer exposure to the endothelial wall is intuitively attractive as this limits the inflammatory exposure to the duration necessary to deliver the antiproliferative drug, thus offering potential for improved late safety and efficacy in comparison with durable polymer stents.[4] The absorbable polymer sirolimus-eluting stent (APSES, MiStent; Micell Technologies, Durham, North Carolina) is a thin-strut, cobalt-chromium stent coated with crystalline sirolimus in a bioabsorbable polymer (Figure 1). The combination of crystalline sirolimus within the bioabsorbable polymer enables the deposition of drug into the surrounding tissue and prolonged elution at a controlled rate, providing therapeutic tissue concentrations of sirolimus up to 9 months after implantation, without an initial burst of drug release.[5] The coating is cleared from the stent in 45 to 60 days—leaving behind a bare metal stent—and is absorbed into the tissue within 90 days. However, comparative efficacy data against benchmark durable polymer DES remain scant. The purpose of this analysis was to compare the 3-year clinical outcomes of the MiStent APSES with the durable polymer everolimus-eluting stent (EES; Xience; Abbot Vascular, Abbott Park, Illinois) using pooled data from 3 trials and propensity score matching to account for baseline differences in patient risk.

Methods

This analysis included patients enrolled in the DES With Sirolimus and a Bioabsorbable Polymer for the Treatment of Patients With De Novo Lesions in the Native Coronary Arteries (DESSOLVE) I (enrolled 2010 to 2011) and II (enrolled 2012 to 2013) trials[6,7] who received a MiStent APSES and a contemporary cohort of patients assigned to the EES from the Intracoronary Stenting and Angiographic Results: Test Efficacy of 3 Limus-Eluting Stents-4 (ISAR-TEST-4) trial (enrolled 2007 to 2008).[8] Full details of the 3 trials have been published. DESSOLVE I was the first-in-human experience with the APSES, enrolling 30 patients at 5 centers with symptomatic coronary artery disease with

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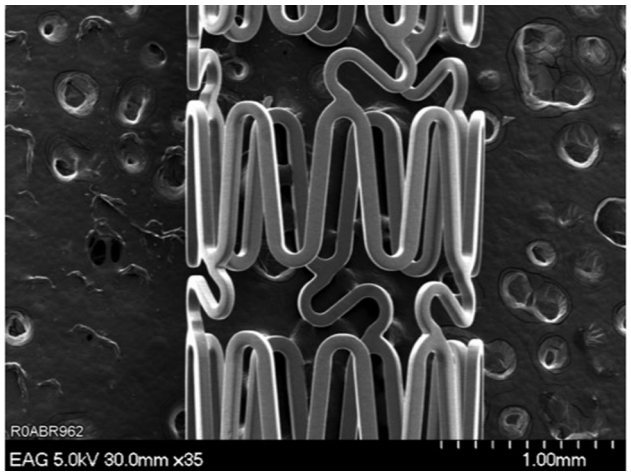

Figure 1. MiStent design.

stable or unstable angina pectoris and lesions with >50% diameter stenosis, amenable to coverage with a ≤23-mm-long stent in vessel sizes of 2.5 to 3.5 mm in diameter.[6] Patients in consecutive groups of 10 underwent repeat angiography, intravascular ultrasound, and optical coherence tomography at 4, 6, or 8 months, and all patients had repeat angiography, intravascular ultrasound, and optical coherence tomography at 18 months of follow-up. The primary end point was angiographic in-stent late lumen loss. DESSOLVE II included 184 patients at 26 centers, randomized in a 2:1 manner to APSES or the zotarolimus-eluting stent (Endeavor Sprint; Medtronic Vascular, Santa Rosa, California). Patients were included if they had stable or unstable angina pectoris, a single, de novo, type A, B1, or B2 lesion of >50% diameter stenosis in a 2.5- to 3.5-mm diameter native coronary artery that could be covered with a ≤30-mm-long stent.[7] Total occlusions, in-stent restenosis, highly calcified or thrombotic lesions, and lesions located at major bifurcations or in highly tortuous vessels were excluded from the study. The primary efficacy hypothesis was superiority of in-stent late lumen loss of APSES compared with ZES. The ISAR-TEST-4 trial was a randomized clinical trial with broad inclusion criteria, enrolling 2,603 patients at 2 clinics in Munich, Germany. Patients were randomized to either bioabsorbable polymer (n = 1,299) or durable polymer DES (n = 1,304); patients treated with durable polymer stents were randomly allocated to Xience EES (n = 652) or SES (Cypher; Cordis, Miami Lakes, Florida) (n = 652).[8] We included only the EES arm of ISAR-TEST-4 in this analysis. The primary end point was the composite of cardiac death, target vessel−related myocardial infarction (MI), or target lesion revascularization (TLR). A detailed comparison of inclusion and exclusion criteria for the DESSOLVE and ISAR-TEST-4 studies is reported in Supplementary Table 1. All patients were prescribed treatment with standard guideline-recommended dual antiplatelet therapy for 12 months.

Clinical end point measures were collected prospectively within each trial using standard definitions, and end points in this analysis are a combination of each study's protocol-defined end points (detailed in Supplementary Table 2). All ISAR-TEST-4 MIs were independently re-adjudicated according to DESSOLVE trial definitions for poolablity of results. The primary clinical end point measure for this analysis was target lesion failure (TLF) defined as the composite of cardiac death, target vessel MI, and clinically indicated TLR. Secondary clinical end points include the patient-oriented composite of major adverse cardiac events defined as death, MI, and all target vessel revascularization. In addition, component end points are reported and include the following: all death, cardiac death, all MI, target vessel MI, clinically indicated TLR, and target vessel revascularization. Target vessel failure was defined as cardiac death, target vessel MI, and target vessel revascularization. Stent thrombosis was adjudicated according to the Academic Research Consortium criteria.[9] An independent Clinical Event Committee adjudicated all events up to 3-year follow-up for each trial (DESSOLVE I and II; Harvard Clinical Research Institute, Boston, Massachusetts; ISAR-TEST-4; ISARESEARCH Center, Munich, Germany). Definitions of end points were similar across the 3 trials. Independent angiographic core laboratories assessed all angiographic end points (DESSOLVE I and II; Yale Cardiovascular Research Group, Yale University, New Haven, Connecticut; ISAR-TEST-4; ISARESEARCH Center) using the same software (CMS, version 7.1/7.2; Medis Medical Imaging Systems, Leiden, The Netherlands), and image acquisition was protocol guided. Baseline and postprocedure angiographic measures are reported in-stent and in-lesion defined as the stented segment and 5 mm on either edge of the stent.

The population for analysis and propensity score modeling was defined using the following rules: (1) only patients with single-vessel intervention who received the study stent were included; (2) those presenting with acute MI were excluded; and (3) those with total occlusions, thrombus, bifurcation lesions requiring side branch intervention, and ostial lesions were excluded. These criteria were selected based on the inclusion and exclusion of the more selective DESSOLVE trial populations. Treatment groups were matched through propensity scores. A logistic regression was fit with treatment (APSES vs EES) as the dependent variable against the following baseline covariates: age, gender, diabetes, smoking, hypertension, hypercholesterolemia, previous MI, PCI, and bypass, and angina status (stable vs nonstable), and whether the lesion required >1 stent and target vessel location (LAD, LCX, and RCA), reference vessel diameter, lesion length, American College of Cardiology/American Heart Association classification, and moderate/severe calcification. The logistic regression model fit was assessed through Hosmer-Lemeshow test. Patients were matched using the "greedy" algorithm with the maximum distance set at 0.1. A box plot of propensity scores before (but after applying exclusion criteria) and after matching was examined (Figure 2). The c-statistic of the propensity score matching was 0.865 demonstrating excellent discrimination.

All statistical analyses were performed using SAS statistical software, and all statistical tests were conducted at the 2-sided, 0.05 significance level. For categorical variables, the number and percentage within each category of the parameter are presented. For continuous variables, the mean, SD, and minimum and maximum values are presented. In the matched sample, data were compared between

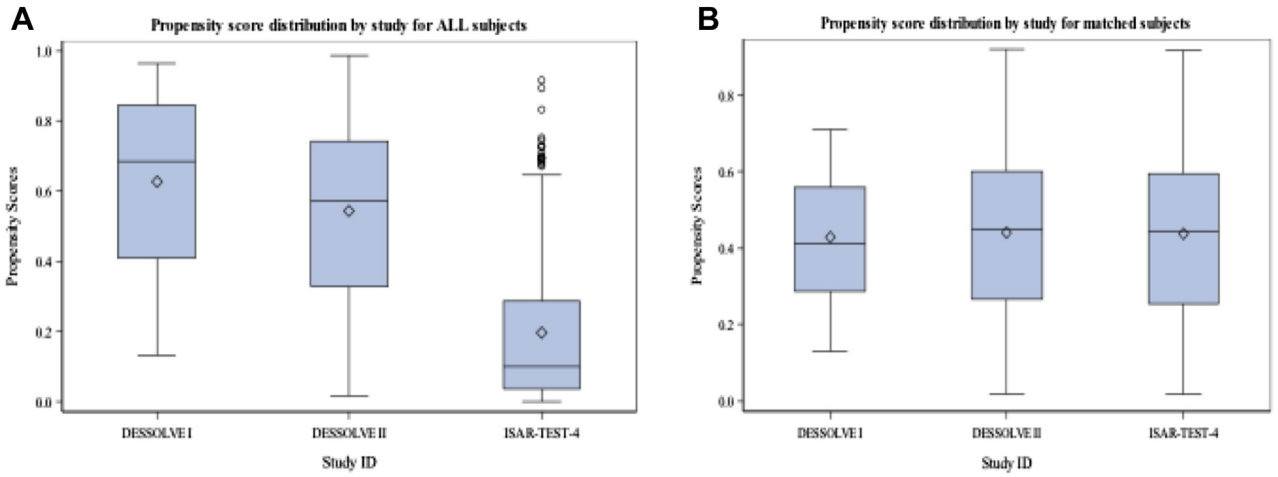

Figure 2. Box plot of propensity scores from the logistic regression *(A)* before and *(B)* after matching.

Table 1
Baseline patient characteristics

Variable	All Patients				Matched Population				
	APSES (N=153)	EES (N=652)	Total (N=805)	P-Value	APSES (N=102)	EES (N=102)	Total (N=204)	P-Value	P-Value From GEE
Age (years)	64.49 ± 10.35	66.74 ± 10.29	66.31 ± 10.34	0.02	65.55 ± 9.48	66.32 ± 9.79	65.93 ± 9.62	0.57	0.55
Male	70% (107/153)	78% (507/652)	76% (614/805)	0.04	71% (72/102)	75% (76/102)	73% (148/204)	0.53	0.48
Diabetes	20% (30/151)	28% (184/652)	27% (214/803)	0.04	22% (22/100)	20% (20/102)	21% (42/202)	0.68	0.66
Insulin Rx	2% (3/151)	9% (60/652)	8% (63/803)	0.003	2% (2/100)	4% (4/102)	3% (6/202)	0.42	0.44
Hypertension	72% (109/152)	68% (442/652)	69% (551/804)	0.35	73% (74/101)	77% (78/102)	75% (152/203)	0.60	0.61
Hyperlipidemia	76% (114/151)	65% (423/652)	67% (537/803)	0.01	72% (72/100)	74% (75/102)	73% (147/202)	0.81	0.8
Current smoker	20% (30/151)	16% (101/652)	16% (131/803)	0.19	15% (15/101)	13% (13/102)	14% (28/203)	0.66	0.68
Prior Myocardial Infarction	22% (33/151)	29% (191/652)	28% (224/803)	0.07	24% (24/101)	21% (21/102)	22% (45/203)	0.59	0.6
Prior Coronary Bypass	3% (5/152)	11% (69/652)	9% (74/804)	0.005	5% (5/102)	6% (6/102)	5% (11/204)	0.76	0.74
Prior PCI	28% (42/153)	53% (348/652)	48% (390/805)	<0.0001	33% (34/102)	31% (32/102)	32% (66/204)	0.76	0.75
Unstable angina pectoris	16% (24/153)	31% (199/652)	28% (223/805)	0.0002	18% (18/102)	29% (30/102)	24% (48/204)	0.048	0.045
Stable angina pectoris	77% (117/153)	59% (383/652)	62% (500/805)	<0.0001	75% (76/102)	71% (72/102)	73% (148/204)	0.53	0.52
Silent ischemia	8% (12/153)	0% (0/0)	8% (12/153)	NA	8% (8/102)	0% (0/0)	8% (8/102)	n/a	n/a

APSES = absorbable polymer sirolimus-eluting stent; EES = everolimus-eluting stent.

groups using methods appropriate for the matched (correlated) nature of the data. The primary outcome variable, TLF, is presented as Kaplan-Meier estimates and compared between groups through marginal hazard ratios (HRs)[10] and 95% confidence intervals (CIs) from the Cox proportional hazards regression using robust sandwich estimates of the variance. The assumption of proportionality was tested using the method of Lin et al.[11]

As late angiographic follow-up was not planned/conducted in the DESSOLVE II study, sensitivity analyses were carried out to assess the robustness of the results to late angiographic follow-up for the primary outcome as follows: (1) all patients were censored at the time of their actual late angiographic follow-up. Patients without late angiographic follow-up were analyzed as usual and censored at their last known follow-up if before 3 years; (2) it was assumed that the covariates "early angiographic follow-up" and "late angiographic follow-up" proportionally affect the hazard of an event. Early and late angiographic follow-up were included in the model for TLF and treated as time-updated covariates for this analysis.

Results

A total of 805 patients (APSES = 153; EES = 652) were included in the overall analysis. Propensity score matching was performed in 204 patients (APSES = 102; EES = 102). Clinical follow-up was available in 98% (100 of 102) of APSES patients versus 88% (90 of 102) of EES patients. Baseline patient characteristics between APSES and EES in the overall population are displayed in Table 1. There were significant differences between the groups. After matching, characteristics were well balanced between the groups (Table 1). Mean age of the matched population was 66.5 years, 21% of them had diabetes and 24% unstable angina. Overlap of the propensity scores was excellent as demonstrated by the box plots (Figure 2). The propensity model fit was good as assessed by the Hosmer-Lemeshow

Table 2
Baseline lesion and angiographic characteristics

Patients/Lesions	All Patients/Lesions				Matched Patients/Lesions				
	APSES (N=153/152)	EES (N=652/850)	Total (N=805/1002)	P-Value	APSES (N=102/101)	EES (N=102/105)	Total (N=204/206)	P-Value	P-Value GEE
Lesions Treated	1.14 ± 0.35	1.30 ± 0.54	1.27 ± 0.51	0.0003	1.14 ± 0.35	1.03 ± 0.17	1.08 ± 0.28	0.005	0.003
Stents Implanted	1.07 ± 0.28	1.26 ± 0.52	1.23 ± 0.50	<0.0001	1.08 ± 0.30	1.04 ± 0.19	1.06 ± 0.25	0.25	NA
Target lesion location									
Left Anterior Descending	43% (65/153)	44% (372/850)	44% (437/1003)	0.77	45% (46/102)	41% (43/105)	43% (89/207)	0.55	0.55
Left Circumflex	22% (34/153)	26% (223/850)	26% (257/1003)	0.30	28% (28/102)	29% (30/105)	28% (58/207)	0.86	0.96
Right	35% (54/153)	30% (255/850)	31% (309/1003)	0.19	28% (28/102)	31% (32/105)	29% (60/207)	0.63	0.67
ACC/AHA classification									
A	32% (49/153)	4.5% (38/850)	8.7% (87/1003)	<0.0001	24% (24/102)	23% (24/105)	23% (48/207)	0.91	0.95
B1	45% (69/153)	25% (208/850)	28% (277/1003)	<0.0001	48% (49/102)	50% (52/105)	49% (101/207)	0.83	0.69
B2	22% (33/153)	46% (390/850)	42% (423/1003)	<0.0001	27% (27/102)	24% (25/105)	25% (52/207)	0.66	0.48
C	1.3% (2/153)	25% (214/850)	22% (216/1003)	<0.0001	2% (2/102)	3.8% (4/105)	2.9% (6/207)	0.43	0.4
TIMI flow grade 3									
Pre-TIMI	92% (140/152)	82% (693/850)	83% (833/1002)	0.001	89% (90/101)	93% (98/105)	91% (188/206)	0.28	0.92
Post-TIMI	99% (150/152)	96% (818/850)	97% (968/1002)	0.12	98% (99/101)	99% (104/105)	99% (203/206)	0.54	0.55
Pre-Procedure									
Lesion Length (mm)	13.50 ± 4.77	15.18 ± 8.89	14.93 ± 8.41	0.02	13.47 ± 4.66	12.97 ± 6.61	13.22 ± 5.73	0.53	0.35
RVD (mm)	2.87 ± 0.37	2.80 ± 0.45	2.81 ± 0.44	0.09	2.83 ± 0.37	2.84 ± 0.41	2.84 ± 0.39	0.78	0.58
MLD (mm)	0.84 ± 0.22	0.99 ± 0.49	0.97 ± 0.47	0.0002	0.83 ± 0.22	1.11 ± 0.35	0.97 ± 0.33	<0.0001	NA
DS (%)	70.48 ± 7.79	64.85 ± 15.98	65.71 ± 15.15	<0.0001	70.31 ± 7.97	60.81 ± 11.69	65.49 ± 11.08	<0.0001	NA
Post Procedure In Stent									
MLD (mm)	2.83 ± 0.34	2.59 ± 0.43	2.63 ± 0.43	<0.0001	2.80 ± 0.34	2.66 ± 0.39	2.73 ± 0.37	0.005	0.15
DS (%)	3.19 ± 7.29	11.83 ± 6.30	10.51 ± 7.17	<0.0001	3.05 ± 7.64	10.92 ± 6.10	7.02 ± 7.93	<0.0001	<0.0001
Post Procedure In-Lesion									
MLD, mm	2.54 ± 0.38	2.25 ± 0.51	2.30 ± 0.50	<0.0001	2.52 ± 0.40	2.29 ± 0.48	2.40 ± 0.46	0.0003	0.0009
DS, (%)	13.47 ± 7.55	23.60 ± 11.44	22.04 ± 11.52	<0.0001	13.20 ± 7.61	23.70 ± 10.20	18.50 ± 10.42	<0.0001	<0.0001

APSES = absorbable polymer sirolimus-eluting stent; DS = diameter stenosis; EES = everolimus-eluting stent; MLD = minimal luminal diameter; RVD= reference vessel diameter; TIMI = thrombolysis in myocardial infarction.

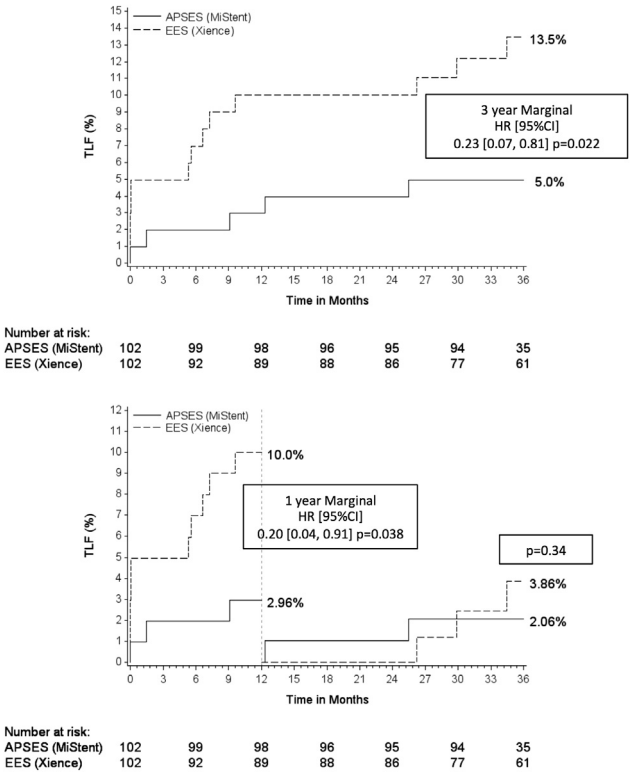

Figure 3. Kaplan-Meier estimates of 3-year TLF *(top)* and 1-year landmark analysis for TLF *(bottom)*.

test (p = 0.28). The assumption of proportionality was not violated.

Baseline lesion characteristics between APSES and EES in the overall population are displayed in Table 2. There were significant differences between the groups. After matching, characteristics were well balanced between the groups (Table 2). The number of stents implanted and procedure success per patient was similar, but the maximum deployment pressure was higher in the EES group. The preprocedure MLD was larger and the postprocedure MLD was smaller in the EES group (p <0.0001), resulting in a higher final in-stent and lesion diameter stenosis in the EES compared with the APSES group (Table 2).

In the matched population, APSES had lower TLF (3% vs 8%, p = 0.08; Figure 3) and TLR (1% vs 6%, p = 0.05; Figure 4) outcomes at 1 year, with no significant differences in target vessel MI (1% vs 2%, p = 0.57) or definite/probable stent thrombosis (0% vs 1%; p = 0.31) compared with EES.

At 3 years, TLF (5.0% vs 12.5%, p = 0.03; Figure 3) was significantly lower with APSES compared with EES, driven by a lower TLR rate (2.0% vs 8.4%, p = 0.05; Figure 4). At 3 years, there were no differences in cardiac death (2.0% vs 2.1%, p >0.99) or target vessel MI between the groups (2.0% vs 3.1%; p = 0.34), and there were no additional late or very late stent thrombosis in either group. The landmark analysis demonstrates no significant difference in TLF or

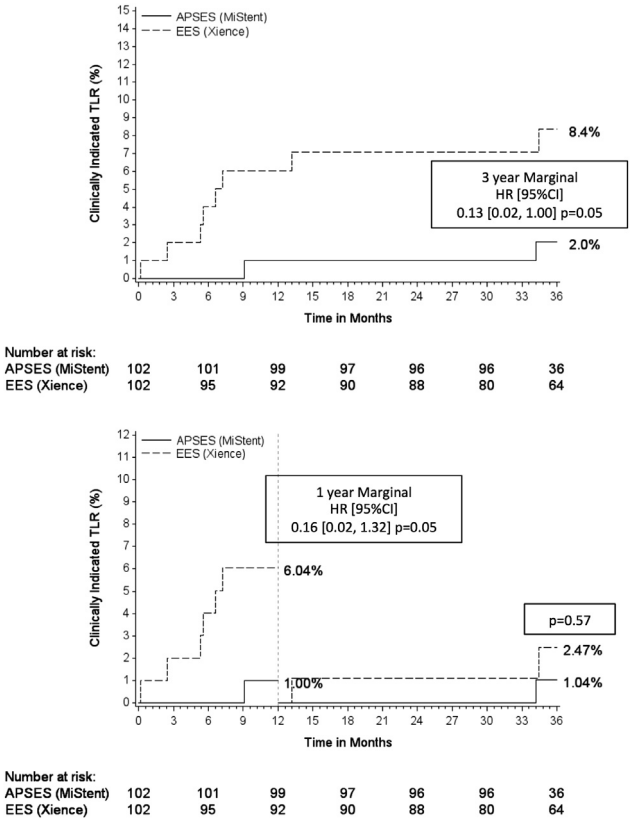

Figure 4. Kaplan-Meier estimates of 3-year ischemia-driven lesion revascularization *(top)* and 1-year landmark analysis for TLR *(bottom)*.

other outcomes in the matched analysis between 1 and 3 years (Figures 3 and 4).

Results for sensitivity analyses were similar for the primary outcome, TLF. When all patients were censored at the time of their actual late angiographic follow-up, TLF remained significantly lower with APSES (5% vs 12%, p = 0.03). Additionally, when "early" and "late" angiographic follow-up are included in the Cox regression, the conclusions are the same. Although late angiographic follow-up was related to an increase in the likelihood of an event (HR 11.1; 95% CI 1.39 to 88.4; p = 0.02), it had little effect on the relation with treatment (HR 3.81; 95% CI 1.26 to 11.48; p = 0.02).

Discussion

In this propensity-matched analysis of pooled data from 3 clinical trials, the thin-strut, cobalt-chromium, MiStent APSES showed lower rates of TLF at 1 year and at 3 years compared with the durable polymer Xience EES. These differences were driven by a significantly lower TLR rate at both time points. Landmark analysis demonstrated that differences in TLF between APSES and EES occurred within the first year and was maintained at 3 years with minimal accrual beyond 1 year, and no difference in events between groups were observed from 1 to 3 years. Definite and probable stent thrombosis was low in both groups with no additional ST events from 1 to 3 years. In view of the dearth of randomized trial data comparing outcomes with both stents, our findings provide preliminary evidence of the comparable safety and effectiveness of the MiStent APSES versus the leading benchmarked Xience EES in a well-matched patient population with 3-year follow-up.

The thin-strut MiStent APSES releases sirolimus in its crystalline form from a bioabsorbable polylactide-co-glycolic acid polymer coating (approximately 3 to 5 μm thick on the luminal and 10 to 15 μm thick on the abluminal stent surfaces).[12] Based on our data, the achieved drug-release kinetic may confer benefit within the first year compared with the benchmark durable polymer EES; moreover, this benefit appears to be sustained between 1 and 3 years. The early benefit of the MiStent APSES may result from the unique combination of crystalline sirolimus within the bioabsorbable polymer, which enables the deposition of drug into the surrounding tissue with prolonged elution at a controlled rate. This unique design provides therapeutic tissue concentrations of sirolimus up to 9 months after implantation, without an initial burst of drug release.[13] Unlike other bioabsorbable polymer DES, the MiStent polymer coating is cleared from the stent in 45 to 60 days and absorbed into the tissue within 90 days, long before complete drug elution. This unique prolonged drug elution resulting from the crystalline formulation of sirolimus (9 months) combined with a shorter polymeric absorption (3 months) may be associated with reduced inflammation[13] and may well account for the observed lower rates of TLF and TLR at 1 year compared with the durable polymer EES platform observed in our study. Another important differentiating factor are the release kinetics of MiStent APSES, which lack the early drug release burst described with conventional DES,[14] and may mitigate an early dose-related exaggerated vascular inflammatory effect.

A number of large-scale randomized clinical trials evaluating bioabsorbable polymer DES compared with the durable polymer EES have been recently reported and demonstrated generally comparable results in TLF at 9 to 12 months. The Clinical Evaluation of New Terumo Drug-Eluting Coronary Stent System in the Treatment of Patients with Coronary Artery Disease (CENTURY II) trial evaluated a thin-strut, cobalt-chromium, stent-releasing sirolimus from a poly-D,L-lactic acid and polycaprolactone co-polymer, which degrades over 3 to 4 months.[15] The 9-month TLF rate of the bioabsorbable polymer DES was similar (4.4% vs 4.9%, p = 0.66) compared with EES. The Ultrathin Strut Biodegradable Polymer Sirolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Stent for Percutaneous Coronary Revascularisation (BIOSCIENCE) randomized trial[16] evaluated a thin-strut, cobalt-chromium, poly-L-lactic acid polymer that degrades over 12 to 24 months. The 12-month TLF rates (6.7% vs 4.1%) were noninferior to the EES. Similar results were seen in the smaller BIOTRONIK-Safety and Clinical PerFormance of the Drug ELuting Orsiro Stent in the Treatment of Subjects With Single de Novo Coronary Artery Lesions-II (BIOFLOW-II) trial.[17] The EVOLVE II randomized trial evaluated a thin-strut, platinum-chromium stent platform that delivers everolimus from a bioabsorbable poly(D,L-lactide-co-glycolide) polymer applied to the abluminal surface; this device has near synchronous drug release (90 days) and polymer absorption (120 days).[18] At 12 months, TLF rates (6.7% vs 6.2%, p = 0.83) were noninferior to the durable polymer Promus Element EES.

The high performance of bioabsorbable polymer DES out to 12 months is encouraging. A number of large meta-analyses comparing durable and bioabsorbable DES have confirmed similar outcomes at 12 months compared with durable polymer DES.[19−22] Comparable outcomes versus benchmark durable polymer DES at this time point should be a sine qua non for their adoption. Unlike the results of these larger series and randomized trials, our matched analysis shows reduced TLF rates with MiStent relative to the durable polymer comparator.

The hypothesized benefit of bioabsorbable polymer DES is expected to become manifest first at late follow-up. In this respect, although the durable polymer EES demonstrates high efficacy at 9 to 12 months, accrual of events beyond 12 months has been described to occur at a rate of 2% to 3% per year in a large series of durable polymer DES.[23] However, clear demonstration of long-term benefit with other bioabsorbable polymer DES remains to be shown. In the 3-year follow-up of the original ISAR-TEST-4 trial, continued accrual of events occurred in both the durable and bioabsorbable polymer DES groups with no significant differences in clinical events discernable at 3 years with the biodegradable DES.[24] Moreover, although long-term follow-up from the Limus Eluted From a Durable Versus Erodable Stent Coating (LEADERS) trial and a pooled analysis including data from ISAR-TEST-3 and ISAR-TEST-4 showed improved late outcomes with bioabsorbable polymer DES, the comparator stent in these analyses was the early-generation Cypher SES.[4,25] Indeed, in a recent analysis of the final 5-year results from ISAR-TEST-4, we showed similar long-term results between bioabsorbable polymer DES and durable polymer EES.[26]

Whether our clinical findings reflect a design-specific advantage of the APSES is difficult to determine from our matched analysis and warrants confirmation in a randomized clinical trial. One cannot exclude that methodologic issues inherent to the design of our study may have played an important role. Indeed, in our series, the 1-year TLF rate for Xience V appears slightly higher than expected from that observed in randomized series (8%), whereas the MiStent appears comparable or lower than previously seen. Many factors could contribute to these differences including patient selection in the context of the DESSOLVE approval trials compared with the selection of the all-comers ISAR population. Nonetheless, at 1 year, the APSES results were excellent and the potential effect of the differential duration of polymer degradation relative to drug release will necessitate further evaluation. Ultimately, our data suggest that the unique design properties of the MiStent APSES may offer early and sustained clinical benefit that warrants large-scale evaluation in a randomized controlled trial setting.

The present study has some important limitations. First, a propensity-matched analysis cannot completely correct for baseline confounding factors between the groups. Therefore, we cannot exclude the possibility that our results are due at least in part to residual unmeasured confounding. Second, the number of patients included is modest, and this limits the ability of our study to detect differences between the groups especially in relation to rarely occurring clinical events. Third, interpretation of angiographic results is limited by that quantitative coronary angiographic analysis was performed by different core laboratories for the DESSOLVE I and II studies in comparison with ISAR-TEST-4. However, the definitions of end points were similar, and the same software packages were used for analysis.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amjcard.2015.11.044.

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