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Biodegradable Polymer- versus Durable Polymer-Coated Sirolimus-Eluting Stents: The Final 5-Year Outcomes of the I-LOVE-IT 2 Trial

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Disclosures

All of the authors and collaborators have no relevant personal conflicts of interest to disclose.

Brief Title: Five-Year Outcomes of the I-LOVE-IT 2 Trial

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Abstract

Aims This analysis presents the final 5-year results of the I-LOVE-IT 2 trial, a noninferiority study comparing BP- sirolimus-eluting stent (SES) with DP-SES in patients with coronary artery disease.

Methods and results Overall, 2737 Chinese patients eligible for coronary stenting were treated with BP- or DP-SES in a 2:1 ratio. Patients who were randomized to BP-SES group were additionally re-randomized to receive either 6-month or 12-month dual antiplatelet therapy (DAPT) in a 1:1 ratio. The primary endpoint was 12-month target lesion failure (TLF: cardiac death, target vessel myocardial infarction, or clinically indicated target lesion revascularization). At five years, overall follow-up rate was 90.8%, and the cumulative incidence of TLF as the primary endpoint was similar between BP-SES and DP-SES (hazard ratio [HR]: 1.01; 95% confidence interval [CI]: 0.79 to 1.28), as was that for patient-oriented composite endpoint (PoCE: all-cause death, all MI and any revascularization) (HR: 1.03, 95% CI: 0.86 to 1.23), or definite/probable ST (HR: 1.11, 95% CI: 0.70 to 1.77). Cumulative events also were similar between 6-month DAPT and 12-month DAPT groups after BP-SES implantation.

Conclusions I-LOVE-IT 2 has shown that the 5-year safety and efficacy of BP-SES and DP-SES were similar, as were those between 6-month and 12-month of DAPT after BP-SES implantations.

CLINICAL TRIAL REGISTRATION: URL: https://www.clinicaltrials.gov. Unique identifier: NCT 01681381.

Key Words: Adjunctive pharmacotherapy, Drug-eluting stent, Clinical trials.

Condensed Abstract

This analysis presents the final 5-year results of the I-LOVE-IT 2 trial, a noninferiority study comparing BP- sirolimus-eluting stent (SES) with DP-SES in patients with coronary artery disease. 2737 patients eligible for coronary stenting were treated with BP- or DP-SES in a 2:1 ratio. At five years, the cumulative incidence of target lesion failure (TLF: cardiac death, target vessel myocardial infarction, or clinically indicated target lesion revascularization) was similar between BP-SES and DP-SES (hazard ratio [HR]: 1.01; 95% confidence interval [CI]: 0.79 to 1.28). I-LOVE-IT 2 has shown that the 5-year safety and efficacy of BP-SES and DP-SES were similar.

Abbreviations

BP=Biodegradable polymers
DAPT=dual antiplatelet therapy
DES=drug-eluting stents
DP=durable polymers
PCI=percutaneous coronary intervention
PoCE=patient-oriented composite endpoint
TLF=target-lesion failure
TLR=target lesion revascularization
TV-MI=target vessel myocardial infarction

Introduction

Biodegradable polymers (BP) were developed to optimize the vascular healing response to drug-eluting stents (DES) by eliminating the detrimental effects of durable polymers (DP).[1,2] By virtue of the transient nature of the carrier, BP-DES were expected to elicit a more physiological vascular response in comparison to DP drug-eluting stents (DP-DES),[3] as appeared to be the case in clinical investigations reporting improved healing and lower thrombogenicity with BP-DES compared with early-generation DP-DES.[4] However, this was not the case in a few studies comparing long-term results between BP with DP on similar stent platforms eluting the same drug. In the prior reported one-year and three-year results of I-LOVE-IT 2 (Evaluate Safety and Effectiveness of the Tivoli DES and the Firebird DES for Treatment of Coronary Revascularization) trial, the biodegradable-polymer sirolimus-eluting stent (BP-SES, TIVOLI™, EssenTech, Beijing, China) was noninferior to the durable-polymer sirolimus-eluting stent (DP-SES) (Firebird2™, Microport Medical, Shanghai, China) in the primary composite safety and efficacy endpoint of target-lesion failure (TLF) at 12 months,[5] and the BP-SES yielded similar safety and efficacy outcomes at 3 years versus the DP-SES.[6] The present analysis presents the final 5-year results of the I-LOVE-IT 2 trial.

Methods

Study design

The design and methods for the I-LOVE-IT 2 trial (NCT01681381) have been described previously and are summarized in the following text.[5] In brief, this was a prospective, multicenter, randomized, assessor-blinded, noninferiority study comparing BP-SES with DP-SES, conducted in 32 centers in China (N=2737). Patients were eligible if they were over 18 years old, and had at least one coronary lesion with stenosis of >70% in a vessel with reference diameter of 2.5 to 4.0 mm. No restriction was placed on total number of treated lesions, treated vessels, lesion length, or number of stents implanted. Patients with multivessel disease had to receive complete revascularization within 30 days using same study stents if needed. Exclusion criteria were known intolerance to a study drug, metal alloys, or contrast media; life expectancy less than one year; restenosis lesions; stent implantation within one year; left ventricular ejection fraction <40%; severe renal or hepatic dysfunction;

hemodynamic instability; planned surgery within 6 months after index procedure; childbearing potential within one year; clinical indications of inability to tolerate dual antiplatelet therapy (DAPT) for 12 months; inability to provide written informed consent; and participation in another trial before reaching the primary endpoint. Patients scheduled for percutaneous coronary intervention (PCI) using DES were to be enrolled with fewer exclusion criteria. A screen-log was required in all centers.

Randomization and Procedures

Patients were randomly assigned to undergo PCI with either BP-SES or DP-SES in a 2:1 ratio. Patients who were randomized to BP-SES group were additionally re-randomized to a 6-month DAPT group or 12-month DAPT group in a 1:1 ratio. Randomization was performed just after angiogram by a web-based allocation system and was stratified by center, after fulfilled the required information, patients were then randomized into 1 of the 3 groups: DP SES, BP-SES with 6-month group, or BP-SES with 12-month group. Angiograms were reviewed by a blinded independent core laboratory (CCRF, Beijing, China), and all adverse events qualifying for primary and secondary endpoints were adjudicated by a blinded clinical events committee.

Balloon angioplasty and stent implantation were performed according to standard techniques; direct stenting (without previous balloon dilatation) was allowed. No mixture of type of stents was permitted for a given patient unless the operator was unable to insert the study stent, in which case crossover to another non-study device of the operator's choice was possible. Staged procedures were permitted, which were defined as procedures planned at the time of index procedure and performed within 30 days with the same type of study stent. In the case of unplanned revascularization procedures requiring stent implantation, it was recommended that physicians use the same type of study stent.

Procedural anticoagulation was achieved with unfractionated heparin at a dose of 70 to 100 IU per kilogram of body weight, and activated clotting time was maintained at 250 seconds or above; the use of glycoprotein IIb/IIIa inhibitors was left to operator's discretion. A loading dose of 300 mg of aspirin and 300 mg of clopidogrel was administered before all procedures. All patients were discharged with a prescription for at least 100 mg of aspirin daily indefinitely and 75 mg of clopidogrel daily for a minimum of 6 months after index procedure.

Qualitative and quantitative coronary angiography (including SYNTAX score and

residual SYNTAX score) was centrally evaluated at CCRF using QAngio XA Version 7.3 Analysis Software (Medis Medical Imaging System Inc., Leiden, The Netherlands).

Study endpoints and follow-up

The primary endpoint was 12-month TLF, a composite of cardiac death, target vessel myocardial infarction (TV-MI), or clinically indicated target lesion revascularization (TLR). Secondary endpoints included TLF components, device/lesion/procedure success rates, definite/probable stent thrombosis, and patient-oriented composite endpoint (PoCE, including all-cause death, all MI and any revascularization).

We defined cardiac death as any death due to an evident cardiac cause, any death related to PCI, unwitnessed death, or death from unknown causes. Spontaneous infarction was defined as a typical rise and fall of troponin or creatine kinase-MB fraction with at least one of the following: ischemic symptoms, development of pathological Q waves, ischemic electrocardiographic changes, or pathological findings of an acute MI. For comparison with other trials using Academic Research Consortium (ARC) MI definitions, we also adjudicated MI data according to ARC definitions.[7] TLR was defined as revascularization for a stenosis within the stent or within the 5-mm borders adjacent to the stent. We regarded revascularization of the target lesion and vessel as clinically indicated if stenosis of any target lesion or vessel was at least 50% of the diameter of the vessel on the basis of quantitative coronary angiography in the presence of objective evidence of ischemia from non-invasive or invasive testing or symptoms. We also regarded revascularization as clinically indicated if stenosis was at least 70% of the diameter of the vessel irrespective of ischemic signs or symptoms. Bleeding events were recorded using the Bleeding Academic Research Consortium (BARC) definition. Net Adverse Clinical and Cerebral Events (NACCE) is defined as a composite of all-cause death, myocardial infarction, stroke, or major bleeding (BARC type ≥ 3 bleeding).

Patients were followed up by telephone or hospital visit at 1, 6, 9, and 12 months and thereafter annually for 5 years, which was predefined in the original protocol.

Statistical Analysis

Sample size calculation has been report previously. [5]A total of 2790 subjects would need to be enrolled. Noninferiority would be achieved if the upper limit of the one-sided 95% confidence interval of the difference was less than the margin.

Following the conduct of the study, based on the observed TLF rate of 6.3% and actual n per group, there was 80% power to exclude a 0.028 noninferiority margin (margin/event ratio 44.5%, same as originally planned).

Categorical variables are reported as counts and percentages, and between-group differences were assessed with Chi-square or Fisher's exact test. Continuous variables are presented as means ±SD and were compared with the use of a two-sample t-test. The Kaplan-Meier method was used to calculate time to clinical endpoints, and the log-rank test was used to compare between-group differences. An exploratory Cox regression analysis was used to identify demographic and clinical factors predictive of endpoint. Unless otherwise specified, a two-sided P value of less than 0.05 was considered to indicate statistical significance. A landmark analysis for primary and secondary endpoints were performed from randomization to 1year and from 1 year to 5 year. Statistical analysis was performed using SAS software (SAS 9.1.3., SAS Institute, Cary, NC).

Results

A total of 2,737 Chinese patients were randomized to treatment with the BP-SES (n=1,829) or DP-SES (n=908) (Figure 1). Baseline information between groups as shown in Supplementary Table 1 and Table 2. Overall, 167 patients (9.1%) allocated to the BP-SES and 85 (9.4%) allocated to the DP-SES group were lost to follow-up before reaching five years, without any between-group differences. Baseline patient characteristics have been previously shown.[5] The two groups of patients were generally well balanced, in terms of their baseline clinical and lesion characteristics[5].

At five years, the incidence of TLF as the primary endpoint was similar between the BP- versus the DP-SES (11.4% vs. 11.1%, P=0.89) (Table 1, Figure 2A). The secondary endpoints for the individual components of TLF, including cardiac death, TV-MI, and CI-TLR, were comparable between the two arms and are illustrated in Figure 2B through 2D. Similarly, there was no difference between two groups in the PoCE (19.6% vs. 18.8%, P=0.68) (Table 2, Figure 2E), or definite/probable ST (1.2% vs. 1.4%, P=0.80) (Table 1, Figure 2F).

In a landmark analysis of the primary endpoint and its components, with the cutoff set at 1 year, we found no difference in rate of late events between 1 and 5 years (Figure 2, Table 1). The very late ST rates were low, with no significant

between-group differences (BP-SES vs. DP-SES, 0.9% vs. 0.8%, P=0.88) (Table 1, Figure 2F). Most patients discontinued DAPT after 1 year, and cumulative event rates were similar between 6 versus 12 months of DAPT groups after BP-SES implantation (Table 2, Supplementary Figure 1).

In the subgroup analysis, the incidence of TLF was not significantly different between the BP- and DP-SES for any prespecified subgroups, except that patients with long lesion tended to benefit more with DP-SES implantation over 5 years (Figure 3). There was also no statistically significant heterogeneity between duration of DAPT and the occurrence of NACCE among the subgroups (Supplementary Figure 2).

Discussion

The current article is the first report on long-term follow-up data out to 5 years, comparing treatment with BP- versus DP-coated cobalt-chromium (CoCr) sirolimus-eluting stents. The major findings of this report were similar rates of: (1) long-term safety and efficacy outcomes between BP-SES and DP-SES; (2) TLF and its components between BP- and DP-SES by landmark analysis after one year, and (3) cumulative events between 6 versus 12 Months of DAPT groups after BP-SES implantation.

Whether there is benefit of the biodegradable polymer stent over the permanent polymer stent has been a topic of discussion in interventional cardiology. To the best of our knowledge, I-LOVE-IT 2 was the first study that directly compared biodegradable and durable-polymer stents, which were quite similar except slight difference in strut thickness, stent profile, coating thickness, and available stent lengths[5] (Supplementary Table 3). Our long-term follow-up results have shown that BP-SES were similar to DP-SES in terms of clinical outcomes at five-year follow-up, including stent thrombosis, which might be explained by firstly, both devices being thin-strut CoCr DES. Previous studies had shown similar safety profile in terms of MI or ST beyond one year for thin-strut BP- and DP-DES,[8,9] and improvement in strut platform and strut thickness of new-generation DP-DES may have resulted in extended safety and efficacy outcomes that are comparable to that of BP-DES. In multicenter, randomized EVOLVE II trial (The EVOLVE II Clinical Trial to Assess the SYNERGY Stent System for the Treatment of Atherosclerotic Lesion[s]), BP-

DES with thin-strut demonstrated comparable outcomes to DP-DES, with low rates of stent thrombosis and adverse events through 5 years of follow-up.[10] A recent study showed that optical coherence tomography (OCT) performed at a median follow-up of 7 months displayed decreased neointimal growth and higher risk for uncovered struts after implantation of thick-struts BP-DES in comparison to new-generation DP-DES,[11] and the subgroup analysis found that thick-struts but not thin-strut BP-DES had less NIH thickness as compared with new-generation DP-DES. Those findings confirmed that thin-struts stents allow for accelerated endothelial recovery, faster integration into the vessel wall and complete re-endothelialization in comparison with thick-struts platforms. Secondly, lesions in patients in the study were of lower complexity (mean baseline SYNTAX score 11.7), and the sample size was calculated based on primary endpoints at one-year. The rates of clinical events in the study were lower than those in other similar studies;[12, 13] and a larger study with greater proportion of with higher lesion complexity are warranted to finally elucidate whether BP-DES is superior to DP-DES or not.

One of hypotheses of the study was that the combination of short-term DAPT and a BP-DES could reduce both the incidence of thrombotic events and bleeding complications. The previously reported 18-month follow-up results showed that incidence of target lesion failure and net adverse clinical and cerebral events were similar between 6-month and 12-month DAPT groups.[14] The present 5-year follow-up results again showed similar results for cumulative events between 6 as 12 months of DAPT groups after BP-SES implantation, which was consistent with a recent study.[15] Some concerns arise when the present data are interpreted in daily practice. Firstly, the incidence of the primary endpoint was lower than expected, suggesting that patients in the study might represent a low-risk cohort. The mean total lesion length in both groups was around 21mm, and average stent diameters were over 3mm in size. Therefore, whether 6-month DAPT after BP-DES implantation is feasible in high-risk patients with more complex lesions needs to be studied. Secondly, new-generation antiplatelet drugs, such as ticagrelor or prasugrel, were not used in our trial. Discontinuation of aspirin and continuation of new-generation antiplatelet drugs may be another option after BP-DES implantation, as suggested by the GLOBAL LEADERS study.[16] Finally, biodegradable polymer–based DES have wide-ranging differences in degradation products and kinetics, which may importantly affect DAPT

duration. Therefore, the results of the study cannot be extrapolated to other biodegradable polymer DES.

Limitations

In addition to the aforementioned points, several important study limitations need to be taken into consideration. Firstly, although this study focused on comparisons between BP-DES and DP-DES, there remains limited evidence supporting the Tivoli as a prototype BP-DES when compared with US Food and Drug Administration-approved new-generation thin-strut BP-DES. Secondly, a double-blinded design was not used for the comparison between the two DAPT strategies within the BP-DES group; and early discontinuation of DAPT (0.3%) and crossing over to prolonged DAPT (6.5%) occurred in a some of patients. Third, 58% of patients presented with unstable angina in the study. In recent years, high-sensitivity cardiac troponin assays have improved the detection of acute myocardial infarction, the number of patients labelled as NSTEMI is increasing instead of unstable angina. Fourth, all patients including those with ACS were treated with clopidogrel, not with more potent antiplatelet agents. Fifth, differences in the available lengths of the two stents may have effects on clinical outcomes. Finally, all patients enrolled in present study were Chinese, so generalizability of the study findings needs to be proved in the future studies.

Conclusions

I-LOVE-IT 2, the largest-scale cardiovascular device randomized trial in China, has shown similar 5-year safety and efficacy for BP-SES and DP-SES, as for patients who had received 6 or 12 months of DAPT after BP-SES implantation. The present long-term analysis adds new valuable data to the evidence pool of randomized comparisons between BP-DES and DP-DES, and shorter- and standard-duration of DAPT.

Impact on daily practice

BP-SES and DP-SES have similar rates of: (1) long-term safety and efficacy outcomes; (2) TLF and its components between BP- and DP-SES by landmark analysis after one year, and (3) cumulative events between 6 versus 12 Months of DAPT groups after BP-SES implantation.

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Appendix

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Figure Legends

Figure 1. Patient Flow. BP-SES = biodegradable polymer sirolimus-eluting stent(s); DP-SES = durable polymer sirolimus- eluting stent(s); DAPT = dual antiplatelet therapy.

Figure 2. Kaplan-Meier Estimates for TLF, PoCE and Def/Prob ST in the Overall Population Through 5 Years. Cumulative incidence of Target Lesion Failure (A), Cardiac Death (B), Target Vessel-MI (C), ID-TLR (D), PoCE (E), and Def/Prob ST (F).
MI = myocardial infarction; ID-TLR = ischemia driven target lesion revascularization; PoCE = patient oriented composite endpoint; Def/Prob ST = definite/probable stent thrombosis; other abbreviations as in Figure 1.

Figure 3. Subgroup Analysis of the 5-Year TLF. Complex lesions were defined by presence of at least one of the following lesion characteristics: unprotected left main coronary artery, bifurcation, ostial lesion, total occlusion, severely tortuous or angulated lesion, and moderate to heavy calcification.
CI = confidence interval; PCI = percutaneous coronary intervention; AMI = acute myocardial infarction; other abbreviations as in Figure 1.

Table 1. Kaplan-Meier Estimates of Clinical Outcomes Through 5 Years

	BP-SES	DP-SES	Hazard Ratio* [95% CI]	Log-rank p value
0 - 5 years	N=1829	N=908		
Target lesion failure	11.4% (203)	11.1% (100)	1.01 [0.79,1.28]	0.89
Patient-oriented composite endpoint	19.6% (352)	18.8% (170)	1.03 [0.86,1.23]	0.68
All-cause death	5.7% (100)	3.9% (35)	1.42 [0.97,2.09]	0.06
Cardiac death	3.0% (52)	2.3% (20)	1.30 [0.77,2.17]	0.29
All myocardial infarction	6.1% (108)	6.8% (61)	0.88 [0.64,1.20]	0.48
Target vessel myocardial infarction	5.0% (89)	5.9% (53)	0.83 [0.59,1.17]	0.32
Any revascularization	12.1% (214)	11.9% (106)	1.01 [0.80,1.27]	0.92
Target vessel revascularization	7.3% (130)	6.6% (59)	1.10 [0.81,1.50]	0.54
Target lesion revascularization	6.0% (107)	5.8% (52)	1.03 [0.74,1.43]	0.88
Ischemia driven target lesion revascularization	5.9% (105)	5.7% (51)	1.03 [0.74,1.44]	0.87
Definite/probable stent thrombosis	1.2% (22)	1.4% (12)	0.91 [0.45,1.85]	0.80
Definite stent thrombosis	0.6% (10)	0.7% (6)	0.83 [0.30,2.28]	0.72
Probable stent thrombosis	0.7% (12)	0.7% (6)	1.00 [0.38,2.66]	0.99
Acute (0-1 day)	0.2% (3)	0.2 (2)	0.74 [0.12,4.45]	0.75
Subacute (2-30 days)	0.2% (3)	0.2 (2)	0.74 [0.12,4.45]	0.75
Late (30-365 days)	0.1% (1)	0.1% (1)	0.50 [0.03,7.92]	0.61
Very late (>365 days)	0.9% (15)	0.8% (7)	1.07 [0.44,2.63]	0.88
1 - 5 years	N=1800	N=897		
Target lesion failure	5.7% (100)	5.5% (49)	0.99 [0.69,1.43]	0.88
Patient-oriented composite endpoint	11.4% (201)	10.1% (90)	1.10 [0.85,1.42]	0.33
All-cause death	4.4% (76)	3.0% (26)	1.49 [0.93,2.39]	0.08
Cardiac death	2.3% (39)	1.7% (15)	1.49 [0.78,2.87]	0.35
All myocardial infarction	2.1% (35)	2.3% (20)	0.81 [0.46,1.44]	0.70
Target vessel myocardial infarction	1.4% (25)	1.7% (15)	0.82 [0.42,1.59]	0.57
Any revascularization	7.4% (128)	7.2% (63)	1.00 [0.73,1.36]	0.88
Target vessel revascularization	4.4% (77)	3.9% (35)	1.04 [0.69,1.58]	0.64
Target lesion revascularization	3.6% (62)	3.6% (32)	0.89 [0.57,1.40]	0.87
Ischemia driven target lesion revascularization	3.4% (60)	3.6% (32)	0.8 0[0.55,1.35]	0.75
Definite/probable stent thrombosis	0.9% (15)	0.8% (7)	1.00 [0.37,2.66]	0.88

Definite stent thrombosis	0.4% (7)	0.2% (2)	1.25 [0.24,6.42]	0.48
Probable stent thrombosis	0.5% (8)	0.6% (5)	0.87 [0.26,2.98]	0.69

Values are % (n). *The value was the hazard ratio in BP-SES group compared with DP-SES group. Target lesion failure was defined as a composite of cardiac death, target vessel myocardial infarction and clinical indicated target lesion revascularization. Patient-oriented composite endpoint was defined as a composite of all-cause death, all myocardial infarction, and any revascularization.

CI = confidence interval; other abbreviations as in Table 1.

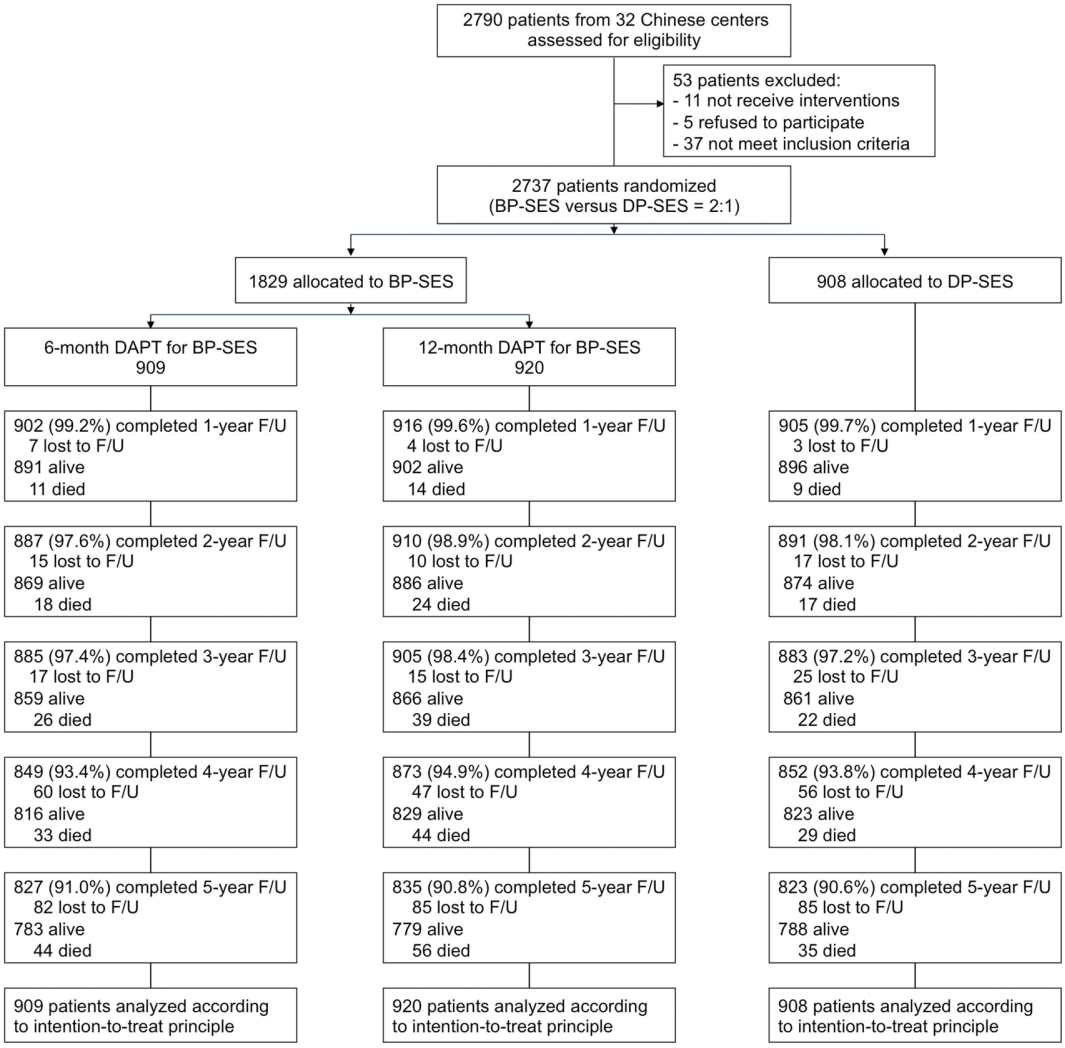
Table 2. Kaplan-Meier Cumulative Events in 6 Versus 12 Months of DAPT After BP-SES Subgroup

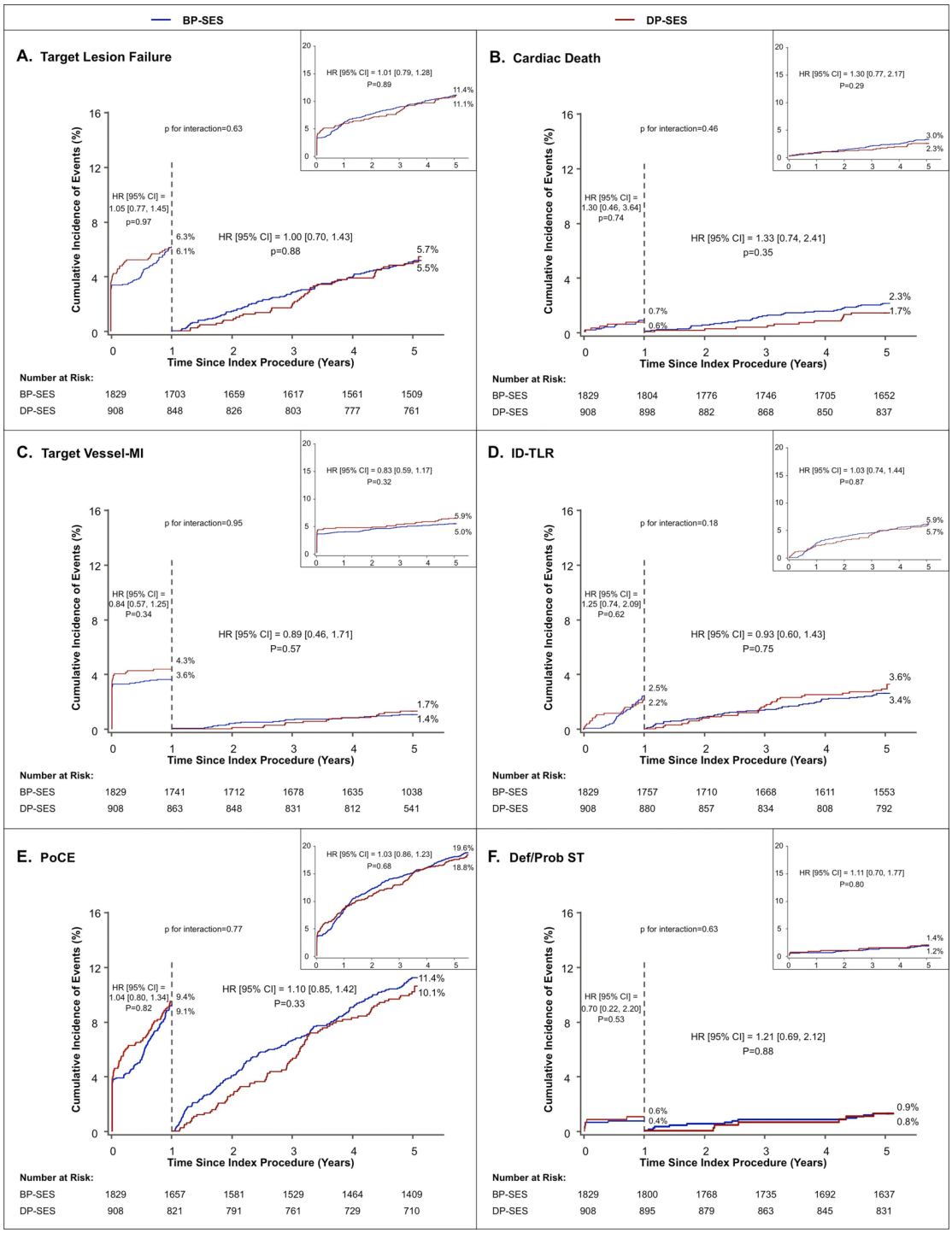
	6-month DAPT group	12-month DAPT group	Hazard Ratio [95% CI]	Log-rank p value
0 - 5 years	N=909	N=920		
Target lesion failure	11.5% (101)	11.2% (102)	0.99 [0.76,1.31]	0.82
NACCE	15.9% (140)	15.5% (140)	0.99 [0.78,1.25]	0.80
All-cause death	5.1% (44)	6.2% (56)	1.27 [0.85,1.88]	0.27
Cardiac death	2.7% (23)	3.2% (29)	1.26 [0.73,2.17]	0.53
All myocardial infarction	6.7% (59)	5.5% (49)	0.82 [0.56,1.20]	0.29
Target vessel myocardial infarction	5.7% (50)	4.3% (39)	0.77 [0.51,1.17]	0.18
Stroke	5.4% (46)	6.2% (55)	1.19 [0.81,1.77]	0.46
Any revascularization	12.0% (106)	12.2% (108)	1.01 [0.77,1.32]	0.94
Target vessel revascularization	7.4% (65)	7.3% (65)	0.99 [0.70,1.39]	0.91
Target lesion revascularization	6.2% (55)	5.8% (52)	0.93 [0.64,1.36]	0.69
Ischemia driven target lesion revascularization	6.1% (54)	5.7% (51)	0.93 [0.64,1.36]	0.69
All bleeding	9.2% (81)	10.4% (94)	1.15 [0.86,1.55]	0.42
Major bleeding	2.2% (19)	1.7% (15)	0.78 [0.40,1.53]	0.37
Definite/probable stent thrombosis	1.6% (14)	0.9% (8)	0.57 [0.24,1.35]	0.19
Definite stent thrombosis	0.7% (6)	0.5% (4)	0.66 [0.19,2.34]	0.51
Probable stent thrombosis	0.9% (8)	0.5% (4)	0.50 [0.15,1.65]	0.24
Acute (0-1 day)	0.2% (2)	0.1% (1)	0.50 [0.05,5.46]	0.56
Subacute (2-30 days)	0.2s% (2)	0.1% (1)	0.50 [0.05,5.46]	0.56
Late (30-365 days)	0.1% (1)	0% (0)	-	0.31
Very late (>365 days)	1.0% (9)	0.7% (6)	0.66 [0.24,1.86]	0.42
18 months - 5 years	N=889	N=902		
Target lesion failure	4.6% (39)	5.5% (49)	1.07 [0.75,1.51]	0.38
NACCE	8.8% (75)	9.5% (84)	1.03 [0.77,1.37]	0.62
All-cause death	3.4% (28)	4.4% (39)	1.27 [0.78,2.09]	0.25
Cardiac death	1.9% (15)	2.4% (21)	1.19[0.60,2.36]	0.44
All myocardial infarction	2.1% (18)	1.7% (14)	0.74 [0.40,1.36]	0.56
Target vessel myocardial infarction	1.7% (15)	1.0% (9)	0.59 [0.26,1.35]	0.20
Stroke	4.1% (34)	4.4% (39)	1.13 [0.75,1.70]	0.69
Any revascularization	5.7% (49)	5.5% (47)	1.03 [0.78,1.36]	0.84

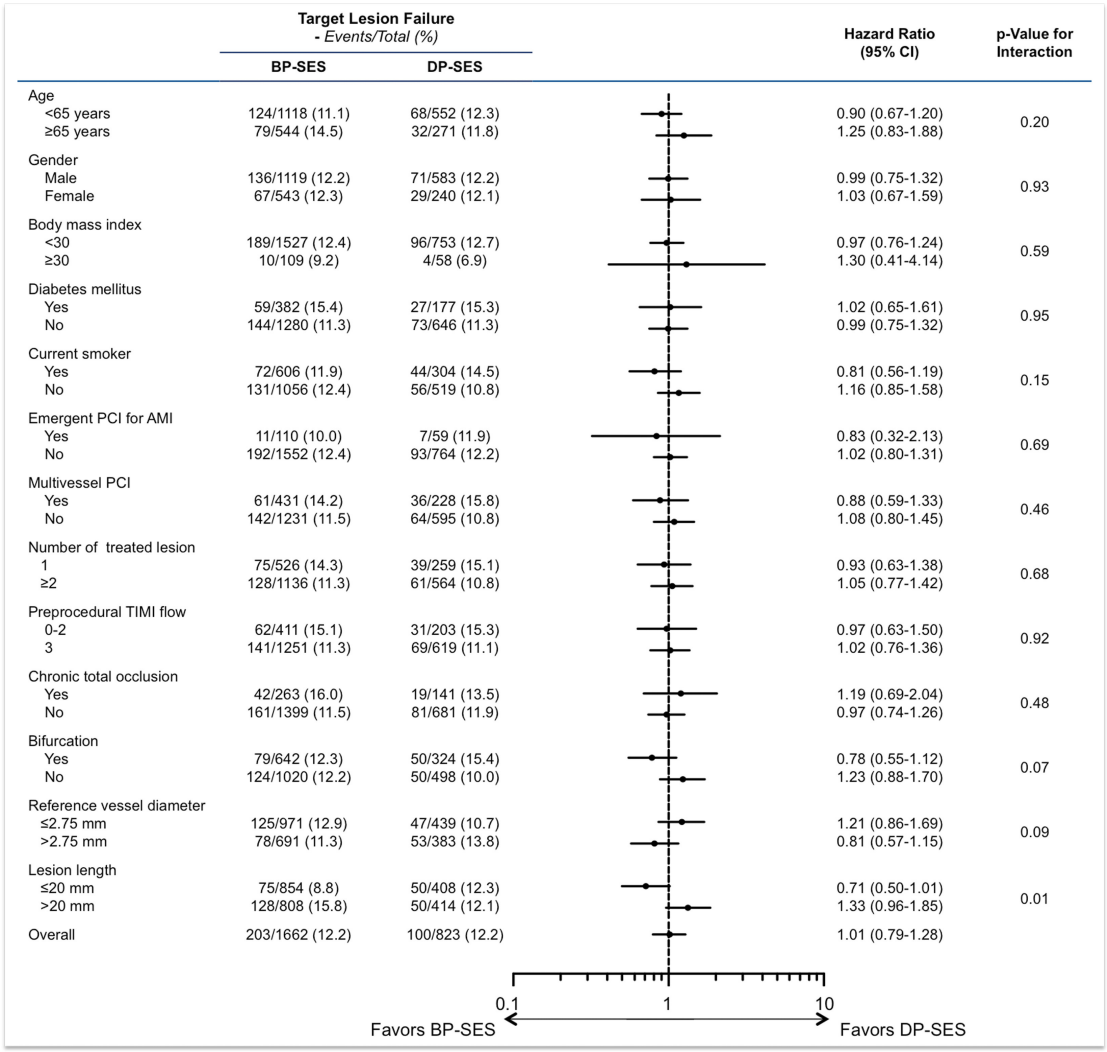
Target vessel revascularization	3.5% (30)	3.8% (33)	1.04 [0.72,1.49]	0.75
Target lesion revascularization	2.8% (24)	3.1% (27)	0.99 [0.66,1.48]	0.72
Ischemia driven target lesion revascularization	2.7% (23)	3.1% (27)	0.99 [0.65,1.48]	0.61
All bleeding	3.3% (28)	4.7% (41)	1.15 [0.84,1.57]	0.17
Major bleeding	1.0% (8)	0.9% (8)	0.79 [0.37,1.68]	0.78
Definite/probable stent thrombosis	1.0% (9)	0.7% (6)	0.55 [0.18,1.64]	0.42
Definite stent thrombosis	0.5% (4)	0.4% (3)	0.74 [0.17,3.31]	0.69
Probable stent thrombosis	0.6% (5)	0.4% (3)	0.40 [0.08,2.04]	0.47

Values are % (n). Net adverse clinical and cerebral events were defined as a composite of all-cause death, all MI, stroke, or major bleeding (BARC type ≥ 3 bleeding).

DAPT = dual antiplatelet therapy; NACCE = net adverse clinical and cerebral events; other abbreviations as in Table 1.







Supplementary Appendix

Supplementary table 1. Baseline Information Between BP-SES and DP-SES.

	BP-SES (1,829 Patients, 2,495 Lesions)	DP-SES (908 Patients, 1,235 Lesions)	p
Age, years	60.2 ± 10.1	60.2 ± 10.0	0.89
Male gender	68.0% (1,243)	70.0% (636)	0.27
Diabetes mellitus	22.6% (414)	21.3% (193)	0.41
Hypertension	62.9% (1,150)	61.6% (559)	0.50
Hyperlipidemia	24.3% (445)	22.5% (204)	0.28
Current smoker	37.5% (685)	36.9% (335)	0.78
Stable angina	14.7% (269)	13.9% (126)	0.56
Unstable angina	72.7% (1,330)	76.1% (691)	0.06
AMI within 24 hours	4.7% (86)	5.6% (51)	0.30
LVEF (%)	60.5 ± 8.3	61.0 ± 8.0	0.18
Target vessel location			0.39
Left main artery	1.8% (44)	2.6% (32)	
Left anterior descending artery	45.6% (1,138)	44.5% (550)	
Left circumflex artery	22.6% (563)	22.8% (281)	
Right coronary artery	30.1% (750)	30.1% (372)	
ACC/AHA lesion classification B2+C	83.5% (2,083)	85.1% (1,051)	0.21
Baseline SYNTAX score	11.7 ± 8.2	11.7 ± 8.5	0.99
Reference vessel diameter, mm	2.79 ± 0.47	2.79 ± 0.44	0.85
Lesion length, mm	20.6 ± 12.3	21.2 ± 12.9	0.25
Procedural characteristics			
Stents per patient	1.70 ± 0.86	1.75 ± 0.89	0.19
Total stent length per patient, mm	41.1 ± 24.4	42.7 ± 24.8	0.11
Post-dilation	51.4% (1,282)	46.2% (571)	0.003
Post-procedural TIMI flow grade 3	99.5% (2,482)	99.4% (1,228)	0.86
Residual SYNTAX score	3.3 ± 5.1	3.2 ± 5.6	0.74
Device success	99.5% (3,116)	99.6% (1,589)	0.62
Lesion success	99.3% (2.478)	99.4% (1,228)	0.67
Procedure success	95.8% (1,752)	95.6% (868)	0.81

Values are mean ± SD or n (%).

ACC/AHA = American College of Cardiology/American Heart Association; AMI = acute myocardial infarction; BP-SES = biodegradable polymer sirolimus-eluting stent; CAD = coronary artery disease; CABG = coronary artery bypass grafting; DP-SES = durable polymer

sirolimus-eluting stent; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; SYNTAX = synergy between percutaneous coronary intervention with taxus and cardiac surgery; TIMI = thrombolysis in myocardial infarction.

Supplementary table 2. Baseline Information Between 6-Month vs. 12-Month DAPT Group.

	6-month DAPT Group (Patient, n=909; Lesion, n=1240)	12-month DAPT Group (Patient, n=920; Lesion, n=1255)	p
Age, years	60.4 ± 10.2	60.0 ± 10.0	0.41
Male gender	611 (67.2)	632 (68.7)	0.50
Diabetes mellitus	23.2% (211)	22.1% (203)	0.56
Hypertension	61.0% (554)	64.8% (596)	0.09
Hyperlipidemia	25.3% (230)	23.4% (215)	0.34
Current smoker	36.6% (333)	38.3% (352)	0.77
Stable angina	14.3% (130)	15.1% (139)	0.63
Unstable angina	58.0% (527)	56.5% (520)	0.53
AMI within 24 hours	4.7% (225)	5.6% (224)	0.84
LVEF (%)	60.8 ± 8.4	60.3 ± 8.2	0.29
Target vessel location			0.88
Left main artery	1.9% (23)	1.7% (21)	
Left anterior descending artery	45.9% (569)	45.3% (569)	
Left circumflex artery	22.9% (284)	22.2% (279)	
Right coronary artery	29.4% (364)	30.8% (386)	
ACC/AHA lesion classification B2+C	83.6% (1,037)	83.4% (1,046)	0.85
Baseline SYNTAX score	11.6 ± 8.1	11.7 ± 8.2	0.68
Reference vessel diameter, mm	2.78 ± 0.46	2.79 ± 0.47	0.78
Lesion length, mm	20.5 ± 12.0	20.6 ± 12.6	0.64
Procedural characteristics			
Stents per patient	1.70 ± 0.87	1.71 ± 0.85	0.68
Total stent length per patient, mm	41.0 ± 25.1	41.2 ± 24.6	0.87
Post-dilation	51.8% (642)	51.0% (640)	0.68
Post-procedural TIMI flow grade 3	99.6% (1,235)	99.4% (1,247)	0.42
Residual SYNTAX score	3.20 ± 4.74	3.41 ± 5.35	0.38
Device success	99.7% (1,541)	99.4% (1,575)	0.21
Lesion success	99.5% (1,234)	99.1 % (1,244)	0.23
Procedure success	95.7% (870)	95.9% (882)	0.86

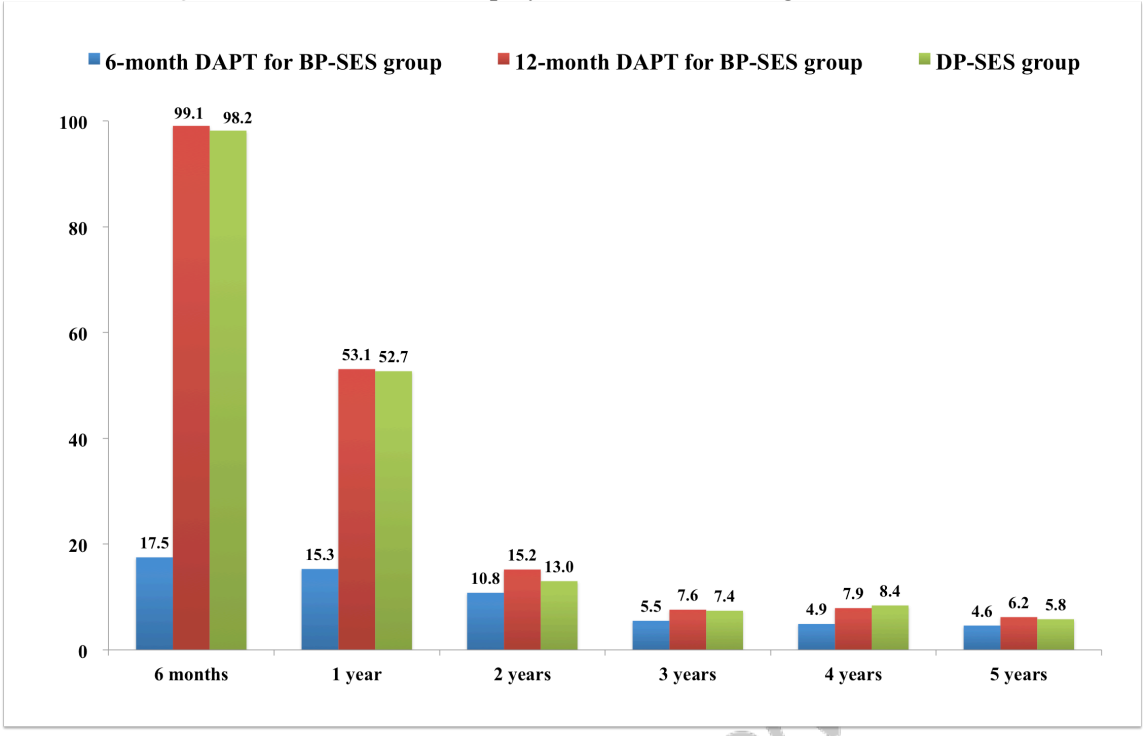
Values are mean ± SD or n (%). Abbreviation as in Table S1.

Supplementary table 3. Comparison of Specifications between BP-SES, DP-SES

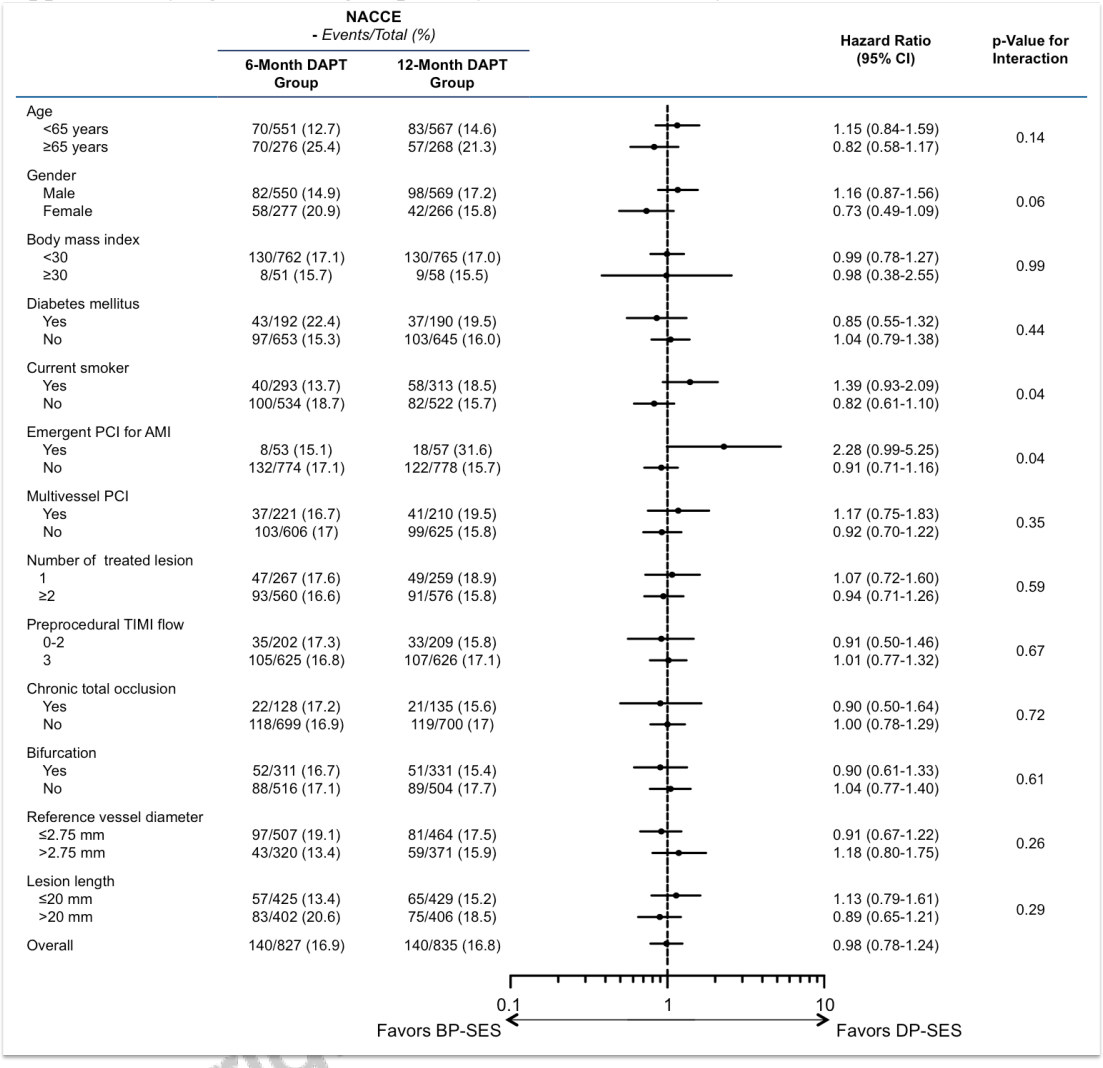
	BP-SES	DP-SES
Stent platform material	cobalt-chromium (L605)	cobalt-chromium (L605)
Strut thickness	0.080 mm	0.086 mm
Stent profile	< 1.10 mm	< 1.12 mm
Diameter	2.50, 2.75, 3.00, 3.50, 4.00 mm	2.50, 2.75, 3.00, 3.50, 4.00 mm
Length	10, 15, 18, 21, 25, 30, 35 mm	13, 18, 23, 29, 33 mm
Drug	sirolimus	sirolimus
Drug dose	8 μg/mm	9 μg/mm
Polymer	PLGA (biodegradable)	SBS (durable)
Polymer thickness	5.5 μm	6.0 μm
Drug release	75% at 28 days	> 80% at 30 days

BP-SES = biodegradable polymer sirolimus-eluting stent; DP-SES = durable polymer sirolimus-eluting stent; PLGA = poly lactide-co-glycolide acid; SBS = styrene-butadiene styrene.

Supplementary figure 1. DAPT Utilization Through 5 Years. BP-SES = biodegradable polymer sirolimus-eluting stent; DP-SES = durable polymer sirolimus-eluting stent.



Supplementary figure 2. Subgroup Analysis of NACCE at 5 years.



NACCE was defined as a composite of all-cause death, all myocardial infarction, stroke, and major bleeding (Bleeding Academic Research Consortium type ≥3 bleeding). NACCE = net adverse clinical and cerebral events; CI = confidence interval; DAPT = dual antiplatelet therapy; PCI = percutaneous coronary intervention; AMI = acute myocardial infarction.