Received: 27 September 2022 | Revised: 22 January 2023 | Accepted: 8 February 2023

DOI: 10.1002/ccd.30600

ORIGINAL ARTICLE - CLINICAL SCIENCE

WILEY

Complex primary percutaneous coronary intervention with ultrathin-strut biodegradable versus thin-strut durable polymer drug-eluting stents in patients with ST-segment elevation myocardial infarction: A subgroup analysis from the BIOSTEMI randomized trial

Juan F. Iglesias MD[1] | Olivier Muller MD, PhD[2] | Sylvain Losdat PhD[3] | Marco Roffi MD[1] | David J. Kurz MD[4] | Daniel Weilenmann MD[5] | Christoph Kaiser MD[6] | Dik Heg PhD[3] | Stephan Windecker MD[7] | Thomas Pilgrim MD, MSc[7]

[1]Department of Cardiology, Geneva University Hospitals, Geneva, Switzerland

[2]Department of Cardiology, Lausanne University Hospital, Lausanne, Switzerland

[3]CTU Bern, University of Bern, Bern, Switzerland

[4]Department of Cardiology, Triemlispital, Zurich, Switzerland

[5]Department of Cardiology, Kantonsspital, St. Gallen, Switzerland

[6]Department of Cardiology, Basel University Hospital, Basel, Switzerland

[7]Department of Cardiology, Bern University Hospital, Bern, Switzerland

Correspondence
Juan F. Iglesias, MD, FESC, FACC, Department of Cardiology, Geneva University Hospitals, Rue Gabrielle-Perret-Gentil 4, 1205 Geneva, Switzerland.
Email: Juanfernando.Iglesias@hcuge.ch

Funding information
Biotronik

Abstract

Background: Ultrathin-strut biodegradable polymer sirolimus-eluting stents (BP-SES) are superior to thin-strut durable polymer everolimus-eluting stents (DP-EES) with respect to target lesion failure (TLF) at 2 years among patients with ST-segment elevation myocardial infarction (STEMI). We sought to determine the impact of primary percutaneous coronary intervention (pPCI) complexity on long-term clinical outcomes with BP-SES versus DP-EES in STEMI patients.

Methods: We performed a post hoc subgroup analysis from the BIOSTEMI (NCT02579031) randomized trial, which included individual data from 407 STEMI patients enrolled in the BIOSCIENCE trial (NCT01443104). STEMI patients were randomly assigned to treatment with ultrathin-strut BP-SES or thin-strut DP-EES, and further categorized into those undergoing complex versus noncomplex pPCI. Complex pPCI was defined by the presence of ≥1 of the following criteria: 3 vessel treatment, ≥3 stents implanted, ≥3 lesions treated, bifurcation lesion with ≥2 stents implanted, total stent length ≥60 mm, and/or chronic total occlusion treatment. The primary endpoint was TLF, a composite of cardiac death, target-vessel myocardial reinfarction, or clinically indicated target lesion revascularization, within 2 years.

Results: Among a total of 1707 STEMI patients, 421 (24.7%) underwent complex pPCI. Baseline characteristics were similar between groups. At 2 years, TLF occurred in 14 patients (7.1%) treated with BP-SES and 25 patients (11.6%) treated with

Abbreviations: BP-SES, biodegradable polymer sirolimus-eluting stent; CAD, coronary artery disease; DES, drug-eluting stent; DP-EES, durable polymer everolimus-eluting stent; PCI, percutaneous coronary intervention; POCE, patient-oriented composite endpoint; STEMI, ST-segment elevation myocardial infarction; TLF, target lesion failure; TLR, target lesion revascularization; TVF, target vessel failure; TVR, target vessel revascularization.

DP-EES (hazard ratio [HR]: 0.62; 95% confidence interval [CI]: 0.32–1.19; $p = 0.15$) in the complex pPCI group, and in 28 patients (4.4%) treated with BP-SES and 49 patients (8.2%) treated with DP-EES (HR: 0.54; 95% CI: 0.34–0.86; $p = 0.008$; p for interaction = 0.74) in the noncomplex pPCI group. Individual TLF components and stent thrombosis rates did not significantly differ between groups.

Conclusion: In a post hoc subgroup analysis from the BIOSTEMI randomized trial, ultrathin-strut BP-SES were superior to thin-strut DP-EES with respect to TLF at 2 years among STEMI patients undergoing both complex and noncomplex pPCI.

KEYWORDS

biodegradable polymer, complex percutaneous coronary intervention, drug-eluting stent, ST-segment elevation myocardial infarction, ultrathin-strut

1 | INTRODUCTION

The advent of newer-generation drug-eluting stent (DES) designs that combine highly deliverable thin-strut stent platforms, biodegradable, or biocompatible permanent polymers and reduced sirolimus analogues concentrations with controlled drug release has rapidly shifted the boundaries of percutaneous coronary intervention (PCI) toward the treatment of more extensive and increasingly complex coronary lesions.[1,2] Patients undergoing complex PCI in the newer-generation DES era remain however at increased long-term risk for myocardial infarction, stent thrombosis, and repeat revascularization compared with those treated for noncomplex coronary lesions, irrespective of baseline clinical presentation.[3] Direct comparisons between contemporary DESs among patients undergoing complex PCI are limited and systematically failed to demonstrate differences in clinical outcomes between newer-generation DESs designs with different stent strut thickness and polymer coatings.[4–6] In addition, there is paucity of data concerning the impact of procedural complexity on the long-term clinical performance of newest-generation DESs among highest-risk patients with acute coronary syndrome undergoing PCI.

Patients with ST-segment elevation myocardial infarction (STEMI) are at increased risk for stent-related adverse outcomes after primary PCI[7] owing to an enhanced prothrombotic and inflammatory environment that may interfere with vascular healing.[8] Ultrathin-strut biodegradable polymer sirolimus-eluting stents (BP-SES) were recently found superior to thin-strut durable polymer everolimus-eluting stents (DP-EES) with respect to target lesion failure (TLF) at up to 2 years of follow-up among patients with STEMI undergoing primary PCI,[9,10] a difference mainly driven by a lower risk of ischemia-driven target lesion revascularization (TLR). However, the long-term impact of procedural complexity on patient- and stent-related adverse events following primary PCI with ultrathin-strut BP-SES versus thin-strut DP-EES in patients with STEMI remains uncertain. We, therefore, sought to investigate the effects of primary PCI complexity on long-term clinical outcomes after ultrathin-strut BP-SES versus thin-strut DP-EES implantation in patients with STEMI.

2 | METHODS

2.1 | Study design and study population

BIOSTEMI was an investigator-initiated, prospective, multicentre, single-blind, open-label, randomized superiority trial that compared ultrathin-strut BP-SES versus thin-strut DP-EES among patients undergoing primary PCI for STEMI. The study rationale and design have been previously described.[11] To summarize, STEMI patients undergoing primary PCI within 24 h after symptom onset, and with at least one infarct-related coronary lesion in one or more native target coronary arteries suitable for DES implantation, were randomly allocated in a 1:1 ratio to treatment with ultrathin-strut BP-SES or thin-strut DP-EES. For the present analysis, we further categorized STEMI patients treated with ultrathin-strut BP-SES or thin-strut DP-EES into those undergoing complex versus noncomplex primary PCI during the index procedure. The study protocol complied with the Declaration of Helsinki and was approved by the institutional ethics committees at participating centers. All patients provided written informed consent for participation. The trial was registered with ClinicalTrials.gov number, NCT02579031. The primary outcome results of the BIOSTEMI trial at 1 and 2 years of follow-up were previously reported.[9,10]

2.2 | Study procedures

The investigational BP-SES (Orsiro; Biotronik AG) combines an ultrathin- (60 μm for stent diameters ≤3.0 mm) or thin-strut (80 μm for stent diameters >3.0 mm) cobalt-chromium metallic stent platform covered by an amorphous silicon-carbide layer, and an asymmetric biodegradable poly-L-lactic acid polymer coating that releases sirolimus at a dose of 1.4 μg/mm^2 stent surface over a period of 12–14 weeks and degrades within 24 months.[12] The comparator DP-EES (Xience Xpedition/Alpine; Abbott Vascular) consists of a thin-strut (81 μm) cobalt-chromium stent platform covered by a

permanent poly-n-butyl-methacrylate, and vinylidene fluoride and hexafluoropropylene co-polymer releasing everolimus.

Web-based randomization was performed using a computer-generated allocation sequence in random blocks of 2, 4, and 6, which was stratified according to center, presence or absence of diabetes, and multivessel coronary artery disease. Primary PCI was performed at the operator's discretion according to current recommendations and techniques at the time of enrollment. Dual antiplatelet therapy (DAPT), consisting in acetylsalicylic acid (loading and maintenance doses, 250–500 and 100 mg daily, respectively) combined with prasugrel (loading and maintenance doses, 60 and 10 mg daily, respectively) or ticagrelor (loading and maintenance doses, 180 and 90 mg twice daily, respectively), alternatively with clopidogrel (loading and maintenance doses, 600 and 75 mg daily, respectively), was initiated before, or at the time of, primary PCI and prescribed for a recommended duration of 12 months.

2.3 | Study definitions

Patients with STEMI who were randomly allocated to treatment with ultrathin-strut BP-SES or thin-strut DP-EES were further categorized into complex and noncomplex primary PCI subgroups according to the index procedure complexity. There is currently no universal definition of complex PCI.[2] For the present analysis, we defined complex primary PCI based on a previous study[13] by the presence of at least one of the following criteria during the index procedure: 3 vessel treatment, ≥3 stents implanted, ≥3 lesions treated, bifurcation lesion with ≥2 stents implanted, total stent length ≥60 mm, and/or chronic total occlusion (CTO) treatment.

2.4 | Study endpoints

The primary endpoint of the present analysis was TLF, defined as the composite of cardiac death, target vessel myocardial reinfarction, or clinically indicated TLR, within 2 years of the index procedure. Primary and secondary endpoint definitions, data collection and monitoring have been previously described.[11] The patient-oriented composite endpoint (POCE) was defined as the composite of all-cause death, any myocardial reinfarction, or any revascularization. Target vessel failure (TVF) was defined as the composite of cardiac death, any myocardial reinfarction, or any target vessel revascularization (TVR). All study endpoints were adjudicated using standard definitions by an independent clinical events committee blinded to treatment assignment.

2.5 | Statistical analysis

We performed a post hoc, nonprespecified, subgroup analysis from the BIOSTEMI trial comparing clinical outcomes according to randomized stent type (BP-SES vs. DP-EES) and primary PCI complexity (complex vs. noncomplex primary PCI) based on a previous study definition.[13] For the present analysis, we included individual patient data from STEMI patients enrolled into the BIOSCIENCE trial[14] (NCT02579031), as with the primary endpoint analysis of the BIOSTEMI trial.[9] All analyses were performed according to the intention-to-treat principle. The results are presented as count (%) for categorical variables and as mean ± standard deviation for continuous variables. p Values were obtained from χ^2 tests, Fisher's exact tests, generalized linear models, or mixed-effect models (for lesion-level analysis), as appropriate. Mantel-Cox heterogeneity tests were used to calculate hazard ratios (HR) and their associated 95% confidence intervals (CI), p values for main effects, and interaction between stent type (BP-EES vs. DP-SES) and patient subgroup (complex vs. noncomplex primary PCI). We used time to first event for each endpoint and reported numbers of patients and Kaplan–Meier estimates of cumulative incidence. A $p \leq 0.05$ was considered statistically significant. Analyses were performed with STATA 15 (Stata Statistical Software: Release 15; StataCorp. 2017).

3 | RESULTS

A total of 1707 STEMI patients (1300 and 407 patients from BIOSTEMI and BIOSCIENCE trials, respectively) were included, of which 421 (24.7%) underwent complex primary PCI (200 patients treated with ultrathin-strut BP-SES, 221 patients treated with thin-strut DP-EES) (Figure 1). Follow-up information at 2 years was available for 405 out of 421 (96.2%) patients in the complex primary PCI group, and 1204 out of 1279 (94.1%) patients in the noncomplex primary PCI group (Figure 1). Baseline clinical, angiographic, and procedural characteristics did not differ between groups (Tables 1 and 2). The most frequent complex primary PCI features were ≥3 stents implanted (72.2%), long lesion treatment with a total stent length ≥60 mm (42.8%), bifurcation lesion treatment with ≥2 stents implanted (31.1%), and ≥3 lesions treated (20%) (Table 3, Figure 2). Among complex primary PCI patients, complex PCI criteria did not significantly differ among those treated with ultrathin-strut BP-SES or DP-EES, except for total stent length ≥60 mm which was significantly more prevalent in the DP-EES group (49.8% vs. 35%; $p = 0.002$) (Table 3). At 2 years of follow-up, 371 (12%) patients were on DAPT (Supporting Information: Table 1). The adherence rates to DAPT at 2 years were similar among patients treated with BP-SES and DP-EES in the complex (10.2% vs. 8.8%; $p = 0.73$) and noncomplex (6.6% vs. 8.8%; $p = 0.18$) primary PCI groups, respectively (Supporting Information: Table 1).

At 2 years of follow-up, the rates of TLF were significantly higher among STEMI patients undergoing complex, as compared with those who underwent noncomplex, primary PCI (9.5% vs. 6.3%; HR: 1.54; 95% CI: 1.05–2.27; $p = 0.03$). The difference was driven by a significantly higher risk for clinically indicated TLR (5.8% vs. 3.4%; HR: 1.75; 95% CI: 1.05–2.93; $p = 0.03$) in the complex primary PCI group (Table 4). STEMI patients undergoing complex primary PCI had a significantly increased risk for repeat revascularization (10.3% vs. 7.0%; HR: 1.50; 95% CI: 1.03–2.17; $p = 0.03$), and definite/probable

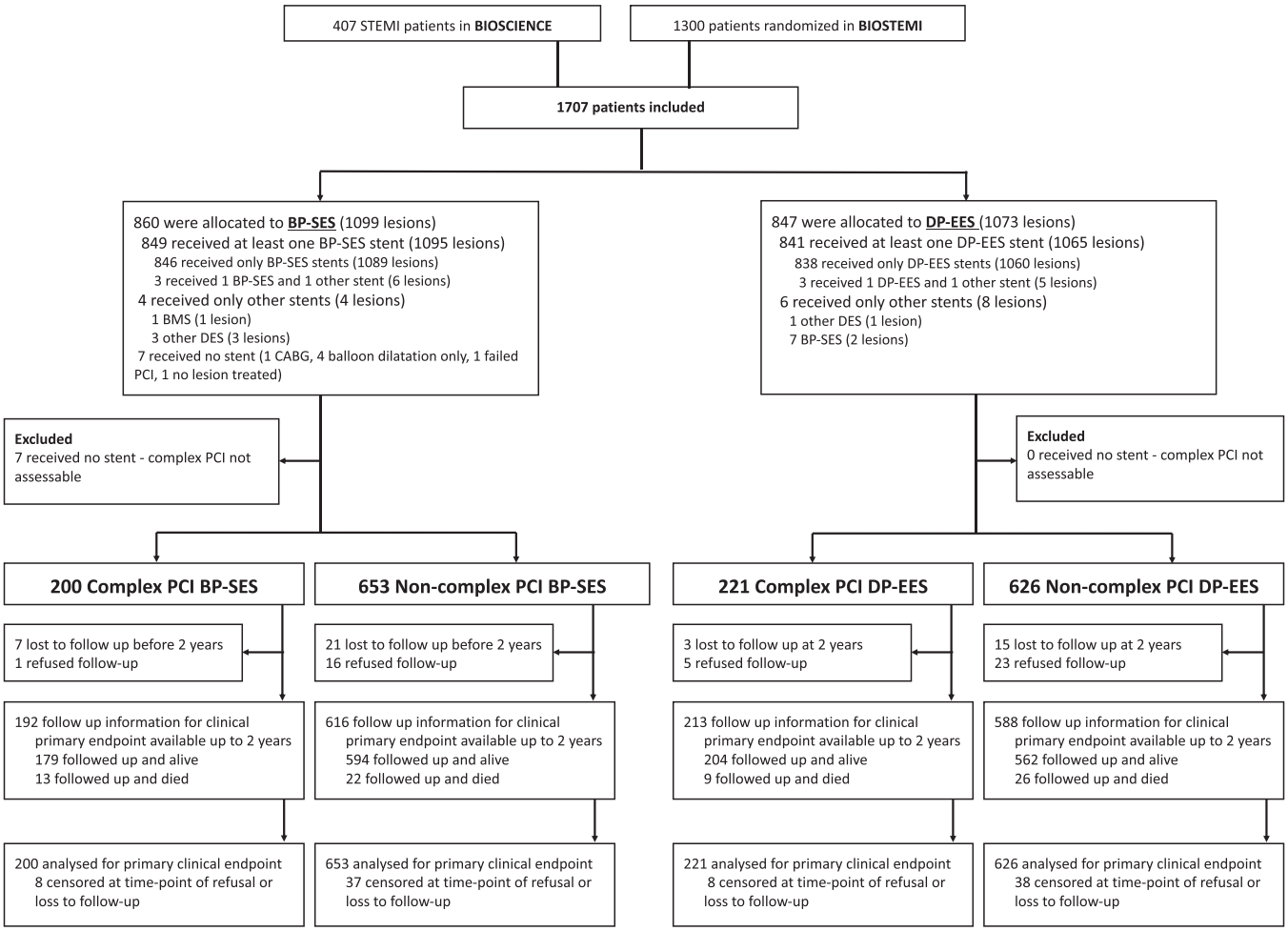

FIGURE 1 Patient flowchart according to the CONSORT statement. BMS, bare metal stent; BP-SES, biodegradable polymer sirolimus-eluting stent; CABG, coronary artery bypass grafting; DES, drug-eluting stent; DP-EES, durable polymer everolimus-eluting stent; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

stent thrombosis (3.9% vs. 2.0%; HR: 1.95; 95% CI: 1.04–3.65; $p = 0.03$) at 2 years of follow-up compared with those undergoing noncomplex primary PCI (Table 4). The increased risk for repeat revascularization resulted in higher rates of POCE at 2 years among STEMI patients undergoing complex, as compared to noncomplex, primary PCI (15.7% vs. 11.0%; HR: 1.48; 95% CI: 1.10–1.99; $p = 0.009$) (Table 4). In addition, the rates of TVF at 2 years were significantly higher among STEMI patients undergoing complex versus noncomplex primary PCI (11.7% vs. 7.3%; HR: 1.63; 95% CI: 1.15–2.32; $p = 0.006$), a difference driven by a significantly lower risk for TVR (8.3% vs. 4.4%; HR: 1.91; 95% CI: 1.23–2.95; $p = 0.003$) (Table 4).

At 2 years, the rates of TLF were numerically lower among STEMI patients treated with ultrathin-strut BP-SES compared with thin-strut DP-EES in the complex primary PCI group (7.1% vs. 11.6%; HR: 0.62; 95% CI: 0.32–1.19; $p = 0.15$) (Table 5, Figure 3). There were no significant differences in the rates of individual TLF components at 2 years between treatment groups, but the risk for target vessel myocardial reinfarction (1.0% vs. 4.3%; HR: 0.24; 95% CI: 0.05–1.13; $p = 0.051$) was numerically lower among complex primary PCI patients treated with ultrathin-strut BP-SES compared with thin-strut DP-EES (Table 5, Figure 3). STEMI patients undergoing complex primary PCI with ultrathin-strut BP-SES had a significantly lower risk for repeat revascularization (5.9% vs. 14.3%; HR: 0.39; 95% CI: 0.20–0.79; $p = 0.006$), and clinically indicated TVR (4.8% vs. 11.0%; HR: 0.43; 95% CI: 0.20–0.92; $p = 0.03$) at 2 years compared with those treated with thin-strut DP-EES (Table 5). Similarly, the rates of TVF were significantly lower among complex primary PCI patients treated with ultrathin-strut BP-SES compared with thin-strut DP-EES (8.2% vs. 14.8%; HR: 0.54; 95% CI: 0.30–0.99; $p = 0.043$), a difference driven by a significantly lower risk for TVR (4.8% vs. 11.5%; HR: 0.41; 95% CI: 0.19–0.88; $p = 0.02$) (Table 5). In addition, compared with those treated with thin-strut DP-EES, STEMI patients undergoing complex primary PCI with ultrathin-strut BP-SES had numerically lower rates of myocardial reinfarction (2.7% vs. 6.2%; HR: 0.42; 95% CI: 0.15–1.19; $p = 0.09$), TLR (3.7% vs. 8.2%; HR: 0.45; 95% CI: 0.19–1.10; $p = 0.07$), and definite/probable stent thrombosis (2.0% vs. 5.5%; HR: 0.37; 95% CI: 0.12–1.14; $p = 0.07$) (Table 5). However, 2-year rates of POCE did not significantly differ between

TABLE 1 Baseline clinical characteristics.

Patients—*n*	Complex primary PCI		Noncomplex primary PCI	
	BP-SES *n* = 200	DP-EES *n* = 221	BP-SES *n* = 653	DP-EES *n* = 626
Age—years (SD)	63.4 ± 11.7	64.4 ± 12.0	61.5 ± 12.0	62.3 ± 12.0
Male gender—*n* (%)	161 (80.5%)	164 (74.2%)	515 (78.9%)	464 (74.1%)
Body mass index—kg/m^2	27.1 ± 4.7	27.3 ± 4.1	26.9 ± 4.2	26.7 ± 4.3
Diabetes mellitus, *n* (%)	31 (15.6%)	26 (11.8%)	71 (10.9%)	83 (13.3%)
Orally treated	21 (10.6%)	17 (7.7%)	46 (7.0%)	60 (9.6%)
Insulin-treated	11 (5.5%)	7 (3.2%)	19 (2.9%)	18 (2.9%)
Hypertension—*n* (%)	97 (49.0%)	114 (51.8%)	281 (43.2%)	281 (45.0%)
Hypercholesterolemia—*n* (%)	109 (55.3%)	111 (50.5%)	304 (46.8%)	292 (47.1%)
Current smoker—*n* (%)	86 (44.1%)	81 (37.9%)	299 (46.6%)	246 (39.9%)
Family history of CAD—*n* (%)	38 (19.1%)	44 (19.9%)	126 (19.4%)	162 (25.9%)
Previous MI—*n* (%)	5 (2.5%)	8 (3.6%)	30 (4.6%)	25 (4.0%)
Previous PCI—*n* (%)	7 (3.5%)	9 (4.1%)	32 (4.9%)	33 (5.3%)
Previous CABG—*n* (%)	3 (1.5%)	1 (0.5%)	4 (0.6%)	8 (1.3%)
Atrial fibrillation—*n* (%)	8 (4.0%)	6 (2.7%)	10 (1.5%)	17 (2.7%)
Previous stroke or TIA—*n* (%)	4 (2.0%)	4 (1.8%)	14 (2.1%)	18 (2.9%)
Peripheral vascular disease—*n* (%)	7 (3.5%)	6 (2.7%)	12 (1.8%)	13 (2.1%)
Renal failure (eGFR < 60 mL/min)—*n* (%)	26 (13.5%)	32 (15.2%)	64 (10.2%)[a]	63 (10.5%)[b]
Left ventricular ejection fraction—%	47.6 ± 11.3[c]	46.9 ± 11.0[d]	49.6 ± 10.8[e]	49.0 ± 11.2[f]
Multivessel disease—*n* (%)	93 (63.3%)[g]	101 (63.1%)[h]	225 (45.4%)[i]	213 (43.4%)[j]
Medication at baseline—*n* (%)				
Aspirin	21 (11.5%)[d]	28 (13.7%)[k]	95 (15.1%)[l]	86 (14.4%)[m]
Clopidogrel	0 (0.0%)[d]	1 (0.5%)[k]	7 (1.1%)[l]	8 (1.3%)[m]
Prasugrel	0 (0.0%)[d]	1 (0.5%)[k]	2 (0.3%)[l]	4 (0.7%)[m]
Ticagrelor	1 (0.5%)[d]	2 (1.0%)[k]	9 (1.4%)[l]	3 (0.5%)[m]
Any dual antiplatelet therapy	1 (0.5%)[d]	3 (1.5%)[k]	14 (2.2%)[l]	10 (1.7%)[m]
Vitamin K oral anticoagulant	4 (2.2%)[d]	5 (2.4%)[k]	5 (0.8%)[l]	7 (1.2%)[m]
Nonvitamin K oral anticoagulant	4 (2.2%)[d]	2 (1.0%)[k]	6 (1.0%)[l]	5 (0.8%)[m]
Any anticoagulant therapy	8 (4.3%)[d]	7 (3.4%)[k]	11 (1.8%)[l]	12 (2.0%)[m]
Statins	29 (15.9%)[d]	25 (12.3%)[k]	89 (14.2%)[l]	97 (16.2%)[m]
ACE inhibitors	14 (7.8%)[d]	20 (9.9%)[k]	63 (10.1%)[l]	65 (10.9%)[m]
ARB	24 (13.3%)[d]	36 (17.7%)[k]	86 (13.7%)[l]	92 (15.4%)[m]
β-Blockers	28 (15.6%)[d]	27 (13.3%)[k]	88 (14.1%)[l]	89 (14.9%)[m]

Note: Data are expressed as sample sizes (*n*) with means (±standard deviations) or counts (%).

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; BP-SES, biodegradable polymer sirolimus-eluting stent; CABG, coronary artery bypass grafting; CAD, coronary artery disease; DP-EES, durable polymer everolimus-eluting stent; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

[a] *n* = 631.
[b] *n* = 599.
[c] *n* = 155.
[d] *n* = 180.
[e] *n* = 403.
[f] *n* = 381.
[g] *n* = 147.
[h] *n* = 160.
[i] *n* = 496.
[j] *n* = 491.
[k] *n* = 203.
[l] *n* = 626.
[m] *n* = 596.

TABLE 2 Baseline angiographic and procedural characteristics.

		Complex primary PCI			Noncomplex primary PCI			
Patients—*n* Lesions—*n*	**All stents *n* = 1699 *N* = 2173**	**BP-SES *n* = 200 *N* = 358**	**DP-EES *n* = 221 *N* = 374**	***p* Value**	**BP-SES *n* = 653 *N* = 742**	**DP-EES *n* = 626 *N* = 699**	***p* Value**	***p* Value for interaction**
Target vessel location—per lesion *n* (%)				0.12			<0.001	0.038
Left main coronary artery	29 (1.3%)	10 (2.8%)	9 (2.4%)		6 (0.8%)	4 (0.6%)		
Left anterior descending artery	892 (41.0%)	125 (34.9%)	167 (44.7%)		295 (39.8%)	305 (43.6%)		
Left circumflex artery	385 (17.7%)	70 (19.6%)	49 (13.1%)		123 (16.6%)	143 (20.5%)		
Right coronary artery	862 (39.7%)	151 (42.2%)	148 (39.6%)		316 (42.6%)	247 (35.3%)		
Saphenous vein graft	5 (0.2%)	2 (0.6%)	1 (0.3%)		2 (0.3%)	0 (0.0%)		
Number of lesions per patient	1.28 ± 0.58	1.79 ± 0.96	1.69 ± 0.78	0.26	1.13 ± 0.34	1.12 ± 0.32	0.32	0.37
Number of lesions per patient—*n* (%)				0.45			0.76	0.66
1	1327 (78.1%)	100 (50.0%)	110 (49.8%)		564 (86.5%)	553 (88.3%)		
2	288 (17.0%)	56 (28.0%)	71 (32.1%)		88 (13.5%)	73 (11.7%)		
3	71 (4.2%)	33 (16.5%)	38 (17.2%)		0 (0.0%)	0 (0.0%)		
≥4	13 (0.8%)	11 (5.5%)	2 (0.9%)		0 (0.0%)	0 (0.0%)		
Primary PCI				0.20			0.72	0.22
Stent implantation only	2126 (97.8%)	344 (96.1%)	366 (97.9%)		730 (98.4%)	686 (98.1%)		
POBA only	46 (2.1%)	13 (3.6%)	8 (2.1%)		12 (1.6%)	13 (1.9%)		
Failed PCI	1 (0.0%)	1 (0.3%)	0 (0.0%)		–	–		
Baseline TIMI flow				0.07			<0.001	<0.001
0 or 1	1216 (56.3%)	157 (44.2%)	178 (47.8%)		450 (61.1%)	431 (62.0%)		
2	307 (14.2%)	49 (13.8%)	69 (18.5%)		96 (13.0%)	93 (13.4%)		
3	635 (29.4%)	149 (42.0%)	125 (33.6%)		191 (25.9%)	170 (24.5%)		
Post TIMI flow				0.88			0.48	0.65
0 or 1	12 (0.6%	3 (0.8%)	2 (0.5%)		3 (0.4%	4 (0.6%)		
2	54 (2.5%)	9 (2.5%)	9 (2.4%)		15 (2.0%)	21 (3.0%)		
3	2104 (97.0%)	344 (96.6%)	363 (97.1%)		723 (97.6%)	674 (96.4%)		
Restenotic lesion	36 (1.7%)	6 (1.7%)	8 (2.1%)	0.65	10 (1.3%)	12 (1.7%)	0.59	1.00
Chronic total occlusion	13 (0.6%)	6 (1.7%)	7 (1.9%)	0.85	–	–	–	–

TABLE 2 (Continued)

Patients—*n* Lesions—*n*	All stents *n* = 1699 *N* = 2173	Complex primary PCI BP-SES *n* = 200 *N* = 358	 DP-EES *n* = 221 *N* = 374	*p* Value	Noncomplex primary PCI BP-SES *n* = 653 *N* = 742	 DP-EES *n* = 626 *N* = 699	*p* Value	*p* Value for interaction
Thrombus aspiration	697 (32.1%)	75 (20.9%)	84 (22.5%)	0.64	280 (37.8%)	258 (37.1%)	0.78	0.58
Type of stent per lesion—*n* (%)				0.92			0.52	0.68
Study BP-SES	1075 (50.6%)	343 (99.7%)	2 (0.5%)		725 (99.3%)	5 (0.7%)		
Study DP-EES	1044 (49.1%)	1 (0.3%)	364 (99.5%)		0 (0.0%)	679 (99.0%)		
Any nonstudy DES	8 (0.4%)	1 (0.3%)	1 (0.3%)		4 (0.5%)	2 (0.3%)		
Any bare-metal stent	2 (0.1%)	0 (0.0%)	0 (0.0%)		1 (0.1%)	1 (0.1%)		
Total number of stents implanted	1.38 ± 0.66	1.81 ± 0.88	1.84 ± 0.87	0.76	1.18 ± 0.38	1.15 ± 0.35	0.09	0.35
Total stent length (mm)	32.17 ± 18.90	41.19 ± 25.41	44.66 ± 26.24	0.10	26.60 ± 10.58	26.90 ± 10.67	0.60	0.15
Overlapping stents	599 (28.2%)	175 (50.9%)	196 (53.6%)	0.51	126 (17.3%)	102 (14.9%)	0.23	0.20
Long lesion (total stent length ≥ 60 mm)	180 (10.6%)	70 (35.0%)	110 (49.8%)	0.002	–	–	–	–
Bifurcation treatment with ≥2 stents	131 (7.7%)	62 (31.0%)	69 (31.2%)	0.96	–	–	–	–
Maximum stent diameter (mm)	3.15 ± 0.51	3.15 ± 0.55	3.08 ± 0.54	0.13	3.18 ± 0.50	3.17 ± 0.48	0.52	0.32
Maximum pressure (atm)	13.65 ± 3.25	13.98 ± 3.58	14.04 ± 3.52	0.82	13.39 ± 3.11	13.54 ± 3.04	0.36	0.80
Predilatation	566 (26.6%)	91 (26.5%)	90 (24.6%)	0.60	205 (28.1%)	180 (26.2%)	0.44	0.98
Postdilatation	1308 (61.6%)	240 (69.8%)	265 (72.4%)	0.51	413 (56.6%)	390 (56.9%)	0.90	0.61
Cardiogenic shock	40 (2.4%)	10 (5.0%)	7 (3.2%)	0.34	11 (1.7%)	12 (1.9%)	0.76	0.36

Note: Data are expressed as sample sizes (*n*) with means (±standard deviations) or counts (%). *p* Values are from Fisher's tests (2 × 2 comparisons) or χ^2 tests (otherwise) for counts. In the case of lesion-level data, *p* values are from mixed models accounting for lesions nested within patients. *p* Value for type of stent per lesion testing any randomized stent(s) implanted versus only other stent(s) implanted.

Abbreviations: BP-SES, biodegradable polymer sirolimus-eluting stent; DES, drug-eluting stent; DP-EES, durable polymer everolimus-eluting stent; PCI, percutaneous coronary intervention; POBA, plain old balloon angioplasty; TIMI, thrombolysis In myocardial infarction.

Complex primary PCI criteria	All patients $n = 421$	BP-SES $n = 200$	DP-EES $n = 221$	p Value
3 vessel treatment	10 (2.4%)	7 (3.5%)	3 (1.4%)	0.20
≥3 stents implanted	304 (72.2%)	149 (74.5%)	155 (70.1%)	0.33
≥3 lesions treated	84 (20.0%)	44 (22.0%)	40 (18.1%)	0.33
Bifurcation treatment with ≥2 stents	131 (31.1%)	62 (31.0%)	69 (31.2%)	1.00
Total stent length ≥ 60 mm	180 (42.8%)	70 (35.0%)	110 (49.8%)	0.002
Chronic total occlusion	12 (2.9%)	6 (3.0%)	6 (2.7%)	1.00

Abbreviations: BP-SES, biodegradable polymer sirolimus-eluting stents; DP-EES, durable polymer everolimus-eluting stents; PCI, percutaneous coronary intervention.

TABLE 3 Individual complex primary percutaneous coronary intervention criteria.

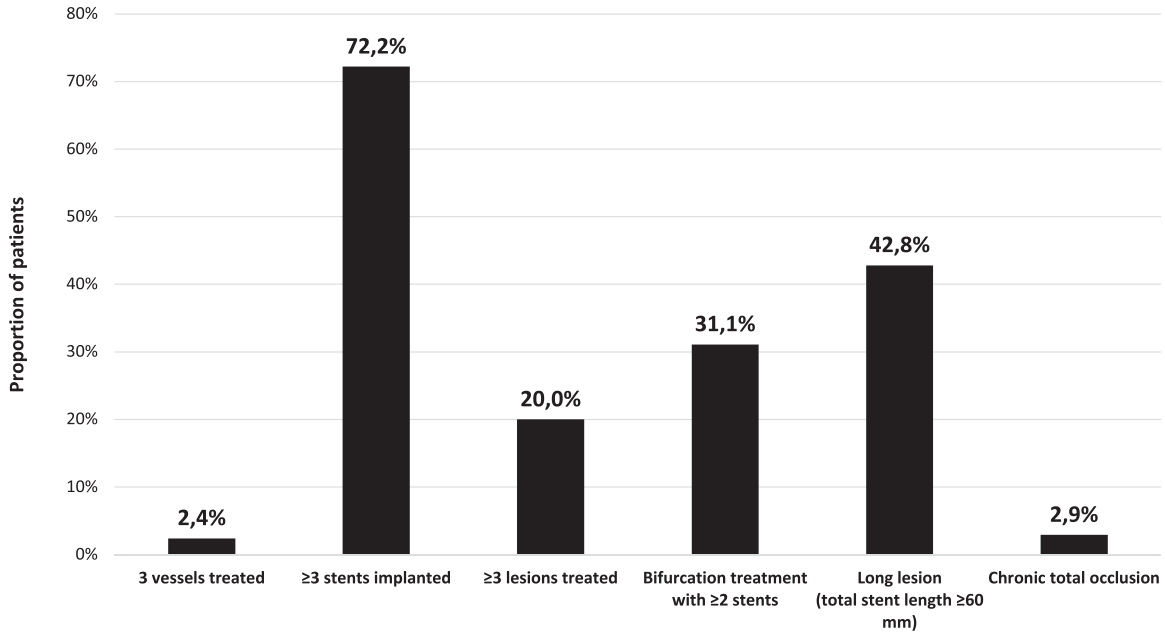

FIGURE 2 Primary percutaneous coronary intervention complexity characteristics in the overall patient population.

STEMI patients undergoing complex primary PCI with BP-SES or DP-EES (12.7% vs. 18.3%; HR: 0.67; 95% CI: 0.41–1.11; $p = 0.12$) (Table 5).

Among STEMI patients undergoing noncomplex primary PCI, 2-year TLF rates were significantly lower with ultrathin-strut BP-SES as compared with thin-strut DP-EES (4.4% vs. 8.2%; HR: 0.54; 95% CI: 0.34–0.86; $p = 0.008$), a difference driven by a lower risk of ischemia driven TLR (2.4% vs. 4.3%; HR: 0.57; 95% CI: 0.30–1.07; $p = 0.08$) (Table 5, Figure 3). Overall, there was however no significant interaction between treatment effect and primary PCI complexity (p for interaction = 0.74) with respect to the primary endpoint of TLF at 2 years (Table 5). In patients with STEMI undergoing noncomplex primary PCI, the risk of TVF at 2 years was significantly lower among those treated with ultrathin-strut BP-SES compared with thin-strut DP-EES (5.7% vs. 9.0%; HR: 0.63; 95% CI: 0.41–0.96; $p = 0.03$) (Table 5).

In a sensitivity analysis comparing clinical outcomes among patients undergoing complex versus noncomplex primary PCI and stratified according to each individual complex primary PCI criteria, there was no significant treatment interaction between ultrathin-strut BP-SES and thin-strut DP-EES with respect to TLF at 2 years for any individual complex PCI features (Supporting Information: Figure 1).

4 | DISCUSSION

The salient findings of the present post hoc subgroup analysis from the BIOSTEMI randomized trial can be summarized as follows[1]: a significant proportion (25%) of all-comer patients with STEMI require complex primary PCI owing to complex anatomical and procedural features, such as multivessel PCI, ≥3 stents implanted, ≥3 lesions treated, bifurcation lesion with ≥2 stents implanted, and/or total stent length ≥60 mm[2]; despite recent innovations in DES designs, STEMI patients undergoing complex primary PCI with newest-generation DESs remain at increased risk for stent- and patient-related adverse outcomes as compared with those who underwent noncomplex primary PCI; and[3] the superiority of ultrathin-strut BP-

TABLE 4 Clinical outcomes at 2 years in patients undergoing complex versus noncomplex primary percutaneous coronary intervention.

Patients—*n*	Complex primary PCI *n* = 421	Noncomplex primary PCI *n* = 1279	HR (95% CI)	*p* Value
Target lesion failure[a]	39 (9.5)	77 (6.3)	1.54 (1.05–2.27)	0.03
All-cause death	22 (5.3)	48 (3.9)	1.39 (0.84–2.30)	0.20
Cardiac death	16 (3.8)	36 (2.9)	1.35 (0.75–2.43)	0.32
Myocardial reinfarction	18 (4.5)	40 (3.3)	1.37 (0.78–2.39)	0.27
Q-wave myocardial reinfarction	4 (1.0)	10 (0.8)	1.21 (0.38–3.87)	0.74
Non Q-wave myocardial reinfarction	15 (3.8)	30 (2.5)	1.51 (0.81–2.81)	0.19
Target vessel myocardial reinfarction	11 (2.7)	20 (1.7)	1.67 (0.80–3.49)	0.17
Target vessel Q-wave myocardial reinfarction	3 (0.7)	9 (0.7)	1.01 (0.27–3.73)	0.99
Target vessel non Q-wave myocardial reinfarction	9 (2.3)	11 (0.9)	2.48 (1.03–5.99)	0.04
Cardiac death or any myocardial reinfarction	33 (8.0)	74 (6.0)	1.36 (0.90–2.04)	0.15
Revascularization (any)	41 (10.3)	84 (7.0)	1.50 (1.03–2.17)	0.03
Target lesion revascularization (any)	24 (6.1)	43 (3.6)	1.70 (1.03–2.80)	0.04
Clinically indicated target lesion revascularization	23 (5.8)	40 (3.4)	1.75 (1.05–2.93)	0.03
PCI	20 (5.1)	39 (3.3)	1.56 (0.91–2.67)	0.11
CABG	3 (0.8)	2 (0.2)	4.54 (0.76–27.17)	0.07
Target vessel revascularization (any)	33 (8.3)	53 (4.4)	1.91 (1.23–2.95)	0.003
Clinically indicated target vessel revascularization	32 (8.1)	50 (4.2)	1.96 (1.26–3.06)	0.002
PCI	29 (7.3)	49 (4.1)	1.81 (1.14–2.86)	0.01
CABG	3 (0.8)	2 (0.2)	4.54 (0.76–27.17)	0.07
Target vessel failure[b]	48 (11.7)	90 (7.3)	1.63 (1.15–2.32)	0.006
POCE[c]	65 (15.7)	135 (11.0)	1.48 (1.10–1.99)	0.009
Cerebrovascular event (any)	7 (1.7)	18 (1.5)	1.18 (0.49–2.83)	0.71
Stroke (any)	4 (1.0)	14 (1.2)	0.87 (0.28–2.63)	0.80
TIA	3 (0.7)	4 (0.3)	2.27 (0.51–10.17)	0.27
Definite stent thrombosis	8 (2.0)	16 (1.3)	1.52 (0.65–3.55)	0.33
Definite or probable stent thrombosis	16 (3.9)	25 (2.0)	1.95 (1.04–3.65)	0.03

Note: Data expressed as number of first events (% cumulative incidence from Kaplan–Meier estimate). Hazard ratios (95% confidence intervals) and log-rank *p* values are derived from Mantel-Cox regressions.

Abbreviations: BP-SES, biodegradable polymer sirolimus-eluting stent; CABG, coronary artery bypass grafting; CI, confidence interval; DP-EES, durable polymer everolimus-eluting stent; HR, hazard ratio; PCI, percutaneous coronary intervention; POCE, patient-oriented composite endpoint; TIA, transient ischemic attack.

[a]Composite of cardiac death, target vessel myocardial reinfarction (Q-wave and non-Q-wave), and clinically indicated target lesion revascularization (primary endpoint).

[b]Composite of cardiac death, any myocardial reinfarction, or any target vessel revascularization.

[c]Composite of all cause death, any myocardial reinfarction, or any revascularization.

SES over thin-strut DP-EES with regard to stent-related adverse outcomes at 2 years among patients with STEMI is consistent regardless of primary PCI complexity.

With iterative developments in DES technology and refinements in procedural techniques, PCI is currently performed in an increasing proportion of patients with high-risk clinical and anatomical features.[1] Previous studies have reported that up to one-third of all-comer patients treated with PCI have serious comorbidities or complex coronary anatomies[2] that require more complex revascularization procedures. PCI complexity has been traditionally associated with an increased risk for adverse ischemic events, particularly stent-related adverse outcomes.[13,15,16] There is however limited data on the prevalence and clinical outcomes following primary PCI with newer-generation DESs in STEMI patients with

TABLE 5 Clinical outcomes at 2 years in patients undergoing complex versus noncomplex primary percutaneous coronary intervention according to randomized drug-eluting stent.

	Complex primary PCI				Noncomplex primary PCI				
Patients—*n*	BP-SES *n* = 200	DP-EES *n* = 221	HR (95% CI)	*p* Value	BP-SES *n* = 653	DP-EES *n* = 626	HR (95% CI)	*p* Value	*p* Value for interaction
Target lesion failure[a]	14 (7.1)	25 (11.6)	0.62 (0.32–1.19)	0.15	28 (4.4)	49 (8.2)	0.54 (0.34–0.86)	0.008	0.74
All-cause death	13 (6.6)	9 (4.1)	1.60 (0.68–3.75)	0.27	22 (3.5)	26 (4.3)	0.81 (0.46–1.42)	0.45	0.18
Cardiac death	8 (4.0)	8 (3.6)	1.11 (0.41–2.95)	0.84	14 (2.2)	22 (3.6)	0.61 (0.31–1.19)	0.14	0.32
Myocardial reinfarction	5 (2.7)	13 (6.2)	0.42 (0.15–1.19)	0.09	23 (3.7)	17 (2.9)	1.29 (0.69–2.42)	0.43	0.06
Q-wave myocardial reinfarction	0 (0.0)	4 (1.9)	0.12 (0.01–2.21)	0.13	6 (1.0)	4 (0.7)	1.42 (0.40–5.06)	0.58	0.05
Non Q-wave myocardial reinfarction	5 (2.7)	10 (4.8)	0.56 (0.19–1.63)	0.28	17 (2.8)	13 (2.2)	1.25 (0.61–2.57)	0.55	0.22
Target vessel myocardial reinfarction	2 (1.0)	9 (4.3)	0.24 (0.05–1.13)	0.051	10 (1.6)	10 (1.7)	0.95 (0.39–2.28)	0.90	0.12
Target vessel Q-wave myocardial reinfarction	0 (0.0)	3 (1.4)	0.16 (0.01–3.08)	0.25	5 (0.8)	4 (0.7)	1.19 (0.32–4.43)	0.80	0.11
Target vessel non Q-wave myocardial reinfarction	2 (1.0)	7 (3.4)	0.32 (0.07–1.53)	0.13	5 (0.8)	6 (1.0)	0.79 (0.24–2.59)	0.70	0.36
Cardiac death or any myocardial reinfarction	12 (6.2)	21 (9.6)	0.63 (0.31–1.28)	0.20	36 (5.7)	38 (6.3)	0.90 (0.57–1.43)	0.66	0.40
Revascularization (any)	11 (5.9)	30 (14.3)	0.39 (0.20–0.79)	0.006	40 (6.5)	44 (7.5)	0.86 (0.56–1.32)	0.50	0.056
Target lesion revascularization (any)	7 (3.7)	17 (8.2)	0.45 (0.19–1.10)	0.07	17 (2.8)	26 (4.5)	0.62 (0.33–1.14)	0.12	0.58
Clinically indicated target lesion revascularization	7 (3.7)	16 (7.7)	0.48 (0.20–1.18)	0.10	15 (2.4)	25 (4.3)	0.57 (0.30–1.07)	0.08	0.78
PCI	5 (2.6)	15 (7.2)	0.37 (0.13–1.01)	0.044	14 (2.3)	25 (4.3)	0.53 (0.27–1.01)	0.051	0.56
CABG	2 (1.1)	1 (0.5)	2.22 (0.20–24.33)	0.50	1 (0.2)	1 (0.2)	0.95 (0.06–15.16)	0.97	0.65
Target vessel revascularization (any)	9 (4.8)	24 (11.5)	0.41 (0.19–0.88)	0.02	23 (3.7)	30 (5.2)	0.72 (0.42–1.25)	0.24	0.23
Clinically indicated target vessel revascularization	9 (4.8)	23 (11.0)	0.43 (0.20–0.92)	0.03	21 (3.4)	29 (5.0)	0.68 (0.39–1.20)	0.18	0.33
PCI	7 (3.7)	22 (10.5)	0.35 (0.15–0.81)	0.01	20 (3.3)	29 (5.0)	0.65 (0.37–1.15)	0.14	0.23
CABG	2 (1.1)	1 (0.5)	2.22 (0.20–24.33)	0.50	1 (0.2)	1 (0.2)	0.95 (0.06–15.16)	0.97	0.65
Target vessel failure[b]	16 (8.2)	32 (14.8)	0.54 (0.30–0.99)	0.043	36 (5.7)	54 (9.0)	0.63 (0.41–0.96)	0.03	0.70
POCE[c]	25 (12.7)	40 (18.3)	0.67 (0.41–1.11)	0.12	64 (10.1)	72 (11.8)	0.86 (0.61–1.20)	0.36	0.44
Cerebrovascular event (any)	2 (1.1)	5 (2.3)	0.44 (0.09–2.28)	0.32	8 (1.3)	10 (1.7)	0.76 (0.30–1.93)	0.56	0.57
Stroke (any)	0 (0.0)	4 (1.9)	0.12 (0.01–2.21)	0.13	8 (1.3)	6 (1.0)	1.27 (0.44–3.67)	0.66	0.056
TIA	2 (1.1)	1 (0.5)	2.23 (0.20–24.38)	0.50	0 (0.0)	4 (0.7)	0.11 (0.01–2.04)	0.057	0.042

TABLE 5 (Continued)

	Complex primary PCI				Noncomplex primary PCI				
Patients—*n*	BP-SES *n* = 200	DP-EES *n* = 221	HR (95% CI)	*p* Value	BP-SES *n* = 653	DP-EES *n* = 626	HR (95% CI)	*p* Value	*p* Value for interaction
Definite stent thrombosis	2 (1.0)	6 (2.8)	0.37 (0.07–1.84)	0.21	8 (1.3)	8 (1.3)	0.95 (0.36–2.53)	0.92	0.32
Definite or probable stent thrombosis	4 (2.0)	12 (5.5)	0.37 (0.12–1.14)	0.07	12 (1.9)	13 (2.2)	0.87 (0.40–1.92)	0.74	0.21

Note: Data expressed as number of first events (% cumulative incidence from Kaplan–Meier estimate). Hazard ratios (95% confidence intervals) and log-rank *p* values are derived from Mantel-Cox regressions. Interaction *p* value for randomized stent × complex primary PCI (yes or no).

Abbreviations: BP-SES, biodegradable polymer sirolimus-eluting stent; CABG, coronary artery bypass grafting; CI, confidence interval; DP-EES, durable polymer everolimus-eluting stent; HR, hazard ratio; PCI, percutaneous coronary intervention; POCE, patient-oriented composite endpoint; TIA, transient ischemic attack.

[a]Composite of cardiac death, target vessel myocardial reinfarction (Q-wave and non-Q-wave), and clinically indicated target lesion revascularization (primary endpoint).

[b]Composite of cardiac death, any myocardial reinfarction, or any target vessel revascularization.

[c]Composite of all cause death, any myocardial reinfarction, or any revascularization.

complex coronary anatomy. In our all-comer study, we found that a quarter of STEMI patients undergoing primary PCI in contemporary practice have complex anatomical features that require complex primary PCI. Our findings suggest that despite improvements in DES designs and the routine use of potent $P2Y_{12}$ receptor inhibitors, patients with STEMI undergoing complex primary PCI have an increased risk of stent- and patient-related adverse outcomes compared with those who underwent noncomplex primary PCI, thus confirming the combined need for future improvements in DES technology and pharmacological strategies to further improve clinical outcomes in this high-risk patient subgroup. We found that complex primary PCI with latest-generation DESs in STEMI patients was associated with a 50% increased risk for repeat revascularization, including a 75% greater risk for ischemia-driven TLR, and a two fold increased risk for definite or probable stent thrombosis at 2 years of follow-up compared with noncomplex primary PCI. These differences translated into a significantly greater risk for both device- and patient-oriented clinical outcomes at 2 years among patients undergoing complex, as compared with those undergoing noncomplex, primary PCI in the contemporary newer-generation DES era. Our findings are consistent with a recent patient-level pooled analysis from randomized trials investigating the same newer-generation DESs as used in our study that demonstrated a nearly two fold increase in TLF and target vessel myocardial infarction rates, and a three fold increased risk for stent thrombosis among all-comer patients undergoing complex PCI.[6]

Randomized evidence on the differential clinical performances of newest-generation DESs among patients undergoing complex versus noncomplex PCI is limited to large-scale retrospective contemporary registries[4,5,17,18] and small-sized post hoc subgroup[2] or pooled analyses[6] from randomized controlled trials that predominately included all-comer PCI patients. These studies yielded conflicting results with respect to the ability of newer-generation DESs to prevent repeat revascularization in patients with complex, compared with noncomplex, coronary lesions.[2,4,5,17,18] The interpretation of these findings is however hampered by important between-studies differences in complex PCI definitions owing to the absence of available consensus documents,[2] and the inclusion of all-comer patients that precludes the extrapolation of the study conclusions to highest-risk patient subsets, such as patients with STEMI who are commonly underrepresented in those trials.

There is currently no universal definition of complex PCI.[2] For the present analysis, we used the definition of complex PCI from a previous large-scale pooled patient-level meta-analysis of six randomized controlled trials that included 9577 all-comer patients who underwent PCI with predominantly newer-generation DESs, of whom 1680 (17.5%) underwent complex PCI.[13] Complex PCI was defined as having at least one of the following features: 3 vessels treated, ≥3 stents implanted, ≥3 lesions treated, bifurcation with 2 stents implanted, total stent length >60 mm, and/or CTO. As compared with those who underwent noncomplex procedures, patients undergoing complex PCI were found to have a significantly higher risk for cardiac death, myocardial infarction,

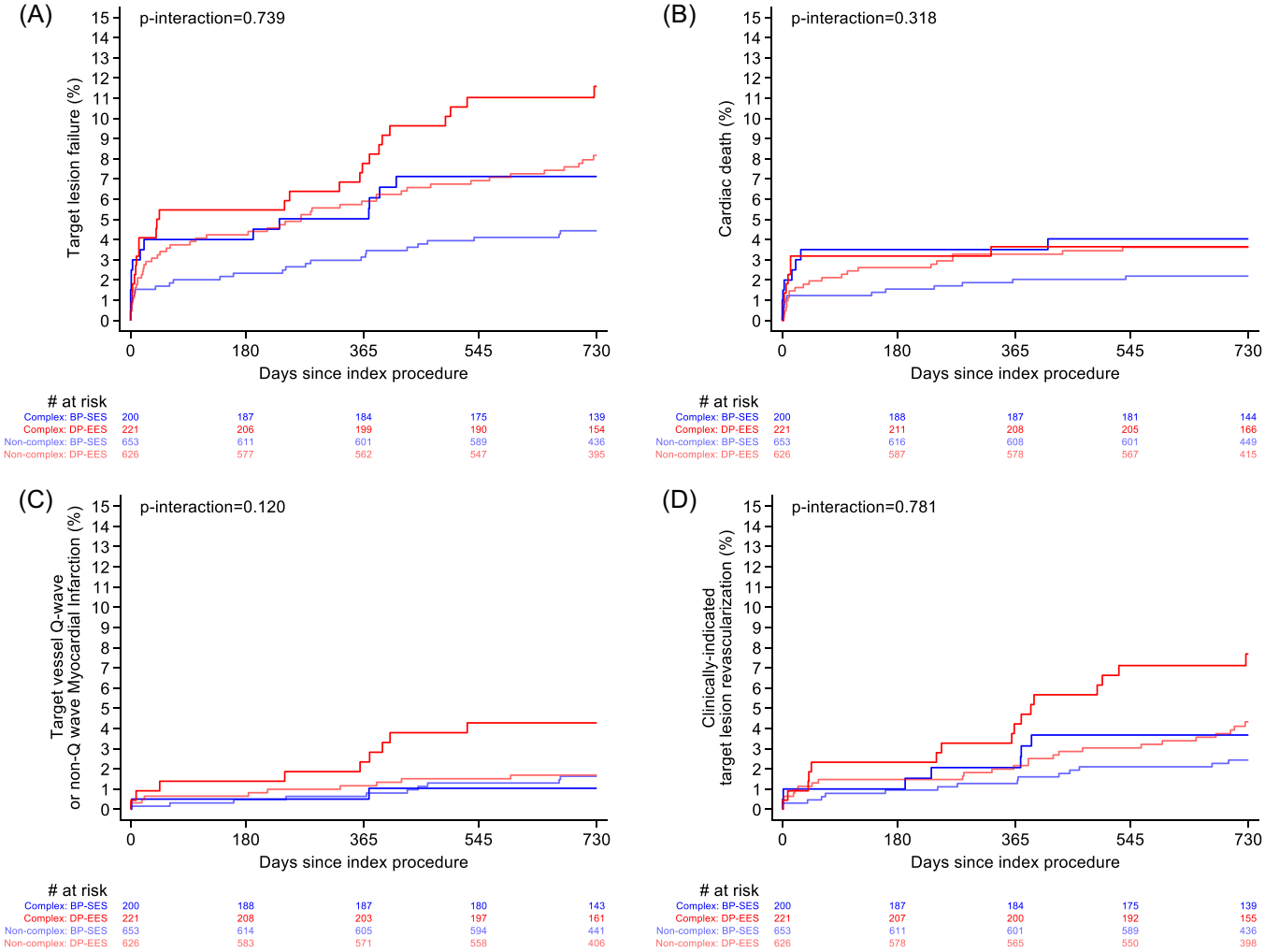

FIGURE 3 Time-to-event curves for the primary composite endpoint target lesion failure and individual components of the primary endpoint at 2 years of follow-up. (A) Target lesion failure; (B) cardiac death; (C) target vessel (TV) myocardial reinfarction; (D) clinically indicated target lesion revascularization (TLR). Dark blue lines indicate biodegradable polymer sirolimus-eluting stent (BP-SES), complex primary percutaneous coronary intervention (PCI) group; light blue lines indicate BP-SES, noncomplex primary PCI group; red lines indicate durable polymer everolimus-eluting stent (DP-EES), complex primary PCI group; orange lines indicate DP-EES, noncomplex primary PCI group.

or stent thrombosis at a median follow-up of 392 days.[13] However, only one out of five patients who underwent complex PCI presented with high-risk acute coronary syndrome, thus underscoring the clinical importance of our study findings in an exclusive STEMI population.

STEMI is associated with a heightened prothrombotic and inflammatory milieu, that further increases the risk for stent-related adverse outcomes compared with chronic or non-ST elevation acute coronary syndromes. Our study is the first to report on the impact of PCI complexity on the clinical performance of newest-generation DESs among patients with STEMI undergoing percutaneous coronary revascularization. We found a consistent treatment effect between ultrathin-strut BP-SES and thin-strut DP-EES with respect to the primary endpoint of TLF at 2 years among STEMI patients undergoing complex or noncomplex primary PCI. Since there was no significant treatment interaction between ultrathin-strut BP-SES and thin-strut DP-EES according to primary PCI complexity, the main treatment effect previously observed in the overall patient population included in the BIOSTEMI trial applies.[9,10] Therefore, our results indicate that ultrathin-strut BP-SES are superior to thin-strut DP-EES with respect to TLF at 2 years among STEMI patients undergoing both complex and noncomplex primary PCI. However, treatment with ultrathin-strut BP-SES might be associated with a lower risk of TLF at 2 years compared with thin-strut DP-EES among STEMI patients undergoing noncomplex primary PCI, a difference caused by a reduced risk for clinically indicated TLR, whereas no significant difference was found among those undergoing complex primary PCI. Among STEMI patients undergoing complex primary PCI, we observed significant reductions in the risks for repeat revascularization, TVR, and TVF at 2 years with ultrathin-strut BP-SES compared with thin-strut DP-EES. In addition, there was a signal toward a lower 2-year risk for target vessel myocardial reinfarction, TLR, and definite/probable stent thrombosis with ultrathin-strut BP-SES compared with thin-strut DP-EES.

Nevertheless, these differences did not translate into improved POCE at 2 years of follow-up with ultrathin-strut BP-SES among STEMI undergoing complex primary PCI. Notably, the 2-year rates of stent thrombosis were low and did not significantly differ between complex primary PCI patients treated with ultrathin-strut BP-SES or thin-strut DP-EES, thus confirming the overall safety of newest-generation DESs among highest-risk STEMI patients undergoing complex primary PCI. These potential differential effects between DESs need however to be considered with caution and warrant confirmation from dedicated randomized clinical trials.

In our study, three out of four STEMI patients undergoing complex primary PCI had ≥3 stents implanted, >40% had long diffuse coronary lesions requiring a total stent length ≥60 mm, and one out of three patients underwent bifurcation PCI with multiple stents, whereas only a minority of patients underwent multivessel or CTO PCI during the index procedure. However, in a sensitivity analysis comparing clinical outcomes among patients who underwent complex versus noncomplex primary PCI and were categorized according to each individual complex primary PCI criteria, there was no significant treatment interaction between ultrathin-strut BP-SES and thin-strut DP-EES with respect to TLF at 2 years for any individual complex primary PCI criteria.

The present analysis has several limitations, which need to be addressed. First, as a post hoc analysis from a randomized trial, the study results should be considered hypothesis-generating rather than conclusive. In the BIOSTEMI trial, patients were not randomized according to primary PCI complexity and unmeasured confounders cannot, therefore, be formally excluded. Second, while the random allocation to study stent platforms may allow for direct comparisons between ultrathin-strut BP-SES and thin-strut DP-EES according to primary PCI complexity, the modest number of patients in the complex primary PCI group prevents from reaching significant data on treatment interaction between study stents and primary PCI complexity with respect to long-term clinical outcomes. Third, there is currently no standardized definition of complex PCI,[2] and existing definitions[13] may not be applicable for STEMI patients. We defined complex primary PCI based on a previous study definition that has been associated with differential stent-related outcomes among all-comer patients undergoing complex versus noncomplex PCI.[13] We did not integrate into our complex PCI definition additional clinical criteria, such as significant patient comorbidities or lesions subsets, including left main disease, that may potentially impact on long-term stent-related outcomes following PCI. Nonetheless, we found consistent treatment effects between ultrathin-strut BP-SES and thin-strut DP-EES with respect to 2-year TLF rates among complex primary PCI patients irrespective of the inclusion or exclusion of left main PCI in the complex primary PCI definition used (Supporting Information: Figure 2).

5 | CONCLUSION

In a post hoc subgroup analysis from the BIOSTEMI randomized trial, we found consistent treatment effects between ultrathin-strut BP-SES and thin-strut DP-EES with respect to TLF at 2 years of follow-up among STEMI patients undergoing complex or noncomplex primary PCI. These results indicate that ultrathin-strut BP-SES are superior to thin-strut DP-EES with respect to TLF at 2 years among STEMI patients, irrespective of primary PCI complexity.

ACKNOWLEDGMENTS

BIOSTEMI was an investigator-initiated study supported by a dedicated research grant from Biotronik AG, Bülach, Switzerland. The funder was not involved in the design, data collection, and management of the study, and had no role in the analysis and interpretation of the study data, writing of the manuscript or decision to submit for publication. Open access funding provided by Universite de Geneve.

CONFLICT OF INTEREST STATEMENT

J. F. I. reports research grants to the institution and personal fees from Biotronik during the conduct of the study; research grants to the institution from Abbott Vascular, AstraZeneca, Biosensors, Biotronik, Concept Medical, Philips Volcano, and Terumo, outside of the submitted work; and personal fees from Astra Zeneca, Biotronik, Bristol/Myers/Squibb, Medalliance, Novartis, Terumo, Medtronic, Philips Volcano, and Cardinal Health, outside the submitted work. S. L. and D. H. are affiliated with Clinical Trials Unit Bern (CTU Bern), University of Bern (Bern, Switzerland), which has a staff policy of not accepting honoraria or consultancy fees. However, CTU Bern is involved in design, conduct, or analysis of clinical studies funded by not-for-profit and for-profit organizations. In particular, pharmaceutical, and medical device companies provide direct funding to some of these studies. For an up-to-date list of CTU Bern's conflicts of interest see www.ctu.unibe.ch/research/declaration_of_interest/index_eng.html. M. R. reports institutional research grants from Terumo, Boston Scientific, Medtronic, Abbott Vascular, and Biotronik, outside the submitted work. D. J. K. reports grants from the University Clinic for Cardiology, Inselspital Bern, Swizerland, during the conduct of the study. S. W. received research grants to their institution from Amgen, Abbott, Bayer, Bristol-Myers Squibb, Boston Scientific, CSL Behring, Edwards Lifesciences, Medtronic, Polares, and Sinomed, outside the submitted work, and research grants from Biotronik during the conduct of the study. T. P. received research grants to the institution and speaker fees from Biotronik during the conduct of this study, research grants to the institution and speaker fees from Boston Scientific, outside the submitted work, and serves as a consultant for HighLife SAS. The remaining authors declare no conflict of interest.

ORCID

Juan F. Iglesias http://orcid.org/0000-0002-1669-6036

REFERENCES

1. Kirtane AJ, Doshi D, Leon MB, et al. Treatment of higher-risk patients with an indication for revascularization: evolution within the field of contemporary percutaneous coronary intervention. *Circulation*. 2016;134(5):422-431.

2. Riley RF, Henry TD, Mahmud E, et al. SCAI position statement on optimal percutaneous coronary interventional therapy for complex coronary artery disease. *Catheter Cardiovasc Interv*. 2020;96(2):346-362.
3. Généreux P, Giustino G, Redfors B, et al. Impact of percutaneous coronary intervention extent, complexity and platelet reactivity on outcomes after drug-eluting stent implantation. *Int J Cardiol*. 2018;268:61-67.
4. Song PS, Park KT, Kim MJ, et al. Safety and efficacy of biodegradable polymer-biolimus-eluting stents (BP-BES) compared with durable polymer-everolimus-eluting stents (DP-EES) in patients undergoing complex percutaneous coronary intervention. *Korean Circ J*. 2019;49(1):69-80.
5. Azzalini L, Baber U, Johal GS, et al. One-year outcomes of patients undergoing complex percutaneous coronary intervention with three contemporary drug-eluting stents. *Catheter Cardiovasc Interv*. 2021;97(7):1341-1351.
6. Hemetsberger R, Abdelghani M, Toelg R, et al. Complex vs. non-complex percutaneous coronary intervention with newer-generation drug-eluting stents: an analysis from the randomized BIOFLOW trials. *Clin Res Cardiol*. 2022;111:795-805. doi:10.1007/s00392-022-01994-4
7. Sarno G, Lagerqvist B, Nilsson J, et al. Stent thrombosis in new-generation drug-eluting stents in patients with STEMI undergoing primary PCI. *J Am Coll Cardiol*. 2014;64:16-24.
8. Nakazawa G, Finn AV, Joner M, et al. Delayed arterial healing and increased late stent thrombosis at culprit sites after drug-eluting stent placement for acute myocardial infarction patients: an autopsy study. *Circulation*. 2008;118:1138-1145.
9. Iglesias JF, Muller O, Heg D, et al. Biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents in patients with ST-segment elevation myocardial infarction (BIOSTEMI): a single-blind, prospective, randomised superiority trial. *Lancet*. 2019;394(10205):1243-1253.
10. Pilgrim T, Muller O, Heg D, et al. Biodegradable- versus durable-polymer drug-eluting stents for STEMI. *JACC Cardiovasc Interv*. 2021;14(6):639-648.
11. Iglesias JF, Muller O, Zaugg S, et al. A comparison of an ultrathin-strut biodegradable polymer sirolimus-eluting stent with a durable polymer everolimus-eluting stent for patients with acute ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: rationale and design of the BIOSTEMI trial. *EuroIntervention*. 2018;14(6):692-699.
12. Iglesias JF, Roffi M, Degrauwe S, et al. Orsiro cobalt-chromium sirolimus-eluting stent: present and future perspectives. *Expert Rev Med Devices*. 2017;14(10):773-788.
13. Giustino G, Chieffo A, Palmerini T, et al. Efficacy and safety of dual antiplatelet therapy after complex PCI. *J Am Coll Cardiol*. 2016;68(17):1851-1864.
14. Pilgrim T, Heg D, Roffi M, et al. Ultrathin strut biodegradable polymer sirolimus-eluting stent versus durable polymer everolimus-eluting stent for percutaneous coronary revascularisation (BIOSCIENCE): a randomised, single-blind, non-inferiority trial. *Lancet*. 2014;384(9960):2111-2122.
15. Yeh RW, Kereiakes DJ, Steg PG, et al. Lesion complexity and outcomes of extended dual antiplatelet therapy after percutaneous coronary intervention. *J Am Coll Cardiol*. 2017;70(18):2213-2223.
16. Ueki Y, Karagiannis A, Zanchin C, et al. Validation of high-risk features for stent-related ischemic events as endorsed by the 2017 DAPT guidelines. *JACC Cardiovasc Interv*. 2019;12(9):820-830.
17. Mohamed MO, Polad J, Hildick-Smith D, et al. Impact of coronary lesion complexity in percutaneous coronary intervention: one-year outcomes from the large, multicentre e-Ultimaster registry. *EuroIntervention*. 2020;16(7):603-612.
18. Endo H, Dohi T, Miyauchi K, et al. Clinical impact of complex percutaneous coronary intervention in patients with coronary artery disease. *Cardiovasc Interv Ther*. 2020;35:234-241.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Iglesias JF, Muller O, Losdat S, et al. Complex primary percutaneous coronary intervention with ultrathin-strut biodegradable versus thin-strut durable polymer drug-eluting stents in patients with ST-segment elevation myocardial infarction: a subgroup analysis from the BIOSTEMI randomized trial. *Catheter Cardiovasc Interv*. 2023;101:687-700. doi:10.1002/ccd.30600