

ORIGINAL STUDIES

Individual patient data analysis of the BIOFLOW study program comparing safety and efficacy of a bioresorbable polymer sirolimus eluting stent to a durable polymer everolimus eluting stent

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Abstract

Objectives: This analysis of pooled individual patient data (IPD) aimed to evaluate the safety and efficacy of a bioresorbable polymer sirolimus eluting stent system (BP-SES; Orsiro) compared to a durable polymer everolimus eluting stent system (DP-EES; Xience) in the pooled population as well as in subgroups.

Methods: IPD with up to 12 months follow-up of the randomized controlled trials BIOFLOW-II (NCT01356888), -IV (NCT01939249), and -V (NCT02389946) as well as the all comers registry BIOFLOW-III (NCT01553526) were pooled. A total of 3,717 subjects (2,923 in BP-SES and 794 in DP-EES) with 5,328 lesions (4,225 lesions in BP-SES and 1,103 in DP-EES) were included in the IPD. The primary endpoint was target lesion failure (TLF) at 12 months follow-up. Subgroups analyzed included diabetes, age (≥ 65 years), gender, complex lesions (B2/C), small vessels (reference vessel diameter ≤ 2.75 mm), multivessel treatment, renal disease, and patients with acute coronary syndrome.

Results: Overall, TLF at 12 months was significantly lower with 5.2% in the BP-SES group versus 7.6% in the DP-EES group ($p = .0098$). Similarly, target vessel myocardial

Abbreviations: BP-SES, bioresorbable polymer sirolimus eluting stent; CD, clinically driven; CI, confidence interval; DES, drug eluting stent; DP-EES, durable polymer everolimus eluting stent; DS, diameter stenosis; IPD, individual patient data; MI, myocardial infarction; OR, odds ratio; RCT, randomized controlled trial; RVD, reference vessel diameter; SD, standard deviation; ST, stent thrombosis; TLF, target lesion failure; TVF, target vessel failure; TV-MI, target vessel MI.

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infarction (TV-MI) was 3.1 versus 5.7% ($p = .0005$). The rate of stent thrombosis was similar in both groups (0.004%). By regression analysis, an independent stent effect in favor of BP-SES was observed for TLF ($p = .0043$) and TV-MI ($p = .0364$) in small vessels.

Conclusion: Results of this IPD analysis suggest that the BP-SES with ultrathin struts is as safe as and more efficacious than DP-EES in the overall cohort and especially in small vessels.

KEYWORDS

drug eluting stent, pooled analysis, small vessel, strut thickness, target lesion failure

1 | INTRODUCTION

Contemporary drug eluting stents (DES) with metallic backbones are characterized by a distinguished safety and efficacy profile compared to previous generations and are therefore the default devices in patients undergoing percutaneous coronary intervention (PCI).¹ The bioresorbable sirolimus eluting stent (BP-SES, Orsiro, BIOTRONIK AG) is a DES, which is known for its ultrathin struts made of cobalt-chromium.² The strut thickness is 60 μm for stent sizes up to 3.0 mm and 80 μm for sizes >3.0 mm in expanded diameter. BP-SES is further characterized by a unique hybrid coating consisting of a bioresorbable drug-polymer combination, which ultimately only leaves the bare metal stent in the vessel covered by a passive coating layer of amorphous silicon carbide.³ The high clinical safety and efficacy profile of BP-SES has been demonstrated in several randomized controlled trials (RCTs) with either de novo lesions⁴⁻⁶ or in all comers populations,⁷⁻¹¹ corroborated by results seen in all comers registries^{11,12} and the SCAAR registry.¹³

The BP-SES has been repeatedly compared to other DES (e.g., the durable polymer everolimus eluting stent [DP-EES], Xience, Abbott, the durable polymer zotarolimus eluting stent [DP-ZES] Resolute Onyx and Resolute Integrity, Medtronic) demonstrating comparable results and safety profiles.^{4,5,8,10} In the BIOFLOW-V trial, a RCT in an almost all-comers population, a significant reduction in both the target lesion failure (TLF) rate and target vessel myocardial infarction rate (TV-MI) was observed for the BP-SES group compared to DP-EES.⁵ Meanwhile, several meta-analyses were conducted comparing the clinical outcomes of BP-SES with contemporary DES.¹⁴⁻¹⁷ In a meta-analysis by Cassese et al. including six RCTs comparing BP-SES against DP-EES, clinical outcomes were comparable between the groups at 12 months follow-up.¹⁷ Similarly, Lipinski et al. assessed the data of eight RCTs comparing BP-SES against various DES. They showed a trend toward reduction of MI, TLF, and stent thrombosis (ST) for patients treated with BP-SES.¹⁴ Zhu et al. considered six RCTs comparing BP-SES with two different durable polymer stents for the meta-analysis, in which a significantly reduced risk for MI in BP-SES treated subjects was found.¹⁵ As the majority of these analyses was performed at publication level, detailed analyses of different patient subgroups were not possible. Hence, this pooled individual patient data (IPD) analysis of the BIOFLOW-II, BIOFLOW-III, BIOFLOW-IV, and BIOFLOW-V studies aimed to evaluate the safety and efficacy of

BP-SES compared to DP-EES in the overall pooled population as well as in certain patient subgroups.

2 | MATERIALS AND METHODS

2.1 | Individual patient data analysis: studies included

BIOFLOW-II was a 2:1 RCT with 452 patients comparing BP-SES with a DP-EES (Xience Prime). The primary endpoint was in stent late lumen loss (LLL): 0.10 ± 0.32 mm in BP-SES versus 0.11 ± 0.29 mm in DP-EES, $p_{\text{non-inferiority}} < .0001$ at 9 months. TLF at 12 months was 6.5% in BP-SES versus 8.0% in DP-EES.¹⁸

BIOFLOW-III was a prospective, multicenter observational all-comers registry with 1,356 patients enrolled. The primary endpoint TLF at 12 month was 5.1% in the overall population.¹²

BIOFLOW-IV was a 2:1 RCT with 525 patients comparing BP-SES with DP-EES (Xience Prime or Xience Xpedition). The primary endpoint non-inferiority related to 12-months target vessel failure (TVF), was met (5.1% in BP-SES patients versus 6.6% in DP-EES patients, $p_{\text{non-inferiority}} < .001$). TLF at 12 months was 4.2% in BP-SES versus 5.4% in DP-EES.⁶

BIOFLOW-V was a 2:1 RCT with 1,334 patients comparing BP-SES with DP-EES. TLF at 12 months rate was 6% in BP-SES versus 10% in DP-EES ($p = .0399$).⁵

In all trials, the endpoint related events used for this analysis were adjudicated by an independent clinical event committee.

This IPD analysis was investigator initiated using the trial data on file hold on property by BIOTRONIK AG, Buelach, Switzerland. The principal investigators of the primary main trials agreed on conducting this analysis. All authors had full access to the data of this analysis and had final responsibility for the decision to submit for publication (Table S1).

2.2 | Endpoint and subgroups

The primary endpoint of this retrospective IPD analysis was TLF at 12 months in the overall population. Secondary endpoints were TLF

at 12 months in pre-defined subgroups such as diabetes, gender, age ≥ 65 years, multivessel treatment, B2/C complex lesions,¹⁹ small vessels ≤ 2.75 mm in diameter, nominal stent size ≤ 3.0 mm diameter, renal disease, as well as subjects presenting with acute coronary syndrome (ACS). Additional secondary endpoints were the individual components of TLF: TV-MI, clinically driven target lesion revascularization (TLR), and cardiac death (CD) at 12 months in the overall population and in the pre-defined subgroups.

2.3 | Statistical methods

The IPD analysis from the four studies was performed according to the intention-to-treat (ITT) principle including all randomized patients. Only complete cases were included with no imputation of missing data. SAS v9.4 was used for analysis.

Categorical baseline variables were summarized as absolute and relative frequencies and compared between the two device groups using Chi-square tests. Continuous baseline variables were listed as means and SDs and compared using the non-parametric Wilcoxon sum-rank test. The aim of the analysis was to estimate the device effect on the binary 1-year TLF rate, applying the Universal MI definition.

Stratified subgroup analyses included diabetes, age (≥ 65 years), gender, complex lesions (B2/C), small vessels (reference vessel diameter [RVD] ≤ 2.75 mm), nominal stent size ≤ 3.0 mm diameter, multivessel treatment, renal disease, and patients with ACS. In order to correct for potential confounding, multivariate mixed effect logistic regression was developed, using the TLF rate at 12 months as the dependent variable and the following independent variables: Device, study (random effect), diabetes, age ≥ 65 years, gender, hypertension, smoking status, renal disease, cancer, complex lesion, multivessel treatment, small vessel ≤ 2.75 mm in diameter, pre-dilatation, post-dilatation, and ACS status. As BP-SES stent sizes vary in strut thickness, the regression analysis was repeated for patients treated with stents ≤ 3.0 mm diameter with only 60 μm strut thickness. An initial model was fitted including interaction terms of every fixed effect with the device. Type III effects *p*-values were used to determine the significance.

As a significant interaction between small vessel ≤ 2.75 mm in diameter and the device was observed ($p = .0109$), two final models were fitted separately without interactions—for small and large vessels. The estimates for individual effect were presented as odds ratios (OR) with 95% confidence intervals (CI) and presented graphically with forest plots.

3 | RESULTS

The overall data of 3,717 subjects (2,923 in BP-SES and 794 in DP-EES) with 5,328 lesions (4,225 lesions in BP-SES and 1,103 in DP-EES) were included in this IPD. The main characteristics of the patients are reported in Table 1. The mean age was 65.5 ± 10.5 years, 73.5% were male. The main risk factors at baseline were hypertension

(77.4%), hypercholesterolemia (69.4%), past or present smoking history (58.5%), and 31.5% diabetes mellitus. Previous MI was observed in 28.2% of cases. There were significantly less patients presenting with hypercholesterolemia in BP-SES than in DP-EES (67.7 vs. 78.2%, $p < .0001$) and more patients with renal disease (9.7 vs. 7.2%, $p < .05$). With respect to ischemic status at baseline, more patients in the BP-SES group presented with stable angina while unstable angina was more frequent for DP-EES subjects (60.4 vs. 52.2% and 25.6 vs. 30.9%, respectively, $p = .0002$). Additionally, more patients suffered from ACS (unstable angina, acute myocardial infarction) for the BP-SES group (36.8% for BP-SES vs. 30.9% DP-SES, $p = .0020$). The lesion characteristics differed between the groups as more patients presented with complex B2/C lesions in the DP-EES group (53.7% for BP-SES and 57.6% for DP-EES, $p = .0296$, Table 2). On the contrary, more patients in the BP-SES group showed a thrombus at baseline (5.4 vs. 0.8%, $p < .0001$). In the overall group, the mean RVD was 2.75 ± 0.52 mm and lesion lengths 14.3 ± 8.01 mm. Diameter stenosis (DS) pre-procedure was higher in the BP-SES group ($73.0 \pm 18.3\%$ vs. $60.2 \pm 14.6\%$, $p < .0001$). There were some significant differences with respect to procedural details, like slightly and physically irrelevant higher implantation pressure in BP-SES, but a higher rate of pre- and post-dilatation in DP-EES (Table 2). Altogether this resulted in a slight but formally significant difference in post-procedural DS ($7.3 \pm 11.7\%$ in BP-SES vs. $7.5 \pm 8.5\%$ in DP-EES, $p < .0001$). However, those minimal differences in lesion length and DS judged by the visual estimation of the investigators have to be taken carefully.

Overall TLF rate at 12 months (Figure 1) was lower in the BP-SES group; 5.2 vs. 7.6% (OR = 0.67, 95% CI [0.49; 0.91]; $p = .0098$). This difference was driven (Figure 2) by a significantly lower rate of TV-MI: 3.1 versus 5.7% (OR = 0.53 with 95% CI [0.37; 0.76]; $p = .0005$). The other composites of TLF (CD and clinically driven TLR) were similar (Figure S1 and Figure S2). The rate of definite or probable ST was also similar and very low in both groups (0.004% [13/2923] vs. 0.004% [3/794]; OR = 1.18 with 95% CI [0.33; 4.14]; $p = .7984$).

When looking at different risk subgroups, TLF rates were significantly lower in BP-SES than DP-EES for subjects presenting with complex lesions (BP-SES 5.4% [89/1,642] vs. DP-EES 8.8% [42/473]; OR 0.59 [0.40; 0.86]; $p = .0060$), RVD ≤ 2.75 mm (BP-SES 5.9% [92/1,545] vs. DP-EES 9.7% [48/495]; OR 0.59 [0.41; 0.85]; $p = .0042$), ACS (BP-SES 5.9% [64/1,075] vs. DP-EES 9.4% [23/245]; OR 0.61 [0.37; 1.01]; $p = .0506$), and stent diameter ≤ 3 mm (BP-SES 5.3% [116/2,169] vs. DP-EES 9.5% [54/566]; OR 0.54 [0.38; 0.75]; $p = .0002$) (Figure 1). Similarly, TV-MI rates were significantly lower in BP-SES compared to DP-EES for complex lesions (BP-SES 3.5% [58/1,642] vs. DP-EES 7.1% [34/473]; OR 0.47 [0.31; 0.73]; $p = .0006$), RVD ≤ 2.75 mm (BP-SES 3.4% [54/1,545] vs. DP-EES 7.2% [36/245]; OR 0.46 [0.30; 0.71]; $p = .0004$), ACS (BP-SES 3.4% [37/1,075] vs. DP-EES 8.6% [21/245]; OR 0.38 [0.22; 0.66]; $p = .0004$), and stent diameter ≤ 3 mm (BP-SES 2.9% [64/2,169] vs. DP-EES 6.8% [39/566]; OR 0.41 [0.27; 0.62]; $p < .0001$) (Figure 2). Because of the imbalance in the number of subjects treated with BP-SES ($N = 2,923$) compared to the number of subjects treated with DP-EES ($N = 794$) in this pooled analysis, we tested if any of the four studies

TABLE 1 Clinical characteristics at baseline

	BP-SES N = 2,923 patients	DP-EES N = 794 patients	Overall N = 3,717 patients	p-value
Mean age years ± SD	65.1 ± 10.5	64.6 ± 10.2	65.5 ± 10.5	—
Age ≥ 65 years (%)	1,602 (54.8)	412 (51.9)	2014 (54.2)	.1434
Male (%)	73.3 (2,144/2923)	74.2 (589/794)	73.5 (2,733/3717)	.64
Female (%)	26.7 (779/2923)	25.8 (205/794)	26.5 (984/3717)	.6375
Hypertension %	77.4 (2,252/2910)	77.7 (609/784)	77.4 (2,861/3694)	.86
Hypercholesterolemia	67.7% (1973/2917)	78.2619/793)	69.9 (2,592/3710)	<.0001
Smoking history (current and past)	58.2 (1701/2922)	59.6 (473/794)	58.5 (2,174/3716)	.49
History of previous MI %	28.2 (818/2905)	26.4 (208/788)	27.8 (1,026/3693)	.33
Diabetes mellitus %	30.9 (902/2921)	33.8 (268/793)	31.5 (1,170/3714)	.12
History of stroke or TIA	6.1179/2920)	6.2 (49/792)	6.1 (228/3712)	.95
Renal disease %	9.7 (283/2921)	7.2 (57/794)	9.2 (340/3715)	<.05
Cancer %	8.5 (249/2919)	10.2 (81/794)	8.9 (330/3713)	.14
Ischemic status at baseline				.0002
Stable angina	60.4 (1,497/2477)	52.2 (414/793)	58.4 (1911/3270)	
Documented silent ischemia	14.0 (347/2477)	16.9 (134/793)	14.7 (481/3270)	
Unstable angina	25.6 (633/2477)	30.9 (245/793)	26.9 (878/3270)	
Acute coronary syndrome ^a	36.8 (1,075/2919)	30.9 (245/793)	35.6 (1,320/3712)	.0020

Abbreviations: BP-SES, bioresorbable polymer sirolimus eluting stent; DP-EES, durable polymer everolimus eluting stent; MI, myocardial infarction; TIA, transient ischemic attack.

^aAcute MI and unstable angina.

TABLE 2 Lesion characteristics and procedural parameters

	BP-SES N = 4,225 lesions	DP-EES N = 1,103 lesions	Overall N = 5,328 lesions	p-value
Multivessel treatment	10.8 (315/2912)	12.6 (99/786)	11.2 (414/3698)	.1606
Lesion				
Complex lesion (B2/C)	53.7 (1906/3548)	57.6 (544/943)	54.5 (2,450/4491)	.0296
Severe calcification	5.3 (190/3554)	4.6 (44/949)	5.2 (234/4503)	.3816
Bifurcation	13.6 (485/3564)	11.3 (107/949)	13.1 (592/4513)	.0585
Thrombus	5.4 (189/3524)	0.8 (8/949)	4.4 (197/4473)	<.0001
Lesion length mm (mean ± SD)	18.7 ± 6.3 (14.3; 14.8)	19.2 ± 7.1 (12.9;13.8)	14.3 ± 8.01 (14.05; 14.52)	<.0001
Reference vessel diameter (mean ± SD and [95% CI])	2.78 ± 0.51 (2.76;2.80) N = 2,908	2.64 ± 0.55 (2.60; 2.68) N = 732	2.75 ± 0.52 (2.74; 2.77) N = 3,700	<.0001
Maximum implantation pressure	14.0 ± 3.0	13.8 ± 2.8	14.0 ± 3.0	<.01
Stent length mm (mean ± SD)	18.8 ± 6.5	18.7 ± 6.3	19.2 ± 7.1	.34
Diameter stenosis pre-procedure (mean ± SD and [95% CI])	73.0 ± 18.3 (72.4;73.6)	60.2 ± 14.6 (59.3; 61.1)	70.3 ± 18.3 (69.7; 70.8)	<.0001
Diameter stenosis post-procedure (mean ± SD and [95% CI])	7.3 ± 11.7 (6.8;7.8)	7.5 ± 8.5 (7.0;8.1)	7.4 ± 10.8 (7.0; 7.8)	.0024
Pre-dilatation	76.7 (2,789/3635)	86.2 (846/981)	78.7 (3,635/4616)	<.0001
Post-dilatation	34.2 (1,243/3634)	42.4 (416/981)	35.9 (1,659/4615)	<.0001

Abbreviations: ACS, acute coronary syndrome, BP-SES, bioresorbable polymer sirolimus eluting stent; DP-EES, permanent polymer everolimus eluting stent; TIA, transient ischemic attack.

had a dominant effect on the results observed which could be excluded.

In order to identify potential predictors for TLF, we performed a regression analysis. Multivessel treatment ($p = .0364$), post-dilatation

($p < .001$), RVD ≤ 2.75 mm ($p = .0075$), and stent diameter ≤ 3.0 mm ($p = .0521$) were identified as predictors of TLF rates at 12 months. In addition, we observed an interaction between both RVD ≤ 2.75 mm and stent type implanted ($p = .0109$) as well as stent

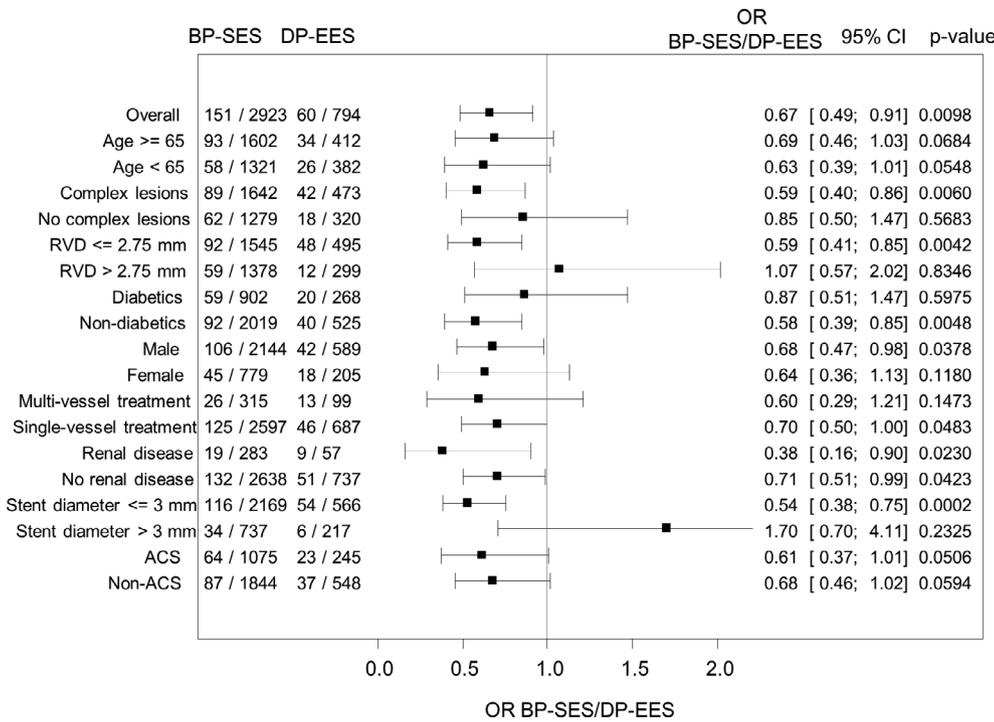


FIGURE 1 Target lesion failure in high risk subgroups

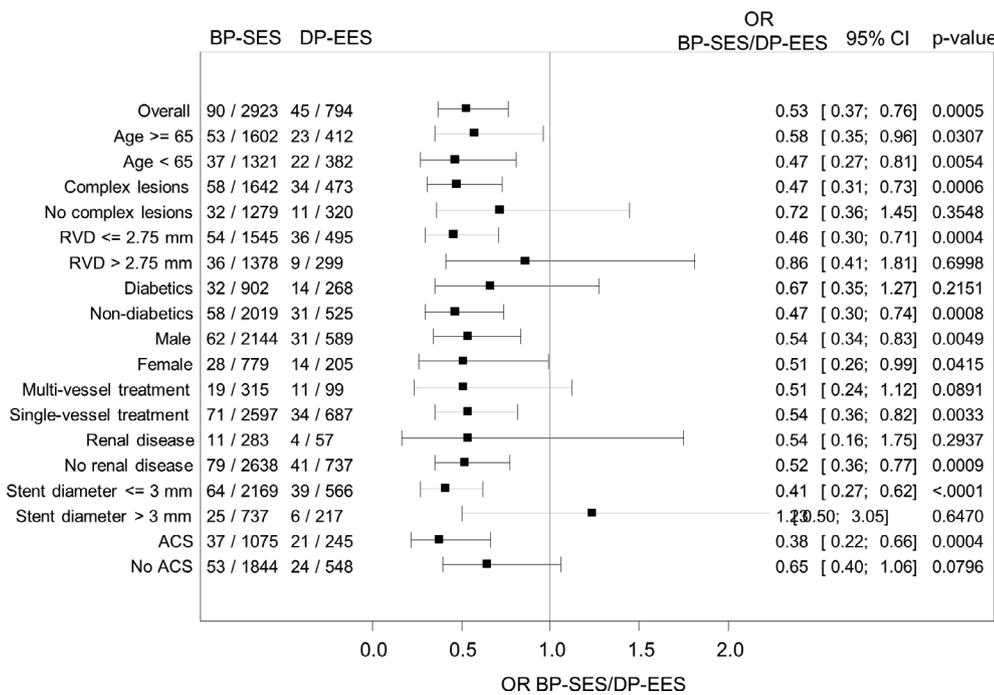


FIGURE 2 Target vessel myocardial infarction in high-risk subgroups

diameter ≤ 3.0 mm and stent type used ($p = .0351$) in favor of BP-SES. On the contrary, no interactions with the type of treatment were found for post-dilatation or multivessel treatment suggesting that those factors influence the clinical outcome independent of the implanted study stent.

In a second step, the model was tested in subjects with RVD ≤ 2.75 mm only to confirm the positive treatment effect of BP-SES in this subgroup; the treatment effect was in favor of the BP-SES stent

for TLF (OR 0.51; 95% CI [0.33; 0.81], $p = .0039$, Figure 3) as well as TV-MI (OR 0.58; 95% CI [0.35; 0.97], $p = .0377$, Figure 4) at 12 months. On the contrary, in patients with RVD > 2.75 mm no treatment effect of the stent type used was detected on either TLF or TV-MI (Figures S3 and S4). As patients with at least one small lesion were predominantly treated with stents up to 3.0 mm in diameter, the model was repeated in the subgroup of subjects treated with at least one stent with a diameter ≤ 3.0 mm. Interestingly, a similar effect in

FIGURE 3 Effect of treatment and possible confounders on TLF in patients with small target vessels (RVD ≤ 2.75 mm)

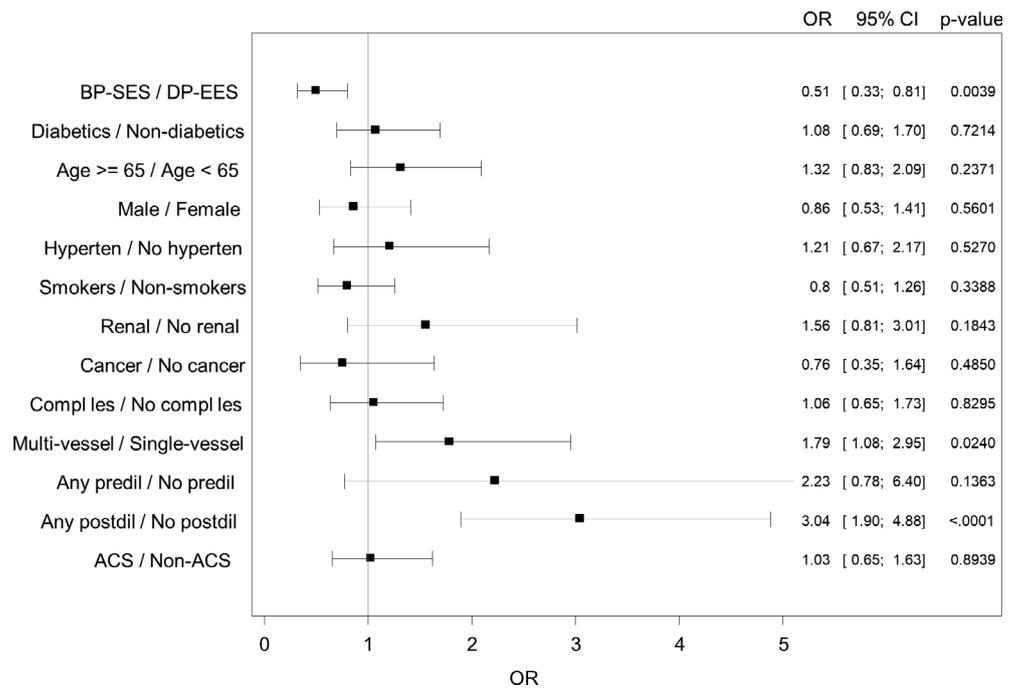
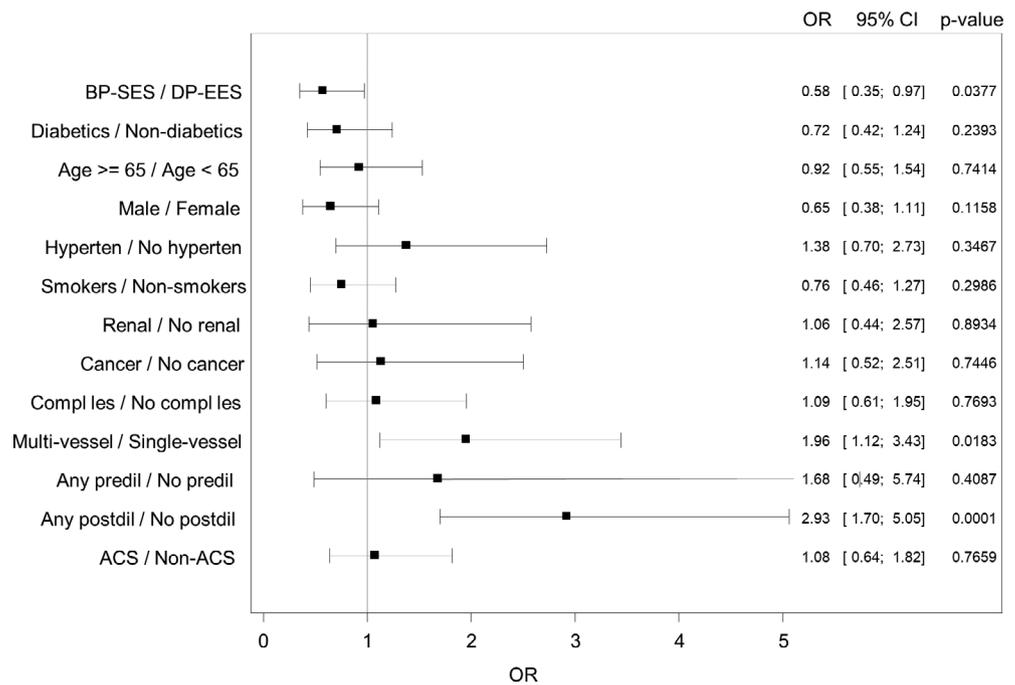


FIGURE 4 Effect of treatment and possible confounders on TV-MI in patients with small target vessels (RVD ≤ 2.75 mm)



favor of BP-SES was seen in those patients for TLF (OR = 0.51 with 95% CI [0.33; 0.79]; $p = .0024$, Figure S5) and TV-MI (OR = 0.55 with 95% CI [0.34; 0.90]; $p = .0165$, Figure S6).

4 | DISCUSSION

As the main finding of this pooled analysis, BP-SES proved to be better with respect to TLF, mainly driven by a significantly lower rate of TV-MI compared to DP-EES. The ST rate was very low without a

difference between the two-stent groups. In a consecutive subgroup analysis, the use of the ultra-thin strut BP-SES in small vessels turned out of significant benefit. Patients with small target vessels of ≤ 2.75 mm in diameter are known to be at increased risk of TLF due to increased rates of restenosis and repeat revascularisation.^{20,21} On the contrary, several DES have been studied in patients with small target vessels with comparable clinical outcomes to those seen for larger vessel sizes.²²⁻²⁴ Further, subgroup analyses of previous studies with the BP-SES (BIOFLOW-II, BIOFLOW-III, and BIOSCIENCE, respectively) demonstrated that BP-SES is safe and effective in the

treatment of lesions in small vessels at a 12-month follow-up.^{7,12,18} A recent post hoc analysis of the BIOSCIENCE trial confirmed that both BP-SES and DP-EES are equally safe and effective for treatment of patients with small target vessels ≤ 3 mm up to 5 years follow-up.²⁵ However, as DES with thinner struts have generally been associated with lower risk for restenosis especially in smaller target vessels, the BP-SES with its ultrathin 60 μm struts is expected to be a very good treatment option for coronary artery disease in small vessels.²⁶⁻²⁹

In this IPD analysis we found in a regression analysis a positive treatment effect in favor of BP-SES for TLF and TV-MI in small target vessels ≤ 2.75 mm RVD as well as in patients treated with stent sizes ≤ 3.0 mm diameter. These findings are in line with the recent results of the BIORESORT trial for the pre-specified subgroup analysis in small vessels up to 2.5 mm in diameter.³⁰ At 36 months, the TLF rates were 7% (36/525) in subjects treated with BP-SES, 9.5% (46/496) in subjects treated DP-EES, and 10% (48/485) in subjects treated with a DP-ZES. Multivariate analysis showed that treatment with BP-SES in small coronary arteries was independently associated with statistically significantly lower TLR rates up to 3 years post procedure.³⁰ It can be speculated that ultra-thin struts cause less arterial injury during intervention, which results in less inflammatory response and improved endothelialization leading to lower event rates.³¹ In addition, stent platforms with thinner struts may also be less thrombogenic compared to stent platforms with thicker struts because of less flow disturbance.³¹ To further investigate whether the positive treatment effect of BP-SES observed in the small vessel subgroup can be linked to the ultrathin struts of 60 μm , we repeated the regression analysis for patients treated with stents ≤ 3.0 mm in diameter corresponding to strut width of only 60 μm . Again, we observed a positive effect on both TLF and TV-MI rates in BP-SES subjects suggesting a positive effect on clinical outcomes by implantation of DES with ultra-thin struts. There are various design elements in all sizes of BP-SES, which are distinct from DP-EES: The antiproliferative drug (sirolimus vs. everolimus), the polymer (bioresorbable vs. durable), and the existence of an additional passive coating on the metallic backbone (amorphous silicon carbide vs. none). It has been speculated if one of these or their combination are advantageous when BP-SES are used. However, this did not translate in a measurable difference in clinical outcome when looking at the large meta-analysis of Cassese et al.¹⁷ However, there is one more relevant distinction of BP-SES which is its differentiated design of ultrathin struts of 60 μm only in stent diameters up to 3 mm compared to 81 μm in DP-EES. Hence, this special design feature appears to be the valid explanation for the benefit of BP-SES with use of stent diameters up to 3 mm, which is the novel finding of this IPD analysis.

5 | LIMITATIONS

First, this IPD was a retrospective analysis and included studies, which all differed in design. Even though we had tested for a study effect, the differences in baseline characteristics and design might have influenced our results (e.g., differences in adjudication of clinical

events). Second, event rates after treatment with second and third generation DES are low. Effects of treatment with either BP-SES or DP-EES might have even been more pronounced in certain subgroups if more IPD would have been available. Third, RVD assessment was not based on corelab assessment only but also the investigators' assessment in quite a large set of patients (BIOFLOW-III). Additionally, subjects were counted in the RVD ≤ 2.75 mm group (or stent size ≤ 3.0 mm diameter) if at least one target lesion RVD was ≤ 2.75 mm (or stent size ≤ 3.0 mm diameter); thus patients who underwent concomitant treatment of a target lesion with RVD > 2.75 mm (or stent size > 3.0 mm diameter) were also counted in this group, which may have impacted the results. Last, even when the components of TLF were consistent over the four included trials, defined as a composite of CD, TV-MI, and clinically driven TLR, in BIOFLOW-V a modified version of the third universal MI definition was used for analysis of the primary endpoint. Because of a more sensitive MI definition more TV-MI were counted in BIOFLOW-V. However, when analyzing the BIOFLOW-V data using the third universal MI definition in a sensitivity analysis, numerically lower rates of TLF were observed as a result of lower rates of TV-MI at 12 months in both treatment groups, compared to the primary analysis. Overall the magnitude and direction of differences in TLF and TV-MI rates between BP-SES and DP-EES were similar between the primary analysis definition and the third Universal definition.

6 | CONCLUSION

Results of this IPD analysis suggest that BP-SES is an equally safe and more efficacious treatment option in patients suffering from coronary artery disease. Patients with small target vessels (RVD ≤ 2.75 mm) or treated with stents of sizes ≤ 3.0 mm in diameter may benefit most from treatment with BP-SES when compared to DP-EES.

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CONFLICT OF INTEREST

Ralph Toelg declares receiving speakers honoraria from BIOTRONIK, Ton Slagboom declares having personal consultancy agreement with BIOTRONIK, Johannes Waltenberger reports personal fees and non-financial support from BIOTRONIK, and personal fees from Bayer, Boehringer Ingelheim and Daiichi-Sankyo, Thierry Lefèvre reports proctoring for Edwards Lifescience, Abbott Vascular and Terumo, David E. Kandzari reports institutional research/grant support from BIOTRONIK, Boston Scientific, Medinol, Medtronic, and Orbus Neich, and personal consultancy honoraria from Boston Scientific, Cardiovascular Systems Inc., and Medtronic, Jacques Koolen reports lecturer and consultant fees from Medtronic, and proctoring for BIOTRONIK, Gert Richardt and Shigeru Saito have no conflict of interest to declare.

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SUPPORTING INFORMATION

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

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