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Biodegradable- Versus Durable-Polymer Drug-Eluting Stents for STEMI

Final 2-Year Outcomes of the BIOSTEMI Trial

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ABSTRACT

OBJECTIVES The aim of this study was to investigate the safety and efficacy of biodegradable-polymer sirolimus-eluting stents (BP-SES) compared with durable-polymer everolimus-eluting stents (DP-EES) in patients with ST-segment elevation myocardial infarction (STEMI).

BACKGROUND Primary percutaneous coronary intervention (PCI) is an effective treatment for patients with STEMI, and long-term outcomes are determined by the safety and efficacy profile of the newest generation drug-eluting stents.

METHODS BIOSTEMI (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) was an investigator-initiated, multicenter, assessor-blind, randomized superiority trial using Bayesian methods. Patients with STEMI undergoing primary PCI within 24 h of symptom onset were randomized in a 1:1 ratio to receive BP-SES (n = 649) or DP-EES (n = 651). The primary endpoint was target lesion failure (TLF), a composite of cardiac death, target vessel myocardial reinfarction, and clinically indicated target lesion revascularization (TLR) at 2 years.

RESULTS Between April 2016 and March 2018, 1,300 patients were included. Baseline characteristics were comparable between the 2 treatment groups. Follow-up through 2 years was complete in 1,221 patients (94%). At 2 years, TLF occurred in 33 patients (5.1%) treated with BP-SES and in 53 patients (8.1%) treated with DP-EES (rate ratio: 0.58; 95% Bayesian credible interval: 0.40 to 0.84; posterior probability of superiority = 0.998). The difference was driven by a lower incidence of clinically indicated TLR in patients treated with BP-SES compared with DP-EES (2.5% vs. 5.1%; rate ratio: 0.52; 95% Bayesian credible interval: 0.30 to 0.87; posterior probability of superiority = 0.993). There were no significant differences in rates of cardiac death, target vessel myocardial reinfarction, and definite stent thrombosis between the 2 treatment arms.

CONCLUSIONS In patients with STEMI undergoing primary PCI, BP-SES were superior to DP-EES with respect to TLF at 2 years. The difference was driven by lower rates of ischemia-driven TLR. (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 [BIOSTEMI]; NCT02579031) (J Am Coll Cardiol Intv 2021;14:639-48) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

BCI = Bayesian credible interval

BP-SES = biodegradable-polymer sirolimus-eluting stent(s)

DP-EES = durable-polymer everolimus-eluting stent(s)

DES = drug-eluting stent(s)

PCI = percutaneous coronary intervention

PLLA = poly-L-lactic acid

RR = rate ratio

STEMI = ST-segment elevation myocardial infarction

Percutaneous coronary intervention (PCI) is an effective strategy to restore myocardial perfusion in patients with acute myocardial infarction that improves prognosis by reducing final infarct size and the risk for infarct-vessel reocclusion (1). Drug-eluting stents (DES) mitigate the need for repeat revascularizations compared with bare-metal stents (2,3) and represent the current standard of care (4).

Recent refinements of newer generation DES involve the reduction of strut thickness of the metallic stent platform and the use of biodegradable polymers as a carrier for the antiproliferative substance. These improvements in stent design mitigate arterial injury, inflammation, and thrombogenicity, facilitate endothelialization, and reduce neointimal hyperplasia (5). A robust body of evidence supporting the noninferiority of biodegradable-polymer sirolimus-eluting stents (BP-SES) compared with second-generation DES (6–9) has recently been challenged by accumulating evidence indicating superiority compared with durable-polymer everolimus-eluting stents (DP-EES) with regard to device-oriented clinical outcomes in patients with chronic and acute coronary syndromes (10–12).

Acute myocardial infarction confers an increased risk for stent-related adverse events due to an exacerbated inflammatory response resulting in delayed arterial healing (13,14). The BIOSTEMI (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) trial was the first randomized trial comparing 2 contemporary DES in patients with acute myocardial infarction and demonstrated the superiority of BP-SES versus DP-EES with regard to target lesion failure at 1 year (12). Here, we report the final 2-year outcomes of the BIOSTEMI trial.

METHODS

STUDY DESIGN AND PATIENTS. The BIOSTEMI trial was an investigator-initiated, single-blind, multicenter, randomized trial investigating the hypothesis that BP-SES are superior to DP-EES in patients undergoing primary PCI for ST-segment elevation myocardial infarction (STEMI) at 10 interventional cardiology centers in Switzerland. The rationale of the trial as well as details of study conduct, randomization, blinding, data management, and data monitoring have been described previously (15). In brief, subjects with STEMI referred for PCI within 24 h of symptom onset qualified for study enrollment if they had at least 1 culprit coronary lesion suitable for stent implantation. Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research. The study was approved by the institutional ethics committees of all participating sites and complied with the Declaration of Helsinki. All patients conscious at the time of intervention provided written informed consent; preliminary consent by proxy was accepted for unconscious patients and had to be confirmed by the patients as soon as possible. The trial is registered with ClinicalTrials.gov (NCT02579031).

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DEVICES AND PROCEDURES. The experimental stent (Orsiro, Biotronik, Bülach, Switzerland) combines a cobalt-chromium platform (60-μm strut thickness for stent diameters up to 3.0 mm, 80-μm strut thickness for stent diameters >3.0 mm) covered with an amorphous hydrogen-rich, silicon-carbide layer (PROBIO, Biotronik) with an asymmetrical biodegradable poly-L-lactic acid (PLLA) polymer matrix releasing sirolimus at a dose of 1.4 μg/mm^2 stent surface, which degrades over a period of 12 to 24 months (16). The control stent (Xience Prime/Xpedition, Abbott Vascular, Santa Clara, California) is based on a cobalt-chromium platform with a strut thickness of 81 μm that releases everolimus from a durable polymer (poly-*n*-butyl-methacrylate and copolymer of vinylidene fluoride and hexafluoropropylene).

ENDPOINT DEFINITIONS AND FOLLOW-UP. The primary endpoint of the trial was target lesion failure, a composite of cardiac death, target vessel myocardial reinfarction, and clinically indicated target lesion revascularization as assessed at 12 months, and has been reported previously (12). Follow-up at 2 years was performed by use of a clinical visit or a

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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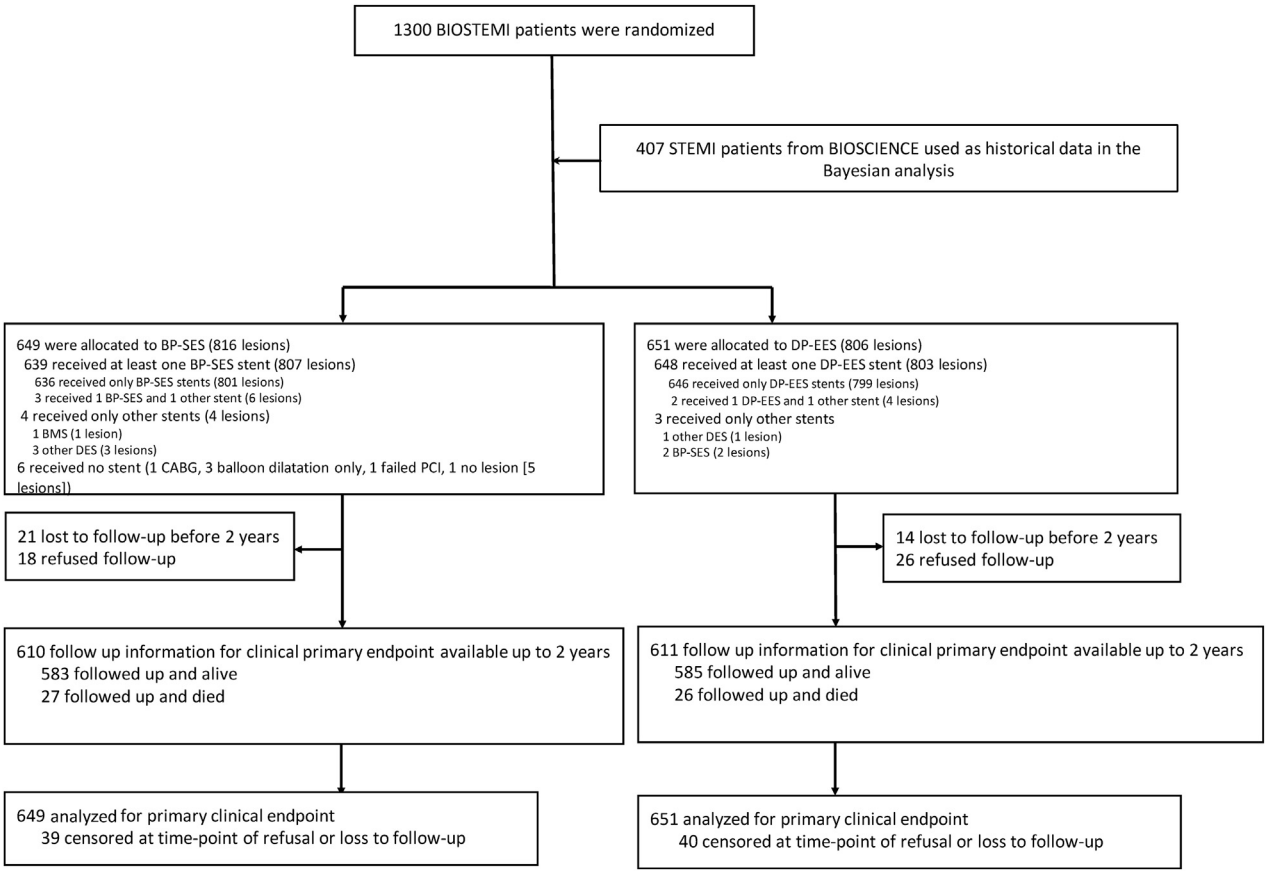
FIGURE 1 Patient Flow According to the Consolidated Standards of Reporting Trials Statement



BIOSCIENCE = Sirolimus-Eluting Stents With Biodegradable Polymer Versus an Everolimus-Eluting Stents; BIOSTEMI = 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; BMS = bare-metal stent(s); BP-SES = biodegradable-polymer sirolimus-eluting stent(s); CABG = coronary artery bypass grafting; DES = drug-eluting stent(s); DP-EES = durable-polymer everolimus-eluting stent(s).

standardized telephone interview. All definitions have been described previously (12). Any death, reinfarction, revascularization, stent thrombosis, cerebrovascular accident, and bleeding events were independently adjudicated by a clinical events committee blinded to treatment arm allocation.

STATISTICAL ANALYSIS. Consistent with the primary endpoint analysis at 1 year (12), we used Bayesian statistical methods with robustified priors incorporating historical data from 407 patients with acute STEMI who had been enrolled in the BIOSCIENCE (Sirolimus-Eluting Stents With Biodegradable Polymer Versus an Everolimus-Eluting Stents) trial (17) to assess the endpoint results at 2 years. All analyses were done with the individual subject as the unit of analysis and according to the intention-to-treat principle. Follow-up time was censored at the time of an event, loss to follow-up, or end of the planned follow-up at 2 years, whichever occurred first.

Bayesian log Poisson models incorporating historical data from the BIOSCIENCE trial were used for the purpose of the present analysis (17). We estimated the log incidence rates of all clinical endpoints from the BIOSCIENCE trial (n = 407) in each of the 2 study arms. We used Bayesian log Poisson models with minimally informative priors ($\mu = 0$, $\tau = 0.111$) and an offset term (log of the time at risk) to model the rates. Then we used the posterior mean and SD of the log incidence rates in BIOSCIENCE as informative priors for the analysis of BIOSTEMI endpoints at 2 years. For each endpoint, the robust prior was a 50:50 mixture between the historical informative prior (μ = posterior

TABLE 1 Medications at 2 Years of Follow-Up

	Biodegradable-Polymer Sirolimus-Eluting Stents (n = 590)	Durable-Polymer Everolimus-Eluting Stents (n = 603)	p Value
At 1-yr follow-up			
Aspirin	563 (95.4)	582 (96.5)	0.378
Clopidogrel	61 (10.3)	65 (10.8)	0.851
Prasugrel	179 (30.3)	202 (33.5)	0.264
Ticagrelor	268 (45.4)	255 (42.3)	0.294
Any dual-antiplatelet treatment	485 (82.2)	501 (83.1)	0.703
Oral anticoagulant agents	14 (2.4)	14 (2.3)	1.000
Novel oral anticoagulant agents	26 (4.4)	32 (5.3)	0.503
Any antithrombotic treatment	40 (6.8)	45 (7.5)	0.655
Statins	524 (88.8)	557 (92.4)	0.037
ACE inhibitors	354 (60.0)	372 (61.7)	0.554
Beta-blockers	417 (70.7)	444 (73.6)	0.272
At 2-yr follow-up			
Aspirin	535 (91.9)	536 (91.9)	1.000
Clopidogrel	15 (2.6)	23 (3.9)	0.248
Prasugrel	14 (2.4)	18 (3.1)	0.591
Ticagrelor	32 (5.5)	21 (3.6)	0.125
Any dual-antiplatelet treatment	49 (8.4)	51 (8.7)	0.917
Oral anticoagulant agents	16 (2.7)	17 (2.9)	1.000
Novel oral anticoagulant agents	26 (4.5)	39 (6.7)	0.125
Any antithrombotic treatment	42 (7.2)	55 (9.4)	0.203
Statins	513 (88.1)	506 (86.8)	0.536
ACE inhibitors	314 (54.0)	325 (55.7)	0.556
Beta-blockers	374 (64.3)	365 (62.6)	0.584

Values are n (%). 1 patient in the biodegradable-polymer sirolimus-eluting stent arm refused to give medication information.

ACE = angiotensin-converting enzyme.

mean [BIOSCIENCE], τ = posterior standard deviation [BIOSCIENCE]) and a vague prior ($\mu = 0$, $\tau = 0.111$) on the basis of Bernoulli distributions. By use of Bayesian log Poisson models with time at risk fitted as an offset, we estimated the incidence rate in both arms for all endpoints at 2 years. The use of robustified priors efficiently controlled the type I error rate by down-weighting the contribution of historical information from the BIOSCIENCE trial if it turned out to be inconsistent with the information collected in the BIOSTEMI trial. Rate ratios (RRs) are reported as the median of the Bayesian posterior distribution, and associated 95% Bayesian credible intervals are reported as the 2.5th and 97.5th percentiles of the Bayesian posterior distribution. Within the framework of this analysis, BCIs were interpreted similarly to frequentist confidence intervals (18).

We performed pre-specified subgroup analyses according to the presence or absence of diabetes and multivessel disease at baseline and post hoc subgroup analyses according to age, sex, body mass index, vessel diameter, lesion length, and renal failure. We also conducted a post hoc landmark analysis with the landmark set at 1 year for the primary endpoint and individual components of the primary endpoint. Subgroup and landmark analyses were conducted using the same approach as in the main analyses. For the subgroup analyses, robustified historical priors were constructed by analysis of the primary endpoint in each subgroup of patients in the BIOSCIENCE trial with acute STEMI. For the landmark analyses, robustified historical priors were constructed by analysis of the given endpoint in each period (before or after landmark) in the BIOSCIENCE trial with acute STEMI. These subgroup-specific or period-specific robustified historical priors were used as priors to analyze the data from the BIOSTEMI patients. For descriptive purposes, we derived Kaplan-Meier curves for patients included in the acute STEMI subgroup of the BIOSCIENCE trial and in the BIOSTEMI trial separately and combined. Full details including model equations and graphical representations of the priors are provided in the statistical analysis plan of the BIOSTEMI trial. Statistical analyses were conducted in R Studio version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria) and Stata 15 (StataCorp, College Station, Texas).

RESULTS

Between April 26, 2016, and March 9, 2018, 1,300 patients with 1,623 lesions were randomly allocated to treatment with BP-SES (n = 649, 817 lesions) or DP-EES (n = 651, 806 lesions). At 2 years, follow-up data were available for 610 of 649 patients receiving BP-SES (94.0%) and 611 of 651 patients receiving DP-EES (93.9%). The median duration of follow-up was 730 days (interquartile range: 710 to 730 days). The trial profile at completion of the BIOSTEMI trial at 2 years is displayed in **Figure 1**.

Baseline clinical, angiographic, and procedural characteristics have been reported previously (12). The mean age of patients was 62.2 ± 11.8 years in the experimental arm and 63.2 ± 11.8 years in the control arm; 136 patients (21%) treated with BP-SES and 174 patients (27%) treated with DP-EES were female.

Medications at 2-year follow-up are summarized in **Table 1** and showed no significant differences between groups. At 2 years, the composite endpoint, target lesion failure, occurred in 33 patients (5.1%) treated with BP-SES and in 53 patients (8.1%) treated with DP-EES (RR: 0.58; 95% BCI: 0.40 to 0.84; posterior probability of superiority = 0.998) (**Table 2, Central Illustration**). The difference remained statistically significant after the exclusion of historical information from the BIOSCIENCE trial (RR: 0.62; 95% BCI: 0.40 to 0.96; posterior probability of superiority = 0.985) (**Table 2** and Supplemental

TABLE 2 Clinical Outcomes at 2 Years of Follow-Up

	Biodegradable-Polymer Sirolimus-Eluting Stent (n = 649)	Durable-Polymer Everolimus-Eluting Stent (n = 651)	BIOSTEMI With Historical Data From BIOSCIENCE		BIOSTEMI Only	
			Rate Ratio (95% BCI)	Bayesian Posterior Probability	Rate Ratio (95% BCI)	Bayesian Posterior Probability
Target lesion failure*	33 (5.1)	53 (8.1)	0.58 (0.40–0.84)	0.998	0.62 (0.40–0.96)	0.985
Cardiac death	19 (2.9)	21 (3.2)	0.77 (0.44–1.35)	0.823	0.91 (0.49–1.69)	0.614
Target vessel MI	10 (1.5)	13 (2)	0.67 (0.33–1.34)	0.875	0.77 (0.33–1.75)	0.731
Clinically indicated TLR	16 (2.5)	33 (5.1)	0.52 (0.30–0.87)	0.993	0.48 (0.26–0.86)	0.993
All-cause death	27 (4.2)	25 (3.8)	1.02 (0.64–1.63)	0.471	1.09 (0.63–1.89)	0.376
MI	24 (3.7)	20 (3.1)	1.01 (0.59–1.71)	0.491	1.20 (0.67–2.20)	0.267
Q-wave	5 (0.8)	5 (0.8)	0.73 (0.25–2.02)	0.727	1.01 (0.30–3.39)	0.495
Non-Q-wave	19 (2.9)	16 (2.5)	1.06 (0.58–1.93)	0.423	1.20 (0.62–2.38)	0.295
Repeat revascularization	35 (5.4)	52 (8)	0.67 (0.46–0.96)	0.985	0.67 (0.43–1.02)	0.969
Any TLR	18 (2.8)	34 (5.2)	0.54 (0.32–0.89)	0.992	0.53 (0.29–0.92)	0.989
Any TVR	22 (3.4)	41 (6.3)	0.58 (0.37–0.89)	0.994	0.53 (0.31–0.88)	0.993
Clinically indicated TVR	20 (3.1)	40 (6.1)	0.56 (0.35–0.87)	0.995	0.50 (0.29–0.84)	0.996
Target vessel failure†	39 (6.0)	61 (9.4)	0.61 (0.43–0.86)	0.998	0.63 (0.42–0.94)	0.988
Death, MI, or any repeat revascularization‡	65 (10.0)	77 (11.8)	0.81 (0.61–1.08)	0.929	0.84 (0.60–1.17)	0.849
Definite stent thrombosis	9 (1.4)	12 (1.8)	0.73 (0.30–1.69)	0.771	0.76 (0.31–1.77)	0.739
Definite or probable stent thrombosis	13 (2.0)	15 (2.3)	0.72 (0.38–1.44)	0.837	0.87 (0.41–1.84)	0.642
BARC bleeding events types 3 to 5	26 (4.0)	24 (3.7)	0.92 (0.58–1.59)	0.625	1.10 (0.63–1.92)	0.372

Values are n (%), unless otherwise indicated. *Primary endpoint, defined as the composite of cardiac death, target vessel Q-wave or non-Q-wave MI, and clinically indicated TLR. †Defined as the composite of cardiac death, any Q-wave or non-Q-wave MI, and any TVR. ‡Patient-oriented composite endpoint.

BARC = Bleeding Academic Research Consortium; BCI = Bayesian credibility interval; MI = myocardial infarction; TLR = target lesion revascularization; TVR = target vessel revascularization.

Figure 1) and was driven by a lower incidence of clinically indicated target lesion revascularization in patients treated with BP-SES (2.5%) compared with DP-EES (5.1%) (RR: 0.52; 95% BCI: 0.30 to 0.87; posterior probability of superiority = 0.993).

The findings for target lesion failure were consistent across various patient subsets in a stratified analysis (**Figure 2**). Patients presenting with multivessel disease had a particular benefit of treatment with BP-SES with a significant interaction (Bayesian posterior probability = 0.994). We found a consistent treatment effect between BP-SES and DP-EES with respect to the occurrence of TLF at 2 years irrespective of stent diameter ≤3.0 mm (**Figure 2**) or ≤2.5 mm (Supplemental Table 1). Event rates of target lesion failure documented at each participating site are provided in Supplemental Table 2.

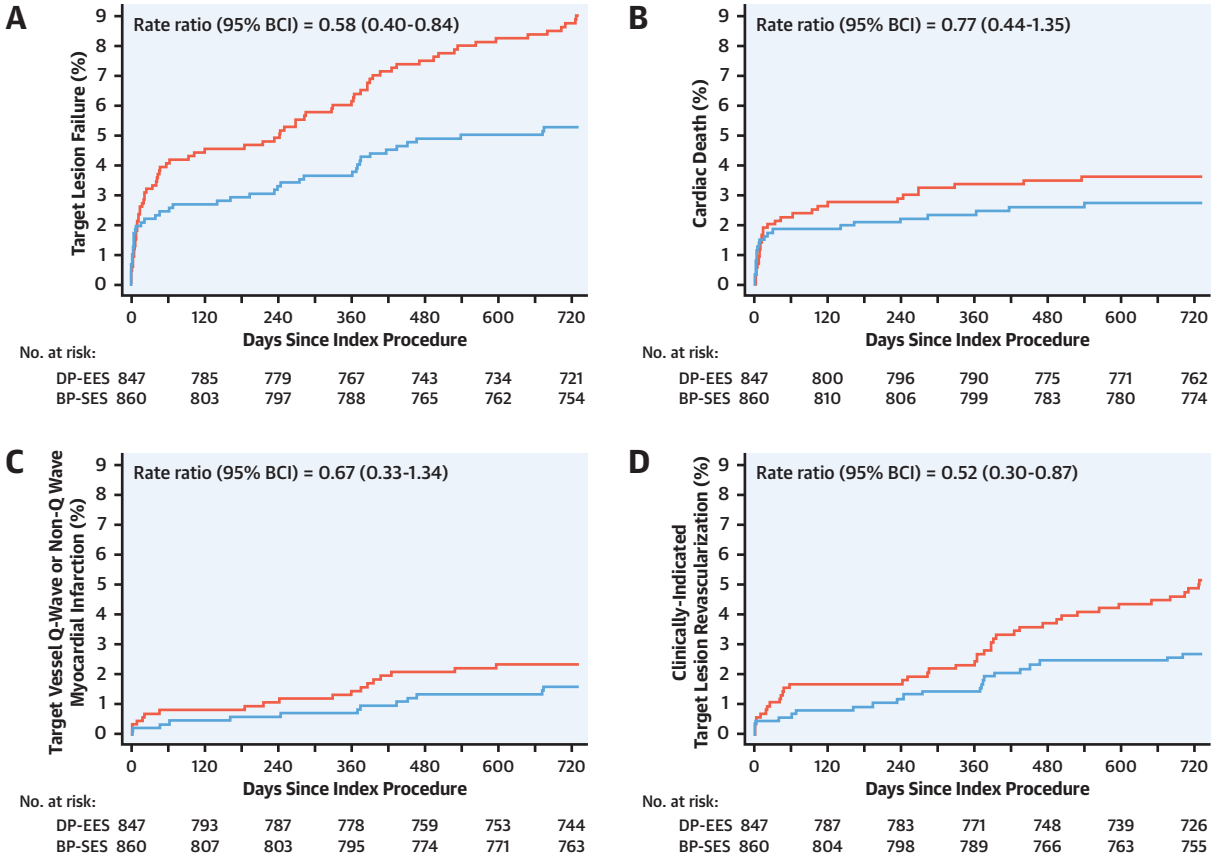
Landmark analyses of clinical endpoints with the landmark set at 1 year are provided in **Figure 3** and indicated no significant interaction between treatment effect and time.

DISCUSSION

The salient findings of the final 2-year outcomes of the BIOSTEMI trial can be summarized as follows. First, BP-SES were superior to DP-EES with regard to target lesion failure in patients undergoing primary PCI for STEMI. The difference was driven by lower rates of ischemia-driven target lesion revascularization in patients treated with BP-SES compared with DP-EES. The effect was robust and maintained after the exclusion of historical information from the BIOSCIENCE trial. And second, despite a significant difference in device-oriented clinical outcomes, there was no significant difference in the composite patient-oriented clinical outcome between patients treated with BP-SES and DP-EES or individual safety endpoints such as death, myocardial infarction, and stent thrombosis.

Different generations of DES have been defined by technical iterations translating into improved clinical outcomes. At 2 years, we found a significant reduction of target lesion failure in patients treated with BP-SES compared with DP-EES in patients undergoing PCI for STEMI, driven by lower rates of ischemia-driven target lesion revascularization in patients treated with BP-SES. The difference remained robust after the exclusion of historical information and was consistent across time with no significant interaction of treatment effect and time. Our findings are consistent with the 3-year data of the BIOFLOW-V (Safety and Effectiveness of the Orsiro Sirolimus Eluting Coronary Stent System in

CENTRAL ILLUSTRATION Time-to-Event Curves for the Composite Endpoint (Target Lesion Failure) and the Individual Components of the Primary Endpoint Up to 2 Years of Follow-Up



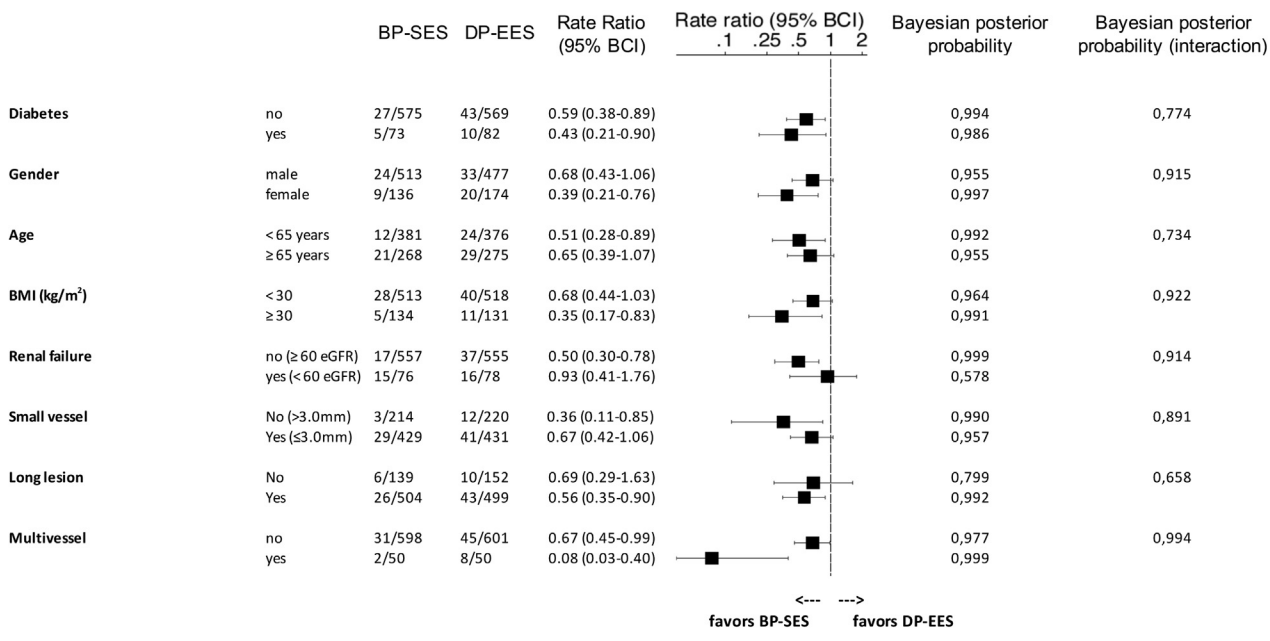
Pilgrim, T. et al. J Am Coll Cardiol Intv. 2021;14(6):639–48.

(A) Target lesion failure, **(B)** cardiac death, **(C)** target vessel myocardial infarction, and **(D)** clinically indicated target lesion revascularization. **Blue lines** indicate biodegradable-polymer sirolimus-eluting stents, and **red lines** indicate durable-polymer everolimus-eluting stents. BCI = Bayesian credible interval; BP-SES = biodegradable-polymer sirolimus-eluting stent(s); DP-EES = durable-polymer everolimus-eluting stent(s).

Subjects With Coronary Artery Lesions) trial, which showed a lower rate of target lesion failure in patients with chronic or acute coronary syndromes treated with BP-SES compared with DP-EES (11). In the latter study, the difference was driven by lower rates of both target vessel myocardial infarction and clinically driven target lesion revascularization in patients treated with BP-SES that emerged beyond 1 year after stent implantation. The detection of early reinfarction in patients presenting with myocardial infarction is challenging and may explain the absence of a difference between the 2 treatment arms in our trial.

In our analysis, patients with multivessel disease seemed to particularly benefit from treatment with BP-SES. The implantation of several stents in patients with multivessel disease may have potentiated the observed difference on a stent level. However, given the small number of patients and the small number of events, the finding may well be a play of chance. Potential mechanistic explanations for the documented differences in clinical outcomes resort to speculation. Two particular features of the experimental stent have been considered as an underlying cause of differences in outcomes. The PLLA polymer of the experimental stent degrades over a period of at least 12 to 24 months before exposing an amorphous hydrogen-rich, silicon-carbide layer designed to mitigate thrombogenicity and facilitate endothelialization. Although the composition of stent strut coverage constantly changes over time because of the degradation

FIGURE 2 Stratified Analyses of the Primary Endpoint (Target Lesion Failure) at 2 Years Across Major Subgroups



The following subgroups were pre-specified: diabetes and multivessel disease. All other subgroups were analyzed post hoc. Values are number of events/number of patients. Bayesian log Poisson models were used to estimate rate ratios and Bayesian credible intervals (BCIs). Bayesian posterior probability is the Bayesian posterior probability of a rate ratio <1.0 within each subgroup. Bayesian posterior probability of the interaction is the Bayesian posterior probability of a difference between the 2 subgroups. Small vessels were defined as stent diameter in any lesion ≤3.0 mm. Long lesions were defined as total stent length in any lesion ≥20 mm. Renal failure was defined as creatinine-estimated glomerular filtration rate (eGFR) <60 ml/min using the MDRD (Modification of Diet in Renal Disease) formula. BMI = body mass index; other abbreviations as in Figure 1.

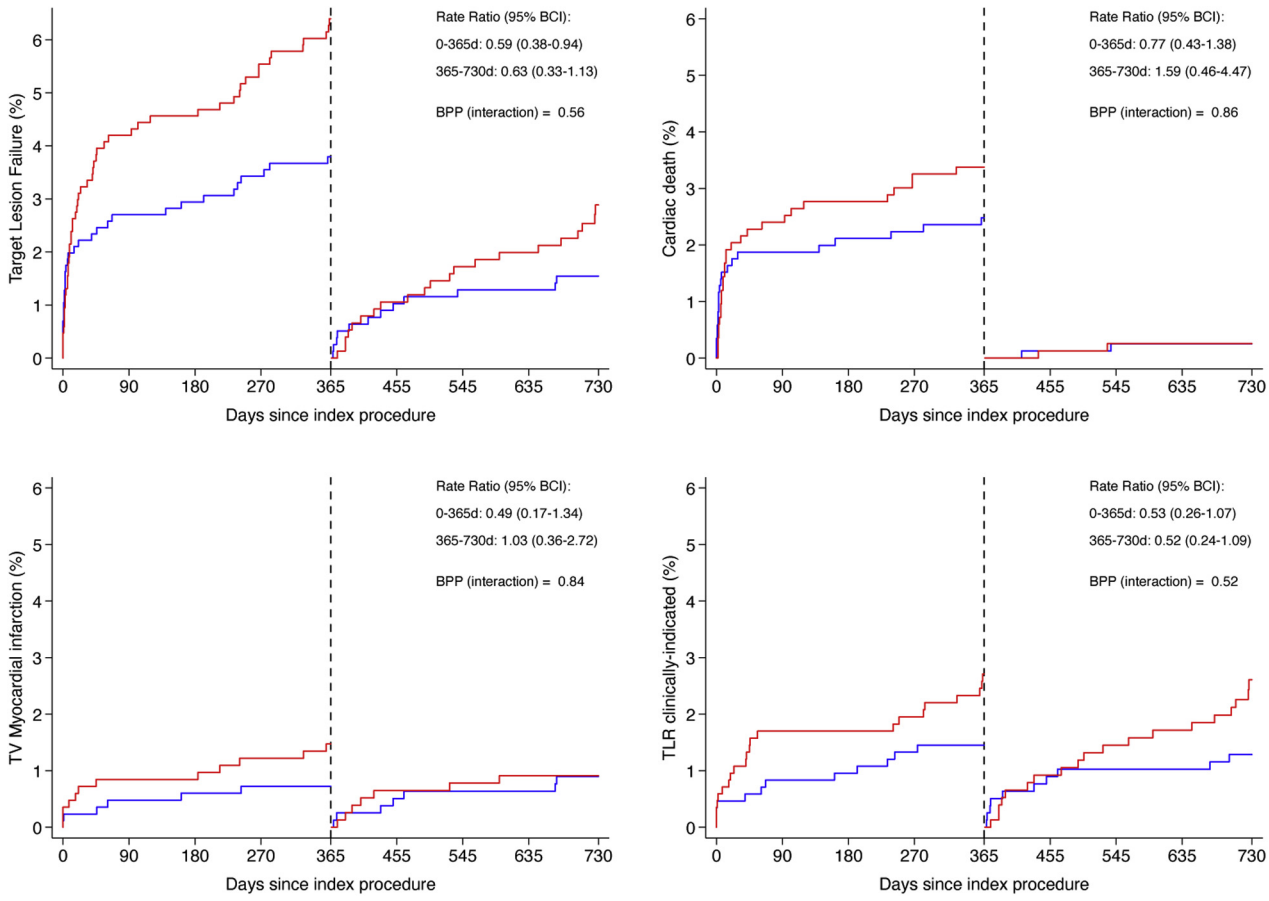
process of the PLLA polymer, the observed effect of a reduction of restenosis and target lesion revascularization remains constant over the follow-up duration of 2 years. An effect of strut coverage on vascular healing and neointimal hyperplasia appears likely but warrants confirmation in future studies including intravascular imaging.

At variance with the polymer matrix, the stent platform remains stable over time and may affect clinical outcomes. Evidence from a meta-analysis of 10 trials with different stent types suggested a significant effect of strut thickness on the risk for target lesion failure (19). However, it is important to note that strut thickness between the experimental stent and the control stent differs with stent diameters ≤3.0 mm (40%), whereas the strut thickness in larger stent diameters is comparable. A stratified analysis according to stent diameters with a cutoff of 3.0 mm as a surrogate to differentiate groups according to strut thickness showed no interaction of the treatment effect in the present study, nor in a previous one (6). Although strut thickness alone may not be the defining factor, the wider context of stent strut geometry affecting flexibility and radial strength may play a seminal role.

Interestingly, other newer generation DES also combining very thin stent platforms with biodegradable polymers were noninferior but not superior to DP-EES with regard to device-oriented primary composite clinical endpoints (20,21). Although these stents share some of the defining characteristics of newer generation DES, they differ with regard to others, such as drug-elution kinetics, time to complete degradation of the polymer, and stent strut geometry, but also with regard to compliance of the balloon used for stent delivery.

A final important finding of our study is that up to one-half of all events within 2 years after myocardial infarction were unrelated to the stent implanted during the index procedure. This finding is consistent with 5-year data from the COMFORTABLE AMI (Biolimus-Eluting Stents With Biodegradable Polymer Versus Bare-Metal Stents in Acute Myocardial Infarction) trial and the EXAMINATION (Everolimus-Eluting Stents Versus Bare-Metal Stents in ST-Segment Elevation Myocardial Infarction) trial

FIGURE 3 Time-to-Event Curves for Target Lesion Failure and Its Individual Components With a Landmark Set at 1 Year



(A) Target lesion failure, **(B)** cardiac death, **(C)** target vessel (TV) myocardial infarction, and **(D)** clinically indicated target lesion revascularization. **Blue lines** indicate biodegradable-polymer sirolimus-eluting stents, and **red lines** indicate durable-polymer everolimus-eluting stents. BCI = Bayesian credible interval; BPP = Bayesian posterior probability; TLR = target lesion revascularization.

and highlights the relative importance of secondary prevention to mitigate disease progression versus device performance (2,3).

Five-year data from the BIOSCIENCE trial suggested a higher all-cause mortality among patients treated with BP-SES compared with DP-EES (6). Although the difference in the BIOSCIENCE trial emerged as early as 2 years (22), we documented comparable rates of all-cause mortality between patients treated with BP-SES and DP-EES in the BIOSTEMI trial at 2 years.

Acute STEMI is the flagship indication for PCI. The BIOSTEMI trial is the first head-to-head comparison of 2 newer generation DES in patients undergoing primary PCI for acute myocardial infarction. In a field of stent comparisons dominated by noninferiority trials, the BIOSTEMI trial stands out by its superiority design, demonstrating a significant difference between 2 contemporary DES. A significant difference between newer generation DES may have clinically relevant implications for routine clinical practice.

STUDY LIMITATIONS. First, the study was powered to show a significant difference between the experimental arm and the control arm with regard to a composite clinical endpoint. Differences in individual clinical endpoints need to be interpreted with caution. However, in contrast to the primary endpoint data at 1 year, 2-year data show a significant difference between the 2 treatment arms not only using Bayesian statistics incorporating a historical

prior from the BIOSCIENCE trial but also when analyzed as an independent clinical trial.

Second, follow-up was limited to 2 years and did not expand well beyond the time of polymer degradation. Differences in the safety profile of the 2 stents may emerge only after discontinuation of dual-antiplatelet therapy. It is important to note that the low adherence to dual-antiplatelet treatment at 2 years in the BIOSTEMI trial, although reflecting current international guidelines, was considerably lower compared with previous STEMI trials (2,3).

Third, follow-up at 2 years was available in 94% of patients. Because provisional study inclusion was possible in unconscious patients by consent by proxy, the majority of patients refusing follow-up dropped out early.

And finally, study participants and physicians were not blinded to treatment allocation.

CONCLUSIONS

The final 2-year outcomes of the BIOSTEMI trial demonstrated superiority of BP-SES versus DP-EES with respect to target lesion failure in patients undergoing primary PCI for STEMI. The difference was robust after the exclusion of historical information from the BIOSCIENCE trial and driven by lower rates of target lesion revascularization in patients treated with BP-SES compared with DP-EES.

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PERSPECTIVES

WHAT IS KNOWN? The long-term clinical outcomes of patients with acute STEMI undergoing primary PCI are determined by the safety and efficacy profile of the newest generation DES.

WHAT IS NEW? BP-SES are superior to DP-EES with respect to target lesion failure at 2-year follow-up among patients undergoing primary for STEMI. The difference is driven by lower rates of ischemia-driven target lesion revascularization.

WHAT IS NEXT? The use of biodegradable-polymer DES may further improve clinical outcomes in patients with acute STEMI undergoing primary PCI.

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KEY WORDS acute myocardial infarction, biodegradable polymer, drug-eluting stent(s), thin strut

APPENDIX For supplemental tables and a figure, please see the online version of this paper.