

# openheart Durable versus biodegradable polymer drug-eluting stents in all-comers

Thierry Witzig, Serban Puricel, Alain Witzig, Pascal Meier, Diego Arroyo, Mario Togni, Stéphane Cook 

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## ABSTRACT

**Background** Drug-eluting stents (DESs) have become the gold standard of coronary angioplasty since their inception in 2002. Biodegradable polymer DESs (BP-DESs) have been postulated to be superior to durable polymer DESs (DP-DESs) due to their more biocompatible polymer. To date, no study has shown the superiority of one type of polymer compared with the other. We aimed to compare outcomes between a broad range of second-generation DP-DES and BP-DES in an all-comer population.

**Methods** We analysed data from 2824 patients who underwent percutaneous coronary intervention (PCI) with BP-DES or DP-DES in the Cardio-FR database. Of these, 2079 (1286 DP-DES and 793 BP-DES) met the inclusion and exclusion criteria and completed a 2-year follow-up: The primary outcome was the device-oriented composite endpoint (DOCE) of cardiac death, non-fatal target vessel myocardial infarction and target lesion revascularisation. **Results** Mean age was 67 years, with 75% male. Despite the DP-DES group exhibiting significantly higher rates of risk factors, such as arterial hypertension (63.1% vs 57.5%,  $p=0.010$ ), a greater average number of stents implanted per patient ( $1.72\pm0.92$  vs  $1.63\pm0.84$ ,  $p=0.040$ ), more acute coronary syndrome (ACS) (55.1% vs 50.2%,  $p=0.031$ ) and a higher rate of post-dilatation (42.2% vs 35.2%,  $p<0.001$ ), the rate of acute stent thrombosis (ST) was significantly lower than in the BP-DES group (HR 0.240, 95% CI 0.075 to 0.766;  $p=0.016$ ). This difference remained significant even after adjusting for covariates using a Cox proportional hazards model and performing a win ratio analysis (4.09, 95% CI 1.28 to 13.09;  $p=0.018$ ). Despite this increased rate of acute ST, there was no difference in DOCE (12.1% vs 14.5%, OR 1.218, 95% CI 0.926 to 1.600;  $p=0.158$ ) between the two groups up to 2 years.

**Conclusion** Clinical follow-up up to 2 years shows similar outcomes between BP-DES and DP-DES. The rate of acute ST is higher in patients with BP-DES.

## INTRODUCTION

Drug-eluting stents (DESs) have become the gold standard for percutaneous coronary intervention (PCI) since their inception in 2002. They have demonstrated their superiority by significantly reducing major adverse cardiac events (MACE), mainly revascularisation rates compared with bare metal stents.<sup>1 2</sup> However, the

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Biodegradable polymer drug-eluting stents (BP-DESs) were developed to improve long-term safety over durable polymer DESs (DP-DESs), but their clinical advantage remains debated.

## WHAT THIS STUDY ADDS

⇒ BP-DES and DP-DES showed similar 2-year clinical outcomes, but BP-DES had a higher risk of acute stent thrombosis.  
⇒ The benefits of BP-DES may be stent-specific rather than due to polymer degradation.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Stent selection should be based on patient-specific factors, not polymer type alone. The increased early thrombosis risk with BP-DES warrants further research into stent design and thrombogenicity.

polymer coating on DES, which delivers growth-inhibiting drugs, may trigger hypersensitivity reactions leading to neoatherosclerosis and late stent thrombosis (ST).<sup>3 4</sup> Because the polymers on biodegradable polymers DES (BP-DES) are degraded in a few months, it was thought that they might outperform traditional first-generation durable polymer DES (DP-DES). However, second-generation DP-DESs have been improved by incorporating more biocompatible polymers and thinner strut design. These developments have contributed to a substantial decrease in the rates of MACEs, ST and the need for revascularisation.<sup>2 5</sup> Thus, while BP-DESs have shown signs of superiority to the first-generation DP-DESs, this remains to be demonstrated when compared with second-generation DP-DESs.<sup>6 7</sup>

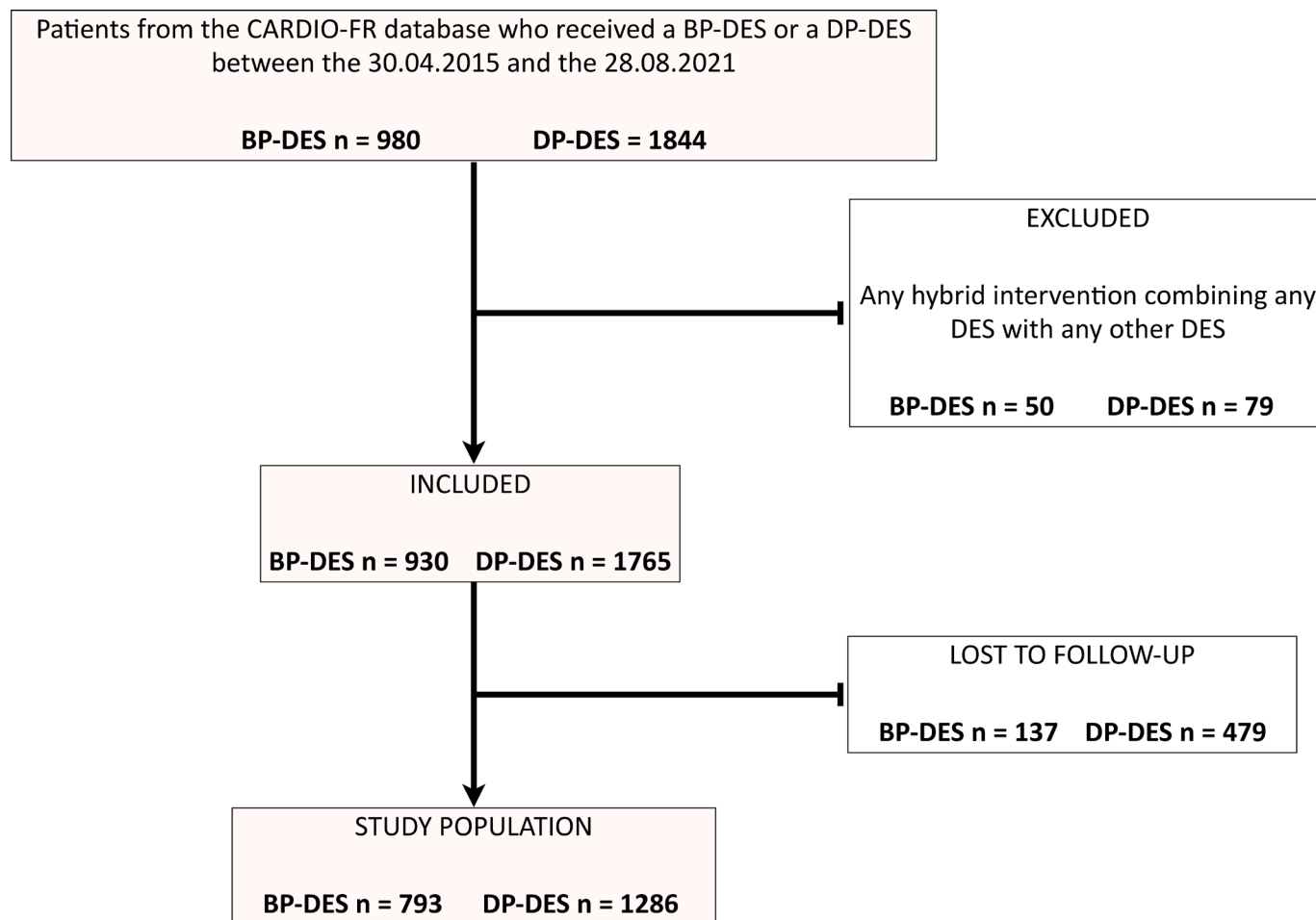
This study aims to compare outcomes between a broad range of second-generation DP-DES and BP-DES in an all-comer population to assess the similarity of outcomes between the two types of devices in a real-world setting.



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Cardiology, University & Hospital Fribourg, Fribourg, Switzerland

**Correspondence to**  
Professor Stéphane Cook;  
[stephane.cook@unifr.ch](mailto:stephane.cook@unifr.ch)



**Figure 1** Flowchart presenting the selection process. BP-DES, biodegradable polymer drug-eluting stent; DES, drug-eluting stent; DP-DES, durable polymer drug-eluting stent.

## METHODS

### Study population

The Cardio-FR registry at the University and Hospital Fribourg includes all patients aged 18+ admitted for PCI who provided written informed consent. It collects data on baseline characteristics, procedural details, in-hospital outcomes and annual clinical follow-ups via phone. The registry has been previously described.<sup>8 9</sup> Briefly, stent allocation is randomised using a preset distribution key based on the annual calendar. We included all patients undergoing PCI with second-generation DP-DES or BP-DES from May 2015 to August 2021, with a completed 2-year follow-up. Exclusion criteria were lack of consent, loss to follow-up or hybrid procedures involving different DES types.

The registry complies with the Helsinki Declaration and was approved by the local ethics committee (003-REP-CER-FR) and registered in ClinicalTrials.gov (NCT04185285).

### PCIs and medications

Procedures were performed via femoral or radial artery with a 6 French guiding catheter using standard techniques per guidelines. Intravascular imaging was at the operator's discretion. Preprocedural antithrombotic

therapy included aspirin (250–500 mg IV bolus if not pretreated, 100 mg/day thereafter) and unfractionated heparin (70 UI/kg); cangrelor and tirofiban were used at operator discretion. All patients received a loading dose of 600 mg clopidogrel, 180 mg ticagrelor or 60 mg prasugrel preprocedure or postprocedure. Long-term antiplatelet therapy included aspirin  $\geq$ 100 mg/day plus either clopidogrel 75 mg, ticagrelor 90 mg two times per day or prasugrel 10 mg for at least 3 months. In patients on oral anticoagulation, aspirin 100 mg was given for at least a week and clopidogrel 75 mg daily for 6 months. Other medications followed standard care. Patients were monitored for 4–12 hours in intermediate care and underwent biomarker and ECG assessments preprocedure and postprocedure.

### Study endpoints

The primary endpoint was device-oriented composite endpoint (DOCE), including cardiac death, non-fatal target vessel myocardial infarction (TVMI) and target lesion revascularisation (TLR). Secondary endpoints included patient-oriented composite endpoint (POCE), individual primary endpoints, all-cause mortality and ST incidence. Endpoints followed the Academic Research Consortium-2 (ARC-2) criteria.<sup>10</sup> Death was cardiac if

**Table 1** Baseline patient, lesion and procedural characteristics

| Patient characteristics                        | BP-DES<br>n=793 | DP-DES<br>n=1286 | P value |
|------------------------------------------------|-----------------|------------------|---------|
| Age, mean±SD                                   | 67.7±11.7       | 67.3±11.7        | 0.441   |
| Male, n (%)                                    | 597 (75.3)      | 963 (74.9)       | 0.838   |
| Body mass index, mean±SD                       | 27.3±4.9        | 27.4±4.6         | 0.625   |
| Diabetes mellitus, n (%)                       | 182 (23.0)      | 289 (22.5)       | 0.800   |
| Non-insulin dependent, n (%)                   | 135 (17.0)      | 197 (15.3)       | 0.303   |
| Insulin dependent, n (%)                       | 47 (5.9)        | 92 (7.2)         | 0.277   |
| Arterial hypertension, n (%)                   | 456 (57.5)      | 812 (63.1)       | 0.010   |
| Current smoker, n (%)                          | 198 (25.0)      | 349 (27.1)       | 0.275   |
| Family history, n (%)                          | 171 (21.6)      | 241 (18.7)       | 0.117   |
| Renal insufficiency, n (%)                     | 257 (32.4)      | 384 (29.9)       | 0.345   |
| Previous MI, n (%)                             | 115 (14.5)      | 174 (13.5)       | 0.534   |
| Previous PCI, n (%)                            | 237 (29.9)      | 336 (26.1)       | 0.062   |
| Previous CABG, n (%)                           | 75 (9.5)        | 114 (8.9)        | 0.648   |
| Multivessel PCI, n (%)                         | 86 (10.8)       | 140 (10.9)       | 0.976   |
| ACS, n (%)                                     | 398 (50.2)      | 708 (55.1)       | 0.031   |
| CCS, n (%)                                     | 376 (47.4)      | 549 (42.7)       | 0.035   |
| Staged PCI, n (%)                              | 19 (2.4)        | 29 (2.3)         | 0.835   |
| Number of vessels treated per patient, mean±SD | 1.13±0.36       | 1.13±0.35        | 0.463   |
| Number of lesions treated per patient, mean±SD | 1.39±0.69       | 1.43±0.68        | 0.062   |
| One lesion, n (%)                              | 558 (70.4)      | 849 (66.0)       | 0.040   |
| Two lesions, n (%)                             | 175 (22.1)      | 341 (26.5)       | 0.023   |
| Three lesions, n (%)                           | 50 (6.3)        | 79 (6.1)         | 0.882   |
| Four and more lesions, n (%)                   | 10 (1.3)        | 17 (1.3)         | 0.905   |
| <b>Lesion and procedural characteristics</b>   | n=1102          | n=1838           |         |
| Target vessel                                  |                 |                  |         |
| Left main, n (%)                               | 21 (2.6)        | 43 (3.3)         | 0.372   |
| Left anterior descending artery, n (%)         | 488 (61.5)      | 783 (60.9)       | 0.767   |
| Left circumflex, n (%)                         | 225 (28.4)      | 378 (29.4)       | 0.619   |
| Right coronary artery, n (%)                   | 349 (44.0)      | 600 (46.7)       | 0.239   |
| Saphenous vein graft, n (%)                    | 18 (2.2)        | 32 (2.5)         | 0.752   |
| Internal mammary artery, n (%)                 | 1 (0.1)         | 2 (0.2)          | 0.863   |
| Number of stents per patient, mean±SD          | 1.63±0.84       | 1.72±0.92        | 0.040   |
| Maximum stent diameter per lesion, mm±SD       | 2.97±0.49       | 3.00±0.54        | 0.495   |
| Total stent length per lesion, mm±SD           | 22.27±11.51     | 23.10±12.70      | 0.501   |
| Maximal inflation pressure, atm±SD             | 14.74±3.51      | 14.30±3.20       | 0.003   |
| Bifurcation treatment, n (%)                   | 179 (16.2)      | 341 (18.6)       | 0.112   |
| Predilatation, n (%)                           | 883 (80.1)      | 1408 (76.6)      | 0.026   |
| Post dilatation, n (%)                         | 388 (35.2)      | 775 (42.2)       | <0.001  |
| Shockwave, n (%)                               | 1 (0.1)         | 9 (0.5)          | 0.072   |

Continued

**Table 1** Continued

| Patient characteristics                                                                                                                                               | BP-DES<br>n=793 | DP-DES<br>n=1286 | P value |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|------------------|---------|
| ACS, acute coronary syndrome; CABG, coronary artery bypass graft; CCS, chronic coronary syndrome; MI, myocardial infarction; PCI, percutaneous coronary intervention. |                 |                  |         |

the cause was evident, unwitnessed or unknown. TLR was defined as repeat revascularisation within the stent or 5 mm proximal/distal. Target-vessel revascularisation was any revascularisation in the stented vessel, considered ischaemia-driven if associated with a positive functional study, stenosis  $\geq 50\%$  with ischaemic symptoms or stenosis  $\geq 70\%$  regardless of symptoms. Myocardial infarction (MI) was defined as new pathological Q waves ( $\geq 0.04$ s in  $\geq 2$  contiguous leads) or creatine phosphokinase elevation  $>2\times$  normal with specific elevation of myocardial enzymes, such as the CK-MB isoenzyme or troponin I.

ST was definite with angiographic thrombus confirmation and ischaemic signs or creatine kinase elevation  $>2\times$  normal within 48 hours. Probable ST included unexplained death within 30 days or MI in the target vessel area without angiographic confirmation. Possible ST included unexplained death beyond 30 days. ST was classified as acute ( $<24$  hours), subacute (24 hours–30 days), late (30 days–1 year) and very late ( $>1$  year).

### Statistical analysis

Categorical variables are reported as counts and percentages while continuous variables are reported as mean and SD. Normality was assessed by the computation of Q-Q plots and the Shapiro-Wilk test. Continuous variables were analysed using the Student's t-test or the Wilcoxon rank-sum test per distribution. Categorical variables were compared using the  $\chi^2$  or Fisher exact test as appropriate. Survival data were analysed with the log-rank test. The proportional hazard condition was assessed with Kaplan Meier plots as well as ln/ln curves. Primary outcomes were also analysed using win ratio and Cox regression or binary logistic regression as appropriate. All statistical analyses except win ratios were performed using SPSS version 29 (SPSS, Chicago, Illinois, USA) at a 2-tailed significance level of  $\alpha=0.05$ . Win ratios were performed with R V.4.4.1 (R Core Team, Vienna, Austria) using the WinRatio package<sup>11</sup> at a 2-tailed significance level of  $\alpha=0.05$ .

## RESULTS

### Population

During the inclusion period, 2824 patients were registered in the Cardio-FR registry. Of these, 2695 met the inclusion and exclusion criteria, but 616 patients were lost to follow-up. Consequently, the study population comprised 2079 patients, divided into two groups: 793 patients in the BP-DES group and 1286 patients in the DP-DES group. The flowchart is shown in figure 1.

**Table 2** Studied stent characteristics and patient distribution across groups

| Stent name       | Polymer type  | Coating   | Alloy     | Strut size (µm) | Drug        | Number of patients, per cent of study group |
|------------------|---------------|-----------|-----------|-----------------|-------------|---------------------------------------------|
| Synergy II       | Biodegradable | Abluminal | PtCr      | 74              | Everolimus  | 561 (70.1)                                  |
| Orsiro           | Biodegradable | Conformal | CoCr      | 60              | Sirolimus   | 158 (19.9)                                  |
| Biomatrix Alpha  | Biodegradable | Abluminal | CoCr      | 84              | Biolimus    | 62 (7.8)                                    |
| Firehawk         | Biodegradable | Abluminal | CoCr      | 86              | Sirolimus   | 6 (0.8)                                     |
| Supraflex Cruz   | Biodegradable | Conformal | CoCr      | 60              | Sirolimus   | 5 (0.6)                                     |
| Ultimaster       | Biodegradable | Abluminal | CoCr      | 80              | Sirolimus   | 1 (0.1)                                     |
| Resolute Onyx    | Durable       | Conformal | Pt-Ir, Co | 81              | Zotarolimus | 856 (66.2)                                  |
| Xience Alpine    | Durable       | Conformal | CoCr      | 81              | Everolimus  | 265 (20.6)                                  |
| Xience Sierra    | Durable       | Conformal | CoCr      | 81              | Everolimus  | 156 (12.1)                                  |
| Xience Xpedition | Durable       | Conformal | CoCr      | 81              | Everolimus  | 9 (0.7)                                     |

Alloy composition: CoCr is for Cobalt-Chromium; PtCr, for Platinum-Chromium and Pt-Ir/Co, for Platinum-Iridium-Cobalt.

The presentation in terms of acute or chronic coronary syndromes is summarised in online supplemental table S1.

### Baseline patient, lesion and procedural characteristics

The DP-DES group exhibited significantly higher rates of arterial hypertension (63.1% vs 57.5%,  $p=0.010$ ), a greater average number of stents implanted per patient ( $1.72\pm0.92$  vs  $1.63\pm0.84$ ,  $p=0.040$ ), a higher proportion of patients with dual lesions (26.5% vs 22.1%,  $p=0.023$ ) and more frequent use of postdilatation (42.2% vs 35.2%,  $p<0.001$ ). Conversely, the BP-DES group demonstrated a significantly higher maximal inflation pressure ( $14.7\pm3.5$  vs  $14.3\pm3.2$  ATM,  $p=0.003$ ), higher rates of predilatation (80.1% vs 76.6%,  $p=0.026$ ) and a numerical, though not statistically significant, difference in the number of patients who had undergone a previous PCI (29.9% vs 26.1%,  $p=0.062$ ). The two groups also differed significantly in presentation, with more acute coronary syndrome (ACS) cases (55.1% vs 50.2%,  $p=0.031$ ) in the DP-DES group and more chronic coronary syndrome cases (47.4% vs 42.7%,  $p=0.035$ ) in the BP-DES group (table 1).

### Studied stent characteristics

Table 2 presents the stents included in this study along with their key characteristics. The BP-DES group primarily comprised the Synergy II BP-DES (70.1%), whereas the DP-DES group mainly consisted of the Resolute Onyx DP-DES (66.2%).

### Clinical outcomes

Table 3 and figure 2 illustrate clinical outcomes at 1-month, 1-year, and 2-year follow-up. At 1 month, treatment with BP-DES was associated with significantly higher rates of MI (7.6% vs 5.0%,  $p=0.015$ ), a greater need for ischaemia-driven revascularisation (3.7% vs 2.0%,  $p=0.024$ ) and a higher incidence of definite/probable ST (1.8% vs 0.8%,  $p=0.040$ ). However, these differences were no longer observed at longer follow-up, and

the occurrence of all events was similar between the two groups up to 2 years: the overall DOCE rate was comparable between the BP-DES and DP-DES groups (12.1% vs 14.5%,  $p=0.132$ ), as was the incidence of TLR (6.3% vs 7.7%,  $p=0.238$ ).

A subanalysis of the timing of ST revealed a notably higher incidence of acute ST in the BP-DES group (1.3% vs 0.3%,  $p=0.010$ ) online supplemental table S2. The antiplatelet status, lesion and patient characteristics, as well as the use of intravascular imaging were similar between groups.

Multivariate analyses to adjust for potential confounders were also conducted. A Cox regression confirmed the significantly higher rate of acute ST (HR 0.240, 95% CI 0.075 to 0.766;  $p=0.016$ ) in the BP-DES group but a similar rate of ST (HR 0.520, 95% CI 0.259 to 1.043;  $p=0.065$ ) between the two groups at 2-year follow-up. Similarly, a binary logistic regression corroborated the comparable incidence of DOCE (OR 1.218, 95% CI 0.926 to 1.600;  $p=0.158$ ) and POCE (OR 1.043, 95% CI 0.855 to 1.274;  $p=0.677$ ) between the two groups at 2-year follow-up (online supplemental table S3).

Finally, an exploratory win ratio analysis was performed, further supporting the higher rate of acute ST (win ratio 4.09, 95% CI 1.28 to 13.09;  $p=0.018$ ) in the BP-DES group, while showing a similar incidence of ST (win ratio 1.86, 95% CI 0.93 to 3.73;  $p=0.081$ ) between the two groups at 2-year follow-up.

### DISCUSSION

In this registry-based study, we observed no significant differences in clinical outcomes between the two groups after 2 years. There was, however, an increased rate of acute ST in the BP-DES group.

The overall event rates reported in this study were comparable to those of similar studies that included an all-comer population and a real-world setting approach, such as those by Zanchin *et al*<sup>12</sup> or the BIOSCIENCE (A

**Table 3** Clinical outcomes

| 1-month follow-up                            | BP-DES<br>n=793 | DP-DES<br>n=1286 | P value |
|----------------------------------------------|-----------------|------------------|---------|
| DOCE, n (%)                                  | 31 (3.9)        | 50 (3.9)         | 0.981   |
| Cardiac death, n (%)                         | 13 (1.6)        | 31 (2.4)         | 0.235   |
| TVMI, n (%)                                  | 13 (1.6)        | 17 (1.3)         | 0.555   |
| TLR, n (%)                                   | 15 (1.9)        | 16 (1.2)         | 0.237   |
| POCE, n (%)                                  | 92 (11.6)       | 118 (9.2)        | 0.073   |
| Death, n (%)                                 | 16 (2.0)        | 38 (3.0)         | 0.191   |
| MI, n (%)                                    | 60 (7.6)        | 64 (5.0)         | 0.015   |
| Ischaemia-driven<br>revascularisation, n (%) | 29 (3.7)        | 26 (2.0)         | 0.024   |
| Stroke, n (%)                                | 4 (0.5)         | 11 (0.9)         | 0.359   |
| Definite/probable ST, n (%)                  | 14 (1.8)        | 10 (0.8)         | 0.040   |
| 1-year follow-up                             |                 |                  |         |
| DOCE, n (%)                                  | 64 (8.1)        | 119 (9.3)        | 0.357   |
| Cardiac death, n (%)                         | 28 (3.5)        | 55 (4.3)         | 0.394   |
| TVMI, n (%)                                  | 18 (2.3)        | 32 (2.5)         | 0.756   |
| TLR, n (%)                                   | 32 (4.0)        | 59 (4.6)         | 0.554   |
| POCE, n (%)                                  | 163 (20.6)      | 265 (20.6)       | 0.938   |
| Death, n (%)                                 | 36 (4.5)        | 80 (6.2)         | 0.103   |
| MI, n (%)                                    | 75 (9.5)        | 101 (7.9)        | 0.191   |
| Ischaemia-driven<br>revascularisation, n (%) | 73 (9.2)        | 125 (9.7)        | 0.729   |
| Stroke, n (%)                                | 17 (2.1)        | 17 (1.3)         | 0.153   |
| Definite/probable ST, n (%)                  | 15 (1.9)        | 12 (0.9)         | 0.060   |
| 2-year follow-up                             |                 |                  |         |
| DOCE, n (%)                                  | 96 (12.1)       | 186 (14.5)       | 0.132   |
| Cardiac death, n (%)                         | 42 (5.3)        | 79 (6.1)         | 0.416   |
| TVMI, n (%)                                  | 22 (2.8)        | 47 (3.7)         | 0.282   |
| TLR, n (%)                                   | 50 (6.3)        | 99 (7.7)         | 0.238   |
| POCE, n (%)                                  | 235 (29.6)      | 389 (30.2)       | 0.832   |
| Death, n (%)                                 | 61 (7.7)        | 127 (9.9)        | 0.088   |
| MI, n (%)                                    | 87 (11.0)       | 130 (10.1)       | 0.500   |
| Ischaemia-driven<br>revascularisation, n (%) | 113 (14.2)      | 200 (15.6)       | 0.446   |
| Stroke, n (%)                                | 28 (3.5)        | 30 (2.3)         | 0.107   |
| Definite/probable ST, n (%)                  | 17 (2.1)        | 15 (1.2)         | 0.078   |

BP-DES, biodegradable polymer drug-eluting stent; DOCE, device-oriented composite endpoint; DP-DES, durable polymer drug-eluting stent; MI, myocardial infarction; POCE, patient-oriented composite endpoint; ST, stent thrombosis; TLR, target lesion revascularisation; TVMI, target vessel myocardial infarction.

Randomized Comparison of a Sirolimus-eluting Stent With Biodegradable Polymer Versus an Everolimus-eluting Stent With a Durable Polymer for Percutaneous Coronary Revascularization)<sup>13</sup> randomised controlled trial (RCT). However, they remained higher than in the registry-based study by De Araujo and colleagues,<sup>14</sup> which applied propensity score matching to select a population with more favourable risk factors.

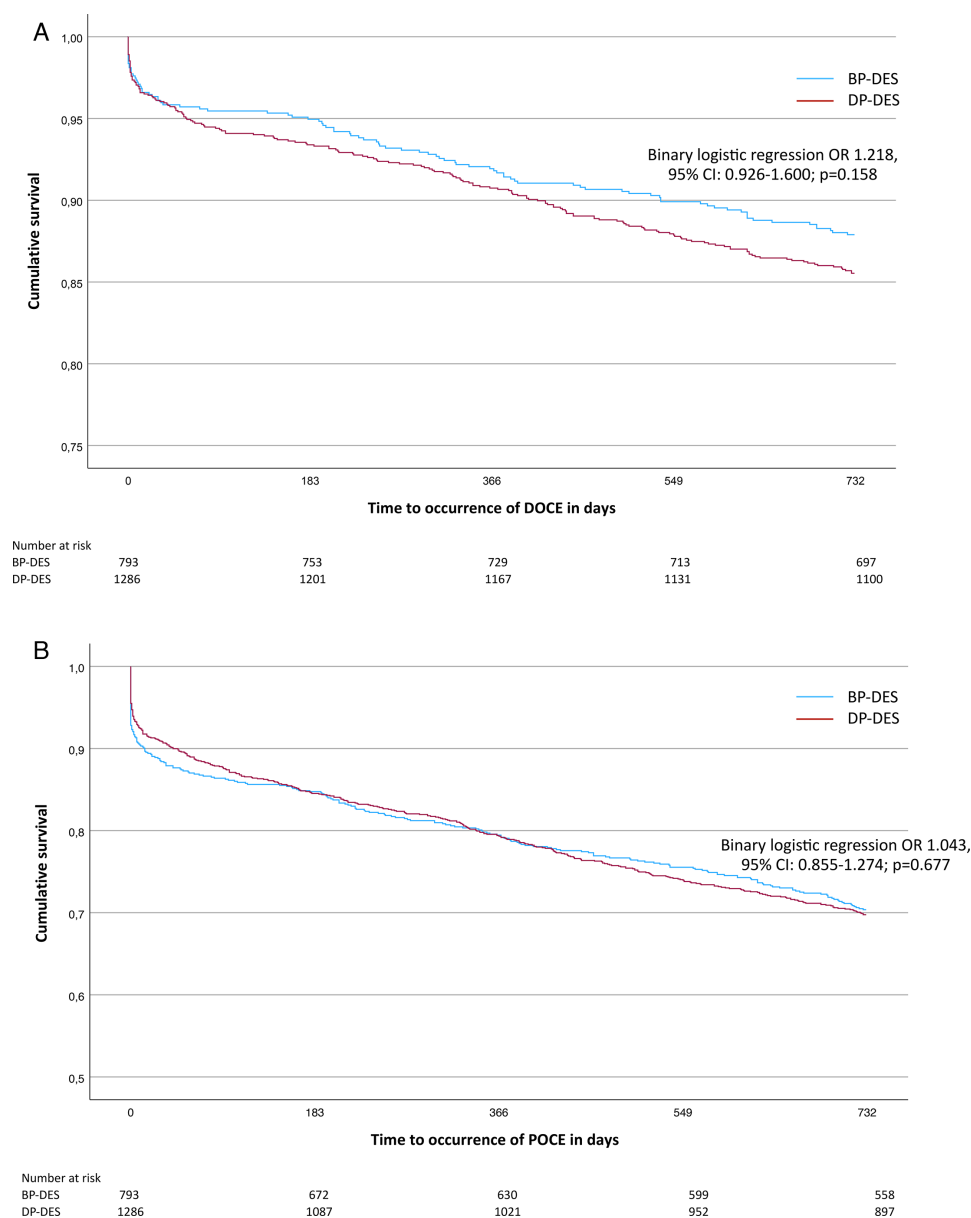
### No net clinical benefit of BP-DES over DP-DES

This study found no significant difference in cumulative endpoints between the two groups. The BP-DES cohort consisted of 70% Synergy II, 20% Orsiro and 8% Biomatrix Alpha. This distribution may have influenced the results, as the most favourable studies supporting BP-DES over DP-DES were conducted with Orsiro.

Indeed, large-scale RCTs with 5-year follow-ups, such as BIOSCIENCE (A Randomized Comparison of a Sirolimus-eluting Stent With Biodegradable Polymer Versus an Everolimus-eluting Stent With a Durable Polymer for Percutaneous Coronary Revascularization),<sup>13</sup> BIO-RESORT (Comparison of Biodegradable Polymer and Durable Polymer Drug-Eluting Stents in an All Comers Population),<sup>15</sup> and COMPARE II (Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent),<sup>16</sup> have shown no significant differences between BP-DES and DP-DES. Similarly, the HOST REDUCE POLYTECH ACS RCT (Harmonizing Optimal Strategy for Treatment of coronary artery diseases—comparison of REDUction of prasugrEl dose or POLYmer TECHnology in ACS patients)<sup>17</sup> reported comparable patient-oriented outcomes between DP-DES and BP-DES after 3 years in an ACS population. However, treatment with BP-DES was associated with a higher risk of device-oriented endpoints (HR 0.73, 95% CI 0.57 to 0.95;  $p=0.020$ ), primarily due to an increased rate of TLR. This heightened risk was attributed to polymer degradation, as the higher incidence of device-oriented endpoints was only observed during the polymer degradation phase (8–16 months).

Conversely, BIOFLOW V (Ultrathin, bioresorbable polymer sirolimus-eluting stents versus thin, durable polymer everolimus-eluting stents in patients undergoing coronary revascularisation)<sup>18</sup> reported significantly lower rates of TVMI (6.6% vs 10.3%,  $p=0.015$ ) and late/very late ST (0.3% vs 1.6%,  $p=0.021$ ) in the BP-DES group compared with the Xience DP-DES. Similarly, the BIOSTEMI (Biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents in patients with ST-segment elevation myocardial infarction)<sup>19</sup> trial also noted a significant reduction in target lesion failure (TLF) in favour of BP-DES versus DP-DES ( $\Delta-3\%$ ; RR 0.70, 95% CI 0.51 to 0.95) in patients with acute ST-segment elevation myocardial infarction. Both studies were conducted with the Orsiro BP-DES.

A 2017 meta-analysis by El-Hayek *et al.*,<sup>7</sup> including 20 000 patients over 26 months, as well as longer 5-year follow-up meta-analyses by Kobayashi *et al.*<sup>20</sup> and Lou *et al.*,<sup>21</sup> found no significant differences between BP-DES and DP-DES. However, Zhu *et al.*<sup>22</sup> and Monjur *et al.*<sup>23</sup> reported a significant reduction in MI risk (RR 0.78, 95% CI 0.62 to 0.98) and TLF risk (OR 0.82, 95% CI 0.69 to 0.98;  $p=0.037$ ) in the Orsiro BP-DES group. Furthermore, a network meta-analysis by Taglieri *et al.*<sup>24</sup> involving 99 039 patients identified the Orsiro BP-DES as potentially the DES with the lowest DOCE after 5 years, while



**Figure 2** Kaplan-Meier survival free from DOCE (panel A) and POCE (panel B) at 2-year follow-up. BP-DES, biodegradable polymer drug-eluting stent; DOCE, device-oriented composite endpoint; DP-DES, durable polymer drug-eluting stent; POCE, patient-oriented composite endpoint.

reporting no significant differences between other BP-DES and DP-DES.

These findings suggest that the overall benefits of BP-DES may be primarily driven by Orsiro and that the predominance of Synergy II in the BP-DES cohort analysed in this study may have influenced the observed results. However, overall, the differences between the two DES classes remain marginal.

### Increased early ST with BP-DES compared with DP-DES

Early ST is influenced by multiple factors, including patient characteristics (eg, diabetes mellitus), clinical setting (eg, ACS), procedural factors (eg, malapposition, malexpansion, stent length) and stent-related properties.<sup>25</sup> The use of BP-DES has been theoretically associated with an increased prothrombotic risk during the polymer

resorption phase, due to its proinflammatory properties. Indeed, experimental models have shown that conformal permanent polymer stents exhibit lower platelet accumulation under single antiplatelet therapy compared with abluminal bioabsorbable polymer-coated stents such as Synergy, which was the most commonly used BP-DES in this study.<sup>26 27</sup>

Consistently, despite the DP-DES group having a higher proportion of ACS cases and more stents per patient, the rate of acute ST was lower in the DP-DES group than in the BP-DES group in our study. The literature remains divided on this matter, with some studies reporting higher acute ST rates with BP-DES like the one by Zanchin *et al*<sup>12</sup> (1.2% vs 0.3%; p=0.03) and others reporting higher unspecified ST rates with BP-DES like the MAUDE

registry<sup>28</sup> (10.0% vs 2.6%,  $p<0.001$ ), while others, like the BIOFLOW V<sup>18</sup> study reported lower late/very late ST rates (0.3% vs 1.6%,  $p=0.021$ ) with BP-DES or the study from de Araujo and colleagues<sup>14</sup> which reported equal unspecified ST rates between DP-DES and BP-DES (1.4% vs 1.4%  $p=1.000$ ).

A possible explanation for this discrepancy is the specific stent used. In this registry, the most frequently implanted BP-DES was Synergy II, which may exhibit prothrombotic characteristics compared with other BP-DES, such as Orsiro<sup>18</sup> or Inspiron.<sup>14</sup> Supporting this hypothesis, an analysis of Synergy stent data from the POEM (Performance of Bioresorbable Polymer-Coated Everolimus-Eluting Synergy Stent in Patients at HBR Undergoing Percutaneous Coronary Revascularization Followed by 1-Month Dual Antiplatelet Therapy) trial,<sup>29</sup> which evaluated 1-month dual antiplatelet therapy discontinuation, reported a higher ST rate (0.94%) (14) than comparable DP-DES cohorts (eg, 0.3% in Xience 28).<sup>30</sup> This may be attributable to the proinflammatory degradation of Synergy's polymer or from the more thrombogenic abluminal coating design.<sup>31</sup>

Finally, there is no reason to assume there was any difference in the implantation technique between the two groups in this study, and the statistical analysis revealed comparable antiaggregation status and lesion and patient characteristics in ST patients. It should be noted that STs are not systematically confirmed by intravascular imaging and that this significant difference in acute ST rates could be a chance finding resulting from the number of analyses from this current study. In any case, these findings should be interpreted with caution, as neither the other trials reporting ST rates<sup>12 14 18 28</sup> nor this study were sufficiently powered to detect such rare events effectively.

## STUDY LIMITATIONS

This open-label single centre study is based on a registry that uses a non-randomised population. However, stent allocation was determined randomly and prospectively, which helped mitigate methodological biases. Nevertheless, differences in baseline characteristics between the groups persist, and this issue has been rigorously addressed in our analyses to minimise the impact on internal validity.

Moreover, the broad range of DES included in this study may also influence results due to other stent factors than polymer, such as differences in strut thickness, polymer degradation kinetics or antiproliferative drugs. The lack of an independent event adjudication committee also threatens internal validity.

Finally, while the study size is sufficient for the analysis of composite endpoints, it remains limited for detecting rare events, such as ST. Low rates of events also severely restrain multivariate analyses by restricting the number of covariables of the model. As such, the differences observed in the analysis of ST may still reflect a type II

error, even if a similar study arrives at the same conclusions. Only meta-analyses and large registries (over 15 000 patients) could specifically address this question.

## CONCLUSION

Clinical follow-up up to 2 years for patients treated with BP-DES or DP-DES shows similar outcomes. While the rate of acute ST remains low across both groups, it appears to be slightly higher in patients with BP-DES.

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## ORCID iD

Stéphane Cook <http://orcid.org/0000-0003-1221-2978>

## REFERENCES

- Piccolo R, Bonaa KH, Efthimiou O, *et al*. Drug-eluting or bare-metal stents for percutaneous coronary intervention: a systematic review and individual patient data meta-analysis of randomised clinical trials. *The Lancet* 2019;393:2503–10.
- Madhavan MV, Kirtane AJ, Redfors B, *et al*. Stent-Related Adverse Events >1 Year After Percutaneous Coronary Intervention. *J Am Coll Cardiol* 2020;75:590–604.
- Nakazawa G, Otsuka F, Nakano M, *et al*. The pathology of neoatherosclerosis in human coronary implants bare-metal and drug-eluting stents. *J Am Coll Cardiol* 2011;57:1314–22.

- 4 Nebeker JR, Virmani R, Bennett CL, *et al.* Hypersensitivity cases associated with drug-eluting coronary stents: a review of available cases from the Research on Adverse Drug Events and Reports (RADAR) project. *J Am Coll Cardiol* 2006;47:175–81.
- 5 Palmerini T, Biondi-Zoccai G, Della Riva D, *et al.* Clinical outcomes with bioabsorbable polymer- versus durable polymer-based drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *J Am Coll Cardiol* 2014;63:299–307.
- 6 Serruys PW, Farooq V, Kalesan B, *et al.* Improved Safety and Reduction in Stent Thrombosis Associated With Biodegradable Polymer-Based Biolimus-Eluting Stents Versus Durable Polymer-Based Sirolimus-Eluting Stents in Patients With Coronary Artery Disease. *JACC: Cardiovascular Interventions* 2013;6:777–89.
- 7 El-Hayek G, Bangalore S, Casso Dominguez A, *et al.* Meta-Analysis of Randomized Clinical Trials Comparing Biodegradable Polymer Drug-Eluting Stent to Second-Generation Durable Polymer Drug-Eluting Stents. *JACC Cardiovasc Interv* 2017;10:462–73.
- 8 Schukraft S, Huwiler T, Ottiger-Mankaka C, *et al.* Bleeding Risk Profile in Patients on Oral Anticoagulation Undergoing Percutaneous Coronary Interventions: A Prospective 24 Months Cohort Study. *Front Cardiovasc Med* 2021;8:589426.
- 9 Volet C, Puricel S, Cook ST, *et al.* Proximal optimization technique and percutaneous coronary intervention for left main disease: POTENTIAL-LM. *Catheter Cardiovasc Interv* 2024;103:417–24.
- 10 Garcia-Garcia HM, McFadden EP, Farb A, *et al.* Standardized End Point Definitions for Coronary Intervention Trials: The Academic Research Consortium-2 Consensus Document. *Circulation* 2018;137:2635–50.
- 11 Duarte K, Ferreira JP. WinRatio: win ratio for prioritized outcomes and 95% confidence interval. R package version 1.0. 2020. Available: <https://CRAN.R-project.org/package=WinRatio>
- 12 Zanchin C, Ueki Y, Zanchin T, *et al.* Everolimus-Eluting Biodegradable Polymer Versus Everolimus-Eluting Durable Polymer Stent for Coronary Revascularization in Routine Clinical Practice. *JACC Cardiovasc Interv* 2019;12:1665–75.
- 13 Pilgrim T, Piccolo R, Heg D, *et al.* Ultrathin-strut, biodegradable-polymer, sirolimus-eluting stents versus thin-strut, durable-polymer, everolimus-eluting stents for percutaneous coronary revascularisation: 5-year outcomes of the BIOSCIENCE randomised trial. *The Lancet* 2018;392:737–46.
- 14 Araujo GN, Machado GP, Moura M, *et al.* Real-World Assessment of an Ultrathin Strut, Sirolimus-Eluting Stent in Patients with ST-Elevation Myocardial Infarction Submitted to Primary Percutaneous Coronary Intervention (INSTEMI Registry). *Arq Bras Cardiol* 2023;120.
- 15 Ploumen EH, Pinxterhuis TH, Buiten RA, *et al.* Final 5-Year Report of the Randomized BIO-RESORT Trial Comparing 3 Contemporary Drug-Eluting Stents in All-Corers. *J Am Heart Assoc* 2022;11:e026041.
- 16 Vlachojannis GJ, Smits PC, Hofma SH, *et al.* Biodegradable Polymer Biolimus-Eluting Stents Versus Durable Polymer Everolimus-Eluting Stents in Patients With Coronary Artery Disease: Final 5-Year Report From the COMPARE II Trial (Abluminal Biodegradable Polymer Biolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Stent). *JACC Cardiovasc Interv* 2017;10:1215–21.
- 17 Kang J, Hwang D, Park KW, *et al.* Durable-polymer versus biodegradable-polymer drug-eluting stents in acute coronary syndromes: three-year outcomes of the HOST REDUCE POLYTECH RCT Trial. *EuroIntervention* 2024;20:e750–9.
- 18 Kandzari DE, Koolen JJ, Doros G, *et al.* Ultrathin Bioresorbable Polymer Sirolimus-Eluting Stents Versus Durable Polymer Everolimus-Eluting Stents: BIOFLOW V Final 5-Year Outcomes. *JACC Cardiovasc Interv* 2022;15:1852–60.
- 19 Iglesias JF, Roffi M, Losdat S, *et al.* Long-term outcomes with biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents in ST-segment elevation myocardial infarction: 5-year follow-up of the BIOSTEMI randomised superiority trial. *The Lancet* 2023;402:1979–90.
- 20 Kobayashi T, Sotomi Y, Suzuki S, *et al.* Five-year clinical efficacy and safety of contemporary thin-strut biodegradable polymer versus durable polymer drug-eluting stents: a systematic review and meta-analysis of 9 randomized controlled trials. *Cardiovasc Interv and Ther* 2020;35:250–8.
- 21 Lou Y, Yu Y, Xi Z, *et al.* Five-Year Outcomes of Biodegradable Polymer Drug-Eluting Stents Versus Second-Generation Durable Polymer Drug-Eluting Stents: a Meta-Analysis of Randomized Controlled Trials. *Cardiovasc Drugs Ther* 2019;33:557–66.
- 22 Zhu P, Zhou X, Zhang C, *et al.* Safety and efficacy of ultrathin strut biodegradable polymer sirolimus-eluting stent versus durable polymer drug-eluting stents: a meta-analysis of randomized trials. *BMC Cardiovasc Disord* 2018;18:170.
- 23 Monjur MR, Said CF, Bamford P, *et al.* Ultrathin-strut biodegradable polymer versus durable polymer drug-eluting stents: a meta-analysis. *Open Heart* 2020;7:e001394.
- 24 Taglieri N, Bruno AG, Ghetti G, *et al.* Target Lesion Failure With Current Drug-Eluting Stents: Evidence From a Comprehensive Network Meta-Analysis. *JACC Cardiovasc Interv* 2020;13:2868–78.
- 25 Cook S, Windecker S. Early stent thrombosis: past, present, and future. *Circulation* 2009;119:657–9.
- 26 Sato Y, Jinnouchi H, Kolodgie FD, *et al.* Acute thrombogenicity of fluoropolymer coated stents versus competitive drug-eluting stents under single antiplatelet therapy. *Int J Cardiol* 2021;338:42–9.
- 27 Jinnouchi H, Kutyna M, Torii S, *et al.* Comparison of acute thrombogenicity and albumin adsorption in three different durable polymer coronary drug-eluting stents. *EuroIntervention* 2021;17:248–56.
- 28 Khan AR, Tripathi A, Farid TA, *et al.* Stent thrombosis with bioabsorbable polymer drug-eluting stents: insights from the Food and Drug Administration database. *Coron Artery Dis* 2017;28:564–9.
- 29 Pivato CA, Reimers B, Testa L, *et al.* One-Month Dual Antiplatelet Therapy After Bioresorbable Polymer Everolimus-Eluting Stents in High Bleeding Risk Patients. *J Am Heart Assoc* 2022;11:e023454.
- 30 Mehran R, Cao D, Angiolillo DJ, *et al.* 3- or 1-Month DAPT in Patients at High Bleeding Risk Undergoing Everolimus-Eluting Stent Implantation. *JACC Cardiovasc Interv* 2021;14:1870–83.
- 31 Bangalore S. Acute Thrombogenicity of SYNERGY Drug-Eluting Stent: The 'Bare Metal' Concern? *JACC Cardiovasc Interv* 2019;12:1676–8.