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Comparison between two biodegradable polymer-based sirolimus-eluting stents with differing drug elution and polymer absorption kinetics: two-year clinical outcomes of the PANDA III trial

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KEYWORDS

- clinical trials
- drug-eluting stents
- stent thrombosis

Abstract

Aims: In the PANDA III trial, the novel poly-lactide-co-glycolide polymer-based BuMA sirolimus-eluting stent (SES) was non-inferior to the polylactide polymer-based Excel SES for the primary endpoint of one-year target lesion failure (TLF), with a lower incidence of stent thrombosis. We sought to investigate whether the effectiveness profile of BuMA SES, with more rapid drug elution and polymer absorption kinetics, would persist at two years.

Methods and results: A total of 2,348 patients (mean age, 61.2±10.6 years; 24.3% diabetics; 31.2% with acute myocardial infarction within one month) were randomly assigned to receive either BuMA SES (n=1,174) or Excel SES (n=1,174) in the "all-comer" PANDA III trial. Two-year clinical follow-up was available for 2,262 (96.3%) patients. The incidence of TLF and the patient-oriented composite endpoint (PoCE) was low and similar between the BuMA and Excel groups (7.4% vs. 6.9%, p=0.67, and 13.1% vs. 10.9%, p=0.11, respectively). The rate of any revascularisation was significantly higher with the BuMA SES (6.8% vs. 4.6%, p=0.03). Definite and probable thrombosis occurred in 0.7% and 1.4% of patients in the BuMA and Excel groups, respectively (p=0.10).

Conclusions: Two-year rates of TLF and PoCE events were low and similar between the two biodegradable polymer-based SES. ClinicalTrials.gov Identifier: NCT02017275.

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Abbreviations

BES	biolimus-eluting stent(s)
BP	biodegradable polymer
DES	drug-eluting stent(s)
DP	durable polymer
OCT	optical coherence tomography
PCI	percutaneous coronary intervention
PoCE	patient-oriented composite endpoint
SES	sirolimus-eluting stent(s)
ST	stent thrombosis
TLF	target lesion failure

Introduction

The advent of drug-eluting stents (DES) to address the limitations of bare metal stents is considered a significant milestone in percutaneous coronary intervention (PCI). However, late stent thrombosis (ST) and neoatherosclerosis have been observed with DES[1-3] which, based on pathological evidence, appears most likely to be a consequence of delayed endothelial healing secondary to hypersensitivity reaction to the durable polymer (DP)[4]. Therefore, stents with a biodegradable polymer (BP) coating were developed with the intention of decreasing inflammatory reaction after full release of the drug, thereby overcoming the risk of a delayed healing process[5]. Previous studies have established similar safety and efficacy profiles of BP-DES compared with DP-DES[6,7] and, in a recent meta-analysis including 16 randomised clinical trials, event rates at the longest available follow-up (mean 26 months) were similar for BP-DES and second-generation DP-DES[8]. However, the influence of the kinetics of polymer degradation or drug release of BP-DES has scarcely been studied.

To focus study of the underlying mechanisms of possible differences in clinical outcomes on the kinetics of polymer degradation and drug elution, clinical outcomes for two BP-DES, both sirolimus-eluting stents (SES) with the same platform material, namely the polylactide (PLA) polymer-based Excel stent (JW Medical Systems, Weihai, China) and the poly-lactide-co-glycolide (PLGA) polymer-based BuMA stent (Sino Medical, Tianjin, China), were compared in the multicentre, randomised controlled PANDA III trial (Comparison of BuMA Electro-grafting Based BioDegradable Polymer Stent With EXCEL Biodegradable Polymer Sirolimus-eluting Stent in "Real-World" Practice)[9]. At one year, the BuMA stent with more rapid drug elution and polymer absorption kinetics proved to be non-inferior to the Excel SES for the primary endpoint of target lesion failure (TLF), along with having a lower incidence of ST. The present study aimed to analyse the outcomes of the PANDA III all-comers population at two years, i.e., long after drug elution and polymer absorption had been completed for both stents.

Methods

STUDY DESIGN AND POPULATION

The study design and detailed methods of the PANDA III trial have been described previously[9]. Briefly, PANDA III was a randomised trial comparing two BP-based SES with different drug elution profiles and polymer biodegradation kinetics in an "all-comer" population. Eligible patients had at least one coronary artery stenosis greater than 50% with visually estimated reference diameter of 2.5 mm to 4.0 mm. Key exclusion criteria were limited to known allergy to contrast and/or device or study medications, and planned surgery within six months after the index procedure. There were no restrictions as to the lesions or vessels.

Ethics committees from each centre approved the study protocol, and all patients provided written informed consent. Patients were randomised in a 1:1 ratio to receive a BuMA or Excel stent using a web-based allocation system stratified by centre.

STUDY ENDPOINTS

The primary outcome of this study was TLF, a composite of cardiac death, target vessel myocardial infarction (MI), or ischaemia-driven target lesion revascularisation (TLR). Secondary endpoints included the patient-oriented composite endpoint (PoCE), a composite of all-cause death, all MI, or any revascularisation, TLF and PoCE components, and ST. Details of the endpoint definitions are as in the previous report[9]. Patients were followed up by telephone, and all adverse events were collected and recorded by the independent data safety and monitoring board (R&G, Beijing, China). An independent clinical events committee adjudicated all clinical events for analysis.

STUDY DEVICES AND PROCEDURES

The BuMA stent and Excel stent share the same platform material and eluting drug **(Supplementary Table 1)**. Both devices have biodegradable polymer, differing in the unique design incorporating an electrografting (eG) base layer between the polymer and stent strut in the BuMA stent, which allows complete elution of sirolimus within 30 days and absorption of the PLGA polymer within three months. In contrast, the PLA polymer-based Excel stent elutes sirolimus completely within 180 days, and the PLA polymer is completely absorbed within six to nine months.

Stent implantation was performed according to standard techniques. Patients were treated with ≥100 mg of aspirin daily for an indefinite period and 75 mg of clopidogrel daily for at least 12 months.

STATISTICAL ANALYSIS

The sample size and power calculation for the study have been reported previously[9]. Data are presented as percentages and frequencies for dichotomous and categorical variables and were compared using the chi-square or Fisher's exact test. Continuous variables are presented as mean±SD and were compared using the Student's t-test. The 95% confidence intervals of the differences between the two treatment arms were calculated by normal approximation for continuous variables and by the Newcombe score method for binary variables. Kaplan-Meier analysis was used to calculate the time to clinical events, and the log-rank test to assess between-group differences. A landmark analysis at one year was performed for adverse clinical endpoints.

Cox proportional hazards regression analysis was used to test for interaction between subgroups and stent type for the clinical endpoint of TLF. Multivariate Cox proportional hazards models were constructed to identify independent predictors of two-year TLF. All statistical analyses were performed using SAS software, version 9.1.3 (SAS Institute, Cary, NC, USA).

Results

A total of 2,348 patients were randomly assigned to treatment with BuMA SES (n=1,174) or Excel SES (n=1,174); 1,136 (96.8%) patients in the BuMA group and 1,126 (95.9%) patients in the Excel group completed follow-up at two years **(Figure 1)**. **Table 1** summarises the baseline demographics, and clinical and lesion characteristics of all patients.

At two years, there were still no significant differences in TLF between the two arms, 7.4% in the BuMA group and 6.9% in the Excel group, with a p-value of 0.67 **(Table 2, Figure 2, Supplementary Figure 1, Supplementary Table 2)**. The patient-oriented outcome was also comparable between the BuMA and Excel groups, 13.1% vs. 10.9%, respectively (p=0.11). In contrast, the incidence of any revascularisation was significantly higher in the BuMA group (6.8% vs. 4.6%, p=0.03), mainly driven by a numerically higher rate of ischaemia-driven target vessel revascularisation (TVR) and TLR events compared to the Excel group (3.2% vs. 2.0%, p=0.07, and 2.4% vs. 1.5%, p=0.14, respectively). All-cause death occurred in 39 patients in the BuMA group and 27 patients in the Excel group, without a significant difference. Myocardial infarction rates were 4.9% vs. 5.6%, respectively (p=0.48).

The incidence of definite/probable stent thrombosis up to two years did not differ significantly, being 0.7% in the BuMA group and 1.4% in the Excel group (p=0.10). The rate of definite stent thrombosis was numerically lower for the BuMA group (BuMA vs. Excel: 0.2% vs. 0.7%, p=0.06). Very late stent thrombosis occurred in two (0.2%) versus one (0.1%) patient, respectively. At two-year follow-up, 38.7% (440 of 1,136) and 39.9% (449 of 1,126) of the surviving patients in the BuMA and Excel groups were still on dual antiplatelet therapy (DAPT) **(Figure 3)**. We additionally analysed the correlation of two-year safety outcomes with DAPT cessation **(Supplementary Table 3)**. The results showed that the incidence of spontaneous MI and definite/probable ST was similar between patients on and off DAPT.

The pre-specified subgroup analysis revealed no significant between-stent difference in TLF at two years across subgroups except for bifurcation lesions **(Figure 4)**. The results showed that, for patients with bifurcation lesions, Excel SES implantation might be associated with a decreased risk of TLF. In multivariable Cox regression analysis, age, baseline SYNTAX score, and total stent length per patient were independent predictors of two-year TLF **(Table 3)**. Stent type was not an independent predictor of TLF.

Discussion

The two-year results of the PANDA III trial showed that the incidence of TLF and PoCE was low and similar between the two groups, while event rates of any revascularisation were significantly higher in the BuMA group, mainly driven by a numerically higher incidence of ischaemia-driven TVR and TLR.

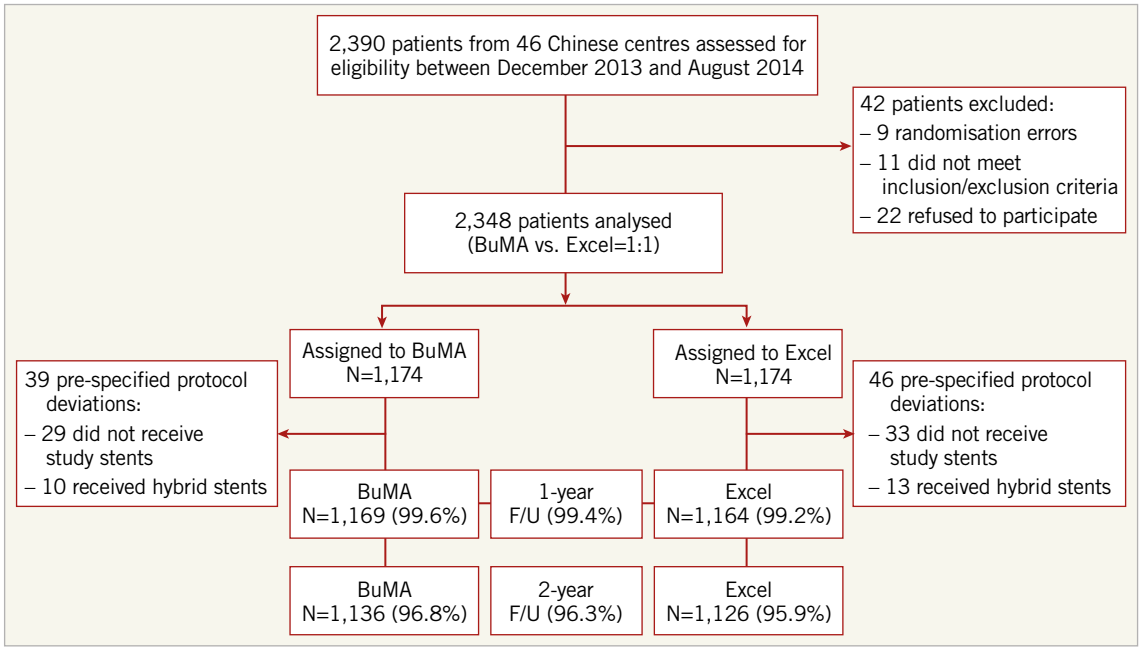

Figure 1. *Patient flow chart. Two-year follow-up includes a window of ±30 days. The per-treatment evaluable population consisted of subjects who received only study device(s) at the target lesion and who had no pre-specified protocol deviations.*

Table 1. Baseline patient and lesion characteristics.

Variable	BuMA (N=1,174, L=1,605)	Excel (N=1,174, L=1,572)	*p*-value
Age, years	60.8±10.6	61.5±10.6	0.11
Men	828 (70.5)	830 (70.7)	0.93
Diabetes mellitus	275 (23.4)	295 (25.1)	0.34
Insulin-requiring	69 (5.9)	86 (7.3)	0.16
Hypertension	724 (61.7)	723 (61.6)	0.97
Hyperlipidaemia	368 (31.4)	364 (31.0)	0.86
Current tobacco use	437 (37.2)	442 (37.7)	0.83
Previous myocardial infarction	464 (39.5)	483 (41.1)	0.42
Clinical presentation			
Silent ischaemia	48 (4.1)	31 (2.6)	0.05
Stable angina	182 (15.5)	164 (14.0)	0.29
Unstable angina	578 (49.2)	613 (52.2)	0.15
Recent myocardial infarction within 30 days	366 (31.2)	366 (31.2)	1.00
STEMI	170 (14.5)	192 (16.4)	0.21
NSTEMI	196 (16.7)	174 (14.8)	0.21
Left ventricular ejection fraction, %	59.2±9.1 (1,116*)	59.4±8.8 (1,115*)	0.56
Baseline SYNTAX score	14.5±9.2 (1,164*)	14.8±9.3 (1,159*)	0.46
Target vessel location			
Left main artery	20 (1.3)	23 (1.5)	0.60
Left anterior descending artery	729 (45.4)	718 (45.7)	0.89
Left circumflex artery/ramus	342 (21.3)	324 (20.6)	0.63
Right coronary artery	514 (32.0)	507 (32.3)	0.89
Reference vessel diameter, mm	2.75±0.47 (1,586¶)	2.76±0.45 (1,558¶)	0.79
ACC/AHA class B2/C lesions	1,325 (82.6)	1,295 (82.4)	0.90
Bifurcation lesions	551 (34.4)	558 (35.5)	0.49
Ostial lesion	59 (3.7)	68 (4.3)	0.35
Total occlusion	210 (13.1)	218 (13.9)	0.52
Stents per patient	1.74±0.96	1.70±0.90	0.34
Total stent length per patient, mm	42.6±26.6	42.0±25.4	0.60
Successful outcome			
Device success	2,035 (99.8)	1,996 (99.95)	0.22
Lesion success	1,586 (98.8)	1,550 (98.6)	0.59
Procedural success	1,117 (95.1)	1,112 (94.7)	0.64

Values are mean±SD or n (%). *Number of patients for whom continuous variables were calculated. ¶Number of lesions for which continuous variables were calculated. ACC/AHA: American College of Cardiology/American Heart Association; L: number of target lesions; N: number of patients; NSTEMI: non-ST-segment elevation myocardial infarction; STEMI: ST-segment elevation myocardial infarction; SYNTAX: Synergy between PCI with Taxus and Cardiac Surgery

Table 2. Overall clinical outcomes at 2 years*.

Variable	BuMA (N=1,136)	Excel (N=1,126)	*p*-value
Target lesion failure¶	84 (7.4)	78 (6.9)	0.67
Patient-oriented composite endpoint‡	149 (13.1)	123 (10.9)	0.11
All-cause death	39 (3.4)	27 (2.4)	0.14
Cardiac	18 (1.6)	17 (1.5)	0.89
Vascular	11 (1.0)	5 (0.4)	0.14
Non-cardiovascular	10 (0.9)	5 (0.4)	0.20
All myocardial infarction	56 (4.9)	63 (5.6)	0.48
Target vessel-related	52 (4.6)	58 (5.2)	0.53
Non-target vessel-related	4 (0.4)	5 (0.4)	0.75
Periprocedural	44 (3.8)	49 (4.2)	0.39
Post-procedural	12 (1.1)	14 (1.2)	0.68
Any revascularisation	77 (6.8)	52 (4.6)	0.03
Ischaemia-driven TVR	36 (3.2)	22 (2.0)	0.07
Ischaemia-driven TLR	27 (2.4)	17 (1.5)	0.14
Definite/probable stent thrombosis	8 (0.7)	16 (1.4)	0.10
Definite	2 (0.2)	8 (0.7)	0.06
Probable	6 (0.5)	8 (0.7)	0.58
Acute (0-24 hours)	3 (0.3)	4 (0.4)	0.73
Subacute (>24 hours-30 days)	0 (0)	5 (0.4)	0.03
Late (>30 days-1 year)	3 (0.3)	6 (0.5)	0.34
Very late (>1 year)	2 (0.2)	1 (0.1)	1.00

Values are n (%). *Two-year follow-up includes a window of ±30 days. ¶Target lesion failure was defined as a composite of cardiac death, target vessel myocardial infarction, or ischaemia-driven target lesion revascularisation. ‡Patient-oriented composite endpoint was defined as a composite of all-cause death, all myocardial infarction, or any revascularisation. TLR: target lesion revascularisation; TVR: target vessel revascularisation

At one year, the BuMA SES with fast drug elution and polymer degradation kinetics was associated with similar safety and efficacy profiles but decreased rates of stent thrombosis events compared with the Excel SES[9]. As previously reported, both devices would have completed polymer absorption before one year, ending up with the same stainless steel platform. Although a numerically lower ST event rate was found at two years, driven mainly by subacute and late ST, the incidence of ST events at one to two years was similar between the two groups. The findings might support

Table 3. Independent predictors of 2-year TLF by multivariable Cox regression analysis.

Variable	Hazard ratio (95% CI)	*p*-value
Age (per 10-year increase)	1.43 (1.22, 1.67)	<0.0001
Baseline SYNTAX score (per 10-point increase)	1.24 (1.06, 1.46)	0.007
Total stent length per patient (per 1-point increase)	1.01 (1.00, 1.01)	0.001

The following variables were included in the multivariable Cox regression analysis: stent type (BuMA vs. Excel), age (per 10-year increase), sex (female vs. male), baseline SYNTAX score (per 10-point increase), acute myocardial infarction within 30 days and total stent length per patient (per 1-point increase). SYNTAX: Synergy between PCI with Taxus and Cardiac Surgery; TLF: target lesion failure

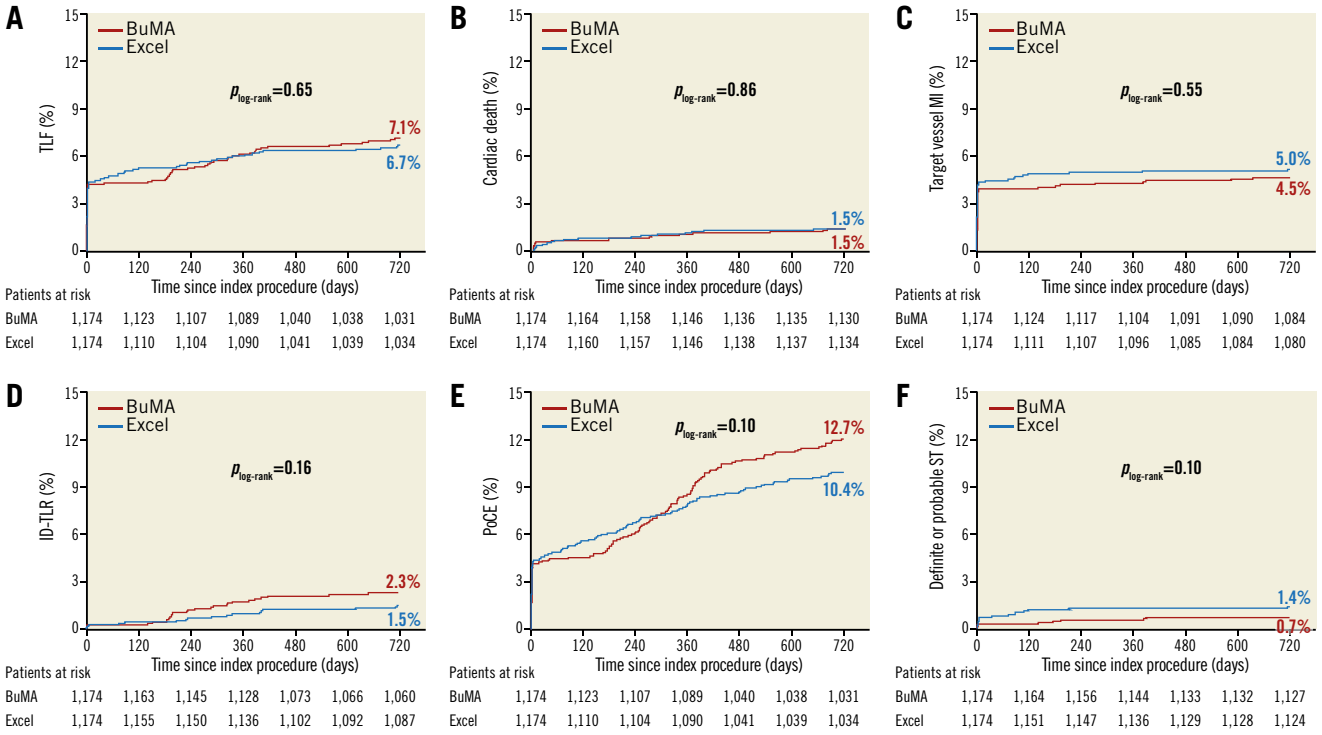

Figure 2. *Kaplan-Meier curves for TLF and ST up to two years. Cumulative event curves up to two years for target lesion failure (A), cardiac death (B), target vessel myocardial infarction (C), ischaemia-driven target lesion revascularisation (D), patient-oriented composite endpoint (E), and definite or probable stent thrombosis (F) for patients receiving BuMA (red line) or Excel (blue line) stents are shown. ID-TLR: ischaemia-driven target lesion revascularisation; MI: myocardial infarction; PoCE: patient-oriented composite endpoint; ST: stent thrombosis; TLF: target lesion failure*

the theory that differences in polymer degradation and elution kinetics may influence early safety outcomes. After the absorption process is completed, the two stents would perform similarly. Results at two years also showed a non-significantly higher incidence of PoCE in the BuMA group, while rates of TLF and myocardial infarction were similar. The difference in PoCE was mainly driven by a higher event rate of TVR as well as TLR, which might raise concern on late efficacy issues of the BuMA stent with fast drug elution kinetics. However, the BIO-RESORT trial, comparing two BP-DES with very different polymer coating and degradation duration and a DP-ZES, documented similar safety and efficacy outcomes as well as comparable thrombosis rates at one year[10]. The strut thickness of the BP-DES in the PANDA III trial was 100-110 µm for BuMA SES and 120-130 µm for Excel SES, while BP-DES in the BIO-RESORT trial had very thin struts (60-80 µm). The incidence of TLF was 1%-2% higher in the PANDA III trial than in the BIO-RESORT trial, suggesting that, beyond drug elution and polymer degradation kinetics, strut thickness might be an important risk factor for long-term prognosis of BP-DES.

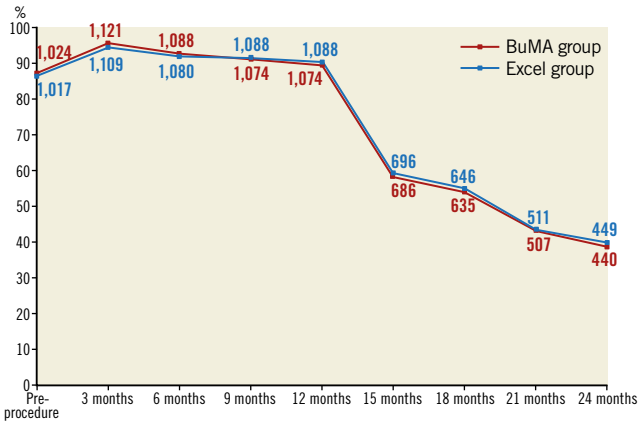

Figure 3. *DAPT utilisation before and after the index procedure. The line chart shows the percentage of patients who continued DAPT; patient numbers are marked in the graph. DAPT: dual antiplatelet therapy*

Studies have suggested better safety and efficacy profiles for the biodegradable polymer DES compared with early-generation DES[11-13]. In the final five-year follow-up of the LEADERS (Limus Eluted From A Durable Versus ERodable Stent Coating), BP biolimus-eluting stents (BES) were associated with a significant reduction in very late ST risk and related composite clinical outcomes[14]. In the pivotal randomised EVOLVE (A Prospective Randomized Multicenter Single-blind Non-inferiority Trial to Assess the Safety and Performance of the Evolution Everolimus-Eluting Monorail

	Target lesion failure, *Events/Total (%)*		Relative risk (95% CI)	*p*-value for interaction
	BuMA, N=1,136	Excel, N=1,126		
Age				
<61 years	21/541 (3.9)	26/516 (5.0)	0.77 (0.44-1.35)	0.16
≥61 years	63/595 (10.6)	52/610 (8.5)	1.24 (0.88-1.76)	
Sex				
Female	28/340 (8.2)	26/337 (7.7)	1.07 (0.64-1.78)	1.00
Male	56/796 (7.0)	52/789 (6.6)	1.07 (0.74-1.54)	
Diabetes				
Present	27/269 (10)	19/289 (6.6)	1.53 (0.87-2.68)	0.15
Absent	57/867 (6.6)	59/837 (7.0)	0.93 (0.66-1.33)	
AMI				
Present	23/342 (6.7)	29/348 (8.3)	0.81 (0.48-1.37)	0.12
Absent	61/794 (7.7)	49/778 (6.3)	1.22 (0.85-1.75)	
Number of target lesions				
1	44/790 (5.6)	51/806 (6.3)	0.88 (0.60-1.30)	0.15
≥2	40/346 (11.6)	27/320 (8.4)	1.37 (0.86-2.18)	
SYNTAX score				
<13	28/553 (5.1)	22/535 (4.1)	1.23 (0.71-2.12)	0.54
≥13	56/573 (9.8)	56/577 (9.7)	1.01 (0.71-1.43)	
Reference vessel diameter				
<2.71 mm	58/625 (9.3)	52/608 (8.6)	1.09 (0.76-1.55)	0.83
≥2.71 mm	26/509 (5.1)	26/515 (5.0)	1.01 (0.60-1.72)	
Lesion length				
<16.4 mm	37/501 (7.4)	35/476 (7.4)	1.00 (0.64-1.57)	0.73
≥16.4 mm	47/633 (7.4)	43/647 (6.6)	1.12 (0.75-1.66)	
ACC/AHA lesion class				
B2/C	76/997 (7.6)	75/979 (7.7)	1.00 (0.73-1.35)	0.13
A/B1	8/139 (5.8)	3/147 (2.0)	2.82 (0.76-10.4)	
LAD lesion				
Yes	60/648 (9.3)	46/644 (7.1)	1.30 (0.90-1.87)	0.08
No	24/488 (4.9)	32/482 (6.6)	0.74 (0.44-1.24)	
Bifurcation lesion				
Yes	50/480 (10.4)	35/485 (7.2)	1.44 (0.95-2.18)	0.04
No	34/656 (5.2)	43/641 (6.7)	0.77 (0.50-1.20)	
Total occlusion				
Yes	16/200 (8.0)	17/196 (8.7)	0.92 (0.48-1.77)	0.62
No	68/936 (7.3)	61/930 (6.6)	1.11 (0.79-1.55)	
Total stent length per patient				
<35 mm	23/511 (4.5)	22/548 (4.0)	1.12 (0.63-1.99)	0.75
≥35 mm	61/625 (9.8)	56/578 (9.7)	1.01 (0.71-1.42)	
All patients	84/1,136 (7.4)	78/1,126 (6.9)	1.07 (0.79-1.44)	

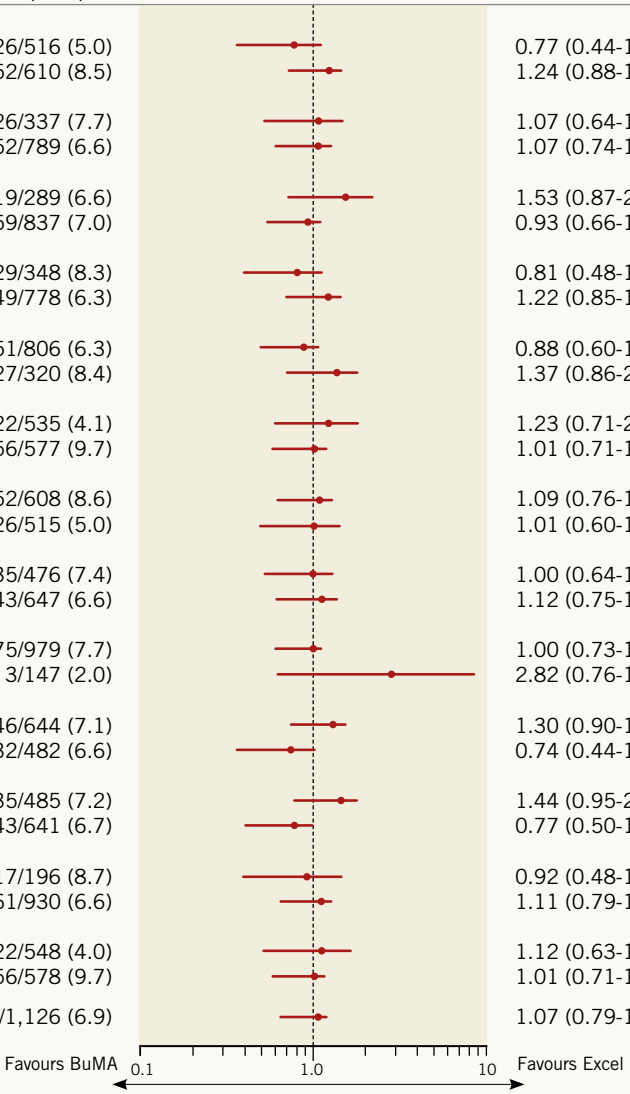

Figure 4. *Subgroup analysis of target lesion failure at two years. The p-value for interaction represents the likelihood of interaction between the variable and the relative treatment effect. ACC: American College of Cardiology; AHA: American Heart Association; CI: confidence interval; DAPT: dual antiplatelet therapy; LAD: left anterior descending artery; SYNTAX: Synergy between PCI with Taxus and Cardiac Surgery*

Coronary Stent System) II trial, the SYNERGY™ coronary stent was non-inferior to the predicate PROMUS Element™ Plus stent (both Boston Scientific, Marlborough, MA, USA) for one-year TLF[15]. Windecker et al demonstrated that, compared with a durable polymer stent, a biodegradable polymer-based stent was non-inferior for nine-month in-stent late lumen loss with comparable clinical event rates[16]. Similar results were reported for the CENTURY II (Clinical Evaluation of New Terumo Drug-Eluting Coronary Stent System in the Treatment of Patients with Coronary Artery Disease) trial[17]. In the three-year outcomes of the SORT OUT VI trial, a DP zotarolimus-eluting stent and a BP biolimus-eluting stent yielded similar safety and efficacy clinical outcomes, including stent thrombosis[11]. However, there are also studies indicating higher event rates for biodegradable polymer stents compared with DP-DES. In a large patient-level pooled analysis of the NEXT (NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-eluting Stent Trial) and COMPARE II (Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent) studies, a higher rate of target vessel MI was observed in the BP-BES group[18].

An optical coherence tomography (OCT) substudy showed that, at two years after stent implantation, stent struts not covered by neointima and evagination were less frequently observed in DP-DES compared with BP-BES (2.1±4.7% vs. 7.9±10.8% respectively, p=0.013)[19]. In terms of the present study, there is a prior single-centre, randomised OCT study that showed that

the BuMA SES had superior strut coverage at three months compared with the Excel SES (94.2% vs. 90.0%, p<0.0001), with a relatively higher proportion of covered struts early at three months[20], which we posited was related to lower thrombosis events at one year with BuMA SES. However, the influence was no longer significant at two years. As compared with DP-DES, BP-DES may provide an advantage by improving late/very late safety outcomes, mainly because durable polymer may contribute to delayed endothelial coverage and impaired stent healing. On the other hand, differing polymer absorption and drug elution profiles may influence the performance of BP-DES, especially at an early stage.

At one year, the incidence of TLF and especially ST was lower in the BuMA group in the acute myocardial infarction subgroup, while there was no between-group difference at two years, which might be secondary to the faster degradation kinetics of the BuMA SES, mainly benefiting the early healing process in patients. In this large-scale all-comer trial, patients appeared to derive little benefit from long-term DAPT use, which was consistent with the ITALIC trial[21] but not the DAPT trial[22]. The optimal duration of DAPT with different types of drug-eluting stent remains a controversial topic, and whether DAPT duration should be shortened or prolonged in patients implanted with BP-DES warrants further investigation. In terms of two-year TLF, patients with bifurcation lesions tended to benefit more from the Excel SES. PCI for bifurcation lesions had been associated with worse clinical outcomes compared with non-bifurcation lesions, and BP-DES yielded at least comparable clinical prognosis compared with DP-DES after treatment of bifurcation lesions[23]. In the subgroup analysis of the LEADERS all-comers trial, BES was associated with comparable safety and superior efficacy when compared with CYPHER® SES (Cordis, Cardinal Health, Milpitas, CA, USA)[24]. Because the subgroup analysis in the present study is limited by the lack of detailed information on bifurcation lesions, such as Medina type, the tendency for bifurcation lesions to benefit from longer elution time of an antiproliferative drug must be regarded as hypothesis-generating.

Limitations

Our study should be interpreted in the light of the following limitations. First, the study was powered for the primary endpoint of TLF; therefore, it was underpowered to detect differences in the individual components of the composite endpoints as well as ST. Second, while all adverse events were adjudicated by an independent blinded clinical events committee, some adverse events, especially revascularisation, might be related to previously implanted stents and not the ones studied. Third, because the BuMA SES is available in diameters from 2.50 mm to 4.00 mm, the study was designed to include patients with an estimated reference diameter of 2.5 mm or greater. Fourth, the two-year event rates were relatively low, which might be partly explained by the relatively longer DAPT duration than that of the clinical routine guidance of one year. Finally, the findings presented should be considered hypothesis-generating and warrant further study.

Conclusions

While the differing polymer absorption and drug elution kinetics of the two BP-DES in the PANDA III trial appeared to influence their performance at an early stage, the two-year follow-up results underscored similar safety and efficacy profiles.

Impact on daily practice

The two-year follow-up of the PANDA III trial documented a low incidence of TLF and PoCE with both BP-DES, which might render BP-DES a favourable choice for PCI. Differing polymer absorption and drug elution profiles may influence the performance of BP-DES.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Figure 1. Landmark analysis at 1 year.

Supplementary Table 1. BuMA and Excel stent specifications.

Supplementary Table 2. Clinical outcomes at 1-2 years.

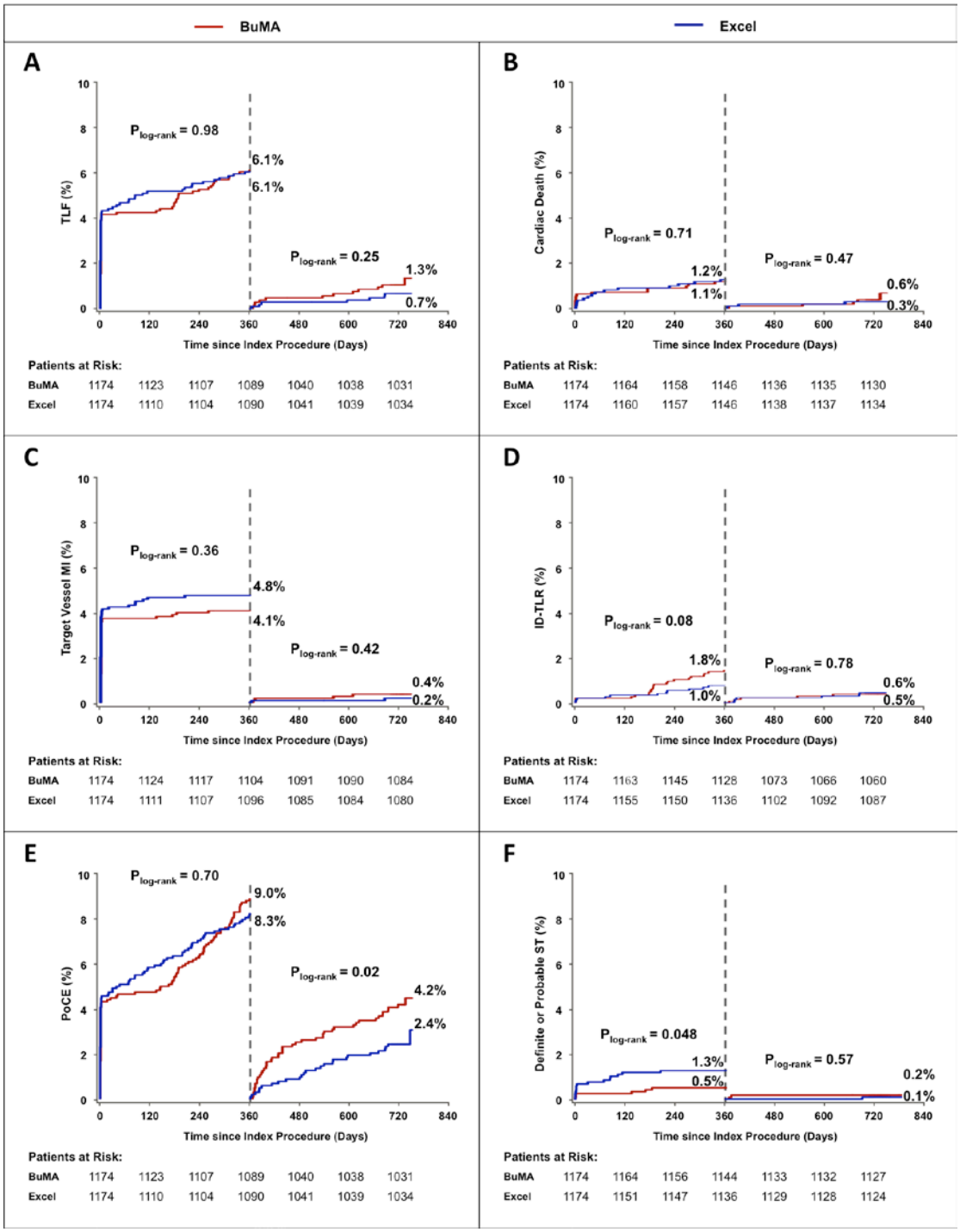
Supplementary Table 3. Correlation of 2-year safety outcomes with DAPT duration.

The supplementary data are published online at: http://www.pcronline.com/eurointervention/142nd_issue/185

Supplementary data

Supplementary Figure 1. Landmark analysis at 1 year.

One-year landmark analyses of target lesion failure (A), cardiac death (B), target vessel myocardial infarction (C), ischaemia-driven target lesion revascularisation (D), patient-oriented composite endpoint (E), and definite or probable stent thrombosis (F) for patients receiving BuMA (red line) or Excel (blue line) are shown.



Supplementary Table 1. BuMA and Excel stent specifications.

	BuMA	**Excel**
Manufacturer	SinoMed, Tianjin, China	JWMS, Weihai, China
Stent platform material	316L stainless steel	316L stainless steel
Strut thickness	100-110 μm	120-130 μm
Stent crossing profile	≤1.05 mm	≤1.25 mm
Diameters	2.50, 2.75, 3.00, 3.25, 3.50, 4.00 mm	2.50, 2.75, 3.00, 3.50, 4.00 mm
Lengths	10, 15, 20, 25, 30, 35 mm	14, 18, 24, 28, 33, 36 mm
Drug	Sirolimus	Sirolimus
Drug dose	6~8 μg/mm	13~14 μg/mm
Polymer	PLGA	PLA
Polymer coating pattern	Circumferential	Abluminal
Base layer (base matrix)	Non-degradable PBMA, chemically bonded to the stent surface by electrografting	None
In vivo drug release	100% in 30 days	100% in 6 months
Polymer biodegradation time	2~3 months	6~9 months

Briefly, the BuMA SES has 100-110 μm 316L stainless steel struts that are circumferentially covered by PLGA polymer, while the Excel SES has 120-130 μm 316L stainless steel struts that are abluminally covered by PLA polymer.

Supplementary Table 2. Clinical outcomes at 1-2 years[*].

Variable	BuMA (N=1,133)	Excel (N=1,122)	*p*-value
Target lesion failure[†]	12 (1.1)	7 (0.6)	0.26
Patient-oriented composite endpoint[‡]	45 (4.0)	25 (2.2)	0.02
All-cause death	16 (1.4)	8 (0.7)	0.11
Cardiac	5 (0.4)	3 (0.3)	0.73
Vascular	5 (0.4)	1 (0.1)	0.22
Non-cardiovascular	6 (0.5)	4 (0.4)	0.75
All myocardial infarction	6 (0.5)	2 (0.2)	0.29
Target vessel-related	4 (0.4)	2 (0.2)	0.69
Non-target vessel-related	2 (0.2)	0 (0.0)	0.50
Periprocedural	-	-	-
Post-procedural	6 (0.5)	2 (0.2)	0.29
Any revascularisation	31 (2.7)	19 (1.7)	0.09
Ischaemia-driven TVR	11 (1.0)	10 (0.9)	0.84
Ischaemia-driven TLR	5 (0.4)	6 (0.5)	0.75
Definite/probable stent thrombosis	2 (0.2)	1 (0.1)	1.00
Definite	0 (0.0)	1 (0.1)	1.00
Probable	2 (0.2)	0 (0.0)	0.50
Acute (0-24 hours)	-	-	-
Subacute (>24 hours-30 days)	-	-	-
Late (>30 days-1 year)	-	-	-
Very late (>1 year)	2 (0.2)	1 (0.1)	1.00

Values are n (%).

* Incidence from 1 to 2 years.

[†] Target lesion failure was defined as a composite of cardiac death, target vessel myocardial infarction, or ischaemia-driven target lesion revascularisation.

[‡] Patient-oriented composite endpoint was defined as a composite of all-cause death, all myocardial infarction, or any revascularisation.

CI: confidence interval; TLR: target lesion revascularisation; TVR: target vessel revascularisation

Supplementary Table 3. Correlation of 2-year safety outcomes with DAPT duration.

	On DAPT	Off DAPT	*p*-value for interaction
Spontaneous MI	1.3% (12/889)	1.0% (14/1,373)	0.47
BuMA SES	1.8% (8/440)	0.6% (4/696)	0.05
Excel SES	0.9% (4/449)	1.5% (10/677)	
Def/prob ST	0.9% (8/889)	1.2% (16/1,373)	0.55
BuMA SES	0.9% (4/440)	0.6% (4/696)	0.21
Excel SES	0.9% (4/449)	1.8% (12/677)	

DAPT: dual antiplatelet therapy; MI: myocardial infarction; ST: stent thrombosis