Supplementary data

Supplementary Appendix 1. Inclusion and exclusion criteria

Patients were eligible if they were at least 20 years old, had chronic stable coronary artery disease or acute coronary syndromes, and had at least one lesion of the coronary arteries or venous or arterial bypass grafts with >50% diameter stenosis that required treatment with a DES. Moreover, the subjects had to have evidence of myocardial ischaemia (e.g., stable, unstable angina, recent infarction, silent ischaemia, positive functional study, or a reversible change in the electrocardiogram consistent with ischaemia). In subjects with diameter stenosis >70%, evidence of myocardial ischaemia did not have to be documented. Angiographically, target lesion(s) had to be located in arteries with diameters of ≥2.5 mm and ≤4.5 mm and had to be amenable to PCI.

The exclusion criteria were life expectancy of <1 year; allergy to aspirin, clopidogrel, ticagrelor, prasugrel, sirolimus, or biolimus; participation in another randomised stent trial; inability to provide written informed consent; cardiogenic shock with Killip class IV; symptomatic heart failure; or non-cardiac comorbid conditions that may result in life expectancy <1 year or protocol non-compliance (per site investigator's medical judgement).

Supplementary Appendix 2. The characteristics of the stents

The Orsiro stent is a cobalt-chromium stent with ultra-thin strut thickness (60 μm for stent diameters of 2.25–3.00 mm and 80 μm for stent diameters of 3.50-4.00 mm). It has a passive silicone carbide stent coating and an active biodegradable poly-L-lactic polymer in a circumferential pattern. The poly-L-lactic polymer is degraded over 12-24 months. The antiproliferative agent, sirolimus, is fully eluted at three months [10]. The BioMatrix stent is made of 316L stainless steel with 120 μm thickness and a polylactic acid abluminal polymer that is degradable at nine months. The antiproliferative agent is biolimus, which is eluted over six months [10].

Supplementary Appendix 3. Antithrombotic therapy

All patients were administered aspirin and one $P2Y_{12}$ inhibitor (clopidogrel, prasugrel, or ticagrelor) before the procedure according to the investigator's discretion. The dose of each drug was at the discretion of each investigator. Aspirin was administered indefinitely and clopidogrel, prasugrel, or ticagrelor was administered for at least one year thereafter. Unfractionated heparin (70-100 IU/kg) was administered before the procedure. Glycoprotein IIb/IIIa inhibitors were used at the operator's discretion.

Supplementary Appendix 4. The definition of endpoints, event detection, site monitoring and event adjudication

Definitions

Cardiac death was defined as any death due to an evident cardiac cause, any death related to PCI, an unwitnessed death, or death from unknown causes. Myocardial infarction was defined according to the third universal definition of myocardial infarction [15]. Myocardial infarction not related to other than the target vessel was defined as any myocardial infarction that was not clearly attributable to a non-target vessel. Target lesion revascularisation was defined as repeat revascularisation with PCI or surgical bypass due to >50% stenosis within the stent or within a 5 mm border proximal or distal to the stent. Target vessel revascularisation was defined as any repeat PCI or surgical bypass of any segment within the entire major coronary vessel that was proximal or distal to a target lesion, including upstream and downstream branches, and the target lesion itself. Revascularisation was considered to be ischaemia-driven if angiography during follow-up showed a diameter stenosis ≥50% with at least one of the following: 1) history of recurrent angina pectoris, presumably related to the target vessel; 2) objective signs of ischaemia at rest or during exercise test by electrocardiography, presumably related to the target vessel; or 3) abnormal test results of invasive functional diagnostic test (fractional flow reserve). Stent thrombosis was defined as definite, probable, or possible stent thrombosis according to the Academic Research Consortium definition [16].

Clinical event detection

Clinically, follow-up of the patients occurred at predetermined schedules at 1, 6, 12 and 18 months. Follow-up comprised preferentially office visits, but telephone contact was also allowed. During the follow-up visits, data on angina class and adverse ischaemic, neurologic, and bleeding events were collected. Original source documents were submitted for any clinical events (death, myocardial infarction, revascularisation, stroke, or any other serious adverse events). If the patient was readmitted in a non-study hospital, all efforts were made to obtain original source documents from that hospital. For myocardial infarctions, electrocardiogram and cardiac enzyme (creatine kinase, creatine kinase MB, and troponin) data were obtained and recorded.

Site monitoring

A designated trial monitor at appropriate intervals reviewed investigational data for accuracy and completeness and to ensure compliance with the protocol. If necessary, this trial monitor inspected all documents and required records that are maintained by the investigator/site, including medical records (office, clinic, or hospital) for the subjects in this trial.

Clinical event adjudication

With the exception of all-cause mortality, most endpoints required clear, pre-specified criteria, and centralised review by an independent clinical events adjudication committee (CEAC) blinded to treatment allocation. These endpoints were captured during patient interview, supplemented by death certificates; hospital record abstracts and related reports (angiography, echocardiography and other clinical information). First, all required

documents, reports, hospital records were identified, made anonymous, and copied to the data coordinating centre (DCC) by clinical staff. Second, the DCC checked to ensure confidentiality and, if required, had the records centrally abstracted onto standard forms by trained DCC staff. Third, centrally prepared forms and documents were circulated to CEAC members for assessment.

Supplementary Appendix 5. Statistical analysis

The trial was powered for the non-inferiority of the Orsiro stent to the BioMatrix stent with respect to the primary endpoint at 18 months. Target lesion failure of second-generation DES at one year had been reported 2.9%-5.6% in Korea [15,16]. We designed 18-month follow-up and recruited centres had performed PCI for acute coronary syndrome at a high percentage. Therefore, we assumed an event rate of 5% in each stent group. The hazard ratio of the historical placebo (bare metal stent) versus DES was 3.22 (95% confidence interval [CI]: 2.04-5.0) [17]. In a recent study showing the inferiority of a DES versus another DES, the hazard ratio was 2.43 (95% CI: 1.50-3.94) [18]. Therefore, we set a non-inferiority margin at 1.5, which was lower than the lower bound of the hazard ratio of the previous inferior DES and was much lower than that of a bare metal stent. Non-inferiority would be acknowledged if the upper limit of the one-sided 95% CI of the risk ratio of TLF was not greater than 1.5. With a sample size of 1,073 patients in each treatment arm, a two-group survival non-inferiority with a one-sided significance level of 0.05 would have 90% power to detect the non-inferiority with a predetermined non-inferiority margin of 1.5. The sample size with 1,192 in each treatment arm assumed a 10% loss-to-follow-up rate.

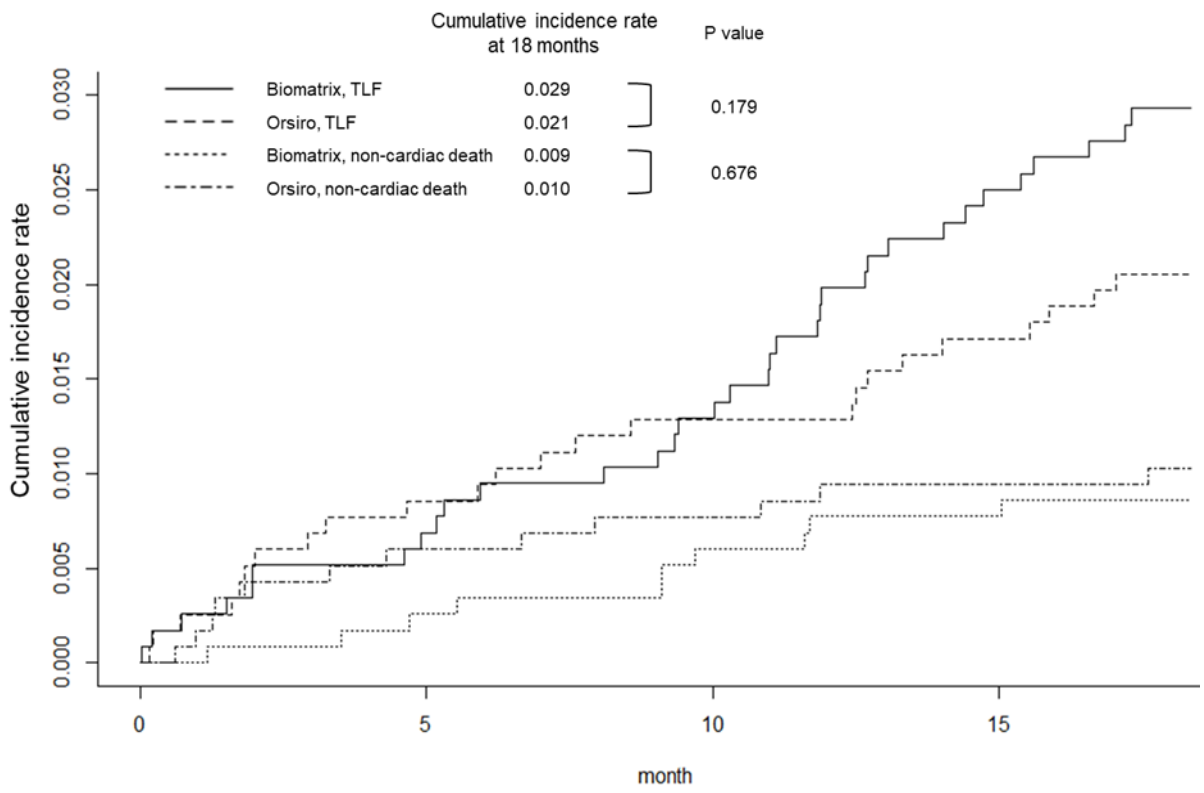
We compared continuous variables between the study groups using the two-sample t-test or the Mann-Whitney U test, depending on whether the data followed a normal distribution. We analysed distributions of categorical variables using the χ^2 test. In the analyses of every endpoint, follow-up continued until the date of an endpoint event, death, or 18 months after stent implantation, whichever came first. We constructed survival curves displaying cumulative incidence rates based on time to events, accounting for the competing risk of death (in cases of death not included in the outcome). Patients who received the BioMatrix stent were used as the reference group for overall and subgroup analyses. We calculated rate ratios for TLF at the 18-month follow-up for pre-specified patient subgroups (based on baseline demographic and clinical characteristics). The intention-to-treat (ITT) principle was used for all analyses. We also performed per-protocol (PP) analyses. Except for the inferiority testing of the primary endpoint, we regarded a two-sided p-value of <0.05 as indicating statistical significance. Statistical analyses were performed using R, version 3.1.0 (R Foundation for Statistical Computing, Vienna, Austria). All the analyses were performed by a professional statistician (S.H. Kim).

Supplementary Appendix 6. A list of centres and investigators

In-Ho Chae[1], MD; Young Jin Choi[2], MD; Myeong-Kon Kim[3], MD; Kwang Soo Cha[4], MD; Seung-Hwan Lee[5], MD; Bum-Kee Hong[6], MD; Seung-Woon Rha[7], MD; Woong Chol Kang[8], MD; Jae-Hwan Lee[9], MD; Sang-Hyun Kim[10], MD; Nam-Ho Lee[11], MD; Kyung-Joo Ahn[12], MD; Hun-Sik Park[13], MD; Dae-Gyun Park[14], MD; Doo-Il Kim[15], MD; Hee-Yeol Kim[16], MD; Sang-Uk Lym[17], MD; Yong Sung Seo[18], MD; Ki-Yuk Chang[19], MD; Tae-Jun Cha[20], MD; Byeong-Hee Hwang[21], MD; Byung-Ryul Cho[22], MD; Byoung-Eun Park[23], MD; Hee-Kyung Jeon[24], MD; Jong-Seon Park[25], MD

1. Seoul National University Bundang Hospital, Seongnam, Republic of Korea;
2. Sejong General Hospital, Bucheon, Republic of Korea;
3. Catholic Kwandong University International St. Mary's Hospital, Incheon, Republic of Korea;
4. Pusan National University Hospital, Pusan, Republic of Korea;
5. Wonju Severance Hospital, Yonsei University College of Medicine, Republic of Korea;
6. Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea;
7. Korea University Guro Hospital, Seoul, Republic of Korea;
8. Gacheon University Gil Medical Center, Incheon, Republic of Korea;
9. Chungnam National University Hospital, Daejeon, Republic of Korea;
10. Seoul Metropolitan Government Seoul National University Boramae Medical Center, Seoul, Republic of Korea;
11. Hallym University Kangnam Sacred Heart Hospital, Seoul, Republic of Korea;
12. KEPCO Medical Center, Seoul, Republic of Korea;
13. Kyoungpook National University Hospital, Daegu, Republic of Korea;
14. Hallym University Kangdong Sacred Heart Hospital, Seoul, Republic of Korea;
15. Inje University Paik Hospital, Pusan, Republic of Korea;
16. The Catholic University of St. Mary's Hospital, Bucheon, Republic of Korea;
17. Cha University Bundang Cha Medical Center, Seongnam, Republic of Korea;
18. Myongji Hospital, Goyangsi, Republic of Korea;
19. The Catholic University of St. Mary's Hospital, Seoul, Republic of Korea;
20. Kosin University Gospel Hospital, Pusan, Republic of Korea;
21. The Catholic University of St Paul's Hospital, Seoul, Republic of Korea;
22. Kangwon National University Hospital, Chuncheon, Republic of Korea;
23. Dankook University Hospital, Cheonan, Republic of Korea;
24. The Catholic University of St. Mary's Hospital, Uijeongbu, Republic of Korea;
25. Yongnam University Medical Center, Daegu, Republic of Korea

Supplementary figure. Cumulative incidence rates with a competing risk, non-cardiac death



Supplementary Figure 1. The cumulative incidence rate of the primary endpoint and a competing risk, non-cardiac death.

Supplementary Table 1. The number of patients per centre.

ID	Centre	Number
1	Seoul National University Bundang Hospital	923
2	Sejong General Hospital	143
3	Catholic Kwandong University International St. Mary's Hospital	139
4	Pusan National University Hospital	124
5	Wonju Severance Hospital, Yonsei University College of Medicine	122
6	Gangnam Severance Hospital, Yonsei University College of Medicine	104
7	Korea University Guro Hospital	96
8	Gacheon University Gil Medical Center	84
9	Chungnam National University Hospital	81
10	Seoul Metropolitan Government Seoul National University Boramae Medical Center	77
11	Hallym University Kangnam Sacred Heart Hospital	73
12	KEPCO Medical Center	71
13	Kyoungpook National University Hospital	62
14	Hallym University Kangdong Sacred Heart Hospital	50
15	Inje University Paik Hospital, Pusan	30
16	The Catholic University of St. Mary's Hospital, Bucheon	29
17	Cha University Bundang Cha Medical Center	26
18	Myongji Hospital	19
19	The Catholic University of St. Mary's Hospital, Seoul	18
20	Kosin University Gospel Hospital	14
21	The Catholic University of St Paul's Hospital	13
22	Kangwon National University Hospital	12
23	Dankook University Hospital, Cheonan	10
24	The Catholic University of St. Mary's Hospital, Uijeongbu	5
25	Yongnam University Medical Center	2

Supplementary Table 2. The results on a per-protocol basis.

	BES	**SES**	HR (95% CI)	*p*-value
TLF	34 (2.9)	24 (2.1)	0.70 (0.41-1.17)	0.175
Cardiac death	16 (1.4)	12 (1.1)	0.74 (0.35-1.57)	0.436
MI	0 (0.0)	3 (0.3)	-	-
TLR	18 (1.6)	10 (0.9)	0.55 (0.25-1.18)	0.125
All-cause death	26 (2.2)	23 (2.0)	0.88 (0.50-1.54)	0.643
TVR	10 (0.9)	15 (1.3)	1.49 (0.67-3.31)	0.331
RR (TLR or TVR)	26 (2.3)	22 (1.9)	0.84 (0.47-1.47)	0.534
CVA	11 (1.0)	7 (0.6)	0.63 (0.24-1.62)	0.335
ST	0 (0.0)	2 (0.2)	-	-
BL	27 (2.4)	27 (2.4)	0.99 (0.58-1.68)	0.964