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A Randomized Comparison of Platinum Chromium-Based Everolimus-Eluting Stents Versus Cobalt Chromium-Based Zotarolimus-Eluting Stents in All-Comers Receiving Percutaneous Coronary Intervention

HOST–ASSURE (Harmonizing Optimal Strategy for Treatment of Coronary Artery Stenosis–Safety & Effectiveness of Drug-Eluting Stents & Anti-platelet Regimen), a Randomized, Controlled, Noninferiority Trial

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Objectives This study sought to test whether the newly developed platinum chromium (PtCr)-based everolimus-eluting stent (EES) is noninferior to the cobalt chromium (CoCr)-based zotarolimus-eluting stent (ZES) in all-comers receiving percutaneous coronary intervention (PCI).

Background PtCr provides improved radial strength, conformability, and visibility compared with the CoCr alloy, but PtCr-based stents have not been tested in a wide range of patients receiving PCI. Also, recent case series have raised the issue of longitudinal stent deformation (LSD) with newer drug-eluting stents.

Methods We randomly assigned 3,755 all-comers receiving PCI to PtCr-EES or CoCr-ZES. The primary outcome was target lesion failure (TLF) at 1-year post-PCI, defined as the composite of cardiac death, nonfatal target vessel–related myocardial infarction, and ischemia-driven target lesion revascularization. Post-hoc angiographic analysis was performed to qualitatively and quantitatively analyze LSD.

Results At 1 year, TLF occurred in 2.9% and 2.9% of the population in the PtCr-EES and CoCr-ZES groups, respectively (superiority $p = 0.98$, noninferiority $p = 0.0247$). There were no significant differences in the individual components of TLF as well as the patient-oriented clinical outcome. Of 5,010 stents analyzed, LSD occurred in 0.2% and 0% in the PtCr-EES and CoCr-ZES groups, respectively ($p = 0.104$). There was no significant difference in post-deployment stent length ratio between the 2 stents ($p = 0.352$).

Conclusions At 1 year, PtCr-EES was noninferior to CoCr-ZES in all-comers receiving PCI. Although LSD was observed only in PtCr-EES, both the stent length ratio and the frequency of LSD were not significantly different between the 2 stent types, and PtCr-EES was not associated with adverse clinical outcomes. (Harmonizing Optimal Strategy for Treatment of Coronary Artery Stenosis–SAfety & EffectiveneSS of Drug-ElUting Stents & Anti-platelet REgimen [HOST–ASSURE]; NCT01267734) (J Am Coll Cardiol 2014;63:2805–16) © 2014 by the American College of Cardiology Foundation

Abbreviations and Acronyms

ARC = Academic Research Consortium
CI = confidence interval
CoCr = cobalt chromium
DES = drug-eluting stent(s)
EES = everolimus-eluting stent(s)
HR = hazard ratio
LSD = longitudinal stent deformation
NSR = nominal stent length ratio
PCI = percutaneous coronary intervention
PtCr = platinum chromium
TLF = target lesion failure
TLR = target lesion revascularization
TV-MI = target vessel–related myocardial infarction
ZES = zotarolimus-eluting stent(s)

Drug-eluting stents (DES) using a cobalt chromium (CoCr) alloy have improved clinical outcomes compared with first-generation DES and have raised the bar for clinical performance (1–5). The CoCr alloy has made it possible to maintain the radio-opacity of coronary stents while reducing the stent strut thickness compared with stainless steel (6,7). The newest addition to the newer-generation CoCr-DES lineup has been the CoCr-based zotarolimus-eluting stent (ZES) (Resolute, Medtronic, Minneapolis, Minnesota), which showed equivalent outcomes compared with the CoCr-based everolimus-eluting stent (EES) in the RESOLUTE All-Comers randomized trial (8,9). However, there still exist unmet needs, such as improved radial strength and visibility, which have driven the development of a novel platinum chromium (PtCr) alloy. PtCr-based stents were shown to have higher radio-opacity, more resistant radial strength, and enhanced conformability (10,11). A recent trial proved the noninferiority of the PtCr-EES (Promus Element, Boston Scientific, Natick, Massachusetts) compared with CoCr-EES in terms of clinical outcomes (12). However, this stent has not been tested in a broader population and compared with the CoCr-ZES. Data suggesting similar safety of PtCr-EES and CoCr-ZES in recent meta-analyses have been from only indirect comparisons (13,14) without evidence from direct, large-scale, head-to-head prospective trials. Further, the issue of longitudinal stent deformation (LSD) has been raised regarding thin-strut stents (15–18), with the PtCr-EES platform implicated as a potential risk factor (19,20).

This randomized trial was performed to test whether the newly developed PtCr-EES is noninferior to the CoCr-ZES in all-comers receiving percutaneous coronary intervention (PCI) with regard to target lesion failure (TLF). Moreover, procedural angiograms of all possible patients were reviewed by a core laboratory to address the issue of LSD.

Methods

Study design. The HOST–ASSURE (Harmonizing Optimal Strategy for Treatment of coronary artery stenosis–sAfety & effectiveneSS of drug-elUting stents & anti-platelet REgimen) was a prospective, randomized, single-blind, blinded endpoint evaluation, multicenter trial conducted at 40 sites in South Korea. The study design has been previously published (21). Briefly, the study had a 2 × 2 factorial design, in which randomization was performed for the type of DES and the type of 1-month intensified antiplatelet therapy followed by conventional dual antiplatelet therapy. Participating patients were randomized 2:1 to either PtCr-EES or CoCr-ZES and 1:1 to either triple antiplatelet therapy or double-dose dual antiplatelet therapy. The trial was coordinated by the investigators at the Cardiovascular Clinical Research Center at Seoul National University Hospital. The data were independently managed by a contract research organization, Dream CIS, Inc. (Seoul, Korea) The primary data analysis was performed by the investigators, with cooperation from Dream CIS, Inc. The executive committee, with assistance from the steering committee, was responsible for the study design, conduct, and management; manuscript preparation; and the decision to submit the paper for publication. An independent data safety monitoring board reviewed the unblinded data. The study was approved by all local ethics committees at the participating centers and was performed in accordance with the Declaration of Helsinki; written informed consent was obtained from all participants.

Patients. Trial participants were 18 years of age or older and had at least 1 clinically significant stenotic lesion amenable to PCI in the coronary artery, venous, or arterial bypass grafts. The trial entry criteria were broad with no exclusion criteria for lesion type, the number of stents used, the number of lesions treated, or the diagnosis at presentation. Major exclusion criteria were severe left ventricular systolic dysfunction (ejection fraction <25%), cardiogenic

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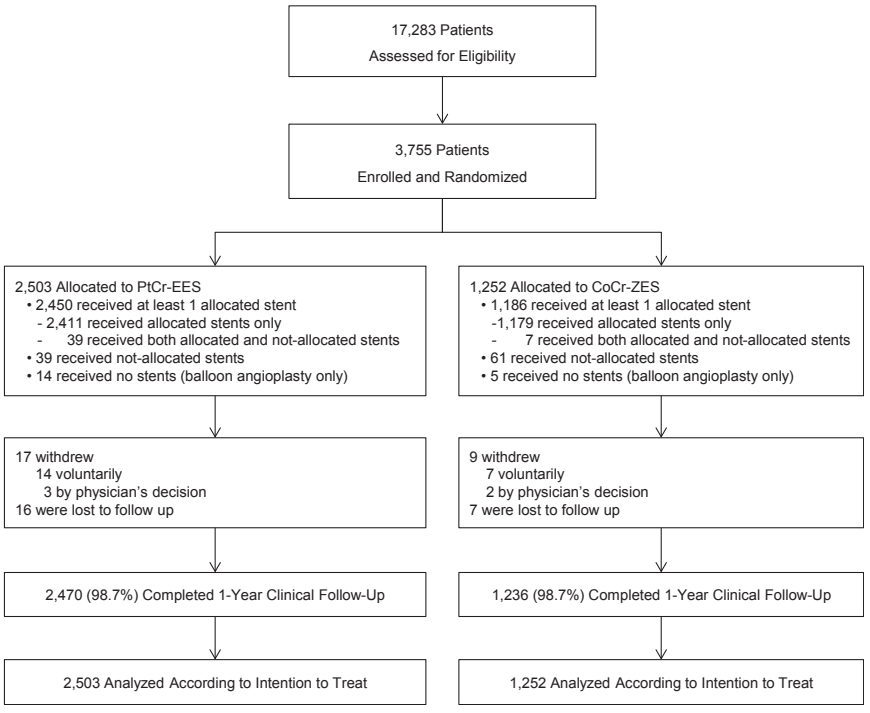

Figure 1 **Trial Profile**

A total of 3,755 patients were randomized 2:1 to platinum chromium (PtCr)-based everolimus-eluting stent (EES) or cobalt chromium (CoCr)-based zotarolimus-eluting stent (ZES). Clinical outcomes were analyzed according to the intention-to-treat basis.

shock, an increased risk of bleeding as evidenced by a history of bleeding diathesis, known coagulopathy, gastrointestinal or genitourinary bleeding within the prior 3 months, or major surgery within 2 months. Details of the eligibility criteria are described in the Online Appendix (Online Table 1).

Study procedures and endpoints. Patients were randomly assigned to either PtCr-EES or CoCr-ZES via a web-based online randomization system after diagnostic angiography and before PCI. The PCI was performed according to the standard techniques. The primary endpoint was TLF at 12 months, defined as a composite of cardiac death, target vessel–related myocardial infarction (TV-MI), and target lesion revascularization (TLR). Secondary endpoints included all of the individual components of the primary outcome along with stent thrombosis, patient-oriented clinical outcome, and all components of patient-oriented clinical outcome (all-cause death, all-cause myocardial infarction, and any repeat revascularization). Clinical events were defined on the basis of the recommendations of the Academic Research Consortium (ARC) (22). All deaths were considered cardiac unless a definite noncardiac cause could be established. Myocardial infarction was defined as the presence of clinical signs of myocardial infarction combined with a creatine kinase MB fraction or troponin-T or -I increase higher than the upper normal limit (23). Cardiac enzyme measurements were not routinely followed serially after PCI for all patients, but were allowed when clinically indicated. Stent thrombosis was defined as definite or probable stent thrombosis according to the ARC classification (22). The independent clinical event adjudication committee, whose members were unaware of the study group assignments, assessed all of the clinical endpoints. The primary analysis was on an intention-to-treat basis.

Angiographic analysis. Detailed methods of angiographic analysis are described in the Online Appendix. In brief, a qualitative analysis was performed to assess the presence of LSD, which was defined as any inconsistency in the radiodensity pattern along the length of the stent, or other gross irregularities or deformities. For quantitative assessment for the possibility of systemic longitudinal shortening of the stent, we measured the nominal stent length ratio (NSR), defined as the ratio of the final stent length after completion of the entire procedure to the nominal stent length.

Statistical analysis. We estimated that 3,750 patients would be required (using a sampling ratio of PtCr-EES to CoCr-ZES at 2:1) in the study to have >80% power with a 1-sided a of 2.5% to show noninferiority of the PtCr-EES compared with CoCr-ZES at hazard ratio (HR) 1.5, with the assumption of a 5% attrition rate and an assumed TLF rate of 6.5% at 12 months for CoCr-ZES. The primary

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Table 1 Baseline Patient Characteristics

	PtCr-EES (n = 2,503)	CoCr-ZES (n = 1,252)
Age, yrs	63.1 ± 10.8	63.5 ± 10.7
Male	1,746 (69.8)	820 (65.6)
Body mass index, kg/m^2	24.6 ± 3.2	24.7 ± 3.2
Hypertension	1,706 (68.2)	852 (68.1)
Diabetes	795 (31.8)	401 (32.0)
Dyslipidemia	1,601 (64.0)	822 (65.7)
Current smoker	823 (32.9)	369 (29.5)
Chronic renal failure	59 (2.4)	36 (2.9)
Peripheral artery disease	41 (1.6)	27 (2.2)
Cerebrovascular disease	172 (6.9)	79 (6.3)
Previous PCI	247 (9.9)	120 (9.6)
Previous bypass surgery	16 (0.6)	10 (0.8)
Previous myocardial infarction	116 (4.6)	49 (3.9)
Congestive heart failure	41 (1.6)	13 (1.0)
Clinical diagnosis		
Silent ischemia	119 (4.8)	63 (5.0)
Stable angina	746 (29.8)	367 (29.3)
Unstable angina	903 (36.1)	476 (38.0)
NSTEMI	452 (18.1)	209 (16.7)
STEMI	283 (11.3)	137 (10.9)
Baseline laboratory findings		
Left ventricular ejection fraction, %	59.9 ± 10.4	60.4 ± 10.2
Hemoglobin, g/dl	13.7 ± 1.7	13.7 ± 1.7
Platelet count × 10^3/mm	227 ± 61	227 ± 64
Serum creatinine, mg/dl	1.00 ± 0.73	1.00 ± 0.87
Total cholesterol, mg/dl	177 ± 43	178 ± 45
Triglyceride, mg/dl	138 ± 87	144 ± 107
HDL cholesterol, mg/dl	44 ± 12	44 ± 11
LDL cholesterol, mg/dl	110 ± 41	109 ± 38
Procedural data		
Angiographic disease extent		
1-vessel disease	1,150 (45.9)	580 (46.3)
2-vessel disease	807 (32.2)	400 (31.9)
3-vessel disease	546 (21.8)	272 (21.7)
Target lesions to be treated		
1	1,766 (70.6)	909 (72.6)
2	570 (22.8)	286 (22.8)
3 or more	167 (6.7)	57 (4.6)
Use of IVUS or OCT	1,037 (41.4)	494 (39.5)
Use of glycoprotein IIb/IIIa inhibitors	55 (2.2)	37 (3.0)
Lesion data	(n = 3,426)	(n = 1,661)
Target vessel location		
Left main artery	74 (2.2)	37 (2.2)
Left anterior descending artery	1,623 (47.4)	852 (51.3)
Left circumflex artery	751 (21.9)	324 (19.5)
Right coronary artery	978 (28.5)	448 (27.0)
ACC/AHA classification B2/C type	1,662 (49.7)	842 (51.7)
Total occlusion	422 (12.3)	193 (11.6)
Thrombus-containing	45 (1.3)	25 (1.5)
Bifurcation	874 (25.6)	420 (25.3)
Medications at discharge		
Aspirin	2,485 (99.3)	1,247 (99.6)
Clopidogrel	2,483 (99.2)	1,246 (99.5)
β-blocker	1,710 (68.3)	845 (67.5)
Calcium-channel blocker	526 (21.0)	236 (18.8)
ACE inhibitor or ARB	1,636 (65.4)	829 (66.2)
Statin	2,122 (84.8)	1,076 (85.9)

Continued in the next column

Table 1 Continued

Values are mean ± SD or n (%).

ACC/AHA = American College of Cardiology/American Heart Association; ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CoCr-ZES = cobalt chromium zotarolimus-eluting stent; HDL = high-density lipoprotein; IVUS = intravascular ultrasound; LDL = low-density lipoprotein; NSTEMI = non–ST-segment elevation myocardial infarction; OCT = optical coherence tomography; PCI = percutaneous coronary intervention; PtCr-EES = platinum chromium everolimus-eluting stent; STEMI = ST-segment elevation myocardial infarction.

analysis was performed on an intention-to-treat basis. Detailed methods of statistical analysis are described in the Online Appendix.

Results

Baseline characteristics and procedural results. From June 2010 to November 2011, a total of 3,755 patients were enrolled at 40 centers in South Korea. These patients were randomly allocated to PtCr-EES (n = 2,503 patients, 3,426 lesions) or CoCr-ZES (n = 1,252 patients, 1,661 lesions). Figure 1 shows the trial profile and the study flow of the patients. The baseline patient characteristics are shown in Table 1 and the baseline lesion and procedural characteristics in Table 2. The baseline characteristics were mostly well balanced and comparable between the 2 groups except for male sex and smoking, which were slightly more frequent in the PtCr-EES group.

Table 3 compares the use of antiplatelet agents in each group during the follow-up duration. There were no significant differences at any follow-up period in terms of the use of aspirin, clopidogrel, or cilostazol. Overall compliance to dual antiplatelet therapy was 91.6% at 1-year follow-up and did not differ significantly at any time between the stent groups.

Clinical outcomes up to 1 year. At 12 months post-PCI, the primary endpoint of TLF (the composite of cardiac death, TV-MI, and TLR) occurred in 72 patients (2.9%) in the PtCr-EES group and 36 patients (2.9%) in the CoCr-ZES group (Table 4, Fig. 2A). We confirmed the non-inferiority of PtCr-EES with an absolute risk difference of 0% and an upper limit of the 1-sided 97.5% HR of 1.499 (p = 0.0247 for noninferiority; pre-specified noninferiority HR margin: 1.5) (Fig. 2B). Regarding superiority, there was no significant difference between the 2 treatment groups (HR: 1.00; 95% confidence interval [CI]: 0.67 to 1.50; p = 0.983 for superiority). The results of the per-protocol analysis were similar to the intention-to-treat analysis (TLF rates: 2.8% vs. 2.8%) with 97.5% upper CI marginally exceeding the pre-specified margin (HR: 1.00; 95% CI: 0.66 to 1.52; p = 0.028 for noninferiority; p = 0.999 for superiority) (Fig. 2C, Online Table 2). The individual rates of cardiac death, TV-MI, and TLR were not significantly different between the 2 groups (Table 4, Figs. 2D to 2F). Patient-oriented outcomes were also similar, and occurred

Table 2 Characteristics of Revascularization Procedures

Variable	PtCr-EES (n = 3,426)	CoCr-ZES (n = 1,661)	p Value
Before index procedure			
Lesion length, mm	19.3 ± 11.8	19.8 ± 12.4	0.229
Reference vessel diameter, mm	3.00 ± 0.50	3.00 ± 0.50	0.457
Minimum lumen diameter, mm	0.81 ± 0.50	0.81 ± 0.50	0.657
Percent stenosis, %	73.1 ± 15.4	72.8 ± 15.5	0.470
SYNTAX score	12.1 ± 8.0	12.4 ± 8.1	0.299
After index procedure			
SYNTAX score	4.0 ± 5.4	4.0 ± 5.4	0.852*
Number of stents			
Per lesion	1.19 ± 0.45	1.17 ± 0.43	0.301
Per patient	1.62 ± 0.92	1.56 ± 0.85	0.061
Maximal stent diameter, mm			
Per lesion	3.15 ± 0.46	3.16 ± 0.44	0.797
Per patient	3.26 ± 0.45	3.24 ± 0.44	0.281
Total stent length, mm			
Per lesion	27.7 ± 13.3	28.7 ± 14.6	0.022
Per patient	37.6 ± 24.2	37.9 ± 25.0	0.764
Adjunctive ballooning	2,369 (69.1)	1,140 (68.6)	0.710
Balloon diameter, mm	3.04 ± 0.56	3.03 ± 0.55	0.532
Maximal Inflation diameter, mm	3.22 ± 0.62	3.20 ± 0.57	0.387
Minimum lumen diameter, mm			
In-stent	2.61 ± 0.43	2.62 ± 0.45	0.465
In-segment	2.23 ± 0.53	2.21 ± 0.52	0.397
Diameter stenosis, %			
In-stent	11.0 ± 7.4	11.2 ± 8.1	0.538
In-segment	21.5 ± 11.2	22.2 ± 11.4	0.051
Acute gain, mm			
In-stent	1.80 ± 0.53	1.81 ± 0.55	0.798
In-segment	1.42 ± 0.58	1.40 ± 0.59	0.275
Successful outcome			
Lesion	3,388 (99.5)	1,643 (99.5)	0.947
Device	3,387 (99.4)	1,649 (99.8)	0.054
Procedure	3,390 (99.5)	1,644 (99.5)	0.875

Values are mean ± SD or n (%). *Comparison was performed with the Wilcoxon rank sum test.
SYNTAX = SYNergy between PCI with TAXUS and Cardiac Surgery; other abbreviations as in Table 1.

in 5.2% and 4.5% of the PtCr-EES and CoCr-ZES groups, respectively (HR: 1.20; 95% CI: 0.88 to 1.64; p = 0.187). Subgroup analyses of the primary outcome showed consistent findings and no significant interaction between different subgroups and the allocated stent except for reference vessel diameter (Fig. 3). There were no significant interactions between the allocated stent and the allocated antiplatelet therapy regimen with regard to any clinical endpoint including TLF.

At 12 months, ARC-defined definite and probable stent thrombosis occurred in 0.4% and 0.7%, respectively, in the 2 groups (p = 0.229). There were no significant differences between the 2 stents regarding definite, probable, and possible stent thrombosis as well as acute, subacute, or late stent thrombosis (Table 5, Online Fig. 1). Details of individual cases of the stent thrombosis are described in Online Table 3.

Angiographic analysis: longitudinal stent deformation. Of 3,755 patients (5,087 lesions) enrolled in the study, the baseline procedural angiograms were available and readable in 3,711 patients (5,010 lesions). The occurrence of LSD was analyzed using the baseline procedural angiograms in these patients: 2,471 patients (3,367 lesions) in the PtCr-EES group and 1,240 patients (1,643 lesions) in the CoCr-ZES group. LSD was observed in 7 patients in the PtCr-EES group (7 stents, incidence rate: 0.21%) and in no patients in the CoCr-ZES group (p = 0.104). The mean NSR was lower in the PtCr-EES group compared with the CoCr-ZES group (mean NSR 0.92 ± 0.07 vs. 0.93 ± 0.07; p < 0.001) (Fig. 4). The specific details of the 7 LSD cases are summarized in Table 6. Of these cases, none were associated with future adverse clinical events up to 1 year. Only 1 case required an additional stent implantation during the baseline procedure (Fig. 5). LSD occurred during stent implantation while advancing adjunctive balloon catheter or while withdrawing the trapped intravascular ultrasound catheter, guidewire, or stent leading to deep engagement of the guiding catheter. In all cases, the proximal part of the stent was the site of deformation and resulted in significant shortening of the stent.

Table 3 Use of Antiplatelet Agents During Follow-Up

	PtCr-EES (n = 2,503)	CoCr-ZES (n = 1,252)	p Value
Aspirin			
At 1 month	2,476/2,490 (99.4)	1,244/1,248 (99.7)	0.314
At 3 months	2,431/2,466 (98.6)	1,218/1,227 (99.3)	0.070
At 9 months	2,351/2,416 (97.3)	1,186/1,213 (97.8)	0.401
At 12 months	2,277/2,373 (96.0)	1,165/1,204 (96.8)	0.232
Clopidogrel			
At 1 month	2,476/2,490 (99.4)	1,242/1,249 (99.4)	0.995
At 3 months	2,426/2,469 (98.3)	1,214/1,228 (98.9)	0.162
At 9 months	2,347/2,412 (97.3)	1,188/1,215 (97.8)	0.393
At 12 months	2,218/2,373 (93.5)	1,140/1,205 (94.6)	0.181
Cilostazol			
At 1 month	1,168/2,490 (46.9)	587/1,248 (47.0)	0.941
At 3 months	172/2,463 (7.0)	95/1,227 (7.7)	0.402
At 9 months	103/2,409 (4.3)	45/1,211 (3.7)	0.422
At 12 months	97/2,364 (4.1)	53/1,201 (4.4)	0.663
Dual antiplatelet therapy			
At 1 month	2,469/2,490 (99.2)	1,242/1,249 (99.4)	0.344
At 3 months	2,415/2,470 (97.8)	1,212/1,228 (98.7)	0.054
At 9 months	2,317/2,416 (95.9)	1,176/1,215 (96.8)	0.187
At 12 months	2,163/2,374 (91.1)	1,116/1,205 (92.6)	0.125

Values are n/N (%).
Abbreviations as in Table 1.

Discussion

This was 1 of the largest direct stent comparison studies ever performed to test the noninferiority of PtCr-EES against the CoCr-ZES, the 2 most recently introduced and now most commonly used DES. Furthermore, we systemically addressed the issue of LSD in over 5,000 lesions. The major findings of this study are as follows:

1. PtCr-EES was noninferior to CoCr-ZES at 1 year regarding TLF, the composite of cardiac death, nonfatal TV-MI, and ischemia-driven TLR. Also, the

Table 4 Cumulative Incidence of Clinical Events Up to 1 Year

	PtCr-EES (n = 2,503)	CoCr-ZES (n = 1,252)	HR (95% CI)	p Value
Target lesion failure	72 (2.88)	36 (2.88)	1.00 (0.67–1.50)	0.983
All-cause death	56 (2.24)	20 (1.60)	1.40 (0.84–2.34)	0.194
Cardiac death	34 (1.36)	17 (1.36)	1.00 (0.56–1.79)	0.997
All-cause MI	28 (1.12)	17 (1.36)	0.83 (0.45–1.51)	0.533
Target vessel-related MI	24 (0.96)	13 (1.04)	0.93 (0.47–1.82)	0.822
Repeat revascularization	74 (2.96)	33 (2.64)	1.13 (0.75–1.70)	0.557
Target lesion revascularization	31 (1.24)	15 (1.20)	1.04 (0.56–1.93)	0.900
Target vessel revascularization	42 (1.68)	23 (1.84)	0.92 (0.55–1.53)	0.746
Cerebrovascular accident	17 (0.68)	8 (0.64)	1.07 (0.46–2.47)	0.879
Ischemic	15 (0.60)	6 (0.48)	1.26 (0.49–3.24)	0.636
Hemorrhagic	2 (0.08)	2 (0.16)	0.50 (0.07–3.55)	0.489
All PLATO bleeding	45 (1.80)	25 (2.00)	0.90 (0.55–1.47)	0.674
Major bleeding	27 (1.08)	16 (1.28)	0.84 (0.45–1.57)	0.591
Major, life-threatening	4 (0.16)	4 (0.32)	0.50 (0.13–2.00)	0.327
Major, other	23 (0.92)	13 (1.04)	0.89 (0.45–1.75)	0.725
Minor bleeding	18 (0.72)	9 (0.72)	1.00 (0.45–2.23)	0.996
Target vessel failure	82 (3.28)	42 (3.35)	0.98 (0.68–1.42)	0.919
Patient-oriented clinical outcome	135 (5.39)	55 (4.39)	1.24 (0.90–1.69)	0.187

Values are n (%). Target vessel failure was a composite of cardiac death, target vessel–related myocardial infarction (MI), and target vessel revascularization; patient-oriented clinical outcome was a composite of all-cause death, all-cause MI, and repeat revascularization.
PLATO = PLATelet inhibition and patient Outcomes; other abbreviations as in Table 1.

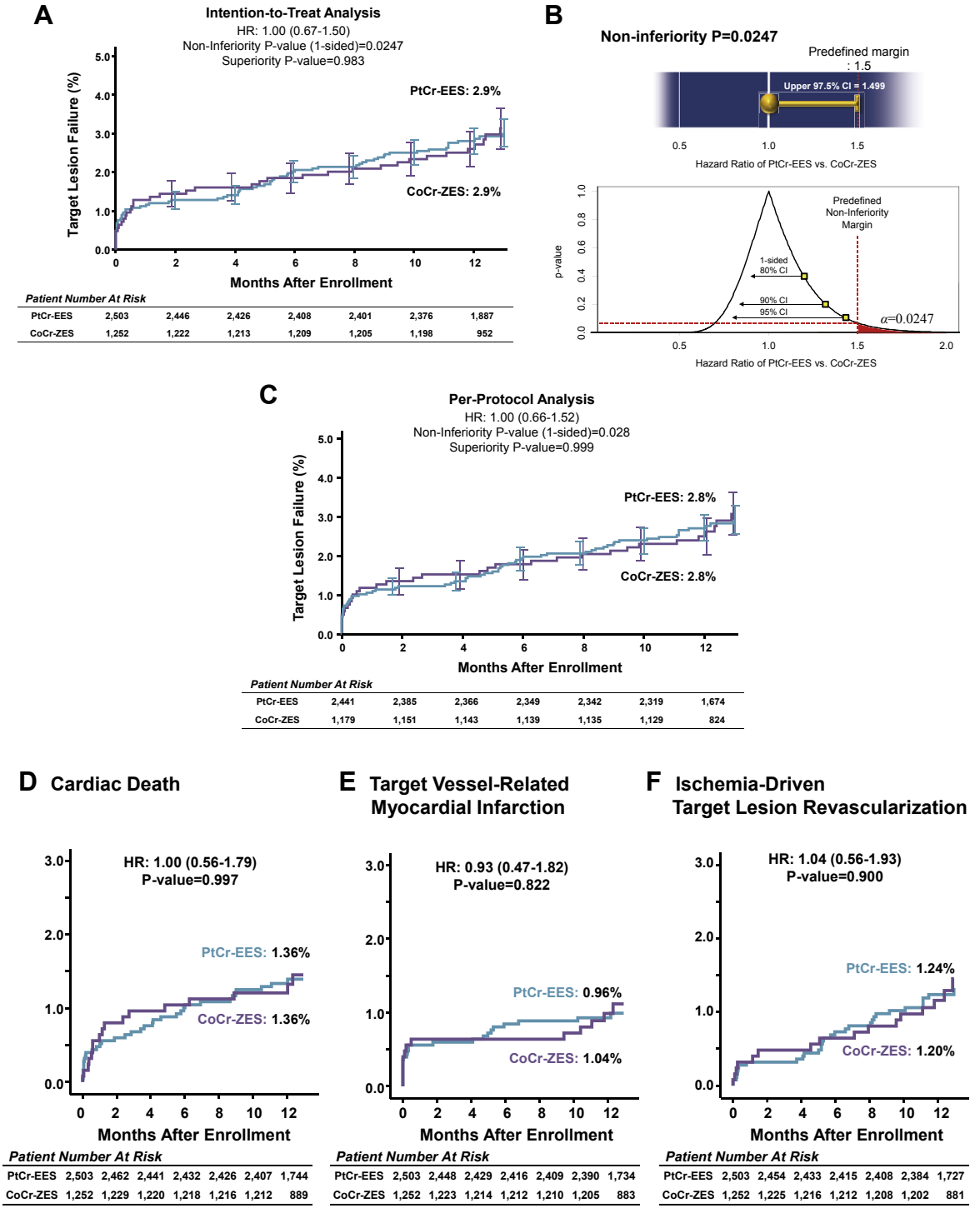

Figure 2 **Clinical Outcomes**

(A) Kaplan-Meier cumulative event curves up to 12 months are shown for target lesion failure. **(B)** A noninferiority margin was pre-defined as hazard ratio (HR) of 1.5 and a p value function curve for hypothesis testing. **(C)** Target lesion failure by per-protocol analysis. **(D to F)** Event curves for cardiac death **(D)**, nonfatal target vessel–related myocardial infarction **(E)**, and ischemia-driven target lesion revascularization **(F)**. CI = confidence interval; other abbreviations as in Figure 1.

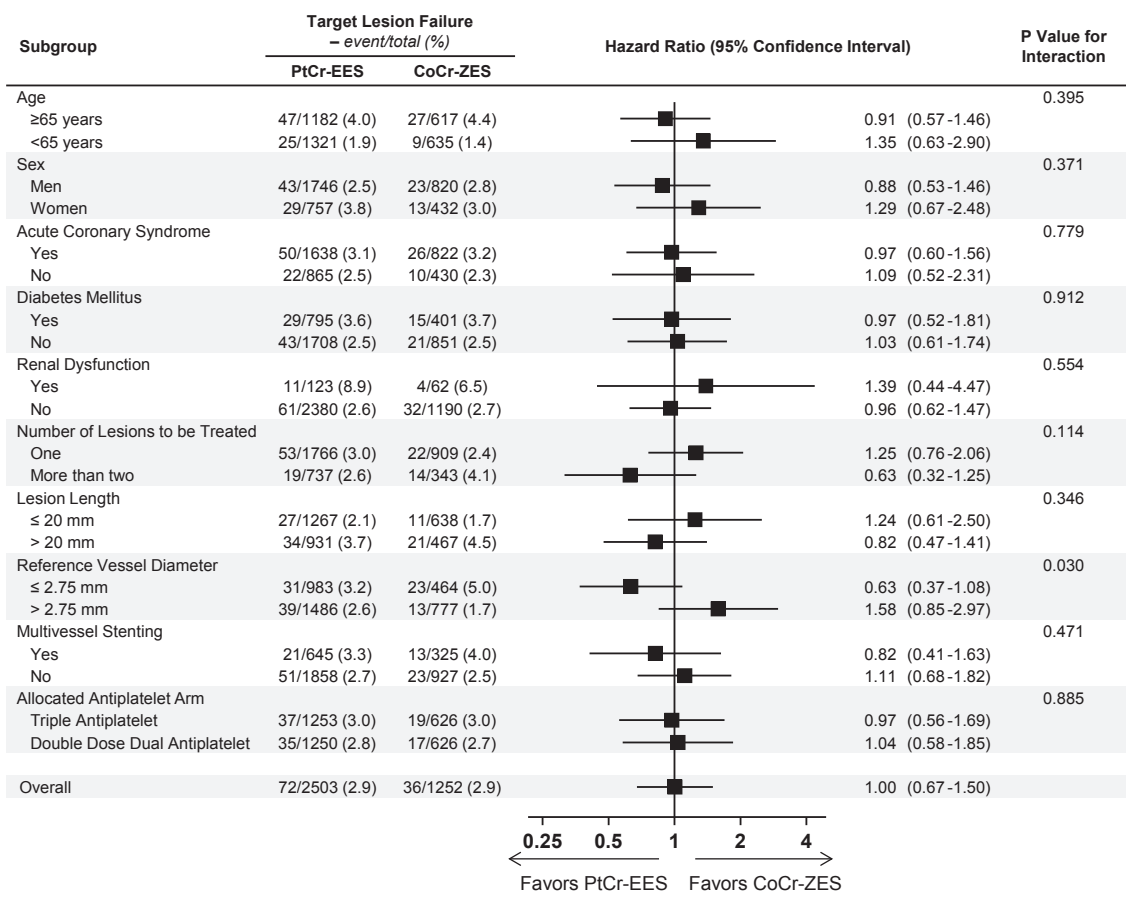

Figure 3 **Subgroup Analysis**

Target lesion failure according to various subgroups. The **squares** indicate the odds ratios and the **horizontal lines** indicate 95% confidence intervals. Abbreviations as in Figure 1.

individual outcomes were very similar between the 2 stents.

2. Both stents demonstrated outstanding safety as well as efficacy, with stent thrombosis rates below 1% and TLF rates below 3% in an enriched PCI population of all-comers.
3. LSD was observed only in PtCr-EES, but its incidence was very rare and it was not associated with future adverse clinical events.

Newer-generation DES have significantly improved clinical outcomes compared with first-generation DES. In particular, CoCr-based EES, the oldest of the newer-generation DES, have shown improved clinical results in various trials and meta-analyses (1–5). The newest addition to the CoCr alloy-based DES line-up has been the CoCr-ZES. In the RESOLUTE All-Comers trial, CoCr-ZES was shown to be noninferior to CoCr-EES regarding stent- and patient-specific clinical outcomes (8,9). We also reported similar clinical performance of the 2 stents from an all-comer registry (24).

Compared with the earlier-generation DES, 1 of the major advantages of the CoCr stent platform was the reduction in stent strut thickness. In previous stainless steel stent platforms, the visibility of the stent decreases significantly as the stent strut thickness is reduced, as was evidenced in the stainless steel-based paclitaxel-eluting stent (Taxus Liberte, Boston Scientific). Thus, the CoCr-based stents have supplanted stainless steel stents as the most commonly used coronary stents in the world. However, CoCr stents have several important limitations. Radial strength and recoil are inferior to stainless steel stents and radio-opacity, although better than with stainless steel stents, is still suboptimal, particularly with the newest thin-strut CoCr stents. The PtCr alloy was developed to address these limitations and was shown to have greater radial strength, less recoil, and greater radio-opacity than its CoCr counterparts (10,11). From bench data, the PtCr alloy showed low thrombogenicity and a high degree of endothelial surface coverage (25). Clinically, PtCr-EES was previously shown to be noninferior to CoCr-EES regarding TLF at 1 and 2 years in the PLATINUM (A Prospective,

Table 5 Cumulative Incidence of Stent Thrombosis Up to 1 Year

	PtCr-EES (n = 2,503)	CoCr-ZES (n = 1,252)	p Value
Definite or probable ST	9 (0.36)	8 (0.67)	0.229
Acute definite or probable ST	1 (0.04)	1 (0.08)	1.000
Subacute definite or probable ST	7 (0.28)	6 (0.50)	0.379
Early definite or probable ST	8 (0.32)	7 (0.58)	0.273
Late definite or probable ST	1 (0.04)	1 (0.08)	1.000
Definite ST	5 (0.20)	3 (0.25)	1.000
Acute definite ST	0 (0.00)	1 (0.08)	0.333
Subacute definite ST	5 (0.20)	1 (0.08)	0.671
Early definite ST	5 (0.20)	2 (0.17)	1.000
Late definite ST	0 (0.00)	1 (0.08)	0.333
Probable ST	4 (0.16)	5 (0.42)	0.171
Acute probable ST	1 (0.04)	0 (0.00)	1.000
Subacute probable ST	2 (0.08)	5 (0.42)	0.045
Early probable ST	3 (0.12)	5 (0.42)	0.127
Late probable ST	1 (0.04)	0 (0.00)	1.000
Possible ST	15 (0.60)	6 (0.50)	0.642
Acute possible ST	0 (0.00)	0 (0.00)	NA
Subacute possible ST	0 (0.00)	0 (0.00)	NA
Early possible ST	0 (0.00)	0 (0.00)	NA
Late possible ST	15 (0.60)	6 (0.50)	0.642

Values are n (%). Stent thrombosis (ST) was defined according to the definition of the Academic Research Consortium consensus.
NA = not available; other abbreviations as in Table 1.

Randomized, Multicenter Trial to Assess an Everolimus-Eluting Coronary Stent System [PROMUS Element] for the Treatment of Up to Two de Novo Coronary Artery Lesions) trial (12). We hypothesized that these potential advantages would lead to at least noninferior clinical results compared with CoCr stents.

Regarding the issue of stent deformation with newer-generation DES, there have been various case reports of

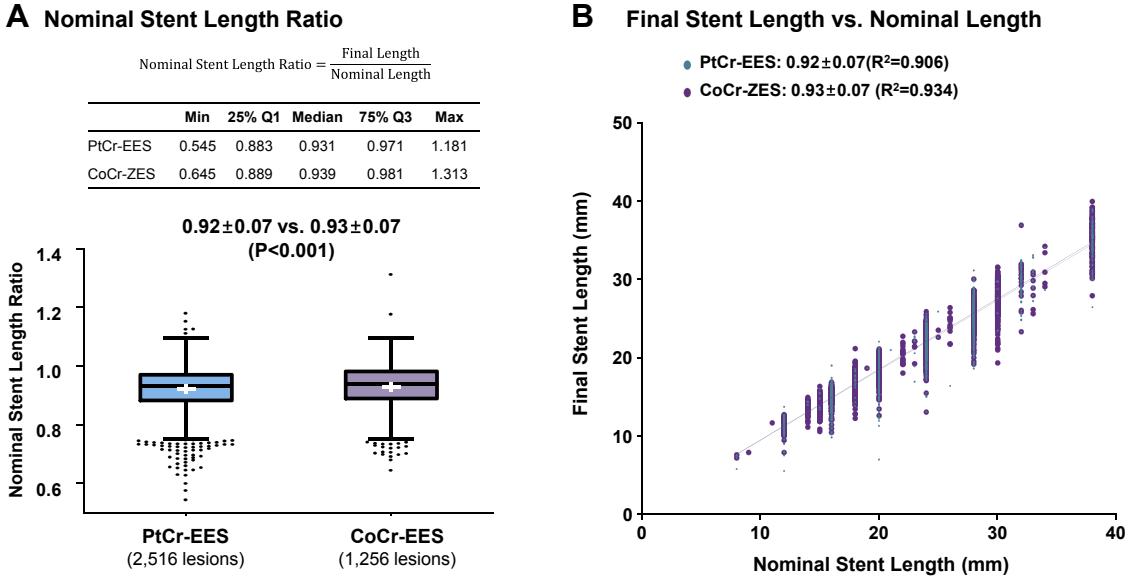

Figure 4 Angiographic Analysis of Stent Length Ratio

(A) Box plots of nominal stent length ratio (NSR) according to allocated arms. The **box** indicates hinges and median, and the **whiskers** show the largest or smallest observation that falls within a distance of 1.5 times the box size from the nearest hinge. The **cross in the box** indicates the mean. **(B)** Dot plotting of nominal and final stent length for both PtCr-EES **(blue)** and CoCr-ZES **(purple)**. Q = quartile; other abbreviations as in Figure 1.

Table 6 Clinical and Angiographic Details of the 7 Patients Who Had Longitudinal Stent Deformation During the Procedure

Patient #	Age/Sex	Lesion Location	Stent Size, mm	Precipitating Factor	Bifurcation	Ostial Lesion	Segment of Stent Involved	Additional Stenting Required	Future Clinical Events
1	61/M	LMCA	P-E 3.0 × 24	Deep engagement of guiding catheter	Yes	Yes	Proximal part	No	No
2	59/M	LMCA	P-E 3.0 × 28	Deep engagement of guiding catheter due to trapped retrograde guidewire (chronic total occlusion)	No	No	Proximal part	No	No
3	50/F	Mid LAD	P-E 4.0 × 28	Deep engagement of guiding catheter due to trapped IVUS catheter	No	No	Proximal part	No	No
4	72/M	Proximal RCA	P-E 3.0 × 28	Deep engagement of guiding catheter due to trapped stent	No	No	Proximal part	No	No
5	39/M	Proximal LAD	P-E 4.0 × 28	Advancing adjunctive balloon catheter	Yes	No	Proximal part	No	No
6	81/F	Mid LAD	P-E 3.0 × 20	Advancing adjunctive balloon catheter	Yes	No	Proximal part	Yes	No
7	68/M	Mid LAD	P-E 3.0 × 28	Advancing adjunctive balloon catheter	No	No	Proximal part	No	No

IVUS = intravascular ultrasound; LAD = left anterior descending artery; LMCA = left main coronary artery; P-E = Promus Element stent (Boston Scientific, Natick, Massachusetts); RCA = right coronary artery.

inadvertent LSD (15–18). LSD raised concerns about possible adverse events or ST. Most reports were anecdotal case reports with no data from comprehensively performed prospective trials. In a study of pooled angiographic evaluation of the PERSEUS (Prospective Evaluation in a Randomized Trial of the Safety and Efficacy of the Use of the TAXUS Element Paclitaxel-Eluting Coronary Stent System for the Treatment of De Novo Coronary Artery Lesions) and PLATINUM trials, PtCr-EES did not differ from stainless steel–based or CoCr-based stents in terms of the nominal stent length ratio, and there were no cases of LSD (16). However, bench testing showed that PtCr-EES had significantly weaker resistance against longitudinal compressive forces compared with other stent platforms, which may be due to its offset peak-to-peak design (15–19,26). In the present study, after meticulous review of over 5,000 stents by an angiographic core laboratory, LSD was observed only in the PtCr-EES group and not in the CoCr-ZES group. However, the events were so rare (0.2% in the PtCr-EES group) that this difference was not statistically significant. The problem observed in this study with the proximal portion of the stent being vulnerable to LSD has recently been addressed by the manufacturer through the addition of connectors to the proximal stent struts in the design of the new version of the PtCr-EES, the Promus Premier stent (Boston Scientific) (27).

Study limitations. First, the observed 1-year TLF rate was 2.9% for the control group (CoCr-ZES), which was lower than the assumed 6.5% used in the study power calculation. If we had assumed an expected event rate of 2.9% instead of 6.5%, the statistical power of this study to detect noninferiority would have been as low as 50%. Second, despite the all-comer nature of the study population, the event rates were very low, which may raise the question of underreporting. However, periodic monitoring and data audits were thoroughly performed during this trial. One possible reason for the low event rates may be that this study had a 2 × 2 factorial design. Also, the fact that some high-risk patients met contraindications to cilostazol and had to be excluded and that all participating patients were treated with intensified antiplatelet therapies for 1 month may have contributed to the lower incidence of TLF. Routine post-PCI cardiac enzyme measurement was not mandated in the study, and it may have also led to the lower incidence of events. There also may be an ethnic or genetic protective factor, as trials done in East Asian populations have consistently reported lower event rates (28–30). Finally, because we used visual assessment for presence of LSD, the likelihood of detecting a deformity would be naturally higher in a more visible stent such as PtCr-EES.

Conclusions

PtCr-EES was noninferior to CoCr-ZES for up to 1 year in all-comers receiving PCI. Although LSD was observed only in PtCr-EES, its incidence was rare and was not associated with future adverse cardiac events.

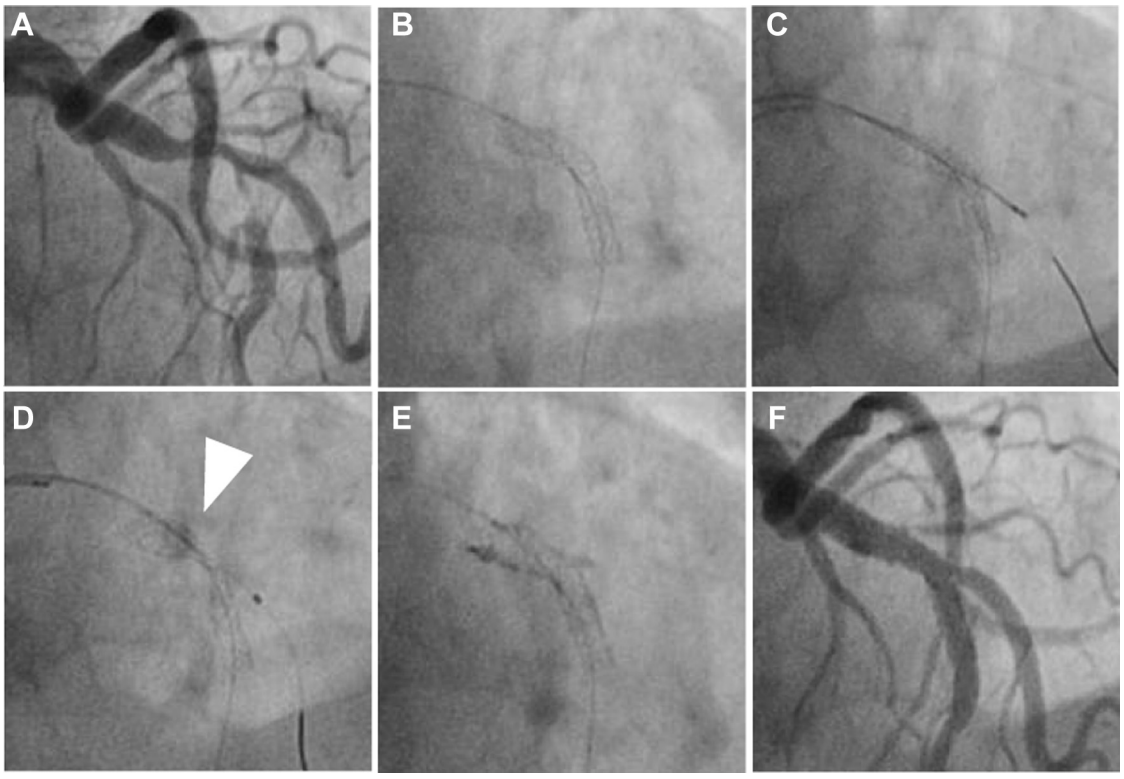

Figure 5 **A Representative Case of Longitudinal Stent Deformation**

An 81-year-old woman presented with stable angina pectoris. **(A)** Baseline angiography showed bifurcation lesion involving an angulated proximal to mid-left anterior descending artery (LAD) and a big diagonal branch. **(B)** A 3.0 × 20-mm Promus Element stent (Boston Scientific, Natick, Massachusetts) was deployed in the left anterior descending artery (LAD) (simple crossover technique). **(C)** After introducing the guidewire to the diagonal branch, no obvious stent deformation was observed. **(D)** Longitudinal stent deformation **(arrowhead)** occurred during advancing adjunctive balloon catheters for kissing ballooning of LAD and diagonal branch. **(E)** An additional 3.5 × 15-mm Promus Element stent was deployed in the proximal LAD overlapping the previous deformed stent. **(F)** Final angiographic result. The patient experienced no clinical events during the 1-year follow-up duration after the procedure.

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Key Words: all-comers trial ▪ clinical outcome ▪ drug-eluting stent(s) ▪ percutaneous coronary intervention.

APPENDIX

For supplemental methods, supplemental tables and a figure, and a list of HOST–ASSURE Trial Investigators, please see the online version of this article.