Comparison of Everolimus- and Sirolimus-Eluting Stents in Patients With Long Coronary Artery Lesions

Duk-Woo Park, MD,* Young-Hak Kim, MD,* Hae-Geun Song, MD,* Jung-Min Ahn, MD,* Won-Jang Kim, MD,* Jong-Young Lee, MD,* Soo-Jin Kang, MD,* Seung-Whan Lee, MD,* Cheol Whan Lee, MD,* Seong-Wook Park, MD,* Sung-Cheol Yun, Ptd,† Ki-Bae Seung, MD,‡ Tae-Hyun Yang, MD,§ Sang-Gon Lee, MD,|| Jae-Hwan Lee, MD,¶ In-Whan Seong, MD,¶ Sang-Sig Cheong, MD,# Bong-Ki Lee, MD,** Nae-Hee Lee, MD,†† Se-Whan Lee, MD,‡‡ Seung-Wook Lee, MD,§§ Keun Lee, MD,||| Hyun-Sook Kim, MD,¶¶ Doo-Soo Jeon, MD,## Min-Kyu Kim, MD,### Deuk-Young Nah, MD,#### Seung-Jea Tahk, MD,##### Seung-Jung Park, MD*

Seoul, Pusan, Ulsan, Daejeon, GangNeung, Chuncheon, Bucheon, Cheonan, Gwangju, Anyang, Incheon, Gyeyongju, and Suwon, Korea

Objectives This study compared everolimus-eluting stents (EES) and sirolimus-eluting stents (SES) for long coronary lesions.

Background Outcomes remain relatively unfavorable for stent-based coronary intervention of lesions with long diseased segments.

Methods This randomized, multicenter, prospective trial compared the use of long EES with SES in 450 patients with long (≥25 mm) native coronary lesions. The primary endpoint of the trial was in-segment late luminal loss at 9-month angiographic follow-up.

Results The EES and SES groups had similar baseline characteristics. Lesion length was 34.0 ± 15.4 mm in the EES group and 34.3 ± 13.5 mm in the SES group (p = 0.85). Nine-month angiographic follow-up was performed in 80% of the EES group and 81% of the SES group (p = 0.69). In-segment late loss as the primary study endpoint was significantly larger in the EES group than in the SES group (0.17 ± 0.41 mm vs. 0.09 ± 0.30 mm, p for noninferiority = 0.96, p for superiority = 0.04). The in-segment binary restenosis rate was also higher in the EES group than in the SES group (7.3% vs. 2.7%, p = 0.046). However, in-stent late loss (0.22 ± 0.43 mm vs. 0.18 ± 0.28 mm, p = 0.29) and in-stent binary restenosis rate (3.9% vs. 2.7%, p = 0.53) were similar among the 2 groups. The incidence of any clinical outcomes (death, myocardial infarction, stent thrombosis, target lesion revascularization, and composite outcomes) was not statistically different between the 2 groups.

Conclusions For patients with long native coronary artery disease, EES implantation was associated with greater angiographic in-segment late loss and higher rates of in-segment restenosis compared with SES implantation. However, clinical outcomes were both excellent and not statistically different. (Percutaneous Treatment of LONG Native Coronary Lesions With Drug-Eluting Stent-III [LONG-DES-III]; NCT01078038) (J Am Coll Cardiol Intv 2011;4:1096–103) © 2011 by the American College of Cardiology Foundation
The use of drug-eluting stents (DES) has had a major clinical impact on the treatment of patients with atherosclerotic coronary artery disease. Early generation DES releasing sirolimus or paclitaxel from durable polymers has reduced angiographic restenosis and the need of repeat revascularization compared with bare-metal stents (BMS) (1). Based on the results of pivotal clinical trials, DES has been widely used for percutaneous coronary intervention (PCI) in routine clinical practice, including more complex clinical and anatomic subsets (2). However, restenosis still occurs, and the incidence of late stent thrombosis is increased with DES compared with BMS, likely as a result of chronic inflammation and delayed healing of the arterial wall (3). These adverse events were more pronounced for “off-label” indications, including higher-risk lesion subsets. Therefore, newer generation DES have been developed with the aim to improve upon the efficacy and safety profiles of early generation devices.

The newer generation everolimus-eluting stent (EES) consists of a thin-strut, cobalt chromium alloy and releases everolimus, a semisynthetic sirolimus analogue from an acrylic and fluoropolymer mixture (4). EES have been shown to improve clinical and angiographic outcomes compared with early generation paclitaxel-eluting stents (5–8). To date, however, there are limited data directly comparing EES with early generation sirolimus-eluting stents (SES), especially in complex lesion subsets. Despite of markedly improved efficacy of DES, long coronary lesions still remain at a higher risk of unfavorable outcomes after PCI, thereby making differences in the performances of comparative DES devices more pronounced. This prospective randomized study, the LONG-DES-III (Percutaneous Treatment of LONG Native Coronary Lesions With Drug-Eluting Stent-III) trial, compared angiographic and clinical outcomes of EES and SES in patients with native long coronary lesions.

Methods

Study design and population. The LONG-DES III trial is a prospective, randomized, single-blind, controlled study conducted in 16 centers in South Korea between June 2008 and August 2009. The study protocol was approved by the ethics committee at each participating center and was conducted according to the principles of the Declaration of Helsinki regarding investigations in humans. All patients provided written, informed consent for participation in this trial. The sponsor of this study contributed to study design but had no role in data collection, monitoring, analysis, interpretation, or writing of the manuscript.

This study involved the consecutive enrollment of eligible patients age 18 years or older with stable angina or acute coronary syndromes or inducible ischemia who had at least 1 native long coronary lesion suitable for stent implantation. Angiographic eligibility for inclusion consisted of a target lesion with a diameter stenosis ≥50%, visual vessel diameter ≥2.5 mm, and visual lesion length ≥25 mm. Inclusion required that the planned total stent length be ≥28 mm. Exclusion criteria were acute ST-segment elevation myocardial infarction (MI) necessitating primary PCI; severely compromised ventricular dysfunction, ejection fraction <30% or cardiogenic shock; allergy to antiplatelet drugs, heparin, stainless steel, contrast agents, everolimus, or sirolimus; left main coronary artery disease (defined as stenosis of >50%); renal dysfunction (serum creatinine level ≥2.0 mg/dl) or dependence on dialysis; terminal illness; elective surgery planned within 6 months after the procedure, necessitating antiplatelet agent discontinuation; and participation in another coronary-device study or inability to follow the protocol.

Randomization, procedures, and adjunct drug therapy. If the inclusion and exclusion criteria were met, randomization was performed after diagnostic angiography and before PCI. Eligible patients were randomly assigned on a 1:1 basis.

Abbreviations and Acronyms

BMS = bare-metal stent(s)  
DES = drug-eluting stent(s)  
EES = everolimus-eluting stent(s)  
MACE = major adverse cardiac events  
MI = myocardial infarction  
PCI = percutaneous coronary intervention  
SES = sirolimus-eluting stent(s)  
TLR = target lesion revascularization

Manuscript received May 13, 2011; accepted May 31, 2011.
to treatment with EES (PROMUS, Boston Scientific, Natick, Massachusetts, or XIENCE V, Abbott Vascular, Santa Clara, California) or SES (Cypher select; Cordis, Johnson & Johnson) by means of an interactive web response system. The allocation sequence was computer generated, stratified according to participating center, and blocked with block sizes of 6 and 10 varying randomly. Patients, but not investigators, were unaware of the treatment assignment.

Stent implantation was performed according to standard techniques. EES were available in diameters of 2.5, 2.75, 3.0, 3.5, and 4.0 mm and in lengths of 8, 12, 15, 18, 23, and 28 mm; SES were available in diameters of 2.5, 2.75, 3.0, and 3.5 mm and in lengths of 8, 13, 18, 23, 28, and 33 mm. In patients with multiple lesions that fulfilled the inclusion and exclusion criteria, the operator determined the hierarchy of lesions and declared the target lesion for each patient before the procedure. The same randomly assigned stent had to be implanted in all lesions in patients requiring multilesion interventions, except when the assigned stent could not be inserted, in which case crossover to another device was allowed. Full lesion coverage was attempted by implanting 1 or several stents.

Before or during the procedure, all patients received at least 200 mg of aspirin and a 300- to 600-mg loading dose of clopidogrel. Heparin was administered throughout the procedure to maintain an activated clotting time of 250 s or longer. Administration of glycoprotein IIb/IIIa inhibitors was at the discretion of the operator. After the procedure, all patients received 100 mg/day of aspirin indefinitely, as well as 75 mg/day clopidogrel for at least 12 months. Use of the standard post-intervention care was recommended (9).

**Study endpoints and definitions.** The primary endpoint was in-segment late luminal loss at 9 months after the index procedure (defined as the difference in the minimal luminal diameter assessed immediately after the procedure and at angiographic follow-up, measured within the margins, 5 mm proximal and 5 mm distal to the stent). Secondary angiographic end points were in-stent and segment binary restenosis and in-stent late loss at 9 months. Secondary clinical endpoints included death, MI, ischemia-driven target lesion revascularization (TLR), ischemia-driven target vessel revascularization, stent thrombosis, a composite of major adverse cardiac events (MACE) (i.e., death, MI, and target vessel revascularization) within 12 months, and device success. All deaths were considered to have been from cardiac causes unless a noncardiac cause could be identified. A diagnosis of MI was based on the presence of new Q waves in at least 2 contiguous leads on an electrocardiogram or an elevation of creatine kinase-myocardial band isoenzyme was assessed before stenting, 8 to 16 h and again 18 to 24 h after the procedure. Clinical follow-up visits were scheduled at 30 days, 9 months, and 12 month and, monitoring of clinical status, rehospitalizations or recatheterization, cardiac-related medications, and occurrence of adverse events was performed. All eligible patients were asked to return for an angiographic follow-up at 9 months after the procedure, or earlier if anginal symptoms occurred.

Clinical, angiographic, procedural, and outcome data were collected using a dedicated, electronic case report form by specialized personnel at the clinical data-management center who were unaware of treatment assignments. All outcomes of interest were confirmed by source documentation collected at each hospital and were centrally adjudicated by an independent clinical events committee, whose members were blinded as to the assigned stent. An independent data and safety monitoring board reviewed the data periodically to identify potential safety issues, but there were no formal stopping rules.

**Quantitative coronary angiography.** Coronary angiograms were digitally recorded at baseline, immediately after the procedure, and at follow-up, and were assessed offline in the angiographic core laboratory (Asan Medical Center, Seoul, Korea) using an automated edge-detection system (CAAS V, Pie Medical Imaging, Maastricht, the Netherlands) by experienced assessors unaware of the allocated stent. All measurements were performed on cineangiograms recorded after the intracoronary administration of nitroglycerin. Standard qualitative and quantitative analyses and definitions were used for angiographic analysis (12). The reference diameter was determined by interpolation.

All quantitative angiographic measurements were obtained within the stented segment (in-stent) and over the entire segment, including the stent and its 5-mm proximal and distal margins (in-segment). Angiographic variables included absolute lesion length, stent length, reference vessel diameter, minimum lumen diameter, percent diameter stenosis, binary restenosis rate, immediate gain, late loss, and patterns of recurrent restenosis. Binary restenosis was defined as percent diameter stenosis of 50% or greater on follow-up angiography, and patterns of angiographic restea-
Analyses were performed using SAS software, version 9.1, by a statistical analyst who was unaware of the type of stent implanted. All p values are 2-sided, apart from those from noninferiority testing of the primary endpoint.

### Results

#### Baseline characteristics and procedural results

A total of 450 patients were randomized to receive the EES (n = 224) or the SES (n = 226). Table 1 shows the baseline demographic and clinical characteristics of the study population. The lesion and procedural characteristics are shown in Table 2. Most of clinical, lesion, and procedural characteristics were similar between the 2 groups except the number of stents used at the target lesion. The number of stents implanted in the target lesion was 1.8 ± 0.7, and the mean total length of the stents was 46.5 ± 17.1 mm. The rate of device success was 99.1% in both groups.

#### Quantitative angiographic results

Quantitative angiographic results at baseline, post-procedure, and follow-up are shown in Table 3. Angiographic measurements of lesions before and after the procedure were similar in the groups. Follow-up angiographic outcomes were quantitatively assessed with the Mehran classification (13).

### Statistical analysis

The primary objective of the study was to assess whether the angiographic outcome of treatment with the EES was not inferior to the outcome of treatment with the SES. To calculate study sample size, we assume an in-segment late luminal loss of 0.24 ± 0.38 mm in SES based on the LONG-DES-II trial (14). Calculation of the study sample size was based on a margin of noninferiority for in-segment late luminal loss of 0.10 mm, which was equal to 40% of an assumed late luminal loss of SES. Using an α level of 0.05 and a statistical power of 80%, we estimated that 180 patients per group were needed to demonstrate noninferiority of the EES. Expecting that approximately 20% patient would not receive follow-up angiography, a total of 450 patients (225 patients per group) was needed to fulfill the primary endpoint. Sample size was calculated using PASS software (NCSS, Kaysville, Utah).

All analyses were based on the intention-to-treat principle. Differences between treatment groups were evaluated by Student t test for continuous variables and by the chi-square or Fisher exact test for categorical variables. Cumulative event curves were generated by means of the Kaplan-Meier method. The noninferiority hypothesis was assessed statistically with Z-test, by which p values for noninferiority were calculated to compare differences between groups with margins of noninferiority, according to the method of Chow and Liu (15). Trial data were held by the trial coordination center at the Asan Medical Center. Analyses were performed using SAS software, version 9.1 (SAS Institute, Cary, North Carolina).
angiography was performed in 179 patients (80%) in the EES group and 184 patients (81%) in the SES group (p = 0.69). The median duration of angiographic follow-up was 274 days (interquartile range: 260 and 299 days) in the EES group and 275 days (interquartile range: 264 and 297 days) in the SES group (p = 0.82). Patients undergoing angiographic follow-up were younger (p = 0.002), less likely to have diabetes (p = 0.03) and previous PCI (p = 0.046), and more likely to have hyperlipidemia (p = 0.001) than those who did not return for angiographic follow-up.

As a primary study endpoint, the mean difference in in-segment late luminal loss between the EES group and the SES group was 0.08 mm (95% confidence interval, 0.02 to 0.14), a result failing to show the noninferiority of the EES (p for noninferiority = 0.96) and instead demonstrating the statistical superiority of the SES (p for superiority = 0.042) (Fig. 1, Table 3). The rates of in-segment binary restenosis were 7.3% in the EES group and 2.7% in the SES group (p = 0.046). However, in-stent late luminal loss (0.22 ± 0.42 mm vs. 0.18 ± 0.28 mm, p = 0.29) and in-stent binary restenosis rate (3.9% vs. 2.7%, p = 0.53) were similar between the EES and the SES groups. The difference in in-segment luminal changes over time between the 2 stents was mainly the result of the larger late luminal loss in the proximal margin of EES than of SES (Table 3). Patterns of in-stent restenosis are shown in Table 4. When

---

**Table 3. Quantitative Angiographic Analysis**

| Characteristics                  | EES (n = 224) | SES (n = 226) | p Value  
|----------------------------------|---------------|---------------|----------
| Before procedure                 |               |               |          
| Lesion length, mm               | 34.0 ± 15.4   | 34.3 ± 13.5   | 0.85     
| Reference vessel diameter, mm   | 3.18 ± 0.47   | 3.14 ± 0.42   | 0.34     
| Minimal luminal diameter, mm    | 1.07 ± 0.45   | 1.06 ± 0.45   | 0.92     
| Diameter stenosis, %            | 66.3 ± 13.5   | 66.1 ± 13.1   | 0.85     
| Immediately after procedure     |               |               |          
| Minimal luminal diameter, mm    |               |               |          
| In-segment                      | 2.33 ± 0.46   | 2.31 ± 0.45   | 0.65     
| In-stent                        | 2.64 ± 0.42   | 2.63 ± 0.40   | 0.80     
| Proximal margin                 | 3.23 ± 0.54   | 3.22 ± 0.53   | 0.82     
| Distal margin                   | 2.35 ± 0.47   | 2.33 ± 0.45   | 0.66     
| Diameter stenosis, %            |               |               |          
| In-segment                      | 17.4 ± 9.3    | 17.2 ± 9.5    | 0.84     
| In-stent                        | 9.7 ± 6.8     | 9.8 ± 6.4     | 0.89     
| Proximal margin                 | 10.1 ± 7.7    | 10.3 ± 8.4    | 0.74     
| Distal margin                   | 16.1 ± 9.4    | 16.3 ± 9.6    | 0.81     
| Acute gain, mm                  |               |               |          
| In-segment                      | 1.27 ± 0.57   | 1.25 ± 0.53   | 0.77     
| In-stent                        | 1.57 ± 0.53   | 1.56 ± 0.51   | 0.91     
| Follow-up at 9 months, %        | 179 (80)      | 184 (81)      | 0.69     
| Late luminal loss, mm           |               |               |          
| In segment (primary end point)  | 0.17 ± 0.41   | 0.09 ± 0.30   | 0.042    
| In stent                        | 0.22 ± 0.42   | 0.18 ± 0.28   | 0.29     
| Proximal margin                 | 0.24 ± 0.52   | 0.13 ± 0.34   | 0.02     
| Distal margin                   | 0.11 ± 0.37   | 0.04 ± 0.28   | 0.051    
| Minimal luminal diameter, mm    |               |               |          
| In-segment                      | 2.17 ± 0.49   | 2.26 ± 0.46   | 0.09     
| In-stent                        | 2.42 ± 0.52   | 2.47 ± 0.47   | 0.31     
| Proximal margin                 | 3.02 ± 0.66   | 3.14 ± 0.50   | 0.047    
| Distal margin                   | 2.25 ± 0.51   | 2.32 ± 0.45   | 0.20     
| Diameter stenosis, %            |               |               |          
| In-segment                      | 23.7 ± 15.3   | 21.4 ± 12.2   | 0.13     
| In-stent                        | 17.8 ± 14.6   | 17.1 ± 12.4   | 0.65     
| Proximal margin                 | 16.5 ± 15.1   | 12.9 ± 9.9    | 0.01     
| Distal margin                   | 18.8 ± 12.3   | 16.9 ± 12.2   | 0.12     
| Angiographic restenosis*        |               |               |          
| In-segment                      | 13 (7.3)      | 5 (2.7)       | 0.046    
| In-stent                        | 7 (3.9)       | 5 (2.7)       | 0.53     
| Proximal margin                 | 6 (3.4)       | 0             | 0.01     
| Distal margin                   | 1 (0.6)       | 0             | 0.49     

Values are mean ± SD or n (%). *In 1 case in the EES group, angiographic restenosis was detected concomitantly in the in-stent area and proximal of the margins. Abbreviations as in Table 1.

---

**Table 4. Angiographic Pattern of Restenosis**

| Characteristics                  | EES (n = 13) | SES (n = 5) | p Value  
|----------------------------------|--------------|-------------|----------
| Focal                            | 12 (92.3)    | 4 (80.0)    | 0.49     
| IA (giant)                       | 0            | 0           | NA       
| IB (margin)                      | 7 (53.8)     | 0           | 0.10     
| IC (focal body)                  | 5 (38.5)     | 4 (80.0)    | 0.29     
| ID (multifocal)                  | 0            | 0           | NA       
| Diffuse                          | 1 (7.7)      | 1 (20.0)    | 0.49     
| II (intrastent)                  | 0            | 1 (20.0)    | 0.28     
| III (proliferative)              | 0            | 0           | NA       
| IV (total occlusion)             | 1 (7.7)      | 0           | >0.99    

Values are n (%). Restenosis is classified using the Mehran criteria (13). NA = not available; other abbreviations as in Table 1.
we compared the primary endpoint in patients with a single long stent for the target lesion, the overall finding was also consistent (0.15 ± 0.43 mm in the EES group vs. 0.04 ± 0.28 mm in the SES group, \( p = 0.10 \)).

**Clinical outcomes.** Major clinical events during follow-up are shown in Table 5. At 1 month, the incidence of clinical events was similar between the 2 groups. All patients completed the 12-month clinical follow-up. At 12 months, the incidence of individual and composite clinical outcomes did not differ significantly between the 2 groups. The overall 12-month cumulative rate of MACE was similar between the EES group and the SES group (Fig. 2). During 12 months, there were only 1 case of stent thrombosis (2 days after the procedure) after use of the EES and no case after use of the SES.

**Discussion**

This randomized trial was designed to compare the efficacy of the newer generation EES with early generation SES for very complex coronary lesions with a long diseased segment. We found that EES implantation was associated with a greater degree of in-segment late luminal loss as well as an increased risk of angiographic in-segment restenosis than was SES implantation. This difference was related to a relatively larger late lumen loss in the proximal margin with the EES than with the SES, with no significant difference in in-stent angiographic parameters. However, clinical outcomes were both excellent and not statistically different, suggesting that both stents appear to be very effective in long coronary lesions with a modest beneficial effect at the proximal margin in SES.

Despite the improved efficacy of newer DES devices, a long diseased segment continued to be a major determinant of worse prognostic outcome in terms of restenosis (16). Therefore, an investigation to identify differential outcomes between first and newer generation stents in the treatment of long coronary lesions is clinically important to the physician’s choice of devices in these common PCI situations. As a surrogate marker of DES efficacy, we chose in-segment late luminal loss at follow-up angiography as the primary endpoint of this trial because it reflects the overall degree of neointimal hyperplasia, the primary cause of restenosis after stent implantation. Although in-stent late loss may be a useful measure of the pure biological potency of DES and a more reliable predictor of restenosis (17), in-segment late loss is the most sensitive measure of the antiproliferative effectiveness of DES and additionally accounts for the magnitude of lumen narrowing that occurs at the margins of the stent, which may reflect stent–balloon mismatch, geographic miss, drug diffusion effects, and so on. Because isolated stenoses at stent edges represent an increasingly greater proportion of TLR events with DES

**Table 5. Clinical Events at Follow-Up**

<table>
<thead>
<tr>
<th>Clinical Outcomes</th>
<th>EES (n = 224)</th>
<th>SES (n = 226)</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up at 1 month</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Cardiac</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Noncardiac</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>21 (9.4)</td>
<td>17 (7.5)</td>
<td>0.48</td>
</tr>
<tr>
<td>Q-wave</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Non–Q-wave</td>
<td>21 (9.4)</td>
<td>17 (7.5)</td>
<td>0.48</td>
</tr>
<tr>
<td>Death or myocardial infarction</td>
<td>21 (9.4)</td>
<td>17 (7.5)</td>
<td>0.48</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>1 (0.4)</td>
<td>0</td>
<td>0.50</td>
</tr>
<tr>
<td>Target lesion revascularization</td>
<td>1 (0.4)</td>
<td>0</td>
<td>0.50</td>
</tr>
<tr>
<td>Target vessel revascularization</td>
<td>1 (0.4)</td>
<td>0</td>
<td>0.50</td>
</tr>
<tr>
<td>Follow-up at 12 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>1 (0.4)</td>
<td>0</td>
<td>0.50</td>
</tr>
<tr>
<td>Cardiac</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Noncardiac</td>
<td>1 (0.4)</td>
<td>0</td>
<td>0.50</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>22 (9.8)</td>
<td>18 (8.0)</td>
<td>0.49</td>
</tr>
<tr>
<td>Q-wave</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Non–Q-wave</td>
<td>22 (9.8)</td>
<td>18 (8.0)</td>
<td>0.49</td>
</tr>
<tr>
<td>Death or myocardial infarction</td>
<td>23 (10.3)</td>
<td>18 (8.0)</td>
<td>0.40</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>1 (0.4)</td>
<td>0</td>
<td>0.50</td>
</tr>
<tr>
<td>Target lesion revascularization</td>
<td>7 (3.1)</td>
<td>5 (2.2)</td>
<td>0.55</td>
</tr>
<tr>
<td>Target vessel revascularization</td>
<td>9 (4.0)</td>
<td>6 (2.7)</td>
<td>0.42</td>
</tr>
<tr>
<td>Major adverse cardiac events*</td>
<td>32 (14.3)</td>
<td>23 (10.2)</td>
<td>0.18</td>
</tr>
<tr>
<td>Target lesion failure, defined post-hoc</td>
<td>29 (12.9)</td>
<td>22 (9.7)</td>
<td>0.28</td>
</tr>
</tbody>
</table>

*Values are n (%). Percentages are from the intention-to-treat analysis. \( p \) values were calculated using the chi-square test or Fisher’s exact test, as appropriate. *The pre-specified major adverse cardiac events were defined as a composite of all-cause death, myocardial infarction, and ischemia-driven target vessel revascularization. †Target lesion failure, defined post-hoc, was a composite of death from cardiac causes, any myocardial infarction (not clearly attributable to a non-target vessel), or ischemia-driven target lesion revascularization. Abbreviations as in Tables 1 and 4.
than with BMS, in-segment measures might be a wise choice as a clinical event surrogate (18). However, it should be stressed that late luminal loss constitutes only a surrogate for clinical endpoints. The limitations of surrogate endpoints have been well described, and our results should therefore be interpreted in this context.

An important issue in our study that requires comment is that a significant discrepancy between in-segment and in-stent late luminal loss exists in stent group comparisons. This phenomenon was mainly attributed to a relatively pronounced neointimal proliferation in the proximal-edge portion observed with EES. This finding differs from the results of most previous stenting trials comparing EES and other DES comparator (5,6). Although the exact mechanism underlying our findings remains unclear, mechanical factors related to the procedures (e.g., residual stenosis or undercoverage of injured segment at the stent margins) presumably might have contributed to this phenomenon, given that an effect similarly mitigated within the stent by the antiproliferative properties of EES and SES resulted in a similar degree of in-stent angiographic parameters. The difference in available longest stent length per se (28 mm in EES and 33 mm in SES) during the study period may also account, at least in part, for differences in the degree of full coverage of diseased segments. There could be the possibility that an appropriate-length stent, sufficient to cover approximately 3 mm of nondiseased tissue on either side of the lesion, might be limited with the use of EES, especially in cases with long coronary lesions of approximately 25- to 28-mm length treated with a single long stent.

Theoretically, the reduced strut thickness (81 μm vs. 140 μm) and a thinner polymer coating (7.6 μm vs. 12.6 μm) in conjunction with improved biocompatibility of the polymer of the EES may favorably affect neointimal hyperplasia. However, this approximation was not compatible with our observed findings. Recently, the relative efficacy of EES versus SES has been reported in randomized trials. ISAR-TEST-4 (Intracoronary Stenting and Angiographic Results: Test Efficacy of 3 Limus-Eluting Stents-4) trial suggested that in-stent late loss is nonsignificantly lower in EES versus SES (0.23 ± 0.52 mm vs. 0.28 ± 0.57 mm, p = 0.08) (19). By contrast, a randomized trial comparing EES and SES in a broader range of lesion complexity showed that in-segment late loss, as a primary endpoint, was significantly larger in the EES group than in the SES (0.10 ± 0.36 mm vs. 0.05 ± 0.34 mm, p = 0.05), a finding consistent with our study (20). However, a large-scale randomized clinical study (SORT-OUT IV [Danish Organisation for Randomised Trials with Clinical Outcome]), including more than 2,600 patients across a wide range of patient and lesion complexity, demonstrated a similar rate of the composite endpoint of MACE between the EES group and the SES group (4.9% vs. 5.2%) (21).

Study limitations. First, our study is an angiographic outcome study not powered for clinical outcomes. Therefore, larger clinical outcome studies are required to detect significant difference in clinical endpoints. Second, the current study findings cannot be directly extrapolated to a patient population with a more favorable and low-risk profile. Another limitation of our study was the relatively short follow-up period of 12 months. Durable polymers of early generation DES have been associated with chronic inflammation of the arterial wall with the potential for delayed restenosis. Furthermore, previous studies comparing EES with paclitaxel-eluting stents, which has been regarded to have a similar safety with SES, also reported benefits in terms of stent thrombosis and MI (8). Therefore, longer-term comparison of newer and early generation DES might be needed to confirm the long-term durability of newer devices.

Conclusions

Both EES and SES appear to be clinically very effective in long coronary lesions with a modest, but statistically significant, beneficial effect at the proximal margin in SES.

Reprint requests and correspondence: Dr. Seung-Jung Park, Department of Cardiology, University of Ulsan College of Medicine, Cardiac Center, Asan Medical Center, 388-1 Poongnap-dong, Songpa-gu, Seoul 138–736, Korea. E-mail: sjpark@amc.seoul.kr.

REFERENCES


20. Kim HS. Efficacy of Xience/Promus versus Cypher to reduce late loss in stent: the EXCELLENT trial. Paper presented at: Transcatheter Cardiovascular Therapeutics (TCT); September 25, 2010; Washington, DC.


Key Words: angioplasty ■ coronary disease ■ stents.

APPENDIX

Data and Safety Monitoring Board: M.S. Lee (University of Ulsan College of Medicine, Seoul, Korea), J.Y. Yang (NHIC Ilsan Hospital, Ilsan, Korea), K.Y. Cho (Seoul National University Hospital, Bundang, Korea).

Event-Adjudication Committee: J.H. Oh (University of Ulsan College of Medicine, Seoul, Korea), S.W. Jo (University of Ulsan College of Medicine, Seoul, Korea), S.H. Kim (University of Ulsan College of Medicine, Seoul, Korea).