Interventional Cardiology

Randomized trial comparing the efficacy between different types of paclitaxel-eluting stents: The comparison of Efficacy between COroflex PLEAs ANd Taxus stent (ECO-PLEASANT) randomized controlled trial

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Aims Paclitaxel-eluting stents (PESs) have been shown to inhibit neointimal hyperplasia after percutaneous coronary intervention. Coroflex Please (B Braun, Melsungen, Germany) is a newly developed PES. We compared the clinical and angiographic efficacy of Coroflex Please with Taxus Liberte (Boston Scientific, Natick, MA) in a real-world practice.

Methods and Results We performed a prospective, open-label, randomized, controlled study that enrolled 945 patients undergoing percutaneous coronary interventions in 18 centers in Korea. The primary end point was clinically driven target vessel revascularization at 9 months. The baseline characteristics were mostly similar and comparable between 2 groups. At 9 months, the incidence of clinically driven target vessel revascularization was 14.6% for Coroflex and 6.4% for Taxus, which was significantly different (hazard ratio 2.43, 95% CI 1.50-3.94, noninferiority P value = 1.000). This is well corroborated by the difference of in-stent late loss between 2 stents (0.71 ± 0.64 mm vs 0.52 ± 0.50 mm, P < .001) by 9-month follow-up angiography (n = 415 vs 215).

Among secondary clinical end points, stent thrombosis (definite and probable) for 1 year was 2.2% in Coroflex and 1.3% in Taxus (P = .317). Also, myocardial infarction for 9 months was higher in Coroflex group than that in Taxus (4.9% vs 1.6%, P = .012), which was partly contributed by the higher incidence of periprocedural myocardial infarction in Coroflex arm (2.2% vs 0.3%, P = .028).

Conclusions Coroflex Please was inferior to Taxus Liberte with regard to clinical and angiographic efficacy. (Am Heart J 2013;165:733-43.)

Numerous paclitaxel-eluting stents (PESs) are available in clinical practice.1,2 We usually expect clinical results of these stents to be similar to the previous standard controls because the coated drug is the same, despite the differences in stent design and polymer technology. However, there have been no studies directly comparing a newly developed PES with its standard control, the Taxus Liberte (Boston Scientific, Natick, MA). The paclitaxel-eluting Coroflex Please (B Braun, Melsungen, Germany) is a recently developed drug-eluting stent using the Coroflex stent platform combined with paclitaxel contained in a polymer coating. In previous

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clinical trials, this new stent showed us comparable results with the first-generation PESs. In the PECOPS I, which was a 1-arm observational study, the results of Coroflex Please were within the range of other PESs. Coroflex Please showed 7.8% of restenosis rate, which was similar to 7.9% in Taxus IV trial. The 3.1% of 30-day major adverse cardiac event (MACE) rate was within the range of other trials with PESs. The 6-month MACE rates in PECOPS I were 8.0%, which was similar to 7.8%, and 8.5% in Taxus II Medium Release and Slow Release, respectively, as well as 8.5% MACE rate at 9 months in Taxus IV. Taxus Liberte was a newer version of Taxus and tested in Taxus ATLAS trial, where Taxus Liberte was proved to be noninferior to TAXUS Express in terms of 9-month target vessel revascularization (TVR), which was 8.0%. Recently, in the PECOPS II, which was a nonrandomized, 1-arm phase II study, the 6-month MACE rate was 17.8%, which was higher than that observed in PECOPS I (8.0%) and in TAXUS II Medium Release and Slow Release (8.6% and 5.5%). In addition, 1-year MACE rate was 19.4%. However, the Coroflex Please has not been compared against any other stent platform in a randomized manner, nor has it been evaluated in a wide range of patient and lesion subgroups, which are usually encountered in real-world practice. Therefore, this study was performed to directly compare the efficacy of the newly developed Coroflex Please against Taxus Liberte in a head-to-head manner.

Methods

Stents description

The Coroflex Please is a 120-μm-thick 316L stainless steel stent coated with a layer of the nonresorbable polymer polysulfone and paclitaxel with a dose of 1 μg/mm² of stent surface. Polysulfone has been used in hemodialysis owing to its low interaction with blood leading to low cell adhesion and platelet activation. It shows thermostability up to 180°C, which is responsible for not losing its physical stability during sterilization, transportation, and storage. The polymer allows for controlled release kinetics of the drug between the Taxus Medium Release and Slow Release. The Taxus Liberte is a 97-μm-thick 316L stainless steel stent coated with a polymer Translute containing 1 μg/mm² of paclitaxel in a slow-release formulation.

Study design and population

The ECO-PLEASANT (comparison of efficacy between Coroflex Please And Taxus stent) trial was a prospective, open-label, blinded end point adjudication, randomized, controlled study that enrolled patients from 18 centers in Korea between June 2008 and June 2009. The study design has been reported elsewhere. 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. All patients provided written, informed consent.

Patients were eligible if they had at least 1 lesion in the native coronary vessel with reference diameter of 2.5 to 4.0 mm, stenosis of more than 50% by visual estimation, and evidence of myocardial ischemia (stable angina, unstable angina, recent myocardial infarction [MI], silent ischemia, positive functional study, or reversible changes in electrocardiogram consistent with ischemia). In those with visually estimated stenosis greater than 70%, evidence of myocardial ischemia did not need to be documented. There were no limitations in the number of lesions, vessels, or the length of the lesions in efforts to reflect real-life clinical practice. Exclusion criteria were ST-segment elevation MI within 48 hours, severely compromised ventricular dysfunction (ejection fraction <25%) or cardiogenic shock, significant left main disease (requiring revascularization therapy), in-stent or in-segment restenosis of a previously implanted stent, true bifurcation lesions requiring a planned 2-stent strategy, allergy to antiplatelet drugs, heparin, stainless steel, contrast agents, paclitaxel, serum creatinine ≥3.0 mg/dL or dependence on dialysis, life expectancy less than 1 year, or active participation in another clinical study.

Randomization and procedures

Patients were randomized 2:1 to Coroflex Please (B Braun) or Taxus Liberte (Boston Scientific). Randomization was done via a Web-based online randomization system after diagnostic angiography and before percutaneous coronary intervention (PCI). To ensure that major factors that could contribute to the primary end point are evenly distributed among the groups, randomization was stratified by enrolling sites, the presence of diabetes mellitus (DM), and lesion length (≥28 mm).

Balloon angioplasty and stent implantation were performed according to the standard techniques. It was recommended that all significant lesions be fully covered by 1 or multiple stents using the same randomly assigned stent, except when the assigned stent could not be inserted, in which case another device was allowed. Staged PCI (defined as procedures planned at the time of index procedure) was allowed as long as the second PCI was performed within 4 weeks of index PCI using the same allocated stent.

Before index procedure, all patients received at least 300 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 longer than 250 seconds. Administration of glycoprotein IIb/IIIa inhibitors was at the discretion of the operator. At discharge, all patients were maintained on at least 75 mg/d of aspirin and 75 mg/d of clopidogrel for at least 6 months.

Follow-up

Clinical follow-up was performed at 1, 4, and 9 months and will be continued annually for up to 3 years. At follow-up, patients were specifically questioned regarding any adverse events or angina symptoms. There was recommended angiographic follow-up at 9 months.

Quantitative coronary angiography

Quantitative and qualitative analyses of all of the baseline and post-PCI coronary angiographic images were performed at a central core laboratory, the Seoul National University Hospital Cardiovascular Clinical Research Center Angiographic Core Lab. All angiograms performed after the index PCI procedure were also evaluated at the central core laboratory. Using the guiding catheter for calibration, the minimal luminal diameter (MLD)
and reference vessel diameter were measured before and after index procedure and at angiographic follow-up if it was performed. Diameter stenosis was defined as the ratio of MLD and diameter of reference segment, and angiographic binary restenosis was denoted as diameter stenosis ≥50% within the target lesion. Late loss (LL) was the difference in MLD between angiogram immediately after index procedure and follow-up angiogram. Acute gain was defined as the increment of MLD immediately after index procedure. All measurements were performed for both the stented segment (in-stent) and 5-mm proximal and distal margins of the stented segment (in-segment).

Study end points
The primary end point for this study was clinically driven TVR (defined as the TVR that was performed when stenosis of >50% with evidence of myocardial ischemia or stenosis >70% was found in target vessel) at 9 months. Secondary clinical end points were MACES (defined as the composite of all-cause death, MI, and TVR), target vessel failure (TVF) (defined as the composite of cardiac death, MI, and clinically driven TVR), stent thrombosis (Academic Research Consortium [ARC] defined definite and probable), and each individual component of the composite outcomes. In patients receiving routine angiographic follow-up, we measured the in-stent binary restenosis rate, in-stent and in-lesion LL, and in-stent and in-lesion MLD and percentage diameter stenosis.

Statistical analysis
On the basis of the results from TAXUS II and IV, ATLAS, and PECOPS I trials, we assumed an incidence of TVR as 8% for Taxus Liberte. Using a sampling ratio of 2:1 for Coroflex Please/Taxus Liberte, enrollment of 915 patients, 610 in the Coroflex Please arm and 305 in the Taxus Liberte arm, would provide the study with a statistical power of 80% to confirm noninferiority within 5% at a 2-sided significance level of .05, allowing for 10% dropout of patients at 9-month clinical follow-up. In addition, we need to test the hypothesis that Coroflex Please is noninferior to Taxus Liberte in terms of neointimal growth inhibition at 9 months. We assumed the in-stent LL as 0.4 ± 0.5 mm for the Taxus Liberte and less than 0.15-mm increases for the Coroflex Please based on the results from TAXUS II and IV, ATLAS, and PECOPS I trials, with type I error set at 0.05, statistical power of 80%, sampling ratio of Coroflex Please/Taxus Liberte at 2:1, and an estimated dropout rate of 30% (for 9-month follow-up angiography). Based on the assumptions above, we would need a total of 450 patients, 300 patients in Coroflex Please arm and 150 in Taxus Liberte arm. Finally, based on the above 2 calculations, we would need a total of 915 patients, 610 patients in Coroflex Please arm and 305 in Taxus Liberte arm.

Categorical variables were analyzed using the χ² test or Fisher exact test, whereas continuous variables were assessed using the Student t test. The time to primary clinical end point was assessed using the Kaplan-Meier method, and the log-rank test was used to compare the incidence of primary clinical end points. All clinical and angiographic outcomes were analyzed by an intention-to-treat basis.

This trial is registered with ClinicalTrials.gov (NCT00699545). This study was supported by a grant from the Clinical Research Center for Ischemic Heart Disease, Seoul, Republic of Korea (0412-CR02-0704-0001) and the Innovative Research Institute for Cell Therapy, Seoul National University Hospital (A062260), sponsored by the Ministry of Health, Welfare and Family, Republic of Korea. We also received unrestricted grants from B Braun. The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the manuscript, and its final contents.

Results
Baseline characteristics and procedural results
Between June 30, 2008, and June 25, 2009, a total of 945 patients (1,170 lesions) from 18 centers in Korea were enrolled in the study and randomly assigned to Coroflex Please (631 patients; 828 lesions) or Taxus Liberte (314 patients; 417 lesions). Figures 1 and 2 show the trial profile and flow, respectively. Baseline patient characteristics are shown in Table I, and baseline lesion and procedural characteristics are shown in Table II. Baseline patient, lesion, and procedural characteristics were mostly similar and comparable between 2 groups, except the frequency of patients with statin medication at discharge, which was more common in Taxus Liberte. There were no restrictions regarding the number of stents or the length of the lesion. The proportion of patients was 52.6% for those presenting with acute coronary syndrome (ACS), 38.8% for those with DM was, 63.6% for those with hypertension, and 54.3% for those with multivessel disease, reflecting the near real-world nature of the patients enrolled in the study. One notable characteristic of the current study was the high percentage of patients undergoing intervention with the aid of use of intravascular ultrasound, which was 50.1% and 51.0% in Coroflex Please and Taxus Liberte, respectively.

Clinical outcomes at 9 months
The cumulative clinical outcomes at 1 and 4-month and up to 9-month follow-up are shown in Table III. At 1 month, the incidence of clinical events such as clinically driven TVR, clinically driven target lesion revascularization (TLR), or cardiac death was similar between 2 groups. However, clinical end points including MI or its associated events showed significant differences. Peri-procedural MI was more common in Coroflex Please than in Taxus Liberte (2.2% vs 0.3%, P = .028). This tendency continued up to 4-month follow-up. Clinical follow-up at 9 months was completed in 927 (98.1%) of the 945 patients. At 9 months, the incidence of clinically driven TVR was 14.6% for Coroflex Please and 6.4% for Taxus Liberte, which was significantly different (hazard ratio 2.43, 95% CI 1.50-3.94, Pnoninferiority = 1.000, Pinferiority < .001) (Figure 3). The rates of MI, clinically driven TLR, or MACE were also higher in Coroflex Please. However, the rate of all-cause death or cardiac death was not statistically different between 2 groups (Table III). As for definite and definite/probable stent thrombosis, the
rates numerically favored Taxus Liberte but were not statistically significant (Table IV).

Angiographic results
Quantitative angiographic results at baseline, postprocedure, and at follow-up are shown in Table V. There were no significant differences in angiographic measurements of lesions before and immediately after the procedure. Angiographic follow-up at 9 months was performed in 415 patients (65.8%) or 551 lesions (66.5%) in Coroflex Please and 215 patients (68.5%) or 287 lesions (68.8%) in Taxus Liberte. Mean ± SD in-stent LL was 0.71 ± 0.64 mm in Coroflex Please and 0.52 ± 0.50 mm in Taxus Liberte. (difference in LL 0.197, 95% upper CI = 0.275, \( p_{\text{inferiority}} = .02 \)). The upper CI was beyond the noninferiority margin and thus did not meet the criteria for noninferiority of Coroflex Please vs Taxus Liberte.
Figure 4 shows the cumulative in-stent and in-segment MLD curves of 2 groups. In addition, Figure 5 shows the cumulative in-stent and in-segment late LL.

Subgroup analysis

Subgroup analysis regarding clinically driven TVR was performed according to the presence of DM, diffuse long lesion, age, sex, multivessel disease, and ACS. The results in various subgroups were similar to those observed in the entire population, except in the non-ACS subgroup (Figure 6). However, even in this non-ACS population, Taxus Liberte showed numerically favorable result over Coroflex Please. As for the angiographic end point of in-stent late LL, subgroup analysis was performed for DM and diffuse long lesion. The angiographic results were almost consistent across the subgroups such that Taxus Liberte bore better angiographic result than did Coroflex Please (Figure 7). In addition, DM and diffuse long lesion are not thought to be interaction variables (interaction \( P = .134 \) and .534, respectively). In those with DM, the difference between 2 stents lessened, although still maintained the favorable outcome for Taxus Liberte. The in-stent late LL of Coroflex Please and Taxus Liberte was 0.69 and 0.57 mm, respectively \( (P = .063) \).

Discussion

In this prospective randomized comparison of Coroflex Please and Taxus Liberte, we found that the clinical and angiographic efficacy of Coroflex Please was inferior to Taxus Liberte. Coroflex Please showed higher incidence of the clinically driven TVR at 9-month follow-up. Other clinical outcomes including MI, clinically driven TLR, or TVF were also worse in Coroflex Please, although all-cause death or cardiac death was similar between 2 stents. The ARC definite and probable stent thrombosis rates were not statistically different between 2 stents, although numerically higher in Coroflex Please. Angiographic results such as in-stent and in-segment LL were also worse in Coroflex Please than in Taxus Liberte.

Introduction of several PESs to the market

Paclitaxel is a lipophilic component derived from the Pacific yew tree Taxus brevifolia. This stabilizes the

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**Table I. Baseline patient characteristics**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coroflex (n = 631)</th>
<th>Taxus (n = 314)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y), mean ± SD</td>
<td>62.4 ± 10.0</td>
<td>63.6 ± 9.8</td>
</tr>
<tr>
<td>Male</td>
<td>398 (63.1)</td>
<td>201 (64.0)</td>
</tr>
<tr>
<td>Body mass index (kg/m²), mean ± SD</td>
<td>25.0 ± 3.2</td>
<td>25.0 ± 3.1</td>
</tr>
<tr>
<td>DM</td>
<td>246 (39.0)</td>
<td>121 (38.5)</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>10 (1.6)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>403 (63.9)</td>
<td>198 (63.1)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>293 (46.4)</td>
<td>146 (46.5)</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>328 (52.0)</td>
<td>162 (51.6)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>118 (18.7)</td>
<td>56 (17.8)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>185 (29.3)</td>
<td>96 (30.6)</td>
</tr>
<tr>
<td>History of MI</td>
<td>31 (4.9)</td>
<td>8 (2.5)</td>
</tr>
<tr>
<td>History of CABG</td>
<td>10 (1.6)</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td>History of PCI</td>
<td>63 (10.0)</td>
<td>25 (8.0)</td>
</tr>
<tr>
<td>History of cerebrovascular disease</td>
<td>45 (7.1)</td>
<td>17 (5.4)</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>345 (54.7)</td>
<td>168 (53.5)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction, %(mean ± SD)</td>
<td>61.1 ± 9.7</td>
<td>61.1 ± 9.6</td>
</tr>
<tr>
<td>Clinical indication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable angina</td>
<td>305 (48.3)</td>
<td>143 (45.5)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>209 (33.1)</td>
<td>109 (34.7)</td>
</tr>
<tr>
<td>Non-ST-segment elevation MI</td>
<td>97 (15.4)</td>
<td>57 (18.2)</td>
</tr>
<tr>
<td>ST-segment elevation MI</td>
<td>20 (3.2)</td>
<td>5 (1.6)</td>
</tr>
<tr>
<td>Medications at discharge</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>624 (98.9)</td>
<td>313 (99.9)</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>623 (98.7)</td>
<td>311 (99.9)</td>
</tr>
<tr>
<td>Statin</td>
<td>490 (77.7)</td>
<td>262 (83.4)</td>
</tr>
<tr>
<td>ACE inhibitor</td>
<td>197 (31.2)</td>
<td>115 (36.6)</td>
</tr>
<tr>
<td>Angiotensin II receptor antagonist</td>
<td>194 (30.7)</td>
<td>88 (28.0)</td>
</tr>
<tr>
<td>( β )-Blocker</td>
<td>415 (65.8)</td>
<td>212 (67.5)</td>
</tr>
<tr>
<td>Calcium channel blocker</td>
<td>147 (23.3)</td>
<td>76 (24.2)</td>
</tr>
</tbody>
</table>

Values are presented as No. (%), unless otherwise indicated. ACE, Angiotensin-converting enzyme.

**Table II. Lesion and procedural characteristics**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coroflex (n = 828)</th>
<th>Taxus (n = 417)</th>
<th>( P^* )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion location</td>
<td></td>
<td></td>
<td>.749</td>
</tr>
<tr>
<td>Left anterior descending artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left circumflex artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right coronary artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main coronary artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACC/AHA B2/C type</td>
<td></td>
<td></td>
<td>.366</td>
</tr>
<tr>
<td>Total occlusion</td>
<td></td>
<td></td>
<td>.956</td>
</tr>
<tr>
<td>Thrombus containing</td>
<td></td>
<td></td>
<td>.398</td>
</tr>
<tr>
<td>Bifurcation lesions</td>
<td></td>
<td></td>
<td>.573</td>
</tr>
<tr>
<td>Calculication</td>
<td></td>
<td></td>
<td>.768</td>
</tr>
<tr>
<td>MLD (mm), mean ± SD</td>
<td>0.78 ± 0.48</td>
<td>0.76 ± 0.49</td>
<td>.612</td>
</tr>
<tr>
<td>Reference vessel diameter (mm), mean ± SD</td>
<td>2.83 ± 0.51</td>
<td>2.80 ± 0.49</td>
<td>.307</td>
</tr>
<tr>
<td>Diameter stenosis (%), mean ± SD</td>
<td>72.5 ± 16.0</td>
<td>72.8 ± 15.6</td>
<td>.668</td>
</tr>
<tr>
<td>Lesion length (mm), mean ± SD</td>
<td>18.8 ± 10.8</td>
<td>20.1 ± 11.2</td>
<td>.070</td>
</tr>
<tr>
<td>Lesion length &gt;20 mm</td>
<td>263 (35.8)</td>
<td>154 (41.5)</td>
<td>.074</td>
</tr>
<tr>
<td>No. of stents per lesion, mean ± SD</td>
<td>1.14 ± 0.38</td>
<td>1.11 ± 0.32</td>
<td>.062</td>
</tr>
<tr>
<td>No. of stents per patient, mean ± SD</td>
<td>1.48 ± 0.81</td>
<td>1.47 ± 0.78</td>
<td>.782†</td>
</tr>
<tr>
<td>Total stent length per lesion (mm), mean ± SD</td>
<td>26.1 ± 12.5</td>
<td>26.4 ± 11.6</td>
<td>.686</td>
</tr>
<tr>
<td>Total stent length per patient, mean ± SD</td>
<td>34.7 ± 22.2</td>
<td>35.0 ± 21.9</td>
<td>.408†</td>
</tr>
<tr>
<td>Use of intravascular ultrasound</td>
<td>316 (50.1)</td>
<td>160 (51.0)</td>
<td>.800*</td>
</tr>
</tbody>
</table>

Values are presented as No. (%), unless otherwise indicated. ACC/AHA, American Heart Association/American College of Cardiology.

*Comparisons were performed using the generalized estimating equations. †Comparisons were performed with the independent t test.
assembly of microtubules by binding β-tubulin dimers and inhibiting their polymerization. In this way, the drug inhibits arterial smooth muscle cell proliferation, migration, and matrix proliferation, leading to inhibition of neointimal hyperplasia after PCI. Taxus is the first PES approved for human use. Its efficacy and safety have been proven in numerous prospective randomized trials. On the other hand, Coroflex Please is a newly developed drug-eluting stent incorporating paclitaxel.

Comparison of efficacy and safety between 2 different PESs

In the present trial, the efficacy of Coroflex Please was inferior to Taxus Liberte. The in-stent LL was 0.71 ± 0.64 and 0.52 ± 0.50 mm, respectively (P < .001). The difference in mean LL was 0.197 mm for in-segment analysis, which was close to the noninferiority margin of 0.15 mm. The results of Taxus Liberte were in accord with previous trial, which showed an in-stent LL of 0.41 ± 0.54 mm in the ATLAS and 0.46 ± 0.52 mm in the ZEST, both at 9 months post-PCI. Although the results of Coroflex Please were thought to be worse in this study than in the previous trials that demonstrated an in-stent LL of 0.47 ± 0.60 and 0.27 ± 0.59 mm in PECOPS I and II, respectively, the observation period was different: 9 months in this study vs 6 months in previous ones. This inferiority of angiographic outcomes agreed with clinical outcomes. The rates of clinically driven TVR at 9 months, the primary end point, were 14.6% and 6.4% for Coroflex Please and Taxus Liberte, respectively. In addition, the rates of clinically driven TLR, which is well correlated with LL, were 14.1% and 5.7%, respectively. In the PECOPS I trial, the TLR rate was 9.4% at 1-year follow-up. However, in the PECOPS II trial, the TLR rate was 14.5% at 1-year follow-up, which was higher than that of the PECOPS I trial. Therefore, the result of the PECOPS II trial is more similar to our results. As for the trial regarding Taxus Liberte, the TLR rate was 5.7% at 9-month follow-up in the TAXUS ATLAS trial. Another trial investigating Taxus Liberte, ZEST trial, showed 7.5% of ischemia-driven TLR at 1 year. Accordingly, our result for Taxus Liberte was not far from the previous trials. In addition, there might be the “occlusostenotic reflex” phenomenon reflected as steeper increase in cumulative incidence curve of clinically driven TVR around 9 months after initial procedure because we performed high rate on angiographic follow-up. Occlusostenotic reflex refers to the phenomenon that if an amenable lesion is found in the coronary angiography, the patients (even asymptomatic) would receive a stent. This reflex is thought to be more likely to happen in the stenotic lesion previously intervened with stent.

There are some differences in stent-particular properties between Coroflex Please and Taxus Liberte. First, the strut is thicker in Coroflex Please than in Taxus Liberte (120 μm vs 97 μm). This would make different physical characteristics of stents such as nominal pressure or time to expansion to nominal diameter. Low compliance or rigid physical characteristics of Coroflex stent may be prone to underexpansion by short inflation time or insufficient inflation pressure. In fact, the thicker strut, the higher LL and restenosis rate would be expected, as shown by Kastrati et al and et al. Second, although the polymer of Coroflex Please is polysulfone, the one of Taxus Liberte is Translute. Polysulfone is biostable at high temperature and biocompatible. This polymer is shown to prevent inflammation and thrombogenesis owing to low cell adhesion and marked reduction of platelet activation. Nonetheless, the outcomes of Coroflex Please were not good as those of Taxus Liberte.

Table III. Clinical adverse events

<table>
<thead>
<tr>
<th></th>
<th>Coroflex (n = 631)</th>
<th>Taxus (n = 314)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 1 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac death</td>
<td>6 (1.0%)</td>
<td>0 (0.0%)</td>
<td>.083</td>
</tr>
<tr>
<td>MI</td>
<td>23 (3.6%)</td>
<td>2 (0.6%)</td>
<td>.007</td>
</tr>
<tr>
<td>Periprocedural MI</td>
<td>14 (2.2%)</td>
<td>1 (0.3%)</td>
<td>.028</td>
</tr>
<tr>
<td>Spontaneous MI</td>
<td>9 (1.4%)</td>
<td>1 (0.3%)</td>
<td>.117</td>
</tr>
<tr>
<td>Clinically driven TLR</td>
<td>10 (1.6%)</td>
<td>1 (0.3%)</td>
<td>.087</td>
</tr>
<tr>
<td>Clinically driven TVR</td>
<td>10 (1.6%)</td>
<td>1 (0.3%)</td>
<td>.087</td>
</tr>
<tr>
<td>Cardiac death + MI</td>
<td>26 (4.1%)</td>
<td>2 (0.6%)</td>
<td>.003</td>
</tr>
<tr>
<td>Target lesion failure‡</td>
<td>27 (4.3%)</td>
<td>2 (0.6%)</td>
<td>.002</td>
</tr>
<tr>
<td>TVF‡</td>
<td>27 (4.3%)</td>
<td>2 (0.6%)</td>
<td>.002</td>
</tr>
<tr>
<td>MACE‡</td>
<td>27 (4.3%)</td>
<td>3 (1.0%)</td>
<td>.006</td>
</tr>
<tr>
<td>At 4 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac death</td>
<td>10 (1.6%)</td>
<td>3 (1.0%)</td>
<td>.434</td>
</tr>
<tr>
<td>MI</td>
<td>26 (4.1%)</td>
<td>3 (1.0%)</td>
<td>.008</td>
</tr>
<tr>
<td>Periprocedural MI</td>
<td>14 (2.2%)</td>
<td>1 (0.3%)</td>
<td>.028</td>
</tr>
<tr>
<td>Spontaneous MI</td>
<td>12 (1.9%)</td>
<td>2 (0.6%)</td>
<td>.130</td>
</tr>
<tr>
<td>Clinically driven TLR</td>
<td>22 (3.5%)</td>
<td>4 (1.3%)</td>
<td>.050</td>
</tr>
<tr>
<td>Clinically driven TVR</td>
<td>23 (3.6%)</td>
<td>5 (1.6%)</td>
<td>.080</td>
</tr>
<tr>
<td>Cardiac death + MI</td>
<td>32 (5.1%)</td>
<td>6 (1.9%)</td>
<td>.020</td>
</tr>
<tr>
<td>Target lesion failure‡</td>
<td>43 (6.8%)</td>
<td>8 (2.5%)</td>
<td>.006</td>
</tr>
<tr>
<td>TVF‡</td>
<td>43 (6.8%)</td>
<td>9 (2.9%)</td>
<td>.012</td>
</tr>
<tr>
<td>MACE‡</td>
<td>46 (7.3%)</td>
<td>11 (3.5%)</td>
<td>.021</td>
</tr>
<tr>
<td>At 9 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac death</td>
<td>11 (1.7%)</td>
<td>5 (1.6%)</td>
<td>.866</td>
</tr>
<tr>
<td>MI</td>
<td>31 (4.9%)</td>
<td>5 (1.6%)</td>
<td>.012</td>
</tr>
<tr>
<td>Periprocedural MI</td>
<td>14 (2.2%)</td>
<td>1 (0.3%)</td>
<td>.028</td>
</tr>
<tr>
<td>Spontaneous MI</td>
<td>17 (2.7%)</td>
<td>4 (1.3%)</td>
<td>.163</td>
</tr>
<tr>
<td>Clinically driven TLR</td>
<td>89 (14.1%)</td>
<td>18 (5.7%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Clinically driven TVR</td>
<td>92 (14.6%)</td>
<td>20 (6.4%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cardiac death + MI</td>
<td>37 (5.9%)</td>
<td>9 (2.9%)</td>
<td>.044</td>
</tr>
<tr>
<td>Target lesion failure‡</td>
<td>111 (17.6%)</td>
<td>25 (8.0%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>TVF‡</td>
<td>113 (17.9%)</td>
<td>27 (8.6%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MACE‡</td>
<td>120 (19.0%)</td>
<td>29 (9.2%)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

* Target lesion failure was defined as a composite of cardiac death, MI, and clinically driven TLR.
† TVF was defined as a composite of cardiac death, MI, and clinically driven TVR.
‡ MACE was defined as a composite of all-cause death, MI, and TVR.
Intek-Apollo stent (Baar 2, Switzerland) uses the same polymer as Coroflex Please. Gavrielatos et al showed favorable outcomes with this stent. At 15-month follow-up, the TVR was 4.6%, which is better than the result of PECOPS I. Considering these results, there might be the negative impact of the stent strut thickness that shadows the possible positive impact of the polymer. Third, the drug-release kinetics of Coroflex Please is between the Taxus Medium Release and Slow Release. However, the drug doses are same between 2 stents system (1 \( \mu \text{g/mm}^2 \) stent surface). This difference might give rise to unfavorable outcome of Coroflex Please.

At 9-month follow-up, the incidence of MI was 4.9% in Coroflex Please and 1.6% in Taxus Liberte, which demonstrated favorable outcome of Taxus Liberte. The higher incidence of MI in Coroflex stent was well corroborated by the trend of higher incidence of definite or combined stent thrombosis. When dividing MI into

---

**Table IV. Incidence of stent thrombosis**

<table>
<thead>
<tr>
<th>ARC stent thrombosis*</th>
<th>Coroflex (n = 631)</th>
<th>Taxus (n = 314)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite stent thrombosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute (0-24 h)</td>
<td>1 (0.2%)</td>
<td>0 (0.0%)</td>
<td>.480</td>
</tr>
<tr>
<td>Subacute (2-30 d)</td>
<td>7 (1.1%)</td>
<td>1 (0.3%)</td>
<td>.160</td>
</tr>
<tr>
<td>Late (31-365 d)</td>
<td>6 (1.0%)</td>
<td>1 (0.3%)</td>
<td>.286</td>
</tr>
<tr>
<td>All (0-365 d)</td>
<td>14 (2.2%)</td>
<td>2 (0.6%)</td>
<td>.076</td>
</tr>
<tr>
<td>Definite or probable ST</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute (0-24 h)</td>
<td>1 (0.2%)</td>
<td>0 (0.0%)</td>
<td>.480</td>
</tr>
<tr>
<td>Subacute (2-30 d)</td>
<td>7 (1.1%)</td>
<td>2 (0.6%)</td>
<td>.481</td>
</tr>
<tr>
<td>Late (31-365 d)</td>
<td>6 (1.0%)</td>
<td>2 (0.6%)</td>
<td>.620</td>
</tr>
<tr>
<td>All (0-365 d)</td>
<td>14 (2.2%)</td>
<td>4 (1.3%)</td>
<td>.317</td>
</tr>
</tbody>
</table>

* Stent was classified according to ARC consensus.

---

**Figure 3**

Cumulative incidence of clinically-driven TVR (%)

- **HR: 2.43 (1.50-3.94)**
- Non-Inferiority P-value = 1.000
- Inferiority P-value < .001

- **Coroflex: 14.6%**
- **Taxus: 6.4%**

---

**Table V. Nine-month angiographic outcomes**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coroflex (n = 834)</th>
<th>Taxus (n = 423)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before procedure, mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lesion length (mm)</td>
<td>18.8 ± 10.8 20.1 ± 11.2</td>
<td>.070</td>
<td></td>
</tr>
<tr>
<td>Reference vessel diameter (mm)</td>
<td>2.83 ± 0.51 2.80 ± 0.49</td>
<td>.307</td>
<td></td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>0.78 ± 0.48 0.76 ± 0.48</td>
<td>.518</td>
<td></td>
</tr>
<tr>
<td>Diameter stenosis (%)</td>
<td>72.5 ± 16.9 73.0 ± 15.2</td>
<td>.544</td>
<td></td>
</tr>
<tr>
<td>Immediately after procedure, mean ± SD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>In stent 2.54 ± 0.45 2.50 ± 0.44</td>
<td>.174</td>
<td></td>
</tr>
<tr>
<td>In segment 2.18 ± 0.52 2.14 ± 0.48</td>
<td>.245</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter stenosis (%)</td>
<td>In stent 8.88 ± 8.71 9.68 ± 8.74</td>
<td>.145</td>
<td></td>
</tr>
<tr>
<td>In segment 19.15 ± 11.52 19.42 ± 11.47</td>
<td>.701</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute gain (mm)</td>
<td>In stent 1.76 ± 0.53 1.74 ± 0.53</td>
<td>.463</td>
<td></td>
</tr>
<tr>
<td>In segment 1.40 ± 0.57 1.38 ± 0.52</td>
<td>.532</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Follow-up at 9 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MLD (mm), mean ± SD</td>
<td>In stent 1.82 ± 0.77 1.97 ± 0.65</td>
<td>.004</td>
<td></td>
</tr>
<tr>
<td>In segment 1.69 ± 0.73 1.80 ± 0.59</td>
<td>.023</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diameter stenosis (%), mean ± SD</td>
<td>In stent 35.15 ± 24.50 28.52 ± 19.51</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>In segment 38.75 ± 23.43 33.43 ± 18.27</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Late luminal loss (mm), mean ± SD</td>
<td>In stent 0.71 ± 0.64 0.52 ± 0.50</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>In segment 0.48 ± 0.61 0.33 ± 0.50</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Binary restenosis, n (%)</td>
<td>In stent 117 (14.1) 40 (9.6)</td>
<td>.034</td>
<td></td>
</tr>
<tr>
<td>In segment 135 (16.3) 47 (11.3)</td>
<td>.025</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restenosis pattern,† n (%)</td>
<td>Focal 88 (62.0) 32 (64.0)</td>
<td>.972</td>
<td></td>
</tr>
<tr>
<td>Diffuse 27 (19.0) 10 (20.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proliferative 14 (9.9) 4 (8.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total occlusion 13 (9.2) 4 (8.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Comparisons were performed using the generalized estimating equations. 
† Comparisons were performed with the Fisher exact test.
periprocedural MI and spontaneous one, we could find that the difference between 2 groups was mainly driven by periprocedural MI (2.2% vs 0.3%, \( P = .028 \)). These results may be caused by the different design of stent, as previously described. In terms of cardiac death, it could not show the differences between Taxus Liberte and Coroflex Please.

Subgroup analysis: diabetes

In subgroup analysis, the inferiority of Coroflex Please was demonstrated in almost all subgroups. The only subgroup where the inferiority of Coroflex Please was not shown was the DM group when investigating in-stent late LL. The in-stent late LL of Coroflex Please and Taxus Liberte was 0.69 and 0.57 mm, respectively. However,
Coroflex Please showed numerically higher LL than did Taxus Liberte, and the difference between 2 stents demonstrated borderline statistical significance ($P = 0.063$). Accordingly, we believe that the DM group was underpowered to detect significant differences in angiographic outcome.
Limitations of the study

There are a couple of limitations to this study. First, the randomization of the stents was not 1:1 but rather 2:1. This leads to sufficient number of patients implanted with Coroflex Please but limited number of patients implanted with Taxus Liberte. This widens the possibility that Taxus Liberte could unexpectedly perform better or worse than its usual performance by chance, which requires cautious attitude at any interpretation of the results. However, the TVR rate of Taxus Liberte in this study was comparable with other studies enrolling the patients receiving Taxus Liberte, namely, the TAXUS ATLAS and ZEST trials.11,19 Second, the selection of control stent could be debatable. In other words, Taxus Liberte might not be an optimal benchmark. However, for example, in the representative trials for everolimus-eluting stents (EESs), namely, the SPIRIT V Diabetes and COMPARE trials that were undertaken at the same period as this ECO-PLEASANT trial, PESs were also selected as comparator stent. SPIRIT V Diabetes was a prospective, single-blind, multicenter trial that compared EES with TAXUS Express, and COMPARE was a prospective, single-center trial that compared EES with TAXUS Liberte.26,27 These trials were designed to compare stents eluting different drugs. Although, the current trial was planned to demonstrate that new PES, Coroflex Please, has equivalent or noninferior efficacy to the established PES, that is to say Taxus Liberte, which elutes the same drug as Coroflex Please. In addition, we intended to show whether all PESs were borne the same or not before automatically assuming data transferability. Therefore, it is arguably more reasonable to select Taxus Liberte as comparator stent in this study than the SPIRIT-IV and COMPARE trials. Lastly, there could be criticism that choice of primary end point was not optimal. However, with regard to TLF and TLR as secondary end points, Coroflex Please was inferior to Taxus Liberte.

In conclusion, in the stent comparison of the ECO-PLEASANT randomized prospective trial, Coroflex Please was inferior to Taxus Liberte in inhibition of neointimal growth after stenting, which was corroborated by the similar tendency of clinical outcomes. In addition, not all PESs were borne the same. Accordingly, head-to-head trials are needed to confirm the efficacy and safety of newly developed stents before automatically assuming data transferability.

Disclosures

We declare that we have no conflict of interest.

References