Final 5-Year Report of the Randomized BIO-RESORT Trial Comparing 3 Contemporary Drug-Eluting Stents in All-Comers

Eline H. Ploumen, MD, PhD; Tineke H. Pinxterhuis, MD, PhD; Rosaly A. Buiten, MD, PhD; Paolo Zocca, MD, PhD; Peter W. Danse, MD, PhD; Carl E. Schotborgh, MD; Martijn Scholte, MD; R. Melvyn Tjon Joe Gin, MD; Samer Somi, MD, PhD; K. Gert van Houwelingen, MD; Martin G. Stoel, MD, PhD; H. A. F. de Man, MD, PhD; Marc Hartmann, MD, PhD; Gerard C. M. Linssen, MD, PhD; Liefke C. van der Heijden, MD, PhD; Marlies M. Kok, MD, PhD; Carine J. M. Doggen, PhD; Clemens von Birgelen, MD, PhD

BACKGROUND: In a previous trial, higher 5-year mortality was observed following treatment with biodegradable polymer Orsiro sirolimus-eluting stents (SES). We assessed 5-year safety and efficacy of all-comers as well as patients with diabetes treated with SES or Synergy everolimus-eluting stents (EES) versus durable polymer Resolute Integrity zotarolimus-eluting stents (ZES).

METHODS AND RESULTS: The randomized BIO-RESORT (Comparison of Biodegradable Polymer and Durable Polymer Drug-Eluting Stents in an All Comers Population) trial enrolled 3514 all-comer patients at 4 Dutch cardiac centers. Patients aged ≥18 years who required percutaneous coronary intervention were eligible. Participants were stratified for diabetes and randomized to treatment with SES, EES, or ZES (1:1:1). The main end point was target vessel failure (cardiac mortality, target vessel myocardial infarction, or target vessel revascularization). Five-year follow-up was available in 3183 of 3514 (90.6%) patients. The main end point target vessel failure occurred in 142 of 1169 (12.7%) patients treated with SES, 130 of 1172 (11.6%) treated with EES, versus 157 of 1173 (14.1%) treated with ZES (hazard ratio [HR], 0.89 [95% CI, 0.71–1.12]; log-rank=0.31; and HR, 0.82 [95% CI, 0.65–1.04]; log-rank=0.10, respectively). Individual components of target vessel failure showed no significant between-stent difference. Very late definite stent thrombosis rates were low and similar (SES, 1.1%; EES, 0.6%; ZES, 0.9%). In patients with diabetes, target vessel failure did not differ significantly between stent-groups (SES, 19.8%; EES, 19.2%; versus ZES, 21.1% [log-rank=0.69 and log-rank=0.63]).

CONCLUSIONS: Orsiro SES, Synergy EES, and Resolute Integrity ZES showed similar 5-year outcomes of safety and efficacy, including mortality. A prespecified stent comparison in patients with diabetes also revealed no significant differences in 5-year clinical outcomes.

REGISTRATION: URL: https://www.clinicaltrials.gov; Unique identifier: NCT01674803.

Key Words: biodegradable polymer, drug-eluting stent, durable polymer, percutaneous coronary intervention, randomized clinical trial

Different drug-eluting stents (DES) have shown similar long-term efficacy in preventing recurrence of lumen obstruction following percutaneous coronary intervention (PCI).1–3 Nevertheless, throughout the years, there have been studies showing that DES can differ in long-term safety.4–6 Consequently, assessing long-term...
safety of novel DES is of interest and may reveal clinically relevant differences, both in all-comers and in high-risk subgroups, such as patients with diabetes. Previously, the 1-year safety and efficacy was similar in patients treated with the very thin-strut biodegradable polymer Synergy everolimus-eluting stent (EES) and ultrathin-strut biodegradable polymer Orsiro sirolimus-eluting stents (SES) versus the thin-strut durable polymer Resolute Integrity zotarolimus-eluting stents (ZES) assessed in the randomized BIO-RESORT (Comparison of Biodegradable Polymer and Durable Polymer Drug-Eluting Stents in an All Comers Population) trial.7 So far, only 1 randomized clinical trial assessed the 5-year outcome of treatment with the Synergy EES, showing no difference versus a thin-strut durable polymer DES in target lesions of low to moderate complexity.8 Recently, an all-comer study with SES showed a higher 5-year mortality rate as compared with a thin-strut durable polymer DES.6 This finding was driven by cancer-related mortality, but there is no valid explanation of why this SES would be carcinogenic. In addition, a subgroup analysis revealed a 5-year mortality rate of >20% in SES-treated patients with diabetes.9 Five-year reports of randomized studies with Orsiro SES are scarce; therefore, it is important to evaluate the long-term mortality of SES-treated patients in another randomized trial. Here, we assessed the 5-year outcome of the randomized BIO-RESORT trial,7 which compared 3 new-generation DES in all-comers: Orsiro SES and Synergy, and Resolute Integrity drug-eluting stents.

### METHODS

Data that support the findings of this study may be made available upon reasonable request. Detailed requests can be made to Cardiovascular Research and Education Enschede and will be evaluated by an independent review committee, identified for this purpose.

### Study Design and Participants

The study design of the BIO-RESORT trial, including details regarding sample size, was previously reported.7 In brief, this investigator-initiated, patient- and assessor-blinded, noninferiority (3.5% noninferiority margin, 2.5% one-sided α level), randomized clinical trial was executed in 4 cardiac centers in the Netherlands (ClinicalTrials.gov NCT01674803). A total of 3514 all-comer patients requiring PCI with DES were randomly assigned in a 1:1:1 fashion to treatment with either Orsiro SES (Biotronik), Synergy EES (Boston Scientific), or Resolute Integrity ZES (Medtronic). Randomization was performed via web-based allocation and was stratified for diabetes.7 There were few exclusion criteria, which included known intolerance.

### CLINICAL PERSPECTIVE

#### What Is New?
- Between Orsiro and Resolute Integrity stents, we found no significant differences in safety and efficacy, including all-cause mortality.
- This randomized study presents the first 5-year follow-up data of the biodegradable polymer Synergy stent, showing in all-comer patients safety and efficacy similar to the durable polymer Resolute Integrity stent.

#### What Are the Clinical Implications?
- All-comer patients and patients with diabetes can be safely and effectively treated with Orsiro, Synergy, and Resolute Integrity drug-eluting stents.

### Nonstandard Abbreviations and Acronyms

| Abbreviation | Description |
|--------------|-------------|
| BIOFLOW III | BIOTRONIK—Safety and Performance Registry for an All-comers Patient Population With the Limus Eluting Orsiro Stent System Within Daily Clinical Practice III |
| BIO-RESORT  | Comparison of Biodegradable Polymer and Durable Polymer Drug-Eluting Stents in an All Comers Population |
| BIOSCIENCE  | Ultrathin Strut Biodegradable Polymer Sirolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Stent for Percutaneous Coronary Revascularization |
| DES          | Drug-eluting stent |
| DUTCH PEERS  | Third-Generation Zotarolimus-Eluting and Everolimus-Eluting Stents in All-Comer Patients Requiring a Percutaneous Coronary Intervention |
| EES          | Everolimus-eluting stent |
| EVOLVE II    | The EVOLVE II Clinical Trial to Assess the SYNERGY Stent System for the Treatment of Atherosclerotic Lesion(s) |
| RESOLUTE US  | Clinical Evaluation of the Medtronic Resolute Zotarolimus-Eluting Coronary Stent System in the Treatment of De Novo Lesions in Native Coronary Arteries With a Reference Vessel Diameter of 2.25mm to 4.2mm |
| SES          | Sirolimus-eluting stents |
| ZES          | Zotarolimus-eluting stents |
to dual antiplatelet therapy, known pregnancy, and life expectancy of <1 year. There was no limit for reference vessel size, lesion length, and number of lesions or vessels to be treated. Patients presenting with any coronary syndrome could participate, and any type of lesion (eg, de novo, restenotic, or coronary bypass lesion) was permitted. The trial was approved by the medical ethics committee Twente and the institutional review boards of all participating centers. In addition, the trial complied with the Declaration of Helsinki. All patients provided written informed consent.

Stents

The Orsiro SES elutes sirolimus within 3 months from a circumferential coating. The 60-μm (for ≤3.0-mm stents) or 80-μm (for >3.0-mm stents) cobalt-chromium struts with a thin passive coating of amorphous silicon carbide are asymmetrically covered with a biodegradable polymer coating that is thicker on the abluminal side (7.4 μm) than on the luminal side (3.5 μm). The biodegradable poly(L-lactide) acid is fully resorbed within =24 months. The Synergy EES elutes everolimus within 3 months from a 4-μm poly(lactic-co-glycolic acid) coating, located only on the abluminal side of 74-μm (for stents ≤2.5 mm), 79-μm (for 3.0–3.5 mm stents), or 81-μm (for 4.0 mm stents) platinum chromium struts. The poly (lactic-co-glycolic acid) coating is resorbed within 4 months. The Resolute Integrity ZES elutes zotarolimus during the first 6 months and has thin, round-shaped, 91-μm cobalt-chromium struts that are circumferentially covered by a 6-μm blend of 3 durable polymers.

Procedures, Clinical Follow-Up, and Event Adjudication

Coronary interventional procedures were performed according to standard techniques. The choice of concomitant medication and type and duration of antiplatelet therapy was based on routine clinical practice, current international guidelines, and operator’s judgment. Cardiovascular Research and Education Enschede (Enschede, the Netherlands) performed trial and data management. The research staff was blinded to the assigned stent type. Clinical follow-up was obtained by telephone, questionnaires, or visits to the outpatient clinic. An independent clinical research organization (Diagram, Zwolle, the Netherlands) performed data monitoring, processing of clinical outcome data, and independent clinical event adjudication. At all times, the clinical event committee was blinded to the assigned stent type. No routine angiographic follow-up was performed.

Clinical End Points

Clinical end points were centrally assessed and pre-specified according to definitions of the Academic Research Consortium. The main end point at 5-year follow-up was target vessel failure (TVF), a composite of cardiac death, target vessel–related myocardial infarction, or clinically indicated target vessel revascularization. Prespecified secondary end points included the individual components of TVF, all-cause mortality, target lesion revascularization, and stent thrombosis. Other secondary composite end points included target lesion failure (cardiac death, target vessel–related myocardial infarction, or clinically driven target lesion revascularization); and the patient-oriented composite end point (all-cause mortality, any myocardial infarction, or any repeat coronary revascularization).

Statistical Analysis

Differences in categorical variables were assessed with chi-square or Fisher exact tests, and continuous variables were compared with ANOVA. Time to main and secondary end points was assessed by Kaplan–Meier analyses, and the approximate log-rank test (Mantel-Cox test) was applied for between-group comparisons. Hazard ratios (HRs) were calculated using Cox proportional hazards analysis. Landmark analyses between 1 and 5 years were performed using 1-year landmarks. Cox regression was performed in order to test for interaction between subgroups and DES type regarding the main clinical end point. The trial was designed to assess the 1-year noninferiority of the primary end point. The 80% power was used to show noninferiority with a margin of 2.5% and an α of 0.05 (1-sided). P values and CIs were 2-sided, and a P value <0.05 was considered significant. Holm-Bonferroni correction was used to correct for testing between multiple groups. Statistical analyses were performed with SPSS version 24 (IBM) and Holm-Bonferroni Sequential Correction (Justin Gaetona, 2013).

RESULTS

All Patients

Between December 2012 and August 2015, 3514 all-comer patients were enrolled and included in the intention-to-treat analysis. Five-year follow-up was available in 3183 of 3514 (90.6%) patients; 88 patients were lost to follow-up, while 244 patients withdrew consent (Figure 1). Trial participants were aged 63.9±10.8 years, ranging from 32 to 93 years; 72.5% were men and 69.7% presented with an acute coronary syndrome. Baseline patient, lesion, and procedural characteristics are presented in Table S1. Dual antiplatelet therapy use at 5 years was low and similar.
for all 3 stent groups (SES 5.9%, EES 3.8%, ZES 4.4%) (Table S2). In addition, ≈15% of the study population used oral anticoagulants.

Five-year clinical outcome is presented in Table 1 (Holm-Bonferroni–corrected P values are presented in Table S3). TVF occurred in 142 of 1169 (12.7%) patients assigned to SES, 130 of 1172 (11.6%) patients assigned to EES, and 157 of 1173 (14.1%) patients assigned to ZES (SES versus ZES: HR, 0.89 [95% CI, 0.71–1.12], Plog-rank=0.31; EES versus ZES: HR, 0.82 [95% CI, 0.65–1.04], Plog-rank=0.10). There was no significant between-stent difference in the individual components of TVF (Figure 2) and other secondary clinical end points. The incidence of definite stent thrombosis (16 of 1169 [1.5%], 11 of 1172 [1.0%], and 13 of 1173 [1.2%], respectively) did not differ significantly (SES versus ZES: HR, 1.22 [95% CI, 0.59–2.54], Plog-rank=0.60; EES versus ZES: HR, 0.84 [95% CI, 0.38–1.88], Plog-rank=0.68). Patients treated with SES had a risk for clinical adverse events that was similar to patients treated with EES during 5-year follow-up (Table S4). The landmark analyses between 1- and 5-year follow-up also showed no statistically significant difference in the main and secondary end points for SES versus ZES and EES.

Figure 1. Trial profile.
Table 1. Clinical Events During 5-Year Follow-Up

| Event                              | SES (n=1169) | EES (n=1172) | ZES (n=1173) | HR (95% CI) SES vs ZES | HR (95% CI) EES vs ZES | P<sub>log-rank</sub> SES vs ZES† | P<sub>log-rank</sub> EES vs ZES† |
|-----------------------------------|-------------|-------------|-------------|------------------------|------------------------|---------------------------------|---------------------------------|
| Death, any                        | 92 (8.2)    | 85 (7.6)    | 106 (9.5)   | 0.86 [0.65–1.14]       | 0.28                   | 0.80 [0.60–1.06]                | 0.12                            |
| Cardiac death                     | 33 (3.0)    | 31 (2.8)    | 40 (3.6)    | 0.82 [0.52–1.30]       | 0.39                   | 0.77 [0.48–1.24]                | 0.28                            |
| MI, any                           | 66 (6.0)    | 56 (5.0)    | 60 (5.4)    | 1.09 [0.77–1.56]       | 0.62                   | 0.93 [0.65–1.34]                | 0.70                            |
| Target vessel MI                  | 50 (4.5)    | 44 (3.9)    | 50 (4.5)    | 1.00 [0.67–1.47]       | 0.98                   | 0.88 [0.59–1.31]                | 0.52                            |
| Coronary revascularization, any   | 153 (13.0)  | 139 (12.7)  | 164 (15.0)  | 0.92 [0.74–1.14]       | 0.44                   | 0.84 [0.67–1.05]                | 0.13                            |
| Target vessel revascularization   | 91 (8.3)    | 79 (7.2)    | 101 (9.3)   | 0.88 [0.67–1.17]       | 0.40                   | 0.78 [0.58–1.04]                | 0.09                            |
| Target lesion revascularization   | 55 (5.0)    | 50 (4.6)    | 62 (5.7)    | 0.88 [0.61–1.26]       | 0.47                   | 0.80 [0.55–1.16]                | 0.24                            |
| Nontarget vessel revascularization| 86 (8.0)    | 79 (7.8)    | 85 (7.3)    | 1.08 [0.80–1.47]       | 0.62                   | 1.08 [0.79–1.46]                | 0.64                            |
| Target vessel failure*            | 142 (12.7)  | 130 (11.6)  | 157 (14.1)  | 0.89 [0.71–1.12]       | 0.31                   | 0.82 [0.65–1.04]                | 0.10                            |
| Target lesion failure             | 113 (10.1)  | 109 (9.7)   | 128 (11.5)  | 0.87 [0.68–1.12]       | 0.28                   | 0.85 [0.66–1.09]                | 0.20                            |
| Major adverse cardiac events      | 178 (15.8)  | 174 (15.4)  | 198 (17.6)  | 0.88 [0.72–1.08]       | 0.23                   | 0.87 [0.71–1.07]                | 0.19                            |
| Patient-oriented composite end point | 256 (22.6) | 237 (21.0)  | 270 (23.9)  | 0.93 [0.79–1.11]       | 0.42                   | 0.87 [0.73–1.03]                | 0.11                            |
| Definite or probable stent thrombosis | 20 (1.8)   | 15 (1.4)    | 19 (1.8)    | 1.05 [0.56–1.96]       | 0.89                   | 0.79 [0.40–1.55]                | 0.49                            |
| Definite stent thrombosis         | 16 (1.5)    | 11 (1.0)    | 13 (1.2)    | 1.22 [0.59–2.54]       | 0.60                   | 0.84 [0.38–1.88]                | 0.68                            |
| Probable stent thrombosis         | 4 (0.4)     | 4 (0.3)     | 6 (0.6)     | 0.66 [0.19–2.35]       | 0.52                   | 0.67 [0.19–2.36]                | 0.53                            |

Data are expressed as number (percentage). EES indicates everolimus-eluting stent; HR, hazard ratio; MI, myocardial infarction; SES, sirolimus-eluting stent; and ZES, zotarolimus-eluting stent.

*Main clinical end point of cardiac death, target vessel–related MI, or clinically indicated target vessel revascularization.
†See Table S3 for P values corrected with Holm-Bonferroni correction.

Patients With Diabetes

Of all 3514 trial participants, 624 (17.8%) had diabetes, without any difference between stent groups. Of all patients with diabetes, 211 were treated with SES, 203 with EES, and 210 with ZES. Baseline patient, lesion, and procedural characteristics of these patients are presented in Table S6. Patients with diabetes were aged 65.5±10.1 years, 67.9% were men, and 22.8% were current smokers. At 5-year follow-up, 6.5% of the patients with diabetes used dual antiplatelet therapy and 21.9% used oral anticoagulants.

TVF occurred in 39 of 211 (19.8%) patients treated with SES, 37 of 203 (19.2%) treated with EES, and 41 of 210 (21.1%) treated with ZES (SES versus ZES: HR, 0.91 [95% CI, 0.59–1.42], P<sub>log-rank</sub>=0.69; EES versus ZES: HR, 0.90 [95% CI, 0.58–1.40], P<sub>log-rank</sub>=0.63 (Figure 3). All-cause and cardiac mortality were lower in patients with diabetes assigned to SES versus ZES (HR, 0.53 [95% CI, 0.30–0.93], P<sub>log-rank</sub>=0.026; and HR, 0.35 [95% CI, 0.14–0.90], P<sub>log-rank</sub>=0.030), but this was not statistically significant after applying the Holm-Bonferroni correction to adjust for testing between multiple groups (Table S7). In addition, no statistically significant difference in all-cause or cardiac mortality was found for treatment with EES versus ZES (HR, 0.71 [95% CI, 0.43–1.20], P<sub>log-rank</sub>=0.20; and HR, 0.49 [95% CI, 0.21–1.14], P<sub>log-rank</sub>=0.10). There was also no significant between-stent difference in other clinical end points (Table 3). Patients treated with EES had a similar risk for clinical adverse events than patients treated with SES during 5-year follow-up (Table S4).

In addition, no significant between-stent difference in clinical outcome was found between patients with insulin-dependent and noninsulin-dependent diabetes, except for a higher rate of definite or probable stent thrombosis in patients with insulin-dependent diabetes treated with ZES as compared with EES (Table S8) (Holm-Bonferroni–corrected P values are presented in Table S9).

DISCUSSION

Main Findings

Five years after PCI, both the novel Orsiro SES and Synergy EES showed no significant difference in the main end point TVF as compared with the Resolute Integrity ZES. In addition, for all 3 stents, similar outcomes were found regarding mortality, myocardial infarction, and repeated revascularization. A landmark analysis between 1- and 5-year follow-up also
Ploumen et al BIO-RESORT at 5 Years

showed no significant between-stent difference in the occurrence of the main end point and its components. Furthermore, in all 3 DES, a low incidence of very late stent thrombosis was found. The favorable long-term safety and efficacy of the 3 stents was consistent in various subgroups. A prespecified analysis of the diabetes subgroup revealed that cardiac mortality was numerically but not significantly lower in patients treated with Orsiro SES or Synergy EES versus Resolute Integrity ZES (3.0% or 4.2% versus 8.3%). Among patients with diabetes, there was no significant between-stent difference in the main end point and secondary end points other than mortality.

Five-Year Clinical Outcome in All-Comers

For Orsiro SES, 5-year follow-up has been reported by only 1 study, the BIOSCIENCE (Ultrathin Strut Biodegradable Polymer Sirolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Stent for Percutaneous Coronary Revascularization) trial (n=2119). It assessed this SES versus a thin-strut durable polymer EES (Xience, Abbott Vascular) in all-comers and showed no difference in 5-year target lesion failure rate (20.2% versus 18.8%). However, 2 other trials with a shorter follow-up and dissimilar study populations showed superiority in target lesion failure of the Orsiro SES versus the Xience EES. One of these 2 trials had a follow-up of 2 years and was performed in patients with ST-segment-elevation myocardial infarction (STEMI), while the other study with a follow-up of 3 years was performed in patients with any clinical syndrome except STEMI. Our present analysis did not find such a difference; yet, there may be too many dissimilarities between the studies.
In addition, at 5-year follow-up of the EVOLVE II trial, the use of dual antiplatelet therapy was disproportionately high (36.4%, versus 4.7% in BIO-RESORT). Nevertheless, the exclusion of patients with STEMI may in fact lead to higher event rates, as patients with STEMI are on average younger and have fewer comorbidities than patients who initially present with stable or unstable angina, in whom atherosclerosis may be more advanced. Comparison of the patient characteristics at baseline supports this thought as the EVOLVE II patient population had more cardiovascular risk factors.

The Resolute Integrity ZES has been previously assessed in the DUTCH PEERS (Third-Generation Zotarolimus-Eluting and Everolimus-Eluting Stents in All-Comer Patients Requiring a Percutaneous Coronary Intervention) randomized trial, which compared it with the Promus Element EES in all-comers. The trial found no difference in 5-year TVF rate, which in the 906 Resolute Integrity ZES–treated patients was comparable to the rate in ZES-treated patients in the present analysis (13.2% and 14.1%).

New-generation DES other than the study stents were compared in several other randomized trials, which also found no between-stent difference in clinical outcome at 5-year follow-up. The results of the current analysis add to the body of evidence that shows in all-comers no significant difference between contemporary stents in 5-year clinical safety and efficacy.

### Five-Year Clinical Outcome of Patients With Diabetes
Patients with diabetes have an increased risk of adverse events following PCI, and it is clinically relevant to assess the long-term outcome of patients with diabetes, treated with contemporary DES. Previously, a subgroup analysis of the BIOSCIENCE trial in all-comer patients with diabetes showed no difference in target lesion failure between Orsiro SES and Xience EES.

| Table 2. Landmark Analysis of Clinical Events Between 1- and 5-Year Follow-Up |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                  | SES (n=1169)    | EES (n=1172)    | ZES (n=1173)    | HR (95% CI) SES vs ZES | EES vs ZES | Difference (95% CI) EES vs ZES | $P_{log-rank}$ SES vs ZES | $P_{log-rank}$ EES vs ZES |
| Death, any       | 73 (6.4)        | 65 (5.7)        | 87 (7.6)        | 0.83 (0.61-1.13) | 0.23         | 0.74 (0.54–1.02) | 0.07            |                     |
| Cardiac death    | 23 (2.0)        | 21 (1.8)        | 30 (2.6)        | 0.76 (0.44-1.30) | 0.31         | 0.60 (0.40–1.22) | 0.20            |                     |
| MI, any          | 37 (3.3)        | 31 (2.8)        | 29 (2.6)        | 1.26 (0.77-2.05) | 0.35         | 1.06 (0.64–1.76) | 0.81            |                     |
| Target lesion failure | 24 (2.1)     | 19 (1.7)        | 19 (1.7)        | 1.24(0.68-2.27) | 0.48         | 0.99 (0.53–1.88) | 0.98            |                     |
| Coronary revascularization, any | 104 (9.5)      | 99 (9.0)        | 112 (10.2)      | 0.90 (0.69-1.18) | 0.45         | 0.87 (0.66–1.14) | 0.31            |                     |
| Target vessel revascularization | 65 (5.8)      | 56 (5.0)        | 71 (6.3)        | 0.90 (0.64-1.25) | 0.50         | 0.78 (0.55–1.11) | 0.16            |                     |
| Target lesion revascularization | 37 (3.3)      | 33 (2.9)        | 45 (4.0)        | 0.81 (0.52-1.24) | 0.33         | 0.73 (0.48–1.14) | 0.16            |                     |
| Nontarget vessel revascularization | 62 (5.5)     | 67 (5.0)        | 57 (5.1)        | 0.70 (1.07-1.54) | 0.70         | 1.18 (0.83–1.67) | 0.37            |                     |
| Target vessel failure* | 87 (7.9)     | 74 (6.7)        | 94 (8.6)        | 0.90 (0.67-1.21) | 0.48         | 0.78 (0.57–1.05) | 0.10            |                     |
| Target lesion failure | 66 (6.0)      | 59 (5.3)        | 75 (6.8)        | 0.86 (0.62-1.19) | 0.36         | 0.78 (0.55–1.09) | 0.15            |                     |
| Major adverse cardiac events | 119 (10.8)    | 114 (10.3)      | 137 (12.4)      | 0.85 (0.66-1.08) | 0.18         | 0.82 (0.64–1.06) | 0.13            |                     |
| Patient-oriented composite end point | 169 (15.7)   | 156 (14.4)      | 180 (16.7)      | 0.91 (0.74-1.13) | 0.40         | 0.85 (0.69–1.06) | 0.15            |                     |
| Definite or probable stent thrombosis | 15 (1.3)      | 10 (0.9)        | 13 (1.1)        | 1.14 (0.54-2.40) | 0.73         | 0.77 (0.34–1.75) | 0.52            |                     |
| Definite stent thrombosis | 12 (1.1)      | 7 (0.6)         | 10 (0.9)        | 1.18 (0.51-2.74) | 0.69         | 0.70 (0.27–1.84) | 0.47            |                     |
| Probable stent thrombosis | 3 (0.3)       | 3 (0.3)         | 3 (0.3)         | 0.99 (0.20-4.90) | 0.99         | 1.00 (0.20–4.94) | 0.997           |                     |

Data are expressed as number (percentage). EES indicates everolimus-eluting stent; HR, hazard ratio; MI, myocardial infarction; SES, sirolimus-eluting stent; and ZES, zotarolimus-eluting stent.

*Main clinical end point of cardiac death, target vessel–related MI, or clinically indicated target vessel revascularization.

†See Table S5 for $P$ values corrected with Holm-Bonferroni correction.
In the present analysis, the target lesion failure rates were higher than in several other studies. For example, the 5-year target lesion failure rate was 14.0% in 402 patients with diabetes who were treated with Orsiro SES in the BIOFLOW III (BIOTRONIK—Safety and Performance Registry for an All-comers Patient Population With the Limus Eluting Orsiro Stent System Within Daily Clinical Practice III) registry,20 and it was 17.0% in 463 patients treated with Synergy EES in the EVOLVE II diabetes substudy.8 In the RESOLUTE US (Clinical Evaluation of the Medtronic Resolute Zotarolimus-Eluting Coronary Stent System in the Treatment of De Novo Lesions in Native Coronary Arteries With a Reference Vessel Diameter of 2.25 mm to 4.2 mm) observational study, patients with diabetes (n=461) also showed a 5-year target lesion failure rate (16.9%) that was comparable to the target lesion failure rate of ZES-treated patients in the present analysis.21

**Five-Year Mortality**

Previous trials reported varying 5-year mortality rates following treatment with the study stents. For Synergy EES–treated patients, 5-year mortality in the EVOLVE II trial was similar to the mortality of Promus Element EES–treated patients (6.9% versus 7.4%).8 EVOLVE II trial participants with diabetes, treated with Synergy EES, also had a low mortality rate (10.3%). These rates are comparable to the all-cause mortality of Synergy EES in our present trial, both in all-comers (7.6%) and in patients with diabetes (13.0%).
For Orsiro SES–treated patients, previous studies reported conflicting results. The BIOSCIENCE trial found a higher mortality for Orsiro SES than for Xience EES (14.1% versus 10.3%), but that difference was driven by cancer-related mortality. In addition, in a diabetes substudy of BIOSCIENCE (n=486) the mortality rate was 20.9% in
patients treated with Orsiro SES and 13.8% with Xience EES (P=0.053).9 Furthermore, a registry of diabetic patients with any clinical syndrome except STEMI observed a 5-year mortality of 15.5% in Orsiro SES–treated patients.20 In our present analysis, all-comer patients treated with Orsiro SES had a relatively low mortality rate (8.2%), and in patients with diabetes we found a mortality rate that was also low and lower than in patients treated with Resolute Integrity ZES (9.4% versus 17.1%).

Notably, the lack of difference in 5-year mortality rates of Orsiro SES– and Resolute Integrity ZES–treated patients in BIO-RESORT challenge the findings of the BIOSCIENCE trial, which suggest an increased mortality in patients treated with Orsiro SES, driven by cancer-related death.6 The poly-L-lactic acid polymer-coating of Orsiro SES gradually degrades into carbon dioxide and hydrogen,22 which both have no systemic carcinogenic effects. Consequently, we cannot think of any reasonable explanation for a higher or lower all-cause mortality risk associated with the Orsiro SES. We feel that the higher mortality rate in the all-comers of BIOSCIENCE may have resulted from a play of chance.

Limitations
The current analysis has some limitations. Although various adverse events (and not only the main end point) were independently adjudicated by a clinical event committee, this large-scale randomized clinical trial was not powered to assess secondary end points. Hence, such findings should be considered hypothesis generating. Furthermore, residual confounding cannot be excluded, but it may be limited by the fact that multiple patient-, target lesion–, interventional procedure–, and medical therapy–related parameters were assessed. Follow-up was not available in 2% (87 of 3514) of patients because of loss to follow-up and in 7% (244 of 3514) consent withdrawal, without any between-stent difference. Of note, a follow-up of 5 years was intended from the very beginning of the current trial. However, as funding was initially not guaranteed beyond 3-year follow-up, the medical ethics committee did not permit consenting patients for a follow-up of 5 years but demanded reconsenting every patient after 3 years, once additional funding was granted. Regrettably, 4% of the study participants refused to reconsent and these patients were classified as “consent withdrawal.” Nevertheless, with only 2% (87 of 3514) of patients, the actual loss to follow-up during all 5 years was low. In addition, the 91% completeness of 5-year follow-up is similar to that of various other randomized stent trials with conventional clinical follow-up.4,7,16,23
CONCLUSIONS

Osiris SES, Synergy EES, and Resolute Integrity ZES showed similar 5-year outcomes of safety and efficacy, including mortality. A prespecified stent comparison in patients with diabetes also revealed no significant differences in 5-year clinical outcomes.

ARTICLE INFORMATION

Received June 16, 2022; accepted September 28, 2022.

Affiliations

Department of Cardiology, Thoraxcentrum Twente, Medisch Spectrum Twente, Enschede, The Netherlands (E.H.P., T.H.P., R.A.B., P.Z., K.G.v.H., M.G.S., H.A.A.M., M.H., L.C.v.d.H., M.M.K., C.v.B.); Department of Health Technology and Services Research, Faculty BMS, Technical Medical Centre, University of Twente, Enschede, The Netherlands (E.H.P., T.H.P., C.J.D., C.v.B.); Department of Cardiology, Rijnstate Hospital, Arnhem, The Netherlands (P.W.D., R.M.G.); Department of Cardiology, Haga Hospital, The Hague, The Netherlands (C.E.S., S.S.); Department of Cardiology, Albert Schweitzer Hospital, Dordrecht, The Netherlands (M.S.); and Department of Cardiology, Hospital Group Twente, Amelo, Hengelo, The Netherlands (G.C.L.).

Sources of Funding

The BIO-RESORT trial was equally funded by Biotronik, Boston Scientific, and Medtronic.

Disclosures

Dr van Bi reports that the research department of Thoraxcentrum Twente has received institutional research grants provided by Abbott Vascular, Biotronik, Boston Scientific, and Medtronic. The remaining authors have no disclosures to report.

Supplemental Material

Tables S1–S9

REFERENCES

1. Wijns W, Valdes-Chavarri M, Richardt G, Moreno R, Íñiguez-Romo A, Barbato E, Camí D, Ando K, Merkely B, Kornowski R, et al. Long-term clinical outcomes after bioresorbable and permanent polymer drug-eluting stent implantation: final 5-year results of the CENTURY II randomised clinical trial. *EuroIntervention*. 2018;14:e343–e351. doi: 10.2446/EIJ-D-18-00358

2. Paradelis V, Vlachojannis GJ, Royaards KJ, Wassing J, van der Ent M, Smits PC. Abluminal biodegradable polymer bioresorbable versus durable polymer everolimus-eluting stent in patients with diabetes mellitus: 5-years follow-up from the COMPARE II trial. *Int J Cardiol*. 2019;290:40–44. doi: 10.1016/j.ijcard.2019.04.054

3. von Birgelen C, van der Heijden LC, Basalus MW, Kok MM, Sen H, von Birgelen C, Kok MM, van der Heijden LC, Danse PW, Schotborgh CE, Scholte M, Tjon Joe Gin RM, Somi S, van Houwelingen KG, Stoel MG, et al. Very thin strut biodegradable polymer everolimus-eluting and sirolimus-eluting stents versus durable polymer zotarolimus-eluting stents in allcomers with coronary artery disease (BIO-RESORT): a three-arm, randomised, non-inferiority trial. *Lancet*. 2019;388:2867–2877. doi: 10.1016/S0140-6736(19)31715-X

4. Kufner S, Sorges J, Mehilli S, Cassese S, Repp J, Wiebe J, Loovahaus R, Lahmann A, Rüdehe T, Ibrahim T, et al. Randomized trial of polymer-free sirolimus- and paclitaxel-eluting stents versus durable polymer zotarolimus-eluting stents: 5-year results of the ISAR-TEST-5 trial. *J Am Coll Cardiol Intv*. 2018;9:764–792. doi: 10.1016/j.jcin.2018.01.009

5. Serruys PW, Farooq V, Kalesan B, de Vries T, Buszman P, Linke A, Ischinger T, Krauss V, Eberli F, Wijns V, et al. Improved safety and reduction in stent thrombosis associated with biodegradable polymer-based biolimus-eluting stents versus durable polymer-based sirolimus-eluting stents in patients with coronary artery disease: final 5-year report of the LEADERS (Limus eluted from a durable versus ERodable stent coating) randomized, noninferiority trial. *J Am Coll Cardiol Intv*. 2013;8:777–789. doi: 10.1016/j.jcin.2013.04.011

6. Pilgrim T, Piccolo R, Heg D, Rofti M, Müller O, Moarof I, Siontis GC, Cook S, Weilennan D, et al. Ultrathin-strut, biodegradable-polymer, sirolimus-eluting stents versus thin-strut, durable-polymer, everolimus-eluting stents for percutaneous coronary revascula- risation: 5-year outcomes of the BIOSCIENCE randomised trial. *Lancet*. 2019;392:737–746. doi: 10.1016/S0140-6736(19)31708-2

7. von Birgelen C, Kok MM, van der Heijden LC, Dansie PW, Schotborgh CE, Scholte M, Tjon Joe Gin RM, Somi S, van Houwelingen KG, Stoel MG, et al. Very thin strut biodegradable polymer everolimus-eluting and sirolimus-eluting stents versus durable polymer zotarolimus-eluting stents in allcomers with coronary artery disease (BIO-RESORT): a three-arm, randomised, non-inferiority trial. *Lancet*. 2019;388:2867–2877. doi: 10.1016/S0140-6736(19)31920-1

8. Kereikais DJ, Windecker S, Jobe RL, Mehta SR, Sarembock IJ, Feldman RL, Stein B, Dubois C, Grady T, Saito S, et al. Clinical outcomes following implantation of thin-strut, bioabsorbable polymer-coated, everolimus-eluting SYNERGY stents. *Circ Cardiovasc Interv*. 2019;12:e008152. doi: 10.1161/CIRCINTERVENTIONS.119.008152

9. Iglesias JF, Heg D, Rofti M, Tüller D, Lanz J, Riganfetti M, Müller O, Moarof I, Cook S, Weilennan D, et al. Five-year outcomes in patients with diabetes mellitus treated with biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents. *J Am Heart Assoc*. 2019;8:e013607. doi: 10.1161/JAHA.119.013607

10. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Strohg A, Poege MA, et al. Five-year outcome after implantation of zotarolimus-eluting stents in allcomers with coronary artery disease (BIOFLOW II): final 2-year outcomes of the BIOFLOW II randomised clinical trial. *J Am Coll Cardiol Intv*. 2021;14:639–648. doi: 10.1016/j.jcin.2020.12.011

11. Ploumen EH, Koolen JJ, Doroza G, Garcia-Garcia HM, Bennett J, Roquin A, Ghario EQ, Cutlip DE, Wakeman R, Investigators BIOFLOWV. Ultrathin bioresorbable-polymer sirolimus-eluting stents versus thin durable-polymer everolimus-eluting stents for coronary revascularisation: 3-year outcomes from the randomized BIOFLOW V trial. *J Am Coll Cardiol Intv*. 2020;13:1543–1553. doi: 10.1016/j.jcin.2020.02.019

12. Ploumen EH, Buiten RA, Zocca P, Doggen CJM, Jessurun GAJ, Schotborgh CE, Roquin A, Dansie PW, Betin A, Aminian A, et al. Acute myocardial infarction treated with novel resolute onyx and osiri stents in the randomized BIONXY trial. *Catheter Cardiovasc Interv*. 2021;98:E188–E196. doi: 10.1002/ccd.29594

13. Zocca P, Kok MM, Tandjung K, Dansie PW, Jessurun GAJ, Hautvast RWM, van Houwelingen KG, Stoel MG, Schramm AR, Tjon Joe Gin RM, et al. 5-year outcome following randomized treatment of all-comers with zotarolimus-eluting resolute integrity and everolimus-eluting PROMUS element coronary stents. *J Am Coll Cardiol Intv*. 2018;11:462–469. doi: 10.1016/j.jcin.2017.11.031

14. Xu K, Xu B, Guan C, Jing Q, Zheng Q, Li X, Zhao X, Wang H, Zhao X, Li Y, et al. Biodegradable polymer-coated versus durable polymer-coated sirolimus-eluting stents: the final 5-year outcomes of the I-LOVE-IT 2 trial. *EuroIntervention*. 2021;16:e1516–e1526. doi: 10.4244/EIJ-D-19-00965

15. Kedhi E, Genèvreux P, Palmerini T, McAndrew TG, Parise H, Mehran R, Dangas GD, Stone GW. Impact of coronary lesion complexity on drug-eluting stent outcomes in patients with and without diabetes mellitus: analysis from 18 pooled randomized trials. *J Am Coll Cardiol Intv*. 2014;63:2111–2118. doi: 10.1016/j.jacc.2014.01.064

16. Koskinas KC, Siontis GC, Piccolo R, Fanzone A, Haynes A, Rat-Wirtzler J, Silber S, Serruys PW, Pilgrim T, Räber L, et al. Impact of diabetic status on outcomes after revascularization with drug-eluting stents in relation to coronary artery disease complexity: patient-level pooled analysis of 6081 patients. *Circ Cardiovasc Interv*. 2016;9:e003255. doi: 10.1161/CIRCINTERVENTIONS.115.003255

17. Chichareon P, Modolo R, Kogame N, Takahashi K, Chang CC, Tomanik M, Botelho R, Eechout H, Hofma S, Trendellova-Lazaroza D, et al. doi: 10.1016/j.jacc.2014.01.064
Association of diabetes with outcomes in patients undergoing contemporary percutaneous coronary intervention: pre-specified subgroup analysis from the randomized GLOBAL LEADERS study. Atherosclerosis. 2020;295:45–53. doi: 10.1016/j.atherosclerosis.2020.01.002

20. Waltenberger J, Brachmann J, van der Heyden J, Richardt G, Fröbert O, Seige M, Friedrich G, Eglis A, Winkens M, Hegeler-Molkewehrum C, et al. Five-year results of the bioflow-III registry: real-world experience with a biodegradable polymer sirolimus-eluting stent. Cardiovasc Revasc Med. 2020;21:63–69. doi: 10.1016/j.carrev.2019.03.004

21. Kirtane AJ, Yeung AC, Ball M, Carr J, O’Shaughnessy C, Mauri L, Liu M, Leon MB. Long-term (5-year) clinical evaluation of the resolute zotarolimus-eluting coronary stent: the RESOLUTE US clinical trial. Catheter Cardiovasc Interv. 2020;95:1067–1073. doi: 10.1002/ccd.28392

22. Hamon M, Niculescu R, Deleanu D, Dorobantu M, Weissman NJ, Waksman R. Clinical and angiographic experience with a third-generation drug-eluting Orsiro stent in the treatment of single de novo coronary artery lesions (BIOFLOW-III): a prospective, first-in-man study. EuroIntervention. 2013;8:1006–1011. doi: 10.4244/EIJY13A155

23. Kufner S, Byrne RA, Valeskini M, Schulz S, Ibrahim T, Hoppmann P, Schneider S, Laugwitz KL, Schunkert H, Kastrati A. Five-year outcomes from a trial of three limus-eluting stents with different polymer coatings in patients with coronary artery disease: final results from the ISAR-TEST 4 randomised trial. EuroIntervention. 2016;11:1372–1379. doi: 10.4244/EIJY14M11_02
Supplemental Material
Table S1. Baseline patient, lesion and procedural characteristics of all patients

|                          | All patients n = 3,514 | SES n = 1,169 | EES n = 1,172 | ZES n = 1,173 |
|--------------------------|------------------------|--------------|---------------|---------------|
| **Age, yrs**             | 63.9 ± 10.8            | 64.2 ± 10.7  | 64.0 ± 10.7   | 63.6 ± 10.9   |
| **Male**                 | 2547 (72.5)            | 854 (73.1%)  | 845 (72.1%)   | 848 (72.3%)   |
| **Body mass index, kg/m²** | 27.4 ± 4.2              | 27.4 ± 4.2   | 27.6 ± 4.2    | 27.3 ± 4.0    |
| **Current smoker**       | 1,031/3,422 (30.1)     | 341/1,144 (29.8) | 336/1,135 (29.6) | 354/1,143 (31.0) |
| **Medical history**      |                        |              |               |               |
| Family history of CAD    | 1,557/3,372 (46.2)     | 516/1,120 (46.1) | 512/1,114 (46.0) | 529/1,138 (46.5) |
| Diabetes, medically treated | 624 (17.8)            | 211 (18.0)   | 203 (17.3)    | 210 (17.9)    |
| Hypertension             | 1624 (46.2)            | 550 (47.0)   | 520 (44.4)    | 554 (47.2)    |
| Hypercholesterolemia     | 1335 (38.0)            | 463 (39.6)   | 422 (36.0)    | 450 (38.4)    |
| Previous MI              | 649 (18.5)             | 209 (17.9)   | 192 (16.4)    | 248 (21.1)    |
| Previous PCI             | 626 (17.8)             | 214 (18.3)   | 214 (18.3)    | 198 (16.9)    |
| Previous CABG            | 267 (7.6)              | 80 (6.8)     | 91 (7.8)      | 96 (8.2)      |
| Previous stroke          | 231 (6.6)              | 76 (6.5)     | 74 (6.3)      | 81 (6.9)      |
| Renal insufficiency*     | 108 (3.1)              | 46 (3.9)     | 29 (2.5)      | 33 (2.8)      |
| **Clinical presentation**|                        |              |               |               |
| Acute coronary syndrome  | 2449 (69.7)            | 818 (70.0)   | 816 (69.6)    | 815 (69.5)    |
| Stable angina            | 1065 (30.3)            | 351 (30.0)   | 356 (30.4)    | 358 (30.5)    |
| **Lesion characteristics**|                        |              |               |               |
| At least 1 complex lesion | 2783 (79.2)           | 942 (80.6)   | 903 (77.0)    | 938 (80.0)    |
| At least 1 bifurcation lesion | 1236 (35.2)       | 412 (35.2)   | 415 (35.4)    | 409 (34.9)    |
| At least 1 chronic total occlusion | 139 (4.0)     | 47 (4.0)     | 44 (3.8)      | 48 (4.1)      |
| At least 1 bypass graft lesion | 70 (2.0)      | 22 (1.9)     | 18 (1.5)      | 30 (2.6)      |
| At least 1 ostial lesion  | 252 (7.2)             | 74 (6.3)     | 97 (8.3)      | 81 (6.9)      |
| At least 1 severely calcified lesion | 783 (22.3) | 266 (22.8)   | 252 (21.5)    | 265 (22.6)    |
| **Procedural details**   |                        |              |               |               |
| Implantation of assigned stents only | 3,446 (98.1) | 1,144 (97.9) | 1,155 (98.5) | 1,147 (97.8) |
| Total stent length per patient, mm | 31 (20-50)      | 30 (18-49)   | 32 (20-48)    | 30 (22-52)    |
| Direct stenting          | 589 (16.8)            | 207 (17.7)   | 208 (17.7)    | 174 (14.8)    |
| Postdilation             | 2833 (80.6)           | 946 (80.9)   | 960 (81.9)    | 927 (79.0)    |
| Multivessel treatment    | 640 (18.2)            | 219 (18.7)   | 201 (17.2)    | 220 (18.8)    |
| Radial approach          | 1597 (45.4)           | 530 (45.3)   | 523 (44.6)    | 544 (46.4)    |
| IVUS                     | 62 (1.8)              | 20 (1.7)     | 20 (1.7)      | 22 (1.9)      |
| OCT                      | 21 (0.6)              | 9 (0.8)      | 7 (0.6)       | 5 (0.4)       |
| FFR                      | 391 (11.1)            | 131 (11.2)   | 133 (11.3)    | 127 (10.8)    |

Values are mean ± SD, n (%) or median (interquartile range, 25th-75th percentile). *Defined as an estimated glomerular filtration rate of < 30 ml/min/1.73m² or the need for dialysis.

**Abbreviations:** CAD = coronary artery disease; CABG = coronary artery bypass grafting; EES = everolimus-eluting stent; FFR = Fractional Flow Reserve; IVUS = Intravascular Ultra Sound; MI = myocardial infarction; OCT = Optical Coherence tomography; PCI = percutaneous coronary intervention; SES = sirolimus-eluting stent; ZES = zotarolimus-eluting stent.
### Table S2. Medication at 5-year follow-up for all patients and for patients with diabetes

| Medication                        | All patients n = 2,950 | SES n = 994 | EES n = 982 | ZES n = 974 | p-value |
|-----------------------------------|------------------------|-------------|-------------|-------------|---------|
| **Aspirin**                       | 2,288 (77.6)           | 779 (78.4)  | 751 (76.5)  | 758 (77.8)  | 0.58    |
| **DAPT**                          | 139 (4.7)              | 59 (5.9)    | 37 (3.8)    | 43 (4.4)    | 0.07    |
| With clopidogrel                  | 103 (3.5)              | 39 (3.9)    | 30 (3.1)    | 34 (3.5)    | 0.58    |
| With prasugrel or ticagrelor      | 36 (1.2)               | 20 (2.0)    | 7 (0.7)     | 9 (0.9)     | 0.02    |
| **Oral anticoagulation**          | 467 (15.8)             | 161 (16.2)  | 161 (16.2)  | 145 (14.9)  | 0.62    |
| Oral anticoagulation with P2Y<sub>12</sub> inhibitor | 23 (0.8) | 12 (1.2) | 3 (0.3) | 8 (0.8) | 0.07 |

| Medication                        | Patients with diabetes n = 493 | SES n = 168 | EES n = 169 | ZES n = 156 | p-value |
|-----------------------------------|---------------------------------|-------------|-------------|-------------|---------|
| **Aspirin**                       | 346 (70.2)                      | 118 (70.2)  | 122 (72.2)  | 106 (67.9)  | 0.71    |
| **DAPT**                          | 32 (6.5)                        | 16 (9.5)    | 8 (4.7)     | 8 (5.1)     | 0.14    |
| With clopidogrel                  | 25 (5.1)                        | 11 (6.5)    | 7 (4.1)     | 7 (4.5)     | 0.56    |
| With prasugrel or ticagrelor      | 7 (1.4)                         | 5 (3.0)     | 1 (0.6)     | 1 (0.6)     | 0.11    |
| **Oral anticoagulation**          | 108 (21.9)                      | 37 (22.0)   | 26 (21.3)   | 35 (22.4)   | 0.97    |
| Oral anticoagulation with P2Y<sub>12</sub> inhibitor | 5 (1.0) | 1 (0.6) | 1 (0.6) | 3 (1.9) | 0.39 |

Numbers are n (%). Data available in 2,950/3,514 patients (SES 994/1,169; EES 982/1,172; ZES 974/1,173), and 493/624 patients with diabetes (SES 168/211; EES 169/203; ZES 156/210).

**Abbreviations:** DAPT = dual Antiplatelet Therapy; EES = everolimus-eluting stent; SES = sirolimus-eluting stent; ZES = zotarolimus-eluting stent.
Table S3. Holm-Bonferroni corrected p-values of 5-year clinical outcomes

| Outcome                                      | Hazard ratio (95% CI) SES vs ZES | \( P_{\text{log-rank}}^{\dagger} \) SES vs ZES | Hazard ratio (95% CI) EES vs ZES | \( P_{\text{log-rank}}^{\dagger} \) EES vs ZES |
|-----------------------------------------------|-----------------------------------|-----------------------------------------------|---------------------------------|-----------------------------------------------|
| Death, any                                    | 0.86 (0.65-1.14)                  | 0.28                                          | 0.80 (0.60-1.06)                | 0.24                                          |
| Cardiac death                                 | 0.82 (0.52-1.30)                  | 0.39                                          | 0.77 (0.48-1.24)                | 0.56                                          |
| Myocardial infarction, any                    | 1.09 (0.77-1.56)                  | 1.00                                          | 0.93 (0.65-1.34)                | 0.70                                          |
| Target vessel myocardial infarction           | 1.00 (0.67-1.47)                  | 0.98                                          | 0.88 (0.59-1.31)                | 1.00                                          |
| Coronary revascularization, any               | 0.92 (0.74-1.14)                  | 0.44                                          | 0.84 (0.67-1.05)                | 0.26                                          |
| Target vessel revascularization               | 0.88 (0.67-1.17)                  | 0.40                                          | 0.78 (0.58-1.04)                | 0.18                                          |
| Target lesion revascularization               | 0.88 (0.61-1.26)                  | 0.47                                          | 0.80 (0.55-1.16)                | 0.48                                          |
| Non-target vessel revascularization           | 1.08 (0.80-1.47)                  | 1.00                                          | 1.08 (0.79-1.46)                | 0.64                                          |
| Target vessel failure*                        | 0.89 (0.71-1.12)                  | 0.31                                          | 0.82 (0.65-1.04)                | 0.20                                          |
| Target lesion failure                         | 0.87 (0.68-1.12)                  | 0.28                                          | 0.85 (0.66-1.09)                | 0.40                                          |
| Major adverse cardiac events                  | 0.88 (0.72-1.08)                  | 0.23                                          | 0.87 (0.71-1.07)                | 0.38                                          |
| Patient-oriented composite endpoint           | 0.93 (0.79-1.11)                  | 0.42                                          | 0.87 (0.73-1.03)                | 0.22                                          |
| Definite-or-probable stent thrombosis         | 1.05 (0.56-1.96)                  | 0.89                                          | 0.79 (0.40-1.55)                | 0.98                                          |
| Definite stent thrombosis                     | 1.22 (0.59-2.54)                  | 1.00                                          | 0.84 (0.38-1.88)                | 0.68                                          |
| Probable stent thrombosis                     | 0.66 (0.19-2.35)                  | 1.00                                          | 0.67 (0.19-2.36)                | 0.53                                          |

\( \dagger \)P'-values are corrected with Holm-Bonferroni correction. *Main clinical endpoint of cardiac death, target vessel-related myocardial infarction, or clinically indicated target vessel revascularization.

*Abbreviations:* EES = everolimus-eluting stent; SES = sirolimus-eluting stent; ZES = zotarolimus-eluting stent.
Table S4. Clinical events during 5-year follow-up, comparison SES vs EES in all-comer patients and in diabetes patients

| Event                                      | SES n = 1,169 | EES n = 1,172 | Hazard ratio (95% CI) EES vs SES | P_{log-rank} EES vs SES |
|--------------------------------------------|---------------|---------------|----------------------------------|------------------------|
| Death, any                                 | 92 (8.2)      | 85 (7.6)      | 0.93 (0.69-1.25)                 | 0.63                   |
| Cardiac death                              | 33 (3.0)      | 31 (2.8)      | 0.94 (0.58-1.54)                 | 0.82                   |
| Myocardial infarction, any                 | 66 (6.0)      | 56 (5.0)      | 0.85 (0.60-1.21)                 | 0.37                   |
| Target vessel myocardial infarction        | 50 (4.5)      | 44 (3.9)      | 0.88 (0.59-1.32)                 | 0.54                   |
| Coronary revascularization, any            | 153 (14.0)    | 139 (12.7)    | 0.91 (0.73-1.15)                 | 0.44                   |
| Target vessel revascularization            | 91 (8.3)      | 79 (7.2)      | 0.88 (0.65-1.18)                 | 0.39                   |
| Target lesion revascularization            | 55 (5.0)      | 50 (4.6)      | 0.92 (0.62-1.34)                 | 0.65                   |
| Non-target vessel revascularization        | 86 (8.0)      | 79 (7.8)      | 1.00 (0.74-1.35)                 | 0.98                   |
| Target vessel failure*                     | 142 (12.7)    | 130 (11.6)    | 0.92 (0.73-1.17)                 | 0.50                   |
| Target lesion failure                      | 113 (10.1)    | 109 (9.7)     | 0.97 (0.75-1.26)                 | 0.83                   |
| Major adverse cardiac events               | 178 (15.8)    | 174 (15.4)    | 0.99 (0.80-1.22)                 | 0.90                   |
| Patient-oriented composite endpoint        | 256 (22.6)    | 237 (21.0)    | 0.93 (0.78-1.11)                 | 0.43                   |
| Definite-or-probable stent thrombosis      | 20 (1.8)      | 15 (1.4)      | 0.75 (0.39-1.47)                 | 0.40                   |
| Definite stent thrombosis                  | 16 (1.5)      | 11 (1.0)      | 0.69 (0.32-1.49)                 | 0.34                   |
| Probable stent thrombosis                  | 4 (0.4)       | 4 (0.3)       | 1.00 (0.25-4.00)                 | 1.00                   |

| Event                                      | SES n = 211 | EES n = 203 | Hazard ratio (95% CI) EES vs SES | P_{log-rank} EES vs ZES |
|--------------------------------------------|-------------|-------------|----------------------------------|------------------------|
| Death, any                                 | 19 (9.4)    | 25 (13.0)   | 1.36 (0.75-2.46)                 | 0.32                   |
| Cardiac death                              | 6 (3.0)     | 8 (4.2)     | 1.38 (0.48-4.00)                 | 0.55                   |
| Myocardial infarction, any                 | 16 (8.3)    | 15 (7.6)    | 0.98 (0.49-1.99)                 | 0.96                   |
| Target vessel myocardial infarction        | 10 (5.1)    | 13 (6.6)    | 1.37 (0.60-3.11)                 | 0.47                   |
| Coronary revascularization, any            | 45 (23.6)   | 35 (18.5)   | 0.78 (0.50-1.22)                 | 0.27                   |
| Target vessel revascularization            | 30 (15.6)   | 21 (11.3)   | 0.70 (0.40-1.22)                 | 0.21                   |
| Target lesion revascularization            | 18 (9.2)    | 13 (6.9)    | 0.73 (0.36-1.49)                 | 0.39                   |
| Non-target vessel revascularization        | 22 (11.9)   | 20 (10.5)   | 0.95 (0.52-1.74)                 | 0.86                   |
| Target vessel failure*                     | 39 (19.8)   | 37 (19.2)   | 0.98 (0.63-1.54)                 | 0.93                   |
| Target lesion failure                      | 29 (14.7)   | 30 (15.5)   | 1.08 (0.65-1.80)                 | 0.77                   |
| Major adverse cardiac events               | 45 (22.2)   | 48 (25.6)   | 1.11 (0.74-1.67)                 | 0.62                   |
Data are n (%). *Main clinical endpoint of cardiac death, target vessel-related myocardial infarction, or clinically indicated target vessel revascularization.

**Abbreviations:** CI = confidence interval; EES = everolimus-eluting stent; SES = sirolimus-eluting stent; ZES = zotarolimus-eluting stent

| Endpoint                                         | Group 1 | Group 2 | Ratio (CI) | p-value |
|--------------------------------------------------|---------|---------|------------|---------|
| Patient-oriented composite endpoint              | 65 (32.2) | 64 (32.7) | 1.02 (0.73-1.45) | 0.90    |
| Definite-or-probable stent thrombosis            | 8 (4.1)  | 4 (2.1)  | 0.51 (0.15-1.69) | 0.26    |
| Definite stent thrombosis                        | 7 (3.6)  | 3 (1.6)  | 0.44 (0.11-1.69) | 0.22    |
| Probable stent thrombosis                        | 1 (0.5)  | 1 (0.5)  | 1.04 (0.07-16.61) | 0.98    |
Table S5. Holm-Bonferroni corrected p-values of landmark analysis between 1 and 5-year follow-up

| Event                                      | Hazard ratio (95% CI) SES vs ZES | \( P_{\text{log-rank}} \uparrow \) SES vs ZES | Difference (95% CI) EES vs ZES | \( P_{\text{log-rank}} \uparrow \) EES vs ZES |
|--------------------------------------------|----------------------------------|-----------------------------------------------|---------------------------------|-----------------------------------------------|
| Death, any                                 | 1.21 (0.89-1.65)                 | 0.23                                          | 0.74 (0.54-1.02)                | 0.14                                          |
| Cardiac death                              | 1.32 (0.77-2.28)                 | 0.31                                          | 0.60 (0.40-1.22)                | 0.40                                          |
| Myocardial infarction, any                 | 0.79 (0.49-1.29)                 | 0.70                                          | 1.06 (0.64-1.76)                | 0.81                                          |
| Target vessel myocardial infarction        | 0.80 (0.44-1.47)                 | 0.98                                          | 0.99 (0.53-1.88)                | 0.98                                          |
| Coronary revascularization, any            | 1.11 (0.85-1.45)                 | 0.45                                          | 0.87 (0.66-1.14)                | 0.62                                          |
| Target vessel revascularization            | 1.12 (0.80-1.57)                 | 0.50                                          | 0.78 (0.55-1.11)                | 0.32                                          |
| Target lesion revascularization            | 1.24 (0.80-1.92)                 | 0.33                                          | 0.73 (0.46-1.14)                | 0.32                                          |
| Non-target vessel revascularization        | 0.93 (0.65-1.33)                 | 0.70                                          | 1.18 (0.83-1.67)                | 0.74                                          |
| Target vessel failure*                     | 1.11 (0.83-1.49)                 | 0.48                                          | 0.78 (0.57-1.05)                | 0.20                                          |
| Target lesion failure                      | 1.17 (0.84-1.62)                 | 0.36                                          | 0.78 (0.55-1.09)                | 0.30                                          |
| Major adverse cardiac events               | 1.18 (0.93-1.51)                 | 0.18                                          | 0.82 (0.64-1.06)                | 0.26                                          |
| Patient-oriented composite endpoint        | 1.10 (0.89-1.35)                 | 0.40                                          | 0.85 (0.69-1.06)                | 0.30                                          |
| Definite-or-probable stent thrombosis      | 0.88 (0.42-1.84)                 | 0.73                                          | 0.77 (0.34-1.75)                | 1.00                                          |
| Definite stent thrombosis                  | 0.85 (0.37-2.00)                 | 0.69                                          | 0.70 (0.27-1.84)                | 0.94                                          |
| Probable stent thrombosis                  | 1.01 (0.20-5.01)                 | 1.00                                          | 1.00 (0.20-4.94)                | 0.997                                         |

\( P^* \)-values are corrected with Holm-Bonferroni correction. *Main clinical endpoint of cardiac death, target vessel-related myocardial infarction, or clinically indicated target vessel revascularization.

Abbreviations: EES = everolimus-eluting stent; SES = sirolimus-eluting stent; ZES = zotarolimus-eluting stent.
Table S6. Baseline patient, lesion and procedural characteristics of patients with diabetes

|                                | All patients with diabetes n = 624 | SES n = 211 | EES n = 203 | ZES n = 210 | p-value |
|--------------------------------|------------------------------------|-------------|-------------|-------------|---------|
| **Age, yrs**                   | 66.5 ± 10.1                        | 67.1 ± 9.6  | 66.7 ± 9.6  | 65.5 ± 10.9 | 0.25    |
| **Male**                       | 424 (67.9)                         | 146 (69.2)  | 142 (70.0)  | 136 (64.8)  | 0.47    |
| **Body mass index, kg/m²**     | 29.3 ± 4.7                         | 29.7 ± 4.4  | 29.3 ± 4.9  | 29.1 ± 4.7  | 0.41    |
| **Current smoker**             | 136/597 (22.8)                     | 46/201 (22.9)| 39/195 (20.0)| 51/201 (25.4)| 0.44    |
| **Medical history**            |                                    |             |             |             |         |
| Family history of CAD          | 250/577 (43.3)                     | 86/193 (44.6)| 79/185 (42.7)| 85/199 (42.7)| 0.91    |
| Hypertension                   | 423 (67.8)                         | 146 (69.2)  | 133 (65.5)  | 144 (68.6)  | 0.69    |
| Hypercholesterolemia           | 321 (51.4)                         | 109 (51.7)  | 102 (50.2)  | 110 (52.4)  | 0.91    |
| Previous MI                    | 149 (23.9)                         | 54 (25.6)   | 40 (19.7)   | 55 (26.2)   | 0.23    |
| Previous PCI                   | 157 (25.2)                         | 56 (26.5)   | 57 (28.1)   | 44 (21.0)   | 0.21    |
| Previous CABG                  | 81 (13.0)                          | 27 (12.8)   | 29 (14.3)   | 25 (11.9)   | 0.77    |
| Previous stroke                | 68 (10.9)                          | 29 (13.7)   | 18 (8.9)    | 21 (13.7)   | 0.25    |
| Renal insufficiency*           | 42 (6.7)                           | 18 (8.5)    | 7 (3.4)     | 17 (8.1)    | 0.07    |
| **Clinical presentation**      |                                    |             |             |             |         |
| Acute coronary syndrome        | 380 (60.9)                         | 129 (61.1)  | 127 (62.6)  | 124 (59.0)  | 0.76    |
| Stable angina                  | 244 (39.1)                         | 82 (38.9)   | 76 (37.4)   | 86 (41.0)   | 0.76    |
| **Lesion characteristics†**   |                                    |             |             |             |         |
| At least 1 complex lesion      | 493 (79.0)                         | 174 (82.5)  | 151 (74.4)  | 168 (80.0)  | 0.12    |
| At least 1 bifurcation lesion  | 235 (37.7)                         | 74 (35.1)   | 74 (36.5)   | 87 (41.4)   | 0.37    |
| At least 1 chronic total occlusion | 33 (5.3)                       | 13 (6.2)    | 12 (5.9)    | 8 (3.8)     | 0.50    |
| At least 1 bypass graft lesion | 19 (3.0)                           | 5 (2.4)     | 5 (2.5)     | 9 (4.3)     | 0.44    |
| At least 1 ostial lesion       | 47 (7.5)                           | 15 (7.1)    | 18 (8.9)    | 14 (6.7)    | 0.67    |
| At least 1 severely calcified lesion | 162 (26.0)               | 54 (25.6)   | 53 (26.1)   | 55 (26.2)   | 0.99    |
| **Procedural details**         |                                    |             |             |             |         |
| Implantation of assigned stents only | 611 (97.9)             | 209 (99.1)  | 199 (98.0)  | 203 (96.7)  | 0.23    |
| Total stent length per patient, mm | 39 (18-49)                  | 38 (18-45)  | 38 (20-50)  | 40 (22-52)  | 0.50    |
| Direct stenting                | 91 (14.6)                         | 33 (15.6)   | 33 (16.3)   | 25 (11.9)   | 0.40    |
| Postdilatation                 | 487 (78.0)                        | 167 (79.1)  | 152 (74.9)  | 168 (80.0)  | 0.41    |
| Multivessel treatment          | 113 (18.1)                        | 34 (16.1)   | 31 (15.3)   | 48 (22.9)   | 0.09    |
| Radial approach                | 321 (51.4)                        | 114 (54.0)  | 108 (53.2)  | 99 (47.1)   | 0.31    |

Values are mean ± SD, n (%), or median (interquartile range, 25th-75th percentile). *Defined as an estimated glomerular filtration rate of < 30 ml/min/1.73m² or the need for dialysis. †Details and definitions of lesion characteristics have been previously reported.

Abbreviations: CAD = coronary artery disease; CABG = coronary artery bypass grafting; EES = everolimus-eluting stent; MI = myocardial infarction; PCI = percutaneous coronary intervention; SES = sirolimus-eluting stent; ZES = zotarolimus-eluting stent.
Table S7. Holm-Bonferroni corrected p-values for 5-year clinical outcome of patients with diabetes

| Event                                      | Hazard ratio (95% CI) SES vs ZES | P_{\text{log-rank}} † SES vs ZES | Hazard ratio (95% CI) EES vs ZES | P_{\text{log-rank}} † EES vs ZES |
|--------------------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| Death, any                                 | 0.53 (0.30-0.93)                 | 0.052                            | 0.71 (0.43-1.20)                 | 0.20                             |
| Cardiac death                              | 0.35 (0.14-0.90)                 | 0.060                            | 0.49 (0.21-1.14)                 | 0.10                             |
| Myocardial infarction, any                 | 1.10 (0.54-2.25)                 | 1.00                             | 1.09 (0.52-2.25)                 | 0.83                             |
| Target vessel myocardial infarction        | 0.80 (0.35-1.85)                 | 1.00                             | 1.10 (0.50-2.40)                 | 0.82                             |
| Coronary revascularization, any            | 1.11 (0.73-1.71)                 | 0.63                             | 0.86 (0.55-1.36)                 | 1.00                             |
| Target vessel revascularization            | 1.21 (0.71-2.07)                 | 0.96                             | 0.84 (0.47-1.51)                 | 0.56                             |
| Target lesion revascularization            | 1.25 (0.62-2.51)                 | 1.00                             | 0.91 (0.43-1.93)                 | 0.80                             |
| Non-target vessel revascularization        | 1.15 (0.62-2.17)                 | 1.00                             | 1.08 (0.57-2.05)                 | 0.81                             |
| Target vessel failure*                     | 0.91 (0.59-1.42)                 | 0.69                             | 0.90 (0.58-1.40)                 | 1.00                             |
| Target lesion failure                      | 0.82 (0.50-1.34)                 | 0.86                             | 0.89 (0.54-1.49)                 | 0.63                             |
| Major adverse cardiac events               | 0.83 (0.56-1.24)                 | 0.74                             | 0.93 (0.63-1.37)                 | 0.71                             |
| Patient-oriented composite endpoint        | 0.90 (0.64-1.26)                 | 1.00                             | 0.92 (0.65-1.29)                 | 0.62                             |
| Definite-or-probable stent thrombosis      | 0.96 (0.36-2.56)                 | 0.94                             | 0.49 (0.15-1.63)                 | 0.48                             |
| Definite stent thrombosis                  | 3.38 (0.70-16.25)                | 0.26                             | 1.47 (0.25-8.81)                 | 0.67                             |
| Probable stent thrombosis                  | 0.16 (0.02-1.31)                 | 0.18                             | 0.16 (0.02-1.35)                 | 0.09                             |

†P'-values are corrected with Holm-Bonferroni correction. *Main clinical endpoint of cardiac death, target vessel-related myocardial infarction, or clinically indicated target vessel revascularization.

**Abbreviations:** EES = everolimus-eluting stent; SES = sirolimus-eluting stent; ZES = zotarolimus-eluting stent.
Table S8. Five-year clinical outcome of patients with insulin-dependent diabetes and non-insulin-dependent diabetes

| Patients with insulin-dependent diabetes | SES n = 70 | EES n = 74 | ZES n = 76 | $P_{\text{log-rank}}$ $^\dagger$ SES vs ZES | $P_{\text{log-rank}}$ $^\dagger$ EES vs ZES |
|-----------------------------------------|------------|------------|------------|--------------------------------|-------------------|
| Death, any                              | 7 (10.4)   | 8 (11.2)   | 14 (19.8)  | 0.12                           | 0.12              |
| Cardiac death                           | 2 (3.1)    | 2 (2.8)    | 7 (10.3)   | 0.10                           | 0.07              |
| Myocardial infarction, any              | 8 (12.6)   | 8 (11.0)   | 5 (7.8)    | 0.39                           | 0.40              |
| Target vessel myocardial infarction     | 4 (6.1)    | 8 (11.0)   | 5 (7.8)    | 0.77                           | 0.40              |
| Coronary revascularization, any         | 19 (30.3)  | 15 (21.4)  | 14 (21.9)  | 0.35                           | 0.88              |
| Target vessel revascularization         | 11 (17.2)  | 10 (14.3)  | 11 (17.6)  | 0.98                           | 0.59              |
| Target lesion revascularization         | 9 (14.1)   | 5 (7.0)    | 8 (12.6)   | 0.79                           | 0.30              |
| Target vessel failure*                  | 14 (21.4)  | 18 (25.2)  | 17 (24.8)  | 0.56                           | 0.95              |
| Target lesion failure                   | 13 (20.1)  | 14 (19.4)  | 15 (21.9)  | 0.71                           | 0.81              |
| Major adverse cardiac events            | 20 (29.9)  | 20 (27.7)  | 21 (29.3)  | 0.90                           | 0.78              |
| Definite-or-probable stent thrombosis   | 4 (6.1)    | 0           | 6 (9.1)    | 0.55                           | 0.010             |
| Definite stent thrombosis               | 4 (6.1)    | 0           | 1 (1.4)    | 0.17                           | 0.32              |

| Patients with non-insulin-dependent diabetes | SES n = 141 | EES n = 129 | ZES n = 134 | $P_{\text{log-rank}}$ $^\dagger$ SES vs ZES | $P_{\text{log-rank}}$ $^\dagger$ EES vs ZES |
|-----------------------------------------------|------------|------------|------------|--------------------------------|-------------------|
| Death, any                                    | 12 (8.8)   | 17 (13.9)  | 20 (15.6)  | 0.10                           | 0.65              |
| Cardiac death                                 | 4 (3.0)    | 6 (5.0)    | 9 (7.3)    | 0.12                           | 0.45              |
| Myocardial infarction, any                    | 8 (6.1)    | 7 (5.7)    | 9 (7.5)    | 0.69                           | 0.65              |
| Target vessel myocardial infarction           | 6 (4.6)    | 5 (4.0)    | 7 (5.9)    | 0.67                           | 0.58              |
| Coronary revascularization, any               | 26 (20.2)  | 20 (16.6)  | 25 (20.6)  | 0.93                           | 0.48              |
| Target vessel revascularization               | 19 (14.7)  | 11 (9.3)   | 13 (10.8)  | 0.35                           | 0.70              |
| Target lesion revascularization               | 9 (6.8)    | 8 (6.8)    | 6 (5.3)    | 0.51                           | 0.55              |
| Target vessel failure*                        | 25 (18.9)  | 19 (15.6)  | 24 (19.2)  | 0.97                           | 0.47              |
| Target lesion failure                         | 16 (11.9)  | 16 (13.2)  | 19 (15.5)  | 0.48                           | 0.67              |
| Major adverse cardiac events                  | 25 (18.3)  | 28 (22.6)  | 31 (24.2)  | 0.30                           | 0.80              |
| Definite-or-probable stent thrombosis         | 4 (3.1)    | 4 (3.3)    | 2 (1.7)    | 0.47                           | 0.40              |
| Definite stent thrombosis                     | 3 (2.4)    | 3 (2.5)    | 1 (1.0)    | 0.36                           | 0.31              |

Data are n (%). $^\dagger$P-values are corrected with Bonferroni correction ($\alpha=0.025$). See Table S9 for p-values corrected with Holm-Bonferroni correction. *Main clinical endpoint of cardiac death, target vessel-related myocardial infarction, or clinically indicated target vessel revascularization.

Abbreviations: EES = everolimus-eluting stent; SES = sirolimus-eluting stent; ZES = zotarolimus-eluting stent.
Table S9. Holm-Bonferroni corrected p-values for 5-year clinical outcome of patients with insulin-dependent diabetes and non-insulin-dependent diabetes

| Patients with insulin-dependent diabetes | \( P'_{\log\text{-rank}} \uparrow \) SES vs ZES | \( P'_{\log\text{-rank}} \uparrow \) EES vs ZES |
|-----------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Death, any                              | 0.24                                          | 0.12                                          |
| Cardiac death                           | 0.10                                          | 0.14                                          |
| Myocardial infarction, any              | 0.78                                          | 0.40                                          |
| Target vessel myocardial infarction     | 0.77                                          | 0.80                                          |
| Coronary revascularization, any         | 0.70                                          | 0.88                                          |
| Target vessel revascularization         | 0.98                                          | 1.00                                          |
| Target lesion revascularization         | 0.79                                          | 0.60                                          |
| Target vessel failure*                  | 1.00                                          | 0.95                                          |
| Target lesion failure                   | 1.00                                          | 0.81                                          |
| Major adverse cardiac events            | 0.90                                          | 1.00                                          |
| Definite-or-probable stent thrombosis   | 0.55                                          | 0.020                                         |
| Definite stent thrombosis               | 0.34                                          | 0.32                                          |

| Patients with non-insulin-dependent diabetes | \( P'_{\log\text{-rank}} \uparrow \) SES vs ZES | \( P'_{\log\text{-rank}} \uparrow \) EES vs ZES |
|---------------------------------------------|-----------------------------------------------|-----------------------------------------------|
| Death, any                                  | 0.20                                          | 0.65                                          |
| Cardiac death                               | 0.24                                          | 0.45                                          |
| Myocardial infarction, any                 | 0.69                                          | 1.00                                          |
| Target vessel myocardial infarction        | 0.67                                          | 1.00                                          |
| Coronary revascularization, any            | 0.93                                          | 0.96                                          |
| Target vessel revascularization            | 0.70                                          | 0.70                                          |
| Target lesion revascularization            | 1.00                                          | 0.55                                          |
| Target vessel failure*                     | 0.97                                          | 0.94                                          |
| Target lesion failure                      | 0.96                                          | 0.67                                          |
| Major adverse cardiac events               | 0.60                                          | 0.80                                          |
| Definite-or-probable stent thrombosis      | 0.47                                          | 0.80                                          |
| Definite stent thrombosis                  | 0.36                                          | 0.62                                          |

\( P' \)-values are corrected with Holm-Bonferroni correction. *Main clinical endpoint of cardiac death, target vessel-related myocardial infarction, or clinically indicated target vessel revascularization.

Abbreviations: EES = everolimus-eluting stent; SES = sirolimus-eluting stent; ZES = zotarolimus-eluting stent.