Coronary bifurcations treated with thin-strut drug-eluting stents: a prespecified analysis of the randomized comparison of biodegradable polymer and durable polymer drug-eluting stents in an all comers population trial

Rosaly A. Buiten,[a,b] Sanne Warta,[a] Eline H. Ploumen,[a,b] Carine J.M. Doggen,[b] Liefke C. van der Heijden,[a] Marc Hartmann,[a] Peter W. Danse,[c] Carl E. Schotborgh,[d] Martijn Scholte,[e] Gerard C.M. Linssen,[f] Paolo Zocca[a,b] and Clemens von Birgelen[a,b]

Background **Treatment of a coronary bifurcation lesion is often required in routine clinical practice, but data on the performance of very thin-strut biodegradable polymer drug-eluting stents are scarce.**

Methods **Comparison of biodegradable polymer and durable polymer drug-eluting stents in an all comers population (BIO-RESORT) is a prospective, multicenter randomized clinical trial that included 3514 all-comer patients, who were randomized to very thin-strut biodegradable polymer-coated sirolimus- or everolimus-eluting stents, versus thin-strut durable polymer-coated zotarolimus-eluting stents. The approach of bifurcation stenting was left at the operator's discretion, and provisional stenting was generally preferred. This prespecified analysis assessed 3-year clinical outcome of all patients in whom treatment involved at least one bifurcation with a side-branch diameter ≥1.5 mm.**

Results **Of all BIO-RESORT trial participants, 1236 patients were treated in bifurcation lesions and analyzed. Single- and two-stent techniques were used in 85.8% and 14.2%, respectively. 'True' bifurcation lesions (main vessel and side-branch obstructed) were treated in 31.1%. Three-year follow-up was available in 1200/1236 (97.1%) patients. The main endpoint target vessel failure (composite of cardiac death, target vessel-related myocardial infarction, or target vessel revascularization) occurred in sirolimus-eluting stents in 42/412 (10.3%) and in zotarolimus-eluting stents in 49/409 (12.1%) patients (*P*-logrank = 0.40). In everolimus-eluting stents, target vessel failure occurred in 40/415 (9.8%) patients (vs. zotarolimus-eluting stents: *P*-logrank = 0.26). There was no between-stent difference in individual components of target vessel failure. Findings were consistent in patients with single-vessel treatment and patients treated with a single-stent technique.**

Conclusions **Three years after stenting all-comers with bifurcation lesions, clinical outcome was similar with the sirolimus-eluting and everolimus-eluting stents versus the zotarolimus-eluting stent. *Coron Artery Dis* XXX: 000–000**

Coronary Artery Disease 2020, **XXX**:000–000

Keywords: bifurcation, clinical trials, coronary artery disease, drug-eluting stents, percutaneous coronary intervention

[a]Department of Cardiology, Thoraxcentrum Twente, Medisch Spectrum Twente, [b]Department of Health Technology and Services Research, Faculty BMS, Technical Medical Centre, University of Twente, Enschede, [c]Department of Cardiology, Rijnstate Hospital, Arnhem, [d]Department of Cardiology, Haga Hospital, The Hague, [e]Department of Cardiology, Albert Schweitzer Hospital, Dordrecht and [f]Department of Cardiology, Hospital Group Twente, Almelo and Hengelo, the Netherlands

Correspondence to Clemens von Birgelen, MD, PhD, Department of Cardiology (A25), Thoraxcentrum Twente, Medisch Spectrum Twente, Koningsplein 1, 7512 KZ Enschede, the Netherlands
Tel: +31 53 487 2105; fax: +31 53 487 2107; e-mail: c.vonbirgelen@mst.nl

Received 10 February 2020 **Accepted** 8 March 2020

Introduction

Treatment of obstructive coronary bifurcation lesions with percutaneous coronary interventions can be technically challenging, due to demanding lesion anatomies or differences in lumen diameter between main and side branch that may interfere with optimal stent sizing [1]. Previous clinical studies in bifurcation lesions showed improved outcomes with second-generation versus first-generation drug-eluting stents (DES)[2–4] and lower repeat revascularization rates with biodegradable polymer-coated versus durable polymer-coated DES that utilized thick stent struts [5,6]. In addition, bench studies have shown that coronary DES can differ in their response to procedural steps that are involved in bifurcation treatment [7–9]. Therefore, the technical characteristics of stents may be important when selecting DES for bifurcation treatment.

Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website, *www.coronary-artery.com*.

0954-6928 Copyright © 2020 Wolters Kluwer Health, Inc. All rights reserved. DOI: 10.1097/MCA.0000000000000891

The metallic backbones of most contemporary DES are characterized by very flexible open-cell designs that use thinner stent struts than their predecessors [10]. In bifurcation lesions, more flexible devices have a theoretical advantage in being easier advanced through complex bifurcation anatomies, and their thinner stent struts may reduce the coverage of side-branch ostia. Several studies have shown excellent outcomes in broad all-comer patient populations with very thin-strut biodegradable polymer DES [11–14], but outcome data after bifurcation treatment are scarce.

Comparison of biodegradable polymer and durable polymer drug-eluting stents in an all comers population (BIO-RESORT) is a large-scale randomized clinical trial that compares two very thin-strut biodegradable polymer-coated DES with a thin-strut durable polymer-coated DES in all-comer patients. In the entire study population, clinical outcome with all three DES was favorable after 3 years of follow-up [15]. The current, prespecified subgroup analysis assesses the 3-year clinical outcome of BIO-RESORT participants who were treated in bifurcation lesions.

Methods

Patient population and study design

This is a prespecified subgroup analysis of the 3-arm, multicenter, investigator-initiated, patient-and assessor-blinded, randomized BIO-RESORT trial (NCT01674803). Details of study design and clinical outcomes until 3 years of follow-up have been published [15,16]. In brief, BIO-RESORT included 3514 all-comer patients with obstructive coronary disease in 4 Dutch cardiac intervention centers between December 2012 and August 2015. Patients were equally randomized to treatment with very thin-strut biodegradable polymer sirolimus-eluting stents (SES; Orsiro, Biotronik, Bülach, Switzerland) or everolimus-eluting stents (EES; Synergy, Boston Scientific, Marlborough, Massachusetts, USA), versus thin-strut durable polymer zotarolimus-eluting stents (ZES; Resolute Integrity, Medtronic, Santa Rosa, California, USA). All coronary syndromes and de novo and restenotic lesions in native vessels or bypass grafts were permitted. There was no limit for lesion length, reference vessel size, or number of lesions or vessels to be treated.

BIO-RESORT complied with the Declaration of Helsinki and was approved by the Medical Ethics Committee Twente and the institutional review boards of all participating centers. All patients provided written informed consent. The present secondary analysis of the trial analyzed all patients who were treated in at least one bifurcation lesion, defined by a side-branch diameter ≥1.5 mm. Bifurcation lesions were classified as 'true' bifurcation lesions, based on the Medina classification, if they had obstructions ≥50% in both main and side branch. Interventional procedures were performed according to current medical guidelines and the operator's judgement. The recommended approach for bifurcation lesion treatment was provisional stenting, but the technique of stenting and the use of final kissing-balloon inflations were left at the operator's discretion. Quantitative coronary angiographic analyses were performed in a core laboratory (Cardiovascular Research and Education Enschede, Enschede, the Netherlands).

Follow-up, event adjudication, and clinical endpoints

Procedures of follow-up and monitoring have been reported [16]. An independent clinical event committee adjudicated adverse clinical events (Diagram, Zwolle, the Netherlands). The prespecified clinical endpoints of the BIO-RESORT trial were defined according to the Academic Research Consortium [17,18]. The main composite endpoint target vessel failure (TVF) included cardiac death, target vessel-related myocardial infarction (MI), or clinically indicated target vessel revascularization. Death was considered as cardiac unless an unequivocal noncardiac cause could be established. MI was defined by any creatine kinase concentration of more than double the upper limit of normal, with confirmatory elevated cardiac biomarkers. A periprocedural MI was defined as an MI occurring during the first 48 hours after the index procedure. Stent thrombosis was defined according to Academic Research Consortium definitions [17].

Technical details of stents

The SES platform is made from very thin cobalt-chromium struts (60 µm for stents ≤3.0 mm and 80 µm for stents >3.0 mm). It has a thin passive amorphous silicon carbide coating and is circumferentially covered with an asymmetrical hybrid biodegradable poly[L-lactide]acid coating that is thicker on the abluminal side (7.4/3.5 µm) that elutes sirolimus in approximately 3 months and is resorbed within 24 months. The EES platform is made from platinum-chromium struts of varying sizes (strut thickness of 74, 79, and 81 µm for stent sizes ≤2.5, 3.0–3.5, and 4.0 mm, respectively). The 4 µm abluminal biodegradable poly[lactic-co-glucolic acid] coating elutes everolimus within 3 months and is resorbed within 4 months. The ZES platform is made from cobalt-chromium and has a strut thickness of 91 µm. Zotarolimus is eluted for 6 months from a 5.6 µm coating that is a blend of 3 durable polymers [9,15].

Statistical analysis

By study design, SES and EES were compared to ZES but not with each other. Categorical variables were compared between groups with the Pearson chi-square test, while continuous variables were assessed with the *t*-test or Wilcoxon rank-sum test, as appropriate. The time to clinical endpoint was calculated with Kaplan–Meier methods, and the log-rank test was applied for between-group comparisons. Hazard ratios (HR), with 2-sided confidence intervals (CI) were computed using Cox

regression analysis. Potential confounders were identified if in univariate analysis a P value < 0.15 was found, and they were then entered into a multivariate Cox regression model using stepwise backward selection. The final model included renal insufficiency and total stent length. Additional analyses were performed in patients treated with a single-stent technique. A 2-sided P value < 0.05 was considered significant. Statistical analyses were performed with SPSS, version 24 (IBM Corp).

Results

A total of 1236 patients were treated in at least one bifurcation lesion (35.2% of all 3514 randomized trial participants). Patient characteristics at baseline are shown in Table 1. There were no differences in baseline characteristics between patient groups, except for previous MI which was less prevalent in SES (17.0%) and EES (13.5%) versus ZES (24.7%) (SES vs. ZES: P = 0.007; EES vs. ZES: P < 0.001). In all 3 stent groups, the most common Medina class was Medina 1,1,0, and provisional stenting was applied in most patients (Table 2). Clinical outcome after 1-year of follow-up is reported in Supplementary Table 1, Supplemental digital content 1, *http://links.lww.com/MCA/A352* and showed no between-DES differences.

At 3 years, clinical follow-up was available in 1200/1236 (97.1%) patients; 17 patients were lost to follow-up and 19 withdrew consent (censored at time of dropout; Fig. 1). The main composite endpoint TVF occurred in SES in 42/412 (10.3%) patients and in ZES in 49/409 (12.1%) patients (HR 0.84, 95% CI 0.56–1.27, P-logrank = 0.40). In EES, TVF occurred in 40/415 (9.8%) patients (EES vs. ZES: HR 0.79, 95% CI 0.51–1.20, P-logrank = 0.26) Fig. 2. There was no significant between-stent difference in any individual component of TVF (Table 3).

Table 1 Patient characteristics at baseline

	SES (n = 412)	EES (n = 415)	ZES (n = 409)
Age, years	64.3 (10.3)	64.0 (10.2)	64.0 (9.9)
Female sex	82 (19.9)	94 (22.7)	96 (23.5)
BMI, kg/m^2	27.1 (3.9)	27.4 (3.9)	27.6 (4.0)
Smoking	104/404 (25.7)	104/401 (25.9)	92/402 (22.9)
Medical history			
Diabetes	74 (18.0)	75 (18.1)	87 (21.3)
Hypertension	193 (46.8)	184 (44.3)	202 (49.4)
Hypercholesterolemia	159 (38.6)	150 (36.1)	151 (36.9)
Prior myocardial infarction	70 (17.0)[a]	56 (13.5)[b]	101 (24.7)
Prior percutaneous coronary intervention	80 (19.4)	72 (17.3)	64 (15.6)
Prior coronary bypass surgery	27 (6.6)	29 (7.0)	22 (5.4)
Renal insufficiency	21 (5.1)	6 (1.4)	12 (2.9)
Clinical syndrome at presentation			
Acute coronary syndrome	269 (65.3)	275 (66.3)	276 (67.5)
Stable angina	143 (34.7)	140 (33.7)	133 (32.5)

Data expressed as mean (SD) or n (%). All other comparisons between SES and EES versus ZES did not differ significantly.
EES, everolimus-eluting stents; SES, sirolimus-eluting stents; ZES, zotarolimus-eluting stents.
[a]SES significantly lower than in ZES, P = 0.007.
[b]EES significantly lower than in ZES, P < 0.001.

In all three DES, stent thrombosis was an infrequent event (Table 3). An exploratory analysis in patients with single-vessel treatment confirmed these findings (data not shown).

Multivariate analysis showed that after adjustment for confounders (i.e., renal insufficiency and total stent length) there was no independent association between type of DES and 3-year TVF rates (adjusted HR for SES vs. ZES: 0.79, 95% CI 0.52–1.20 and adjusted HR for EES vs. ZES: 0.81, 95% CI 0.54–1.23).

A total of 1059/1236 patients (85.7%) were treated with a single-stent technique. In these patients, TVF rates were similar between the very thin-strut SES and EES versus the thin-strut ZES (SES 10.4% and EES 9.2%, vs. 11.6%, P = 0.59 and P = 0.26, respectively). In addition, periprocedural target vessel MI rates did not differ significantly between DES groups (SES 2.2% and EES 1.7%, vs. ZES 2.9%, P = 0.58 and P = 0.29, respectively). Supplementary Table 2, Supplemental digital content 1, *http://links.lww.com/MCA/A352* presents other secondary clinical outcomes in these patients.

Three-year clinical outcome in patients treated with two- versus single-stent technique was similar, except for periprocedural MI which was more prevalent in patients treated with a two-stent technique [9/176 (5.1%) vs. 24/1059 (2.3%); HR 2.27, 95% CI 1.05–4.88, P = 0.03].

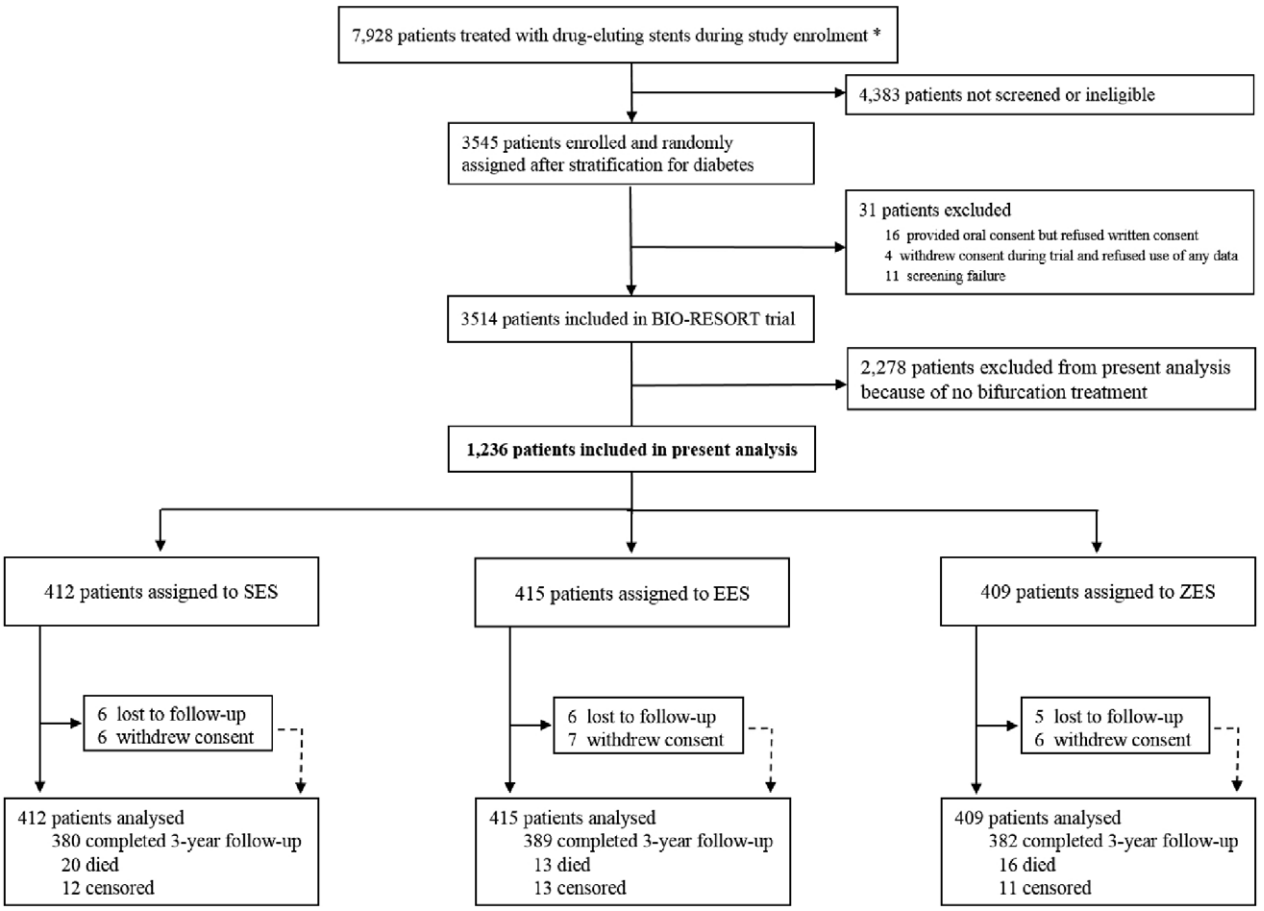
Patients treated in 'true' bifurcation lesions (i.e., lesions obstructed in main and side branch) represented almost one-third of the study population (385/1236; 31.1%). These patients showed 3-year adverse event rates that were non-significantly different to the rates of patients

Table 2 Procedural and lesion characteristics at baseline

	SES (n = 412)	EES (n = 415)	ZES (n = 409)
Medina classification			
0.0.1	27 (6.6)	39 (9.4)	38 (9.3)
0.1.0	78 (18.9)	58 (14.0)	55 (13.4)
0.1.1	21 (5.1)	17 (4.1)	21 (5.1)
1.0.0	17 (4.1)	29 (7.0)	18 (4.4)
1.0.1	13 (3.2)	20 (4.8)	13 (3.2)
1.1.0	168 (40.8)	162 (39.0)	162 (39.6)
1.1.1	88 (21.4)	90 (21.7)	102 (24.9)
Multivessel treatment	127 (30.8)	114 (27.5)	124 (30.3)
Right coronary artery	96 (23.3)	95 (22.9)	102 (24.9)
Left anterior descending artery	304 (73.8)	278 (67.0)	279 (68.2)
Circumflex artery	129 (31.3)	149 (35.9)	145 (35.5)
Stenting approach[a]			
Single-stent approach	359 (87.1)	353 (85.3)	347 (84.8)
Two-stent approach	53 (12.9)	61 (14.7)	62 (15.2)
T-stenting	29 (54.7)	40 (65.6)	42 (67.7)
(Mini) crush	15 (28.3)	15 (24.6)	9 (14.5)
Culotte	2 (3.8)	1 (1.6)	4 (6.5)
Other	7 (13.2)	5 (8.2)	6 (9.7)
Final kissing-balloon inflation	72 (17.5)	86 (20.7)	71 (17.4)
Total stent length	37 (22–57)	36 (20–58)	38 (24–60)

Data expressed as median (interquartile range) or n (%).
EES, everolimus-eluting stents; SES, sirolimus-eluting stents; ZES, zotarolimus-eluting stents.
[a]One patient in the EES group did not receive a stent, and the stenting technique was marked as missing.

Fig. 1



Study flow diagram. *This is the number of patients treated with drug-eluting stents during the period of study enrollment, irrespective of inclusion or exclusion criteria. BIO-RESORT, comparison of biodegradable polymer and durable polymer drug-eluting stents in an all comers population; EES, everolimus-eluting stents; SES, sirolimus-eluting stents; ZES, zotarolimus-eluting stents.

with 'non-true' bifurcation lesions (Supplementary Table 3, Supplemental digital content 1, *http://links.lww.com/MCA/A352*).

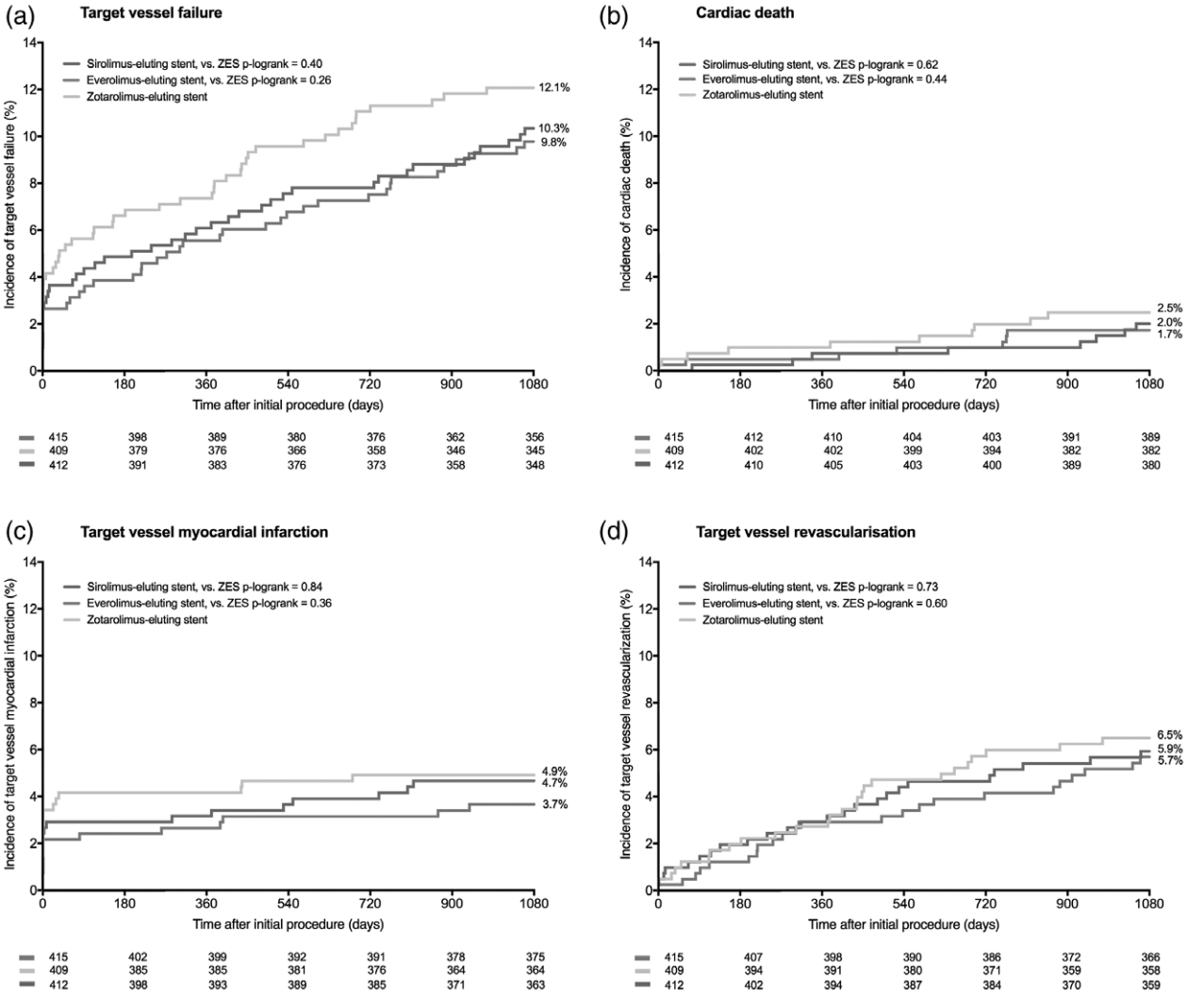
Discussion main findings

Three years after treating all-comer patients who had bifurcated target lesions with very thin-strut SES and EES, there was no significant difference in the incidence of the main clinical endpoint TVF as compared to treatment with thin-strut ZES. In addition, for SES and EES, there were no differences in the occurrence of safety (cardiac death, MI, stent thrombosis) or efficacy (repeat revascularization) endpoints versus ZES. Intuitively, one might expect that the lower strut thickness of the very thin-strut SES and EES could result in fewer periprocedural MI due to less side-branch strut coverage. However, the findings of the present study (including a subanalysis in patients with single-stent treatment) do not provide any signal that supports this hypothesis. Previous research in bifurcation lesions has shown lower repeat revascularization rates after implantation of biodegradable polymer-coated versus durable polymer-coated thick-strut stents [4,5]. Although, in the current study, some clinical endpoints showed numerically somewhat lower event rates in the biodegradable polymer SES and EES groups, none reached statistical significance versus the durable polymer ZES group. Moreover, multivariate analysis showed no independent association of DES type with clinical outcome.

Previous studies using the same drug-eluting stents

Only few other clinical studies assessed patients with bifurcation lesions treated with exactly the same DES as in the present study. A pilot-study in 52 patients, who received the very thin-strut SES in complex bifurcation lesions (Medina 1,1,1 or 1,0,1) with at least 2.5 mm wide side branches, using a new two-stent nano-crush stenting technique, found no adverse clinical events after a mean follow-up of 12 months [19]. The very thin-strut SES was also used in a study that compared two different

Fig. 2



Kaplan–Meier cumulative event curves at 3 years. The main endpoint target vessel failure (a) and its individual components; cardiac death (b), target vessel-related myocardial infarction (c), or clinically indicated target vessel revascularization (d). ZES, zotarolimus-eluting stents.

Table 3 Clinical outcome at 3-year follow-up

	SES (n = 412)	EES (n = 415)	ZES (n = 409)	SES vs. ZES HR (95% CI)	Logrank *P*	EES vs. ZES HR (95% CI)	Logrank *P*
Target vessel failure	42 (10.3)	40 (9.8)	49 (12.1)	0.84 (0.56–1.27)	0.40	0.79 (0.52–1.20)	0.26
Cardiac death	8 (2.0)	7 (1.7)	10 (2.5)	0.79 (0.31–2.00)	0.62	0.69 (0.26–1.81)	0.44
Target vessel myocardial infarction	19 (4.7)	15 (3.7)	20 (4.9)	0.94 (0.50–1.75)	0.84	0.73 (0.38–1.43)	0.36
Periprocedural myocardial infarction	10 (2.4)	9 (2.2)	14 (3.5)	0.71 (0.31–1.59)	0.39	0.63 (0.27–1.46)	0.28
Target vessel revascularization	24 (5.9)	23 (5.7)	26 (6.5)	0.91 (0.52–1.58)	0.73	0.86 (0.49–1.51)	0.60
Target lesion failure	34 (8.4)	35 (8.5)	43 (10.6)	0.77 (0.49–1.21)	0.26	0.79 (0.50–1.23)	0.29
Target lesion revascularization	14 (3.4)	16 (3.9)	18 (4.5)	0.77 (0.38–1.54)	0.45	0.87 (0.44–1.70)	0.68
Definite or probable stent thrombosis	4 (1.0)	5 (1.2)	6 (1.5)	0.66 (0.19–2.34)	0.52	0.82 (0.25–2.69)	0.74
Definite stent thrombosis	3 (0.7)	3 (0.7)	4 (1.0)	0.74 (0.17–3.32)	0.70	0.74 (0.17–3.30)	0.69

Event rates, expressed as n (%), were calculated with the use of the Kaplan–Meier method at 3 years; therefore, percentages may differ slightly from straightforward 'nominator divided by denominator' calculations.
EES, everolimus-eluting stents; SES, sirolimus-eluting stents; ZES, zotarolimus-eluting stents.

two-stent techniques (the nano-crush and Culotte techniques) in patients with unprotected left main bifurcations, but provisional stenting with this SES was not assessed [20].

The CELTIC bifurcation study compared the performance of the very thin-strut EES versus a thin-strut durable polymer EES (Xience, Abbott Vascular, Santa Clara, California, USA) [21]. Participants in that study

underwent treatment in de novo bifurcation lesions (Medina 1,1,1) with a minimum diameter of 2.5 mm in both main vessel and side branch, using the Culotte technique. The study population comprised 170 selected patients, excluding patients with acute ongoing ST-segment elevation MI and patients with left main stem or bypass graft lesions. After 2 years of follow-up, both DES had similar rates of the main composite clinical endpoint (17.7% vs. 18.8%), which included death, MI, cerebrovascular accident, stent thrombosis, target vessel revascularization, and complete or subtotal re-occlusion in the stented vessel or presence of a binary angiographic in-stent restenosis (Hanratty C. The Celtic Bifurcation study: 2-year clinical outcomes. Presented at: EuroPCR 2019; 22 May 2019). Because of the substantial differences in patient population, technique of stenting, duration of follow-up, and clinical endpoint, a meaningful comparison with the present study cannot be made.

The thin-strut ZES was assessed in a substudy of the randomized DUTCH PEERS trial that reported a 2-year TVF rate of 9.8% after bifurcation treatment with thin-strut ZES in 244 all-comer patients [22]. Another study that assessed the clinical performance of the same ZES and its predecessor in 577 patients who underwent percutaneous coronary intervention for bifurcation lesions showed that 8.2% of patients reached the main composite endpoint (cardiac death, MI, or target vessel revascularization) after a mean follow-up of 27 months [23]. A direct comparison with the event rates of the present study cannot be made due to the differences in follow-up duration.

Technique of stenting and clinical outcome

Current guidelines and expert panels generally recommend provisional stenting for most bifurcation lesions [24,25]. A meta-analysis of several randomized clinical trials investigated the clinical outcomes of patients with bifurcation lesions, who were treated with a systematic two-stent approach versus provisional stenting, and found no clear benefit for one or the other approach [26]. In the present study, the majority of patients were treated with single-stenting, which most likely reflects the use of a provisional stenting approach in the majority of patients; nevertheless, the operators' motivation for selecting a certain approach was not recorded. In patients treated with the single-stent technique, there were no between-DES differences in clinical outcome.

In general, crush, Culotte, and T- and protrusion are the most widely used two-stent techniques [25], which is also reflected in the current study. Because of the relatively low number of patients in whom two-stent techniques were applied, we did not perform a comparison between different two-stent techniques. Previous studies that compared crush versus Culotte technique found no solid evidence in favor of one of these techniques [27,28]. In pursuit of the best strategy for treating bifurcation lesions, the series of DK CRUSH studies applied a modified double-kissing crush technique that showed promising 3-year results [29,30]. Nevertheless, these dedicated bifurcation studies were performed in selected patient populations with true left main bifurcation lesions, and the highly skilled operators were probably more familiar with this technically more demanding approach. Consequently, while dedicated bifurcation studies provide extremely important insights from treating challenging bifurcation lesions, such trials may be somewhat less representative of the all-comer patients with bifurcation lesions who are currently treated in routine clinical practice.

Limitations

The results of this substudy of the randomized BIO-RESORT trial are hypothesis-generating as the trial was not powered for subgroup analyses. As quantitative coronary angiographic analyses were restricted to stented coronary segments, no measurements were available of lumen size in untreated side branches. Furthermore, the number of patients who were treated with a two-stent technique was limited, preventing a stent-level comparison of different techniques. Moreover, the decision to apply a certain technique was left at the operator's discretion, and the motivation for their choice was not recorded.

Clinical implications

The present prespecified analysis of the randomized BIO-RESORT trial reassures the safety and efficacy of contemporary DES with dissimilar stent characteristics in treating all-comer patients with bifurcated target lesions. The findings were consistent in patients treated with the single-stent technique, which is generally recommended for most bifurcation lesions[24] and was applied in the majority of patients. Dedicated bifurcation stents are available but have not (yet) been able to show significant, clinically relevant improvements in outcomes as compared to conventional contemporary DES [31].

Conclusion

In this prespecified analysis of a randomized drug-eluting stent trial in all-comers, 3-year clinical outcomes after bifurcation stenting were similar between the very thin-strut SES and EES versus the thin-strut ZES.

Acknowledgements

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

Conflicts of interest

C.v.B. reports that the research department of Thoraxcentrum Twente has received research grants provided by Abbott Vascular, Biotronik, Boston Scientific, and Medtronic. There are no conflicts of interest for the remaining authors.

References

1 von Birgelen C, van Houwelingen KG, Lam MK. Coronary bifurcations: still the touchstone of drug-eluting stents and bioresorbable vascular scaffolds? *Rev Esp Cardiol (Engl Ed)* 2014; **67**:787–789.

2 Kang SH, Ahn JM, Lee JB, Lee CH, Kang DY, Lee PH, *et al*. Temporal changes in characteristics, treatment strategies, and outcomes of coronary bifurcation lesion interventions. *Coron Artery Dis* 2019; **30**:33–43.

3 Ferenc M, Buettner HJ, Gick M, Comberg T, Rothe J, Khoury F, *et al*. Clinical outcome after percutaneous treatment of de novo coronary bifurcation lesions using first or second generation of drug-eluting stents. *Clin Res Cardiol* 2016; **105**:230–238.

4 Costopoulos C, Latib A, Ferrarello S, Naganuma T, Sticchi A, Filippo F, *et al*. First- versus second-generation drug-eluting stents for the treatment of coronary bifurcations. *Cardiovasc Revasc Med* 2013; **14**:311–315.

5 Grundeken MJ, Wykrzykowska JJ, Ishibashi Y, Garg S, de Vries T, Garcia-Garcia HM, *et al*. First generation versus second generation drug-eluting stents for the treatment of bifurcations: 5-year follow-up of the LEADERS all-comers randomized trial. *Catheter Cardiovasc Interv* 2016; **87**:E248–E260.

6 Chen SL, Mintz G, Santoso T, Zhang JJ, Ye F, Xu YW, *et al*. Comparison of paclitaxal vs. Sirolimus eluting stents with bio-degradable polymer for the treatment of coronary bifurcation lesions: subgroup analysis from DKCRUSH-I and DKCRUSH-II studies. *Chin Med J (Engl)* 2012; **125**:3382–3387.

7 Derimay F, Souteyrand G, Motreff P, Rioufol G, Finet G. Influence of platform design of six different drug-eluting stents in provisional coronary bifurcation stenting by repot sequence: a comparative bench analysis. *Eurointervention* 2017; **13**:e1092–e1095.

8 Burzotta F, Mortier P, Trani C. Characteristics of drug-eluting stent platforms potentially influencing bifurcated lesion provisional stenting procedure. *Eurointervention* 2014; **10**:124–132.

9 Basalus MW, van Houwelingen KG, Ankone MJ, Feijen J, von Birgelen C. Micro-computed tomographic assessment following extremely oversized partial postdilatation of drug-eluting stents. *Eurointervention* 2010; **6**:141–148.

10 Byrne RA, Stone GW, Ormiston J, Kastrati A. Coronary balloon angioplasty, stents, and scaffolds. *Lancet* 2017; **390**:781–792.

11 Kereiakes DJ, Meredith IT, Windecker S, Lee Jobe R, Mehta SR, Sarembock IJ, *et al*. Efficacy and safety of a novel bioabsorbable polymer-coated, everolimus-eluting coronary stent: the EVOLVE II Randomized Trial. *Circ Cardiovasc Interv* 2015; **8**:e002372.

12 de Winter RJ, Katagiri Y, Asano T, Milewski KP, Lurz P, Buszman P, *et al*. A sirolimus-eluting bioabsorbable polymer-coated stent (mistent) versus an everolimus-eluting durable polymer stent (xience) after percutaneous coronary intervention (DESSOLVE III): a randomised, single-blind, multicentre, non-inferiority, phase 3 trial. *Lancet* 2018; **391**:431–440.

13 Pilgrim T, Heg D, Roffi M, Tüller D, Muller O, Vuilliomenet A, *et al*. Ultrathin strut biodegradable polymer sirolimus-eluting stent versus durable polymer everolimus-eluting stent for percutaneous coronary revascularisation (BIOSCIENCE): a randomised, single-blind, non-inferiority trial. *Lancet* 2014; **384**:2111–2122.

14 von Birgelen C, Zocca P, Buiten RA, Jessurun GAJ, Schotborgh CE, Roguin A, *et al*. Thin composite wire strut, durable polymer-coated (resolute onyx) versus ultrathin cobalt-chromium strut, bioresorbable polymer-coated (orsiro) drug-eluting stents in allcomers with coronary artery disease (BIONYX): an international, single-blind, randomised non-inferiority trial. *Lancet* 2018; **392**:1235–1245.

15 Buiten RA, Ploumen EH, Zocca P, Doggen CJM, Danse PW, Schotborgh CE, *et al*. Thin, very thin, or ultrathin strut biodegradable or durable polymer-coated drug-eluting stents: 3-year outcomes of BIO-RESORT. *JACC Cardiovasc Interv* 2019; **12**:1650–1660.

16 von Birgelen C, Kok MM, van der Heijden LC, Danse PW, Schotborgh CE, Scholte M, *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* 2016; **388**:2607–2617.

17 Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, *et al*.; Academic Research Consortium. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007; **115**:2344–2351.

18 Vranckx P, Cutlip DE, Mehran R, Kint PP, Silber S, Windecker S, Serruys PW. Myocardial infarction adjudication in contemporary all-comer stent trials: balancing sensitivity and specificity. Addendum to the historical MI definitions used in stent studies. *Eurointervention* 2010; **5**:871–874.

19 Rigatelli G, Dell'Avvocata F, Zuin M, Vassiliev D, Mazza A, Dinh HD. Complex coronary bifurcation revascularization by means of very minimal crushing and ultrathin biodegradable polymer DES: feasibility and 1-year outcomes of the "nano-crush" technique. *Cardiovasc Revasc Med* 2017; **18**:22–27.

20 Rigatelli G, Zuin M, Vassilev D, Dinh H, Giatti S, Carraro M, *et al*. Culotte versus the novel nano-crush technique for unprotected complex bifurcation left main stenting: difference in procedural time, contrast volume and X-ray exposure and 3-years outcomes. *Int J Cardiovasc Imaging* 2019; **35**:207–214.

21 Walsh SJ, Hanratty CG, Watkins S, Oldroyd KG, Mulvihill NT, Hensey M, *et al*. Culotte stenting for coronary bifurcation lesions with 2nd and 3rd generation everolimus-eluting stents: the CELTIC bifurcation study. *Eurointervention* 2018; **14**:e318–e324.

22 van der Heijden LC, Kok MM, Lam MK, Danse PW, Schramm AR, Jessurun GA, *et al*. Bifurcation treatment with novel, highly flexible drug-eluting coronary stents in all-comers: 2-year outcome in patients of the DUTCH PEERS trial. *Clin Res Cardiol* 2016; **105**:206–215.

23 Burzotta F, Summaria F, Latib A, De Vita M, Fantoni C, Benedetto S, *et al*. Prospective multicentre clinical performance evaluation of second and third generation zotarolimus-eluting stents to treat patients with bifurcated coronary lesions. *Catheter Cardiovasc Interv* 2016; **87**:15–22.

24 Banning AP, Lassen JF, Burzotta F, Lefèvre T, Darremont O, Hildick-Smith D, *et al*. Percutaneous coronary intervention for obstructive bifurcation lesions: the 14th consensus document from the european bifurcation club. *Eurointervention* 2019; **15**:90–98.

25 Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, *et al*.; ESC Scientific Document Group. 2018 ESC/EACTS guidelines on myocardial revascularization. *Eur Heart J* 2019; **40**:87–165.

26 Gao XF, Zhang YJ, Tian NL, Wu W, Li MH, Bourantas CV, *et al*. Stenting strategy for coronary artery bifurcation with drug-eluting stents: a meta-analysis of nine randomised trials and systematic review. *Eurointervention* 2014; **10**:561–569.

27 Erglis A, Kumsars I, Niemelä M, Kervinen K, Maeng M, Lassen JF, *et al*.; Nordic PCI Study Group. Randomized comparison of coronary bifurcation stenting with the crush versus the culotte technique using sirolimus eluting stents: the nordic stent technique study. *Circ Cardiovasc Interv* 2009; **2**:27–34.

28 Zheng XW, Zhao DH, Peng HY, Fan Q, Ma Q, Xu ZY, *et al*. Randomized comparison of the crush versus the culotte stenting for coronary artery bifurcation lesions. *Chin Med J (Engl)* 2016; **129**:505–510.

29 Chen S, Xu B, Han Y, Sheiban I, Zhang J, Ye F, *et al*. Clinical outcome after DK crush versus culotte stenting of distal left main bifurcation lesions: the 3-year follow-up results of the DKCRUSH III study. *J Am Coll Cardiol Intv* 2015; **8**:1335–1342.

30 Chen X, Li X, Zhang JJ, Han Y, Kan J, Chen L, *et al*.; DKCRUSH-V Investigators. 3-year outcomes of the DKCRUSH-V trial comparing DK crush with provisional stenting for left main bifurcation lesions. *J Am Coll Cardiol Intv* 2019; **12**:1927–1937.

31 Rawasia WF, Alkhouli M. Dedicated bifurcation stents vs. conventional stenting strategy for coronary bifurcation lesions: Insights from randomized clinical trial. *Cardiovasc Revasc Med* 2020; **pii**:S1553–8389(20)30003-8. – *in press*.