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2-Year Clinical and Angiographic Outcomes From a Randomized Trial of Polymer-Free Dual Drug-Eluting Stents Versus Polymer-Based Cypher and Endeavor, Drug-Eluting Stents

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Objectives In the ISAR-TEST-2 (Intracoronary Stenting and Angiographic Results: Test Efficacy of Three Limus-Eluting Stents) randomized trial, a new-generation sirolimus- and probucol-eluting stent (Dual-DES) demonstrated a 12-month efficacy that was comparable to sirolimus-eluting stents (SES) (Cypher, Cordis Corp., Warren, New Jersey) and superior to zotarolimus-eluting stents (ZES) (Endeavor, Medtronic CardioVascular, Santa Rosa, California). The aim of the current study was to investigate the comparative clinical and angiographic effectiveness of SES, Dual-DES, and ZES between 1 and 2 years.

Background Long-term polymer residue is implicated in adverse events associated with delayed vessel healing after drug-eluting stent therapy. The second-generation ZES utilizes an enhanced biocompatibility polymer system whereas a new-generation Dual-DES employs a polymer-free drug-release system.

Methods A total of 1,007 patients undergoing coronary stenting of de novo lesions in native vessels were randomized to treatment with SES (n = 335), Dual-DES (n = 333), or ZES (n = 339). Clinical follow-up was performed to 2 years. Angiographic follow-up was scheduled at 6 to 8 months and 2 years.

Results There were no significant differences between groups regarding death/myocardial infarction (SES: 10.2% vs. Dual-DES: 7.8% vs. ZES: 9.2%; p = 0.61) or definite stent thrombosis (SES: 0.9% vs. Dual-DES: 0.9% vs. ZES: 0.6%; p = 0.87). Two-year target lesion revascularization (TLR) was 10.7%, 7.7%, and 14.3% lesions in the SES, Dual-DES, and ZES groups, respectively (p = 0.009). Incident TLR between 1 and 2 years in the Dual-DES group (0.9%) was significantly lower than in the Cypher SES group (3.6%) (p = 0.009), but comparable to the Endeavor ZES group (0.7%) (p = 0.72). These findings mirrored those observed for binary restenosis.

Conclusions At 2 years, there was no signal of a differential safety profile between the 3 stent platforms. Furthermore, the antirestenotic efficacy of both Dual-DES and ZES remained durable between 1 and 2 years, with Dual-DES maintaining an advantage over the entire 2-year period. (Intracoronary Stenting and Angiographic Results: Test Efficacy of Three Limus-Eluting Stents [ISAR-TEST-2]; NCT00332397) (J Am Coll Cardiol 2010;55:2536–43)

First-generation drug-eluting stent (DES) systems deliver high antirestenotic efficacy in comparison with bare-metal stents, but do so at the cost of a delay in structural and functional healing of the stented segment (1). This pathophysiological process likely underlies the surfeit of late adverse events seen with this technology in comparison with

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bare-metal stents. These events are comprised of a small, but significant, excess of stent thrombosis, but also perhaps, a marginal erosion of antirestenotic efficacy (2–5). Although multifactorial in origin, pathological and pre-clinical research data strongly implicate polymer residue as a key etiological factor (1,6).

The ISAR-TEST-2 (Intracoronary Stenting and Angiographic Results: Test Efficacy of Three Limus-Eluting Stents) study is a 2-center, investigator-initiated randomized trial (7). We enrolled 1,007 patients across the spectrum of coronary disease presentations and allocated participants to treatment with the first-generation permanent polymer sirolimus-eluting stent (SES) (Cypher, Cordis Corp., Warren, New Jersey), a polymer-free sirolimus- and probucol-eluting stent (Dual-DES), or a biocompatible polymer zotarolimus-eluting stent (ZES) (Endeavor, CardioVascular, Santa Rosa, California) in a trial powered for an angiographic end point. At 6 to 8 months, there was a significant difference in the primary end point across the treatment groups: binary restenosis in the Dual-DES group (11.0%) was significantly lower than that in the ZES group (19.3%; $p = 0.002$), but comparable to that in the SES group (12.0%; $p = 0.68$) (7).

As potential differences between first-, second-, and next-generation DES may be expected to appear with longer-term follow-up, we investigated safety and efficacy outcomes of patients enrolled in the ISAR-TEST-2 trial by analyzing clinical and angiographic data out to 2 years.

Methods

Study population and protocol. The methods of the ISAR-TEST-2 trial have been previously reported (7). In brief, eligible patients were older than age 18 years with ischemic symptoms or evidence of myocardial ischemia in the presence of ≥50% de novo stenosis located in native coronary vessels. Key exclusion criteria included patients with target lesion located in the left main stem, in-stent restenosis, cardiogenic shock, malignancies or other comorbid conditions with life expectancy <12 months, known allergy to the study medications (aspirin, clopidogrel, sirolimus, stainless steel), or pregnancy or positive pregnancy test.

Full details of treatment allocation, study devices, and adjunctive antithrombotic therapy are previously reported (7). An oral loading dose of 600 mg clopidogrel was administered to all patients prior to the intervention. After the intervention, all patients received 200 mg/day aspirin indefinitely, clopidogrel 150 mg for the first 3 days (or until discharge) followed by 75 mg/day for 12 months, and other cardiac medications according to the judgment of the patient's physician (e.g., beta-blockers, ACE inhibitors, statins, and so on).

Data management and follow-up. Patients were followed-up either by physician office visit or by telephone at 6 to 8 months, 1 year, and 2 years. Relevant clinical data were collected and entered into a computer database by specialized personnel of the ISAResearch Centre, Deutsches Herzzentrum. Clinical events were adjudicated by an independent Clinical Event Adjudication Committee. End point adjudication was fully blinded to randomly assigned stent type. Angiographic follow-up was scheduled at 2 time points following coronary intervention, namely 6 to 8 months and 2 years. Baseline, post-procedural, and follow-up coronary angiograms were digitally recorded and assessed offline in the independent quantitative angiographic core laboratory (ISAR-esearch Centre, Deutsches Herzzentrum) with an automated edge-detection system (CMS version 7.1, Medis Medical Imaging Systems, Leiden, the Netherlands) by 2 experienced operators unaware of the treatment allocation. All measurements were performed on cineangiograms recorded after the intracoronary administration of nitroglycerin using the same single worst-view projection at all times. The contrast-filled nontapered catheter tip was used for calibration. Quantitative analysis was performed on both the "in-stent" and "in-segment" areas (including the stented segment, as well as both 5-mm margins proximal and distal to the stent).

Abbreviations and Acronyms

DES = drug-eluting stent(s)
Dual-DES = sirolimus- and probucol-eluting stent(s)
SES = sirolimus-eluting stent(s)
TLR = target lesion revascularization
ZES = zotarolimus-eluting stent(s)

End points and definitions. The principal safety end points of interest in the current analysis were the composite of death and myocardial infarction and the rate of definite stent thrombosis at 2 years. The principal efficacy end point was target lesion revascularization (TLR) at 2 years. Delta-TLR was the difference in TLR events between 1 and 2 years. The adjudication of TLR required the documentation of symptoms or objective signs of ischemia prior to performance of coronary angiography. The angiographic end point of interest was overall binary in-segment restenosis. In analyzing 2-year angiographic outcomes, we used a composite analysis based on the latest angiographic follow-up available for an individual patient (whether at 6 to 8 months or 2 years) (4). The diagnosis of myocardial infarction required the presence of new Q waves on the electrocardiogram and/or elevation of creatine kinase or its MB isoform to at least 3 times the upper limit of normal in no fewer than 2 blood samples. Stent thrombosis was classified according to Academic Research Consortium criteria.

Statistical analysis. The results of the primary analysis have already been published, and this additional analysis is exploratory in nature. Baseline descriptive statistics are presented as frequencies and percentages for categorical variables and mean ± SD or median (interquartile range) for continuous variables. Survival and event-free status were assessed using the methods of Kaplan-Meier. Differences across groups were checked for significance (depending on the distribution of the data) with analysis of variance or Kruskal-Wallis test (continuous data), contingency table analysis (categorical variables), or log-rank test (survival analysis). Intergroup outcome comparisons were assessed using the Student *t* test (continuous data), chi-square or

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Fisher exact test (categorical variables), or log-rank test (survival analysis). Statistical software S-PLUS, version 4.5 (Insightful Corp., Seattle, Washington) was used for all analyses.

Results

As previously reported, a total of 1,007 patients were enrolled in this study: 335 patients received SES, 333 were treated with Dual-DES, and 339 received ZES. Baseline clinical, angiographic, and procedural characteristics were similar across all 3 treatment groups (Table 1).

2-year clinical outcomes. Clinical follow-up data at 2 years were available for all but 65 of the 1,007 enrolled patients (Table 2). Among these 65 patients, median follow-up was 21 months (interquartile range 20 to 22 months).

Regarding safety outcomes, the composite of death or MI at 2 years had occurred in 34 cases (10.2%) with SES, 26 cases (7.8%) in Dual-DES, and 31 cases (9.2%) with ZES ($p = 0.61$) (Fig. 1). Definite stent thrombosis occurred in 3 patients (0.9%) each with SES and Dual-DES and 2 cases (0.6%) with ZES ($p = 0.88$). There were no additional cases of definite stent thrombosis after 12 months.

At 2 years, TLR had been performed in 45 of 419 (10.7%), 33 of 427 (7.7%), and 60 of 420 (14.3%) lesions in the SES, Dual-DES, and ZES groups, respectively ($p = 0.009$). In terms of pairwise comparisons, only the difference between Dual-DES and ZES was significant ($p = 0.006$).

Table 1 Baseline Characteristics

	SES	Dual-DES	ZES	p Value
Patients	335	333	339	
Female	76 (22.7)	76 (22.8)	83 (24.5)	0.83
Age, yrs	66.6 ± 11.1	67.0 ± 11.2	67.2 ± 10.9	0.65
Diabetes	91 (27.2)	96 (28.8)	89 (26.3)	0.75
Hypertension	214 (63.9)	229 (64.9)	229 (67.6)	0.58
Current smoker	58 (17.3)	66 (19.8)	61 (18.0)	0.69
Hyperlipidemia	231 (69.0)	209 (62.8)	222 (65.5)	0.24
Coronary disease				0.30
1-vessel	48 (14.3)	64 (19.2)	59 (17.4)	
2-vessel	85 (25.4)	86 (25.8)	74 (21.8)	
3-vessel	202 (60.3)	183 (55.0)	206 (60.8)	
Multivessel disease	287 (85.7)	269 (80.8)	280 (82.6)	0.23
Clinical presentation				0.50
Myocardial infarction	45 (13.4)	40 (12.0)	49 (14.5)	
Unstable angina	85 (25.4)	101 (30.3)	101 (29.8)	
Stable angina	205 (61.2)	192 (57.7)	189 (55.8)	
Prior myocardial infarction	100 (29.9)	84 (25.2)	88 (26.0)	0.35
Prior aortocoronary bypass surgery	27 (8.1)	33 (9.9)	29 (8.6)	0.68
Left ventricular ejection fraction	52.4 ± 12.0	53.0 ± 12.0	54.5 ± 10.4	0.19
Number of lesions treated per patient	1.25 ± 0.53	1.28 ± 0.51	1.24 ± 0.45	0.42
Lesions	419	427	420	
Target vessel				0.10
Left anterior descending artery	204 (48.7)	187 (43.8)	172 (41.0)	
Left circumflex artery	106 (25.3)	107 (25.1)	128 (30.5)	
Right coronary artery	109 (26.0)	133 (31.1)	120 (28.6)	
Ostial	56 (13.4)	48 (11.2)	55 (13.1)	0.60
Bifurcational	86 (20.5)	78 (18.3)	94 (22.4)	0.33
Total occlusion	48 (11.5)	50 (11.7)	52 (12.4)	0.91
Chronic	17 (4.1)	24 (5.6)	16 (3.8)	0.39
Complex (type B2/C) lesions	306 (73.0)	297 (69.6)	315 (75.0)	0.20
Lesion length, mm	14.8 ± 8.3	14.0 ± 8.2	14.7 ± 8.0	0.17
Vessel size, mm	2.75 ± 0.46	2.69 ± 0.52	2.71 ± 0.49	0.10
Balloon-to-vessel ratio	1.10 ± 0.07	1.11 ± 0.07	1.11 ± 0.08	0.11
Minimal luminal diameter post-procedure, mm				
In-stent	2.55 ± 0.43	2.49 ± 0.48	2.51 ± 0.47	0.07
In-segment	2.20 ± 0.51	2.18 ± 0.58	2.14 ± 0.54	0.20
Diameter stenosis post-procedure, %				
In-stent	10.8 ± 5.7	11.6 ± 5.0	10.7 ± 7.0	0.014
In-segment	23.5 ± 11.0	23.2 ± 11.8	24.2 ± 11.7	0.18

Values are n, n (%), or mean ± SD.
Dual-DES = sirolimus- and probucol-eluting stent(s); SES = sirolimus-eluting stent(s); ZES = zotarolimus-eluting stent(s).

Table 2 Clinical Events at 1 and 2 Years

	SES	Dual-DES	ZES	p Value
Patients	335	333	339	
1 yr				
Definite stent thrombosis	3 (0.9)	3 (0.9)	2 (0.6)	0.87
Probable stent thrombosis	0	0	1 (0.3)	0.37
Possible stent thrombosis	2 (0.6)	3 (0.9)	1 (0.3)	0.59
Death	9 (2.7)	8 (2.4)	12 (3.5)	0.66
Myocardial infarction	12 (3.6)	14 (4.2)	11 (3.2)	0.80
Death/myocardial infarction	20 (6.0)	20 (6.0)	21 (6.2)	0.99
Death/myocardial infarction/target lesion revascularization	46 (13.7)	44 (13.2)	66 (19.5)	0.045
2 yrs				
Definite stent thrombosis	3 (0.9)	3 (0.9)	2 (0.6)	0.87
Probable stent thrombosis	1 (0.3)	0	2 (0.6)	0.37
Possible stent thrombosis	4 (1.2)	4 (1.2)	2 (0.6)	0.67
Death	18 (5.4)	14 (4.2)	21 (6.2)	0.52
Myocardial infarction	18 (5.4)	15 (4.5)	13 (3.9)	0.65
Death/myocardial infarction	34 (10.2)	26 (7.8)	31 (9.2)	0.61
Death/myocardial infarction/target lesion revascularization	68 (20.4)	52 (15.6)	77 (22.7)	0.06

Data are shown as n (%); percentages are Kaplan-Meier estimates.
Abbreviations as in Table 1.

Incident TLR between 1 and 2 years in the Dual-DES group (4 lesions [ΔTLR: 0.9%]) was significantly lower than with the Cypher SES (15 lesions [ΔTLR: 3.6%]) (p = 0.009) but comparable to that observed with the Endeavor ZES (3 lesions [ΔTLR: 0.7%]) (p = 0.72) (Fig. 2).

Serial angiographic follow-up at 2 years. Of the 828 patients with first angiographic follow-up, 80 patients underwent a re-intervention procedure during the same angiographic session, and 15 died prior to the scheduled second angiographic follow-up. Of the remaining 733 eligible patients, 493 patients (67.3%) had re-angiography at 2 years. Relevant angiographic follow-up data are shown in Table 3.

Two-year composite binary restenosis (based on latest angiographic follow-up available for an individual patient) occurred in 65 of 350 (18.6%) lesions with SES, 48 of 345 (13.9%) lesions with Dual-DES, and 75 of 358 (20.9%) lesions with ZES (p = 0.047). In terms of pairwise comparisons, only the difference between Dual-DES and ZES was significant (p = 0.014). Incident binary restenosis between 1 and 2 years in the Dual-DES group (10 lesions [delta-restenosis: 2.9%]) was signifi-

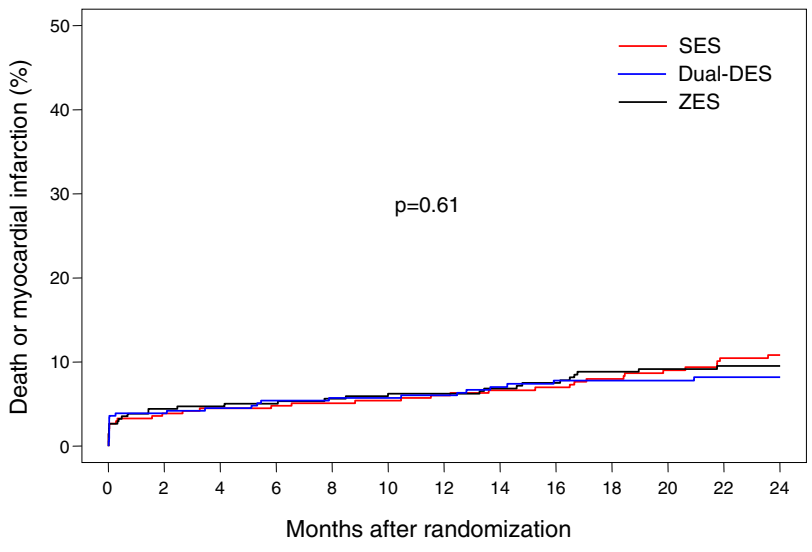

Figure 1 Kaplan-Meier Estimates of Death/Myocardial Infarction Out to 2 Years

Dual-DES = sirolimus- and probucol-eluting stent(s); SES = sirolimus-eluting stent(s); ZES = zotarolimus-eluting stent(s).

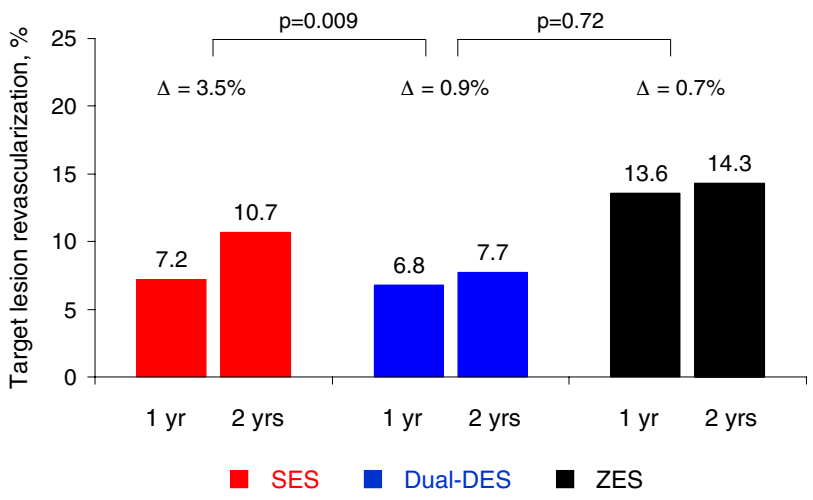

Figure 2 Clinical Restenosis

Target lesion revascularization at 1 and 2 years. Abbreviations as in Figure 1.

cantly lower than with the Cypher SES (23 lesions [delta-restenosis: 6.6%]) (p = 0.023) but comparable to that observed with the Endeavor ZES (6 lesions [delta-restenosis: 1.6%]) (p = 0.28) (Fig. 3).

We checked whether there were significant differences across the 3 study groups among the eligible patients who did not undergo 2-year re-angiography (n = 240). We observed no significant differences in any of the baseline, lesion, or procedural characteristics listed in Table 1 with the exception of luminal caliber pre-intervention (minimal luminal diameter with SES: 0.90 ± 0.50 mm, Dual-DES: 0.99 ± 0.51 mm, ZES: 1.10 ± 0.47 mm; p = 0.028; stenosis: 67.8 ± 16.2%, 65.3 ± 16.1%, 61.3 ± 13.5%; p = 0.018).

Discussion

The ISAR-TEST-2 trial was a 2-center randomized trial comparing the safety and efficacy of 3 limus-eluting stents, namely, the first-generation Cypher SES, a novel polymer-free dual sirolimus- and probucol-eluting stent, and the second-generation Endeavor ZES. The 2-year results are of interest for 2 reasons: 1) the occurrence of safety events beyond 12 months was rare; there was no signal of a differential safety profile across the groups out to 2 years; and 2) the antirestenotic efficacy of both Dual-DES and ZES remained durable between 1 and 2 years, with Dual-DES maintaining an advantage over the entire 2-year period; against this there was evidence of a slight decrement

Table 3 Angiographic Data at 6 to 8 Months and Composite Angiographic Data at 2 Years

	SES	Dual-DES	ZES	p Value
Lesions	350	345	358	
6–8 months				
Minimal luminal diameter, in-stent, mm	2.32 ± 0.63	2.26 ± 0.64	1.95 ± 0.72	<0.001
Minimal luminal diameter, in-segment, mm	1.99 ± 0.59	1.98 ± 0.59	1.79 ± 0.66	<0.001
Diameter stenosis, in-stent	20.1 ± 16.8	20.0 ± 17.1	30.0 ± 21.2	<0.001
Diameter stenosis, in-segment	31.8 ± 15.4	30.5 ± 16.6	35.3 ± 19.4	<0.001
Late luminal loss, in-stent, mm	0.24 ± 0.51	0.23 ± 0.50	0.58 ± 0.55	<0.001
Binary restenosis, in segment	42 (12.0)	38 (11.0)	69 (19.3)	
2-yr composite				
Minimal luminal diameter, in-stent, mm	2.22 ± 0.69	2.19 ± 0.69	1.96 ± 0.73	<0.001
Minimal luminal diameter, in-segment, mm	1.95 ± 0.63	1.95 ± 0.65	1.83 ± 0.69	0.030
Diameter stenosis, in-stent	23.6 ± 20.4	22.4 ± 19.0	29.3 ± 21.8	<0.001
Diameter stenosis, in-segment	33.1 ± 18.2	31.0 ± 17.8	34.1 ± 20.4	0.20
Late luminal loss, in-stent, mm	0.35 ± 0.60	0.30 ± 0.54	0.57 ± 0.57	<0.001
Binary restenosis, in segment	65 (18.6)	48 (13.9)	75 (20.9)	0.047

Data shown as mean ± SD or n (%), unless otherwise specified.
Abbreviations as in Table 1.

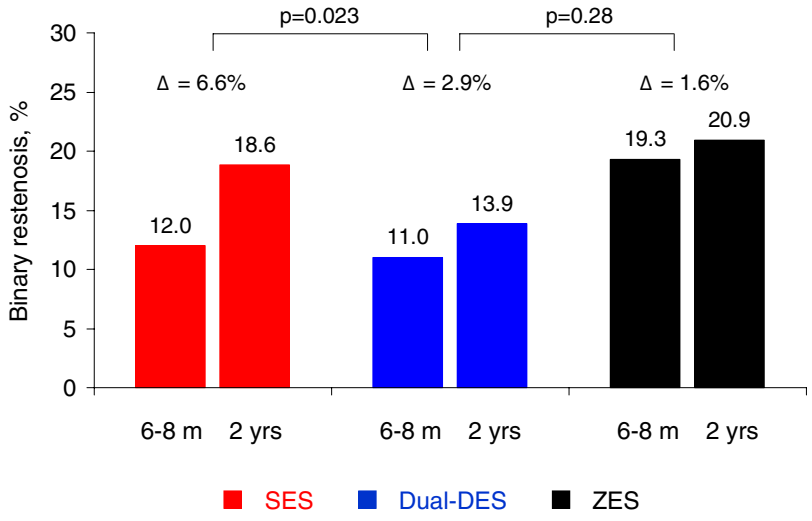

Figure 3 **Angiographic Restenosis**

Binary angiographic restenosis at 6 to 8 months and composite binary angiographic restenosis at 2 years. Abbreviations as in Figure 1.

in angiographic and clinical antirestenotic efficacy with the SES.

With the passage of time, we have come to realize that the undoubted efficacy of first-generation DES in preventing coronary restenosis has been achieved at the expense of a delay in healing of the stented arterial segment. Although multifactorial in origin, pathological and pre-clinical research data strongly implicate polymer residue as a key etiological factor (1,6). This concern has focused attention on the development of newer DES providing high antirestenotic efficacy with lesser impact on arterial healing. The current trial deals with 2 such devices and permits some insight into the comparatively late performance of both platforms.

The second-generation Endeavor ZES has attempted to address the issue of impaired vascular healing by utilizing a thin-strut (91-μm) cobalt chromium backbone—which causes less acute arterial injury—and an enhanced biocompatibility polymer system—which is hypothesized to reduce medium- to long-term inflammatory response. Pre-clinical research studies support the validity of this design concept with evidence of earlier and more complete endothelialization in both porcine and rabbit iliac models (8,9). The drawback of this device is that the polymer system employed results in relatively rapid drug-release kinetics (95% of drug dissociated at 14 days), which translate into a somewhat reduced early antirestenotic efficacy (10). The 2-year results of the ISAR-TEST-2 trial support the characterization of the Endeavor ZES as a rapid-release, early-healing DES device: 6- to 8-month late loss and binary restenosis were relatively high, and there was a low incidence of TLR and binary restenosis between 1 and 2 years. These findings are in keeping with the early and late performance of the ZES in the recently reported ENDEAVOR-IV (Randomized Comparison of Zotarolimus-Eluting and Paclitaxel-Eluting Stents in Patients with Coronary Artery Disease) clinical trial (11,12).

The Dual-DES also incorporates a thin-strut stent backbone (87-μm stainless steel), but uses a polymer-free drug-release system. In order to offset the somewhat lower antirestenotic efficacy of a quick-release polymer-free platform, the Dual-DES incorporates a second drug—probucol—targeted at a different element of the restenotic response cascade. In addition, by virtue of its lipophilicity, it retards the release of the sirolimus (such that approximately 50% of the drug is eluted at 14 days) (13). Probucol is a potent lipophilic antioxidant typically orally administered and has proven effective in inhibiting this restenotic response to balloon injury both in animal models and clinical trials (14,15). It has a low therapeutic index when administered systemically (15)—a feature that makes it better suited to local tissue-specific delivery systems.

Porcine model research has demonstrated signs of improved vascular healing with the Dual-DES at 30 days (13), and this device has demonstrated high antirestenotic efficacy at 6 to 8 months (mean late loss: 0.23 $\pm$ 0.50 mm), comparable to that of the Cypher SES in the current relatively unselected cohort of patients with intermediate-to-high disease complexity (7). The present 2-year analysis supports the durability of antirestenotic efficacy with this device with a low rate of incident TLR and binary restenosis between 1 and 2 years (ΔTLR: 0.9%). This is in keeping with the conjectured late performance advantage of a polymer-free drug-elution system over a durable polymer-based device. In addition, a polymer-free DES might obviate the need for a prolonged duration of dual antiplate-

let therapy after stenting, though this issue remains hypothetical at present.

In the current report, there was a slight decrement in antirestenotic efficacy with the Cypher SES between 1 and 2 years. In particular, the rate of ΔTLR with the Cypher stent (3.5%) was significantly higher than that with both the Dual-DES and ZES. The observation of a small magnitude "catch up" in antirestenotic efficacy with polymer-based DES has previously been described in earlier reports (4,5,16,17).

A central feature of the ISAR-TEST-2 study was the scheduling of serial angiographic follow-up for all patients at 2 time points post-stent implantation, namely, 6 to 8 months and 2 years. Surveillance angiographic follow-up has proven useful in the evaluation of the temporal course of antirestenotic efficacy following plain balloon angioplasty, bare-metal stenting, and DES therapy (4,18,19). However, such follow-up is likely to inflate the rates of revascularization in a manner that is not reflective of routine clinical practice. Although this may distort the absolute magnitude of differences in interdevice efficacy, the relative magnitude may be expected to be real (20). An important caveat relating to angiographic surveillance concerns the issue of missing data. In particular, patients with higher initial restenosis at 6 to 8 months tend not to be represented in 2-year angiographic data as they are likely to have undergone initial TLR. Reporting composite data analysis attempts to capture information on these patients (4). Furthermore, serial angiographic observations should never be considered in isolation but rather always in parallel with overall 2-year TLR. Finally, it should be acknowledged that the proportion of eligible patients who underwent 2-year angiography is relatively low (67.3%). This is unlikely to have introduced significant bias for 2 reasons. First, characteristics of patients who did not undergo angiographic follow-up were well matched across the groups. Second, the results of angiographic restenosis are concordant with results relating to clinical restenosis for which data were available on a very high proportion of patients.

Some additional limitations of our report should be acknowledged. The ISAR-TEST-2 trial was a comparative efficacy trial with a 6- to 8-month primary angiographic end point. Data comparisons at 2 years may be regarded as post hoc and hypothesis generating. Regarding safety outcomes, this study was not powered to detect a difference in relatively rarely occurring clinical events such as death, myocardial infarction, and stent thrombosis. In fact, to date, it has not been possible for any study to show a significant difference in rates of stent thrombosis between newer generation polymer-free or biodegradable polymer DES as compared with established polymer-based DES. This is likely related to the rarity of this complication. It is hoped that aggregate long-term data from recent large-scale studies will provide a framework for testing the hypothesized safety advantage of these platforms over the years to come (21,22).

Conclusions

The results of the ISAR-TEST-2 trial revealed no evidence of a differential safety profile between the Cypher SES, a novel polymer-free sirolimus- and probucol-eluting Dual-DES, and the Endeavor ZES out to 2 years. Furthermore, the antirestenotic efficacy of both the Dual-DES and the ZES remained durable between 1 and 2 years, with Dual-DES maintaining an advantage over the entire 2-year period.

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