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5-Year Outcome Following Randomized Treatment of All-Comers With Zotarolimus-Eluting Resolute Integrity and Everolimus-Eluting PROMUS Element Coronary Stents

Final Report of the DUTCH PEERS (TWENTE II) Trial

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ABSTRACT

OBJECTIVES The study sought to evaluate for the first time the 5-year outcomes after treating an all-comers population with newer-generation cobalt chromium-based Resolute Integrity zotarolimus-eluting stents (ZES) (Medtronic, Santa Rosa, California) versus platinum chromium-based PROMUS Element everolimus eluting stents (EES) (Boston Scientific, Natick, Massachusetts).

BACKGROUND The DUTCH PEERS (TWENTE II) (DUrable polymer-based sTent CHallenge of Promus ElemEnt versus ReSolute integrity: TWENTE II) trial is a randomized, multicenter, single-blinded, investigator-initiated all-comers trial that found at its main analysis similar 1-year safety and efficacy for both drug-eluting stents. It is the first randomized trial ever to investigate the Resolute Integrity ZES and the first trial to compare both devices.

METHODS In total, 1,811 patients were 1:1 randomized to ZES versus EES. We performed a pre-specified assessment of the 5-year clinical outcomes in terms of safety and efficacy. The main endpoint target vessel failure (TVF) is a composite of cardiac death, target vessel–related myocardial infarction, or target vessel revascularization. Secondary endpoints included the individual components of TVF, and stent thrombosis. The study was independently monitored, and adverse clinical events were independently adjudicated.

RESULTS Five-year clinical follow-up data was available in 1,798 (99.3%) patients. The ZES and EES groups showed favorable outcomes, with similar 5-year incidence of TVF (13.2% vs. 14.2%; $p_{log\text{-}rank} = 0.62$) and its individual components: cardiac death (4.5% vs. 4.9%; $p_{log\text{-}rank} = 0.69$), target vessel–related myocardial infarction (3.1% vs. 2.6%; $p_{log\text{-}rank} = 0.47$), and target vessel revascularization (7.6% vs. 8.6%; $p_{log\text{-}rank} = 0.46$). The 5-year incidence of definite or probable stent thrombosis was similar (1.5% vs. 1.3%; $p_{log\text{-}rank} = 0.83$).

CONCLUSIONS At 5-year follow-up, the Resolute Integrity ZES and PROMUS Element EES showed similar and sustained results in terms of safety and efficacy for treating a broad population of all-comers. (J Am Coll Cardiol Intv 2018;11:462–9) © 2018 The authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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Second-generation metallic drug-eluting stents (DES) have resolved the issue of late and very late coronary stent thrombosis, which occurred with first generation DES in the late post-implantation period, by improvements in stent design and polymer coatings, and the use of newer antiproliferative drugs (1). The cobalt-chromium-based Resolute Integrity zotarolimus-eluting stent (ZES) (Medtronic, Santa Rosa, California) and the platinum chromium-based PROMUS Element everolimus-eluting stent (EES) (Boston Scientific, Natick, Massachusetts) are examples of newer-generation DES that were developed to facilitate deliverability and improve DES apposition while maintaining the same durable polymer coatings and antiproliferative drugs as used in the second-generation DES (2–4). Both DES were compared for the first time in the randomized DUTCH PEERS (DUrable polymer-based sTent CHallenge of Promus ElemEnt versus ReSolute integrity) trial, which demonstrated in 1,811 all-comer patients noninferiority of ZES versus EES for the primary endpoint target vessel failure (TVF) at 1-year follow-up (6.1% vs. 5.2%; noninferiority $p = 0.006$) (2).

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Long-term data from comparative clinical DES trials are of significant interest as certain between-stent differences, such as late restenosis and very late stent thrombosis, may only be discovered after several years. However, published reports of long-term clinical outcome data are limited and not yet available for the 2 aforementioned DES. In this final report of the DUTCH PEERS trial we present the 5-year assessment of safety and efficacy of treating a broad population of all-comers by percutaneous coronary interventions (PCIs) with these newer-generation DES.

METHODS

STUDY DESIGN AND PATIENT POPULATIONS. The design of the DUTCH PEERS trial has previously been reported (5). In short, this multicenter, patient-blinded, investigator-initiated, randomized clinical trial (NCT01331707) enrolled 1,811 patients between November 2010 and May 2012 at 4 PCI centers in the Netherlands (Thoraxcentrum Twente, Enschede; Rijnstate Hospital, Arnhem; Treant Zorggroep, Emmen; Alkmaar Medical Center, Alkmaar). Patients 18 years of age and older and capable of providing informed consent with an indication for PCI with DES were randomized in a 1:1 fashion for treatment with Resolute Integrity ZES or PROMUS Element EES. Exclusion criteria were limited and all coronary syndromes, de novo and restenotic lesions, and coronary artery or bypass stenosis were permitted. There was no limit for lesion length, reference size, or number of lesions to be treated (2). Generally, dual antiplatelet therapy consisted of aspirin and clopidogrel and was prescribed in patients without anticoagulation therapy for 1 year. In patients on oral anticoagulation, triple therapy was generally prescribed for 1 to 3 months, followed by a period with clopidogrel as a single antiplatelet agent.

The contract research organization CardioResearch Enschede (Enschede, the Netherlands) coordinated the trial and data management. Follow-up data were obtained by the treating physician or cardiologist or dedicated research nurses every 12 months during routine visits to outpatient clinics (if they coincided with the time of follow-up) or by telephone call or medical questionnaire. Clinical outcome monitoring and event adjudication was performed by the independent external CRO Diagram (Zwolle, the Netherlands). The DUTCH PEERS trial complied with the CONSORT 2010 statement (6) and 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 clinical outcome of the DUTCH PEERS trial has not been reported beyond the 3-year follow-up (7).

CLINICAL ENDPOINTS. Clinical endpoints were defined according to the Academic Research Consortium, including the addendum on definition of myocardial infarction (MI) (8,9). The main endpoint was TVF at 5-year follow-up, a composite of cardiac death, target vessel-related MI or clinically indicated target vessel revascularization. Pre-specified secondary endpoints included the individual

ABBREVIATIONS AND ACRONYMS

DES = drug-eluting stent(s)

EES = everolimus-eluting stent(s)

MACE = major adverse cardiac event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

TLF = target lesion failure

TVF = target vessel failure

ZES = zotarolimus-eluting stent(s)

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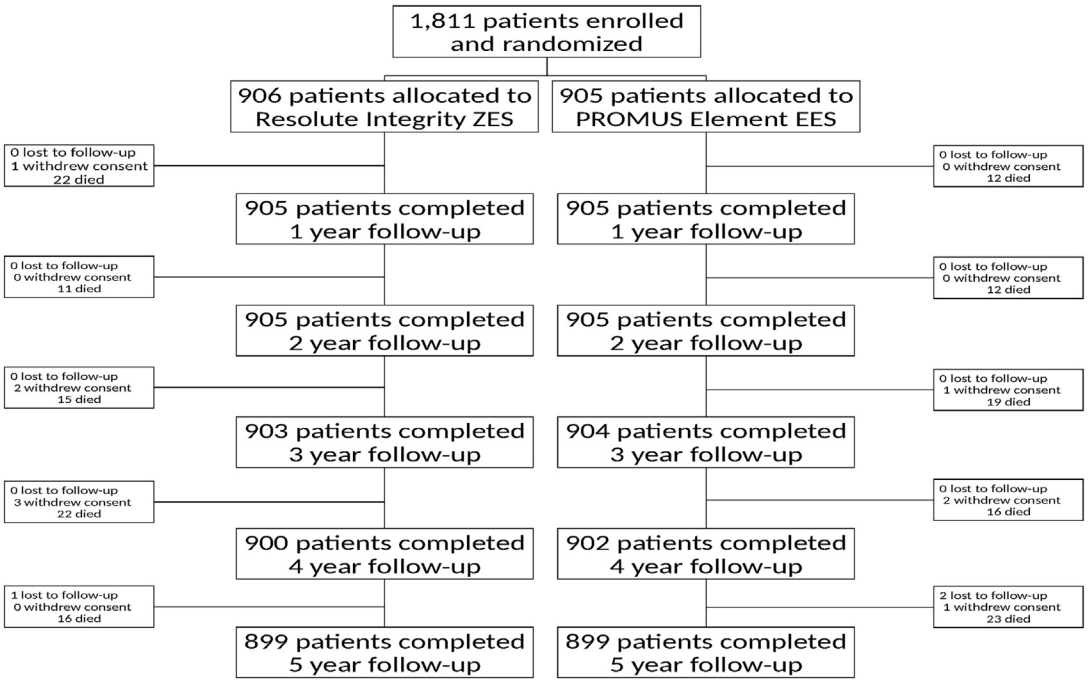
FIGURE 1 Study Flow Chart



Study flow chart of the DUTCH PEERS (DUrable polymer-based sTent CHallenge of Promus ElemEnt versus ReSolute integrity) trial. EES = everolimus-eluting stent(s); ZES = zotarolimus-eluting stent(s).

components of TVF, all-cause mortality, and definite or probable stent thrombosis. Further composite clinical endpoints were: target lesion failure (TLF) (cardiac death, any MI which was not clearly attributable to a nontarget vessel, or clinically indicated target lesion revascularization), major adverse cardiac events (MACE) (all-cause death, any MI, emergent coronary artery bypass surgery, or repeat clinically indicated target lesion revascularization), and a more global patient-oriented composite endpoint (all-cause death, any MI, or any coronary revascularization).

Besides this, we assessed very late clinical adverse events in all patients who had stents implanted with longitudinal stent deformation during the index procedure (2). Of all cases of longitudinal stent deformation, 6 of 9 (66.7%) cases were detected by angiography (i.e., no intracoronary imaging modalities were used) by the operator whereas all 9 cases were detected post-procedurally by the analysts. All stent deformations were located in the proximal stent entrance; additional proximal stents were implanted in 7 of 9 (77.8%) cases and post-dilation was performed in 8 of 9 (88.9%) cases.

Death was regarded as cardiac unless an unequivocal noncardiac cause could be established. MI was defined by creatine kinase concentrations of more than double the upper limit of normal with raised confirmatory cardiac biomarkers. Revascularization procedures were regarded as clinically indicated if the angiographic diameter stenosis of the then treated lesion was 50% or more in the presence of ischemic signs or symptoms, or if the diameter stenosis was 70% or more irrespective of ischemic signs or symptoms (9).

STATISTICAL ANALYSES. Categorical variables were assessed with the chi-square test, whereas continuous variables were assessed with the Student *t* test or the Wilcoxon rank sum test, as appropriate. The time to clinical endpoints was assessed by Kaplan-Meier analyses and the log-rank test was applied to compare groups. Hazard ratios were calculated using Cox proportional hazards regression analysis. The p values and confidence intervals were 2-sided and p values < 0.05 were considered significant. Further details on statistical methods have been reported previously (2). SPSS version 22.0 (IBM Corporation, Armonk, New York) was used.

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RESULTS

Out of all 1,811 patients, 5-year clinical follow-up data were available in 1,798 patients (99.3% follow-up: 3 patients were lost to follow-up and 10 withdrew consent) (Figure 1). As previously reported, there were no differences in baseline clinical and lesion characteristics between patients randomized to treatment with ZES versus EES (Table 1) (2). In both groups, large proportions of patients with acute MI presentation (46.5% vs. 43.7%) were included. Target lesion and interventional characteristics were also similar for both groups, including high rates of complex coronary lesions (American College of Cardiology/American Heart Association class B2 or C: 65.8% vs. 65.6%), with the only exception of more frequent stent post-dilation in EES (73.6% vs. 78.9%; p = 0.002) (Table 2). This is probably related to the excellent radiographic visibility of the PROMUS Element EES and has been reported in other trials (4).

At discharge, most patients (99%) were treated with antiplatelet therapy that included aspirin and clopidogrel; only 18 (1%) patients received prasugrel and 3 (<1%) patients received ticagrelor in addition to aspirin. Information regarding medication use at 5-year follow-up was available in ≥93.9% of all patients. In both DES groups, there was no statistically significant difference in the use of aspirin (78.7% vs. 81.3%; p = 0.17), $P2Y_{12}$ receptor inhibitors (12.1% vs. 10.2%; p = 0.22), dual antiplatelet therapy (6.6% vs. 6.4%; p = 0.88), oral anticoagulant agents (15.8% vs. 15.8%; p = 0.85), or statins (86.4% vs. 85.0%; p = 0.42).

The 5-year incidence of the main clinical endpoint TVF was favorable and similar for the ZES and EES groups (13.2% vs. 14.2%; log-rank p = 0.62) (Table 3, Figure 2 and 3). The rates of the individual components of TVF were also similar for both stent arms: cardiac death (4.5% vs. 4.9%; log-rank p = 0.69); target vessel-related MI (3.1% vs. 2.6%; log-rank p = 0.47); and target vessel revascularization (7.6% vs. 8.6%; log-rank p = 0.46), respectively (Figure 2). In addition, the rates of the composite endpoints TLF (12.0% vs. 12.5%; log-rank p = 0.86), MACE (17.0% vs. 17.2%; log-rank p = 0.97), and the patient-oriented composite endpoint (22.8% vs. 23.3%; log-rank p = 0.86) were similar for both groups (Table 3).

As shown in Table 3, the rates of definite or probable stent thrombosis were low for patients treated with ZES and EES (1.5% vs. 1.3%; log-rank p = 0.83). Due to an apparent dissimilarity between the Resolute Integrity ZES and PROMUS Element EES groups in the course of their time-to-event curves for definite or probable stent thrombosis, an additional post hoc landmark analysis at 12-month follow-up is displayed

TABLE 1 Baseline Demographics

	Resolute Integrity ZES (n = 906)	PROMUS Element EES (n = 905)	p Value
Age, yrs	63.9 ± 10.6	63.9 ± 11.0	0.97
Men	665 (73.4)	657 (72.6)	0.70
Body mass index, kg/m^2*	28.1 ± 4.8	27.8 ± 4.6	0.39
Diabetes mellitus (any)	167 (18.4)	157 (17.3)	0.55
Chronic renal failure†	35 (3.9)	28 (3.1)	0.37
Arterial hypertension	500 (55.2)	484 (53.5)	0.47
Hypercholesterolemia	418 (46.1)	430 (47.5)	0.56
Current smoker‡	213 (23.6)	231 (25.5)	0.32
Family history of coronary artery disease§	452 (50.1)	451 (49.9)	0.98
Previous myocardial infarction	207 (22.8)	190 (21.0)	0.34
Previous percutaneous coronary intervention	182 (20.1)	167 (18.5)	0.38
Previous coronary bypass surgery	84 (9.3)	89 (9.8)	0.68
Clinical syndrome at presentation			0.07
Stable angina	372 (41.1)	377 (41.7)	
Unstable angina	113 (12.5)	132 (14.6)	
Non-ST-segment elevation myocardial infarction	246 (27.2)	201 (22.2)	
ST-segment elevation myocardial infarction	175 (19.3)	195 (21.5)	
Acute coronary syndrome (any)	534 (58.9)	528 (58.3)	0.80
Left ventricular ejection fraction <30%	15 (1.7)	13 (1.4)	0.71
De novo coronary lesions only	817 (90.2)	810 (89.5)	0.64
At least 1 chronic total occlusion	38 (4.2)	38 (4.2)	0.99
At least 1 bifurcation	244 (26.9)	221 (24.4)	0.22
At least 1 in-stent restenosis	27 (3.0)	28 (3.1)	0.89
At least 1 small vessel (RVD <2.75 mm)	551 (60.8)	517 (57.1)	0.11
At least 1 lesion length >27 mm	161 (17.8)	157 (17.3)	0.81
Glycoprotein IIb/IIIa antagonist	262 (28.9)	259 (28.6)	0.89
Lesions treated per patient			0.32
1	668 (73.7)	668 (76.0)	
2	191 (21.1)	182 (20.1)	
3 or more	47 (5.2)	35 (3.9)	

Values are mean ± SD or n (%). *Data from 721 patients in the zotarolimus-eluting stent(s) (ZES) group and 703 patients in the everolimus-eluting stent(s) (EES) group. †Chronic renal failure defined by serum creatinine level ≥130 μmol/l. ‡Data from 903 patients in the ZES group and 905 patients in the EES group. §Data from 903 patients in the ZES group and 902 patients in the EES group.

RVD = reference vessel diameter.

TABLE 2 Target Lesion Characteristics and Interventional Procedure

	Resolute Integrity ZES (n = 1,205 Lesions)	PROMUS Element EES (n = 1,166 Lesions)	p Value
De novo lesion*	1,147 (95.2)	1,103 (94.6)	0.51
ACC/AHA lesion class B2/C	793 (65.8)	765 (65.6)	0.92
Reference vessel diameter, mm	2.68 ± 0.59	2.70 ± 0.59	0.32
Implantation of assigned stents only	1,195 (99.2)	1,161 (99.6)	0.22
Stents per lesion	1.35 ± 0.68	1.36 ± 0.70	0.70
Total stent length per lesion, mm	28.60 ± 18.51	29.71 ± 19.11	0.15
Direct stenting	352 (29.2)	326 (28.0)	0.50
Stent post-dilation	887 (73.6)	920 (78.9)	0.002

Value are n (%) or mean ± SD. Details of lesion characteristics and interventional procedure have previously been reported. *Including chronic total occlusion, but not grafts or in-stent restenosis.

ACC/AHA = American College of Cardiology/American Heart Association; other abbreviations as in Table 1.

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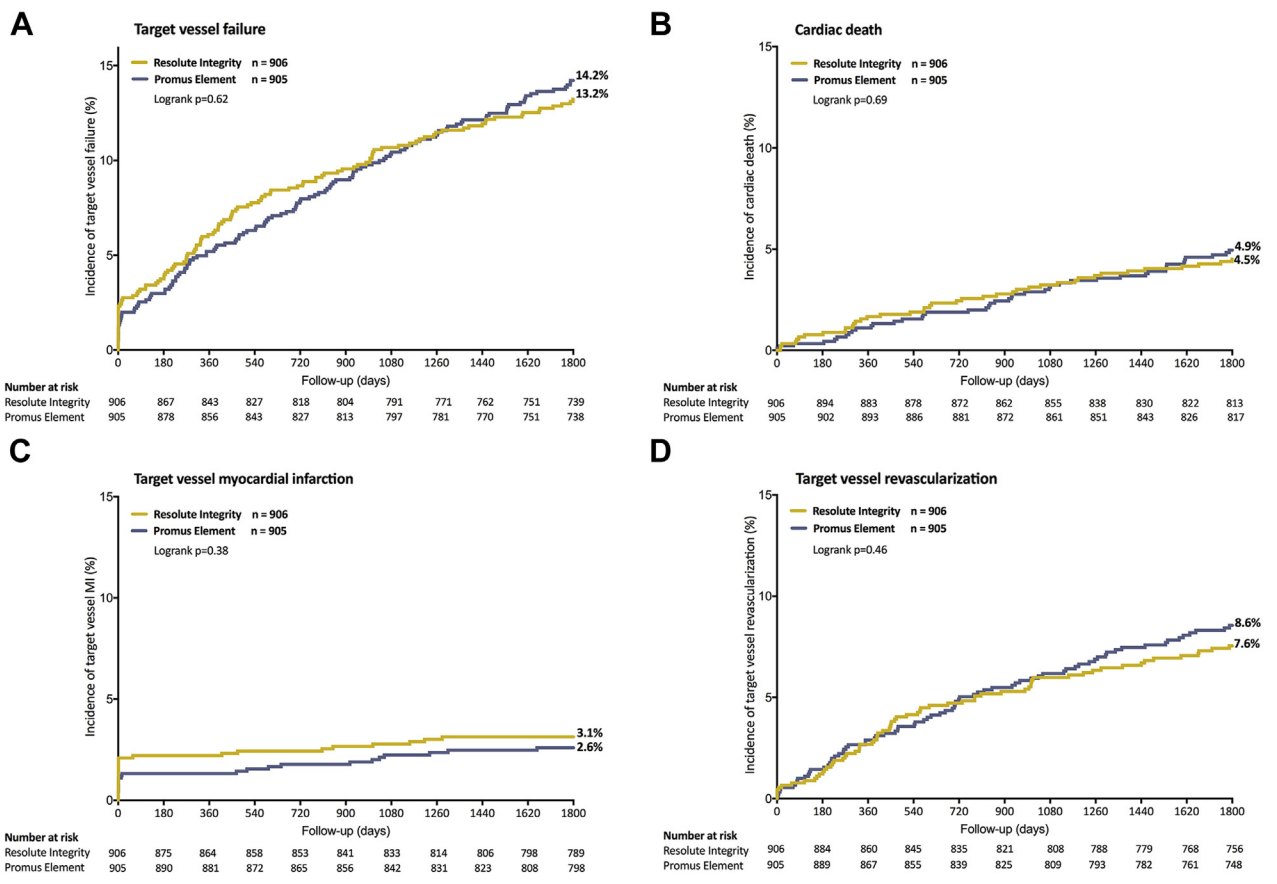
TABLE 3 Clinical Outcomes at 5-Year Follow-Up

	Outcome at 5 Years				Outcome Difference Between 1 and 5 Years			
	Resolute Integrity ZES	PROMUS Element EES	Hazard Ratio (95% CI)	$p_{log\text{-}rank}$	Resolute Integrity ZES	PROMUS Element EES	Difference (95% CI)	p Value
Target vessel failure	118 (13.2)	127 (14.2)	0.94 (0.73 to 1.21)	0.62	63 (7.5)	80 (9.3)	−1.9 (−4.5 to 0.8)	0.17
Death (any)	86 (9.5)	82 (9.1)	1.06 (0.78 to 1.43)	0.72	64 (7.2)	70 (7.8)	−0.6 (−3.1 to 1.9)	0.64
Cardiac death	40 (4.5)	44 (4.9)	0.92 (0.60 to 1.41)	0.69	25 (2.8)	34 (3.8)	−1.0 (−2.6 to 0.7)	0.25
Target vessel myocardial infarction	28 (3.1)	23 (2.6)	1.23 (0.71 to 2.13)	0.47	8 (0.9)	11 (1.2)	−0.3 (−1.3 to 0.7)	0.52
Target vessel revascularization	66 (7.6)	75 (8.6)	0.88 (0.64 to 1.23)	0.46	42 (4.9)	49 (5.7)	−0.8 (−2.9 to 1.3)	0.48
Target lesion failure	109 (12.0)	113 (12.5)	0.98 (0.75 to 1.27)	0.86	58 (6.8)	72 (8.4)	−1.5 (−4.0 to 1.0)	0.24
Major adverse cardiac events	154 (17.0)	156 (17.2)	1.00 (0.80 to 1.25)	0.97	96 (11.3)	112 (13.0)	−1.7 (−4.8 to 1.4)	0.29
Patient-oriented composite endpoint	207 (22.8)	211 (23.3)	0.98 (0.81 to 1.19)	0.86	125 (15.2)	137 (16.5)	−1.3 (−4.8 to 2.2)	0.47
Definite-or-probable stent thrombosis	13 (1.5)	12 (1.3)	1.09 (0.50 to 2.39)	0.83	8 (0.9)	4 (0.5)	0.4 (-0.3 to 1.2)	0.24
Definite stent thrombosis	10 (1.1)	10 (1.1)	1.00 (0.42 to 2.41)	0.99	7 (0.8)	4 (0.5)	0.3 (-0.4 to 1.1)	0.36

Values are n (%).
CI = confidence interval; other abbreviations as in Table 1.

FIGURE 2 Kaplan-Meier Curves for Target Vessel Failure and the Individual Components Thereof



Kaplan-Meier curves for **(A)** target vessel failure, **(B)** cardiac death, **(C)** target vessel–related myocardial infarction, and **(D)** target vessel revascularization for patients treated with the Resolute Integrity ZES **(yellow)** versus PROMUS Element EES **(gray)**. Abbreviations as in Figure 1.

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in Figure 4, Table 3. Definite or probable stent thrombosis occurred in 0.6% versus 0.9% (log-rank p = 0.41) of patients during the first year and in 0.9% vs. 0.5% (p = 0.24) during the second to fifth years.

Longitudinal stent deformation during the index procedure was observed in 9 of the patients treated with EES and in none of the patients treated with ZES. Between 1- and 5-year follow-up, 1 of these EES patients died from progressive heart failure (unrelated to the implanted study stent) whereas all other patients experienced no adverse event.

DISCUSSION

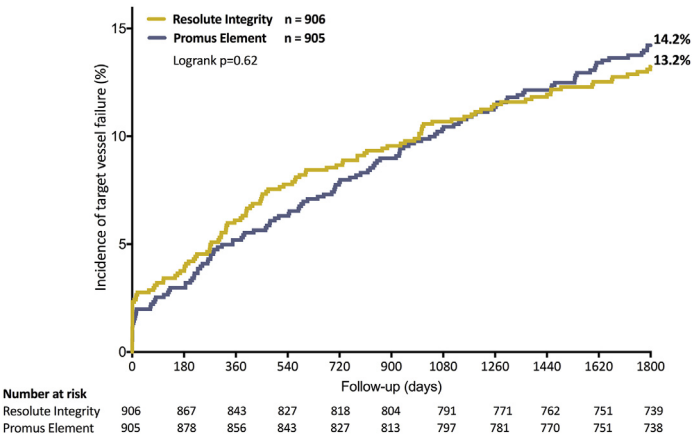
MAIN RESULTS. The present study reports the final 5-year clinical outcome of the randomized DUTCH PEERS trial, which assessed the safety and efficacy of the Resolute Integrity ZES versus PROMUS Element EES in treating all-comer patients (2). The rates of the main clinical endpoint TVF (13.2% vs. 14.2%) were relatively low and similar for both stent groups. There was also no significant between-group difference in the individual components of TVF (i.e., cardiac death, target vessel related MI, and clinically driven target vessel revascularization). Very late stent thrombosis was rare and the 5-year incidence of stent thrombosis was low and comparable in both groups (definite or probable, 1.5% vs. 1.3%). The present 5-year results are consistent with the main outcome of DUTCH PEERS trial at 1-year follow-up, which demonstrated noninferiority of ZES versus EES (2). Furthermore, landmark analyses at 1-year showed for all endpoints no statistically significant difference between the stent groups.

PREVIOUS STUDIES. A meta-analysis of randomized trials, comparing different types of ZES versus EES, showed comparable safety and efficacy at short-term to midterm follow-up (10). The same meta-analysis suggested that in real-world observational studies EES may be more safe and efficacious, a finding that was greatly driven by the outcome of studies that compared EES versus the no longer available Endeavor ZES, which was known to have a higher repeat revascularization risk (10,11). This underlines the importance of obtaining long-term outcome data from large-scale randomized all-comer trials to evaluate the clinical value of modified stents that may be considered to be derivatives. However, 5-year long-term outcomes of all-comers, treated either with Resolute Integrity ZES or with PROMUS Element EES, have not been reported yet (1).

The SORT OUT VI (Scandinavian Organization for Randomized Trials with Clinical Outcome VI) trial is the only other large-scale randomized trial that assessed the Resolute Integrity in all-comers (3). That study compared 1,502 patients treated with Resolute Integrity ZES versus 1,497 patients treated with biodegradable polymer-based biolimus-eluting BioMatrix Flex stents (Biosensors, Singapore) and showed at 3-year follow-up for both stents similar rates of the primary endpoint MACE (8.6% vs. 9.6%; p = 0.36) and all secondary endpoints, including definite or probable stent thrombosis (1.3% vs. 1.2%; p = 0.86) (12). In addition, some previous randomized studies compared the predecessor of the Resolute Integrity ZES (i.e., the Resolute ZES) with EES in broad patient populations and showed favorable 5-year outcomes for both devices (13–15).

So far, the PLATINUM (a Prospective, Randomized, Multicenter Trial to Assess an Everolimus-Eluting Coronary Stent System [PROMUS Element] for the Treatment of Up to Two de Novo Coronary Artery Lesions) trial is the only large-scale randomized study besides the DUTCH PEERS trial that has published 3-year follow-up data of PROMUS Element EES (13). In the PLATINUM trial, 758 patients treated with the platinum-chromium PROMUS Element EES were compared to 749 patients treated with the cobalt-chromium Xience V EES (Abbott Vascular, Santa Clara, California) (4). The study showed a favorable safety and efficacy for both stent groups: the TLF rate was 5.9% versus 7.1% (p = 0.40); the rate of a composite endpoint of all-cause death, MI, or target vessel revascularization was 11.4% versus 12.7% (p = 0.48); and the incidence of definite or probable stent thrombosis was low and comparable in both treatment arms (0.7% vs. 0.5%; p = 0.76) (4).

FIGURE 3 Kaplan-Meier Curves for Target Vessel Failure



Kaplan-Meier curves for target vessel failure for patients treated with Resolute Integrity zotarolimus-eluting **(yellow)** versus PROMUS Element everolimus-eluting stents **(gray)**.

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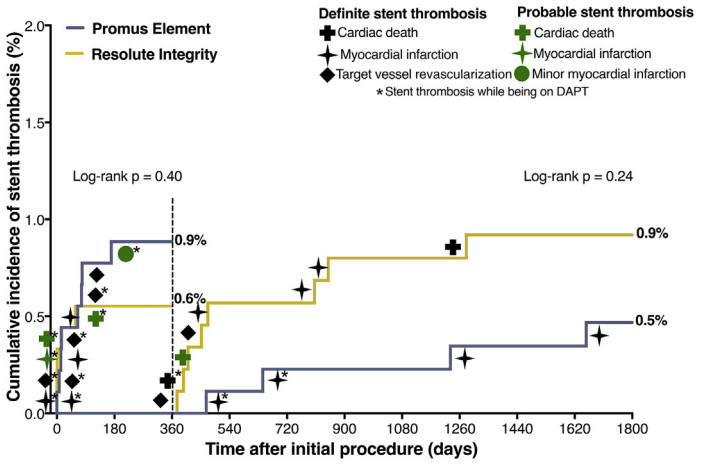
FIGURE 4 Landmark Analysis for Definite or Probable Stent Thrombosis



Kaplan-Meier curve of stent thrombosis for patients treated with the Resolute Integrity ZES **(yellow)** versus the PROMUS Element EES **(gray)**. Dual antiplatelet therapy (DAPT) means acetylsalicylic acid plus $P2Y_{12}$ receptor antagonist. Abbreviations as in Figure 1.

Nevertheless, the PLATINUM trial did not assess all-comers but rather a population of low- to medium-risk patients who experienced stable or unstable angina and required PCI for up to 2 de novo coronary lesions in vessels with a diameter of at least 2.5 mm. The present 5-year follow-up of the DUTCH PEERS trial supports the favorable 3-year findings of the PLATINUM trial in a much broader patient population. Besides this, our results are consistent with long-term outcomes in the COMPARE II (Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent) trial, which compared the predecessor of the PROMUS Element (i.e., the PROMUS EES) or Xience V EES to a biodegradable-polymer biolimus-eluting stent (14).

STENT THROMBOSIS. Although the risk of very late stent thrombosis is attenuated with the introduction of second-generation DES (15-18), each individual case represents an important adverse event that can result in a large MI or death. A recent study in 64 patients with very late DES thrombosis, assessed by optical coherence tomography, revealed a median time from DES implantation until very late stent thrombosis of 4.7 years (interquartile range: 3.1 to 7.5 years) (19). This emphasizes the need for a prolonged follow-up of clinical DES trials. It is reassuring that the rate of very late stent thrombosis is low in the present 5-year analysis of the DUTCH PEERS trial, as well as in other studies with 5-year follow-up (14,20-22).

LONGITUDINAL STENT DEFORMATION. Longitudinal stent deformation has been identified as a potential trade-off of newer-generation DES due to a decreased longitudinal stability caused by thinner stent struts and a reduced number of connectors (23,24). However, in the DUTCH PEERS trial, longitudinal stent deformation was observed only in 0.6% of the implanted PROMUS Element EES and in none of the Resolute Integrity ZES (2). A recent meta-analysis of randomized trials showed a higher risk of observing longitudinal stent deformation in PROMUS Element EES than in other newer-generation DES that was not associated with worse clinical outcome at 1-year follow-up (25). The findings of the present analysis of the DUTCH PEERS trial extend our knowledge, as they show that longitudinal stent deformation, which was recognized and directly managed by the operator in the majority of cases, was not associated with very late adverse clinical events.

STUDY LIMITATIONS. This analysis of the 5-year follow-up was pre-specified but the findings should be considered hypothesis generating. The high 5-year follow-up rate (>99%) and the independent monitoring and adjudication support the validity of the data, but our study is not powered to assess low-incidence adverse events. Nevertheless, in the absence of long-term data from other or even larger randomized all-comer studies to compare both DES, we believe that these data are of interest. From baseline to 5-year follow-up there was an increase in the proportion of patients on oral anticoagulation from 8.8% to 15.8%, which may be most likely related to an increase in the prevalence of atrial fibrillation during this study with long-term follow-up; the latter remains hypothetical, as we did not assess reasons for starting oral anticoagulation. We cannot exclude some degree of selection during enrollment, as 56.2% of all eligible patients were enrolled (2). Nevertheless, it may be fair to state that this enrollment rate is relatively high for an all-comer DES trial, and the high proportion of patients who underwent the index PCI for an acute MI (45.1%) underlines that this trial provides information that is relevant to routine clinical practice.

CONCLUSIONS

At 5-year follow-up, the Resolute Integrity ZES and PROMUS Element EES showed similar and sustained results in terms of safety and efficacy for treating a broad population of all-comers.

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PERSPECTIVES

WHAT IS KNOWN? Newer-generation DES are superior to first-generation DES. The DUTCH PEERS randomized trial has shown low rates of adverse clinical events, such as target vessel MI, repeat target vessel revascularization, and stent thrombosis for 2 newer-generation DES: the Resolute Integrity ZES and the PROMUS Element EES. However, data on the 5-year safety and efficacy of both stents are not available yet.

WHAT IS NEW? The present long-term results of the DUTCH PEERS trial provide a strong signal of similar and sustained safety and efficacy of both metallic DES after 5 years of follow-up in a broad population of all-comer patients.

WHAT IS NEXT? These data are useful to interpret the long-term outcome of novel DES and to put the long-term clinical outcome after treatment with bioresorbable vascular scaffolds into perspective.

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KEY WORDS DES, long-term outcome, newer-generation drug-eluting stent(s), PCI, percutaneous coronary intervention, PROMUS Element everolimus-eluting stent(s), Resolute Integrity zotarolimus-eluting stent(s)

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