One-Year Outcomes in "Real-World" Patients Treated With a Thin-Strut, Platinum-Chromium, Everolimus-Eluting Stent (from the PROMUS Element Plus US Post-Approval Study [PE-Plus PAS])

David E. Kandzari, MD[a,*], Nima Amjadi, MD[b], Christopher Caputo, DO[c], Steven K. Rowe, MD[d], Jerome Williams, MD[e], Hoshedar P. Tamboli, MD[f], Thomas Christen, MD[g], Dominic J. Allocco, MD[g], and Keith D. Dawkins, MD[g]

The PROMUS Element Plus US Post-Approval Study (PE-Plus PAS) was a prospective, open-label, multicenter, observational study designed to examine outcomes in everyday clinical practice in patients treated with everolimus-eluting, platinum-chromium PROMUS Element Plus stents at 52 centers in the United States. This is the first report of results from this large study. The primary end point of the PE-Plus PAS was 12-month cardiac death or myocardial infarction in the more restricted population of "PLATINUM-like" patients pooled from the PE-Plus PAS, PE-PROVE (PROMUS Element European post-approval study), and PLATINUM Workhorse/Small Vessel trials. Additional clinical end points were tested in the overall PE-Plus PAS patient population. Of the 2,683 patients enrolled in PE-Plus PAS, 70% were men, mean age was 64 years, 33% had diabetes, and 29% were "PLATINUM-like." Among the PLATINUM-like patients, 12-month cardiac death or myocardial infarction was 1.8% (33 of 1,855) with an upper 1-sided 95% confidence interval of 2.3%, which was significantly less than the prespecified performance goal of 3.2% ($p_{noninferiority}$ <0.001). In the overall PE-Plus population, 12-month target vessel failure (defined as death, MI, or revascularization related to the target vessel) was 6.7% (170 of 2,554), cardiac death was 1.4% (37 of 2,554), MI was 1.1% (28 of 2,554), and ARC-definite/probable stent thrombosis was 0.7% (19 of 2,554). A prespecified secondary end point of 12-month target vessel failure in diabetic patients demonstrated a rate of 4.2% (14 of 332) with an upper 1-sided 95% confidence interval of 6.03%, which was significantly less than the performance goal of 12.6% ($p_{noninferiority}$ <0.001). In conclusion, in this large registry of unselected patients, coronary artery revascularization with the PROMUS Element Plus everolimus-eluting stent demonstrates favorable results with low 1-year clinical event rates. **© 2015 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2015;■:■−■)**

The PLATINUM clinical trial program evaluated the safety and efficacy of the PROMUS Element Plus everolimus-eluting platinum-chromium coronary stent system (Boston Scientific Corporation, Marlborough, Massachusetts) and supported US and Japanese approval of PROMUS Element.[1−4] These trials showed that the PROMUS Element stent was noninferior to the predicate cobalt-chromium PROMUS stent, with low rates of clinical events for both stents throughout follow-up. However, the strict enrollment criteria required led to many patients being excluded from the trials, such that those outcomes may not be readily applicable to all patients in routine clinical practice. The PROMUS Element Plus US Post-approval Study (PE-Plus PAS) was a prospective, open-label, observational study. The objectives of this study were to (1) assess safety and efficacy in a broad, unselected patient population representative of everyday clinical practice and (2) compare clinical outcomes to a prespecified performance goal after PROMUS Element percutaneous coronary intervention (PCI) in selected patients from 3 studies.

Methods

The device tested in the PE-Plus PAS was the PROMUS Element Plus everolimus-eluting platinum-chromium coronary stent that incorporates the following key components: the antiproliferative drug everolimus, 2 polymers, and the platinum-chromium alloy Element stent. This stent is coated

[a]Interventional Cardiology, Piedmont Hospital, Atlanta, Georgia; [b]Cardiac Cath Lab, Texas Heart and Vascular, South Austin Hospital, South Austin, Texas; [c]Interventional Cardiology, North Florida Regional Medical Center, Gainesville, Florida; [d]Interventional Cardiology, Cox Medical Centers, Springfield, Missouri; [e]Interventional Cardiology, Novant Health Heart and Vascular Institute Presbyterian Medical Center, Charlotte, North Carolina; [f]Cardiology, Brandon Regional Hospital, Brandon, Florida; and [g]Boston Scientific Corporation, Marlborough, Massachusetts. Manuscript received September 8, 2015; revised manuscript received and accepted November 12, 2015.

Clinical Trial Registration Information: *www.clinicaltrials.gov* (NCT01589978).

This study was sponsored and funded by Boston Scientific Corporation (Marlborough, Massachusetts).

See page 6 for disclosure information.

*Corresponding author: Tel: (+404) 605-5526; fax: (+404) 720-0911.
E-mail address: david.kandzari@piedmont.org (D.E. Kandzari).

0002-9149/15/$ - see front matter © 2015 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.amjcard.2015.11.043

conformally with 2 layers: a primer layer (poly-n-butyl methacrylate) and a drug matrix layer. The drug matrix layer contains a copolymer of vinylidene fluoride and hexafluoropropylene blended with everolimus (100 μg/cm^2 total weight of drug per unit of stent surface area). This combination of drug, polymer, and platform is identical to the PROMUS Element everolimus-eluting coronary stent (Boston Scientific Corporation). The PROMUS Element Plus stent system differs from the PROMUS Element stent system by incorporating a stent delivery balloon design change (single layer to dual layer), with resultant smaller crossing profile, to enhance flexibility and reduce balloon withdrawal resistance.

PE-Plus PAS was a prospective, open-label, multicenter study designed to collect "real-world" clinical outcome data for patients receiving ≥1 Plusstents as part of PCI for any indication or lesion complexity. Participating physicians enrolled up to 200 patients per center; a patient was considered enrolled once an informed consent form was signed and there was an attempt to implant at least 1 PROMUS Element Plus stent. Per protocol, patients with PROMUS Element Plus implant failures were followed through hospital discharge following the initial attempted index procedure.

Procedures were to be performed according to the PROMUS Element Plus Everolimus-Eluting Platinum Chromium Coronary Stent System Directions for Use,[5] with angiography performed per local standard practice. Staged procedures were allowed when they (1) were planned at the time of the index procedure and (2) occurred within 30 days of the index procedure and the PROMUS Element Plus stent implanted during the staged procedure was implanted in a vessel not previously treated with a PROMUS Element Plus stent as part of this study. Antiplatelet treatment was recommended according to American College of Cardiology Foundation/American Heart Association/Society for Cardiovascular Angiography and Interventions guidelines for PCI.[6] Follow-up was scheduled at 30 days, 180 days, and annually through 5 years after study stent implantation.

The primary end point of the study was the rate of 12-month cardiac death or myocardial infarction (CD/MI) post-stent implantation in PLATINUM-like[1] patients who received a PROMUS Element Plus stent. PLATINUM-like patients[1] were defined as those without acute MI, graft stenting, chronic total occlusion, in-stent restenosis, failed brachytherapy, bifurcation lesions, ostial lesions, severe tortuosity, moderate or severe calcification by visual estimate in the target lesion or target vessel proximal to target lesion, 3-vessel stenting, cardiogenic shock, left main disease, or acute or chronic renal dysfunction (serum creatinine >2.0 mg/dl or subject on dialysis). PLATINUM-like lesions were defined as follows: (a) lesion length ≤24 mm and diameter ≥2.50 and ≤4.25 mm or (b) lesion length ≤28 mm and diameter ≥2.25 and <2.50 mm. Patients in the primary end point analysis of PE-Plus PAS were pooled from the PE-Plus study, the PLATINUM Workhorse/Small Vessel studies (WH/SV),[1,4] and the single-arm, European post-approval PE-PROVE (PROMUS Element European post-approval study)[7] registry (Figure 1). Statistical testing was used to determine if the 12-month CD/MI rate in the pooled population met the prespecified performance goal of 3.2%

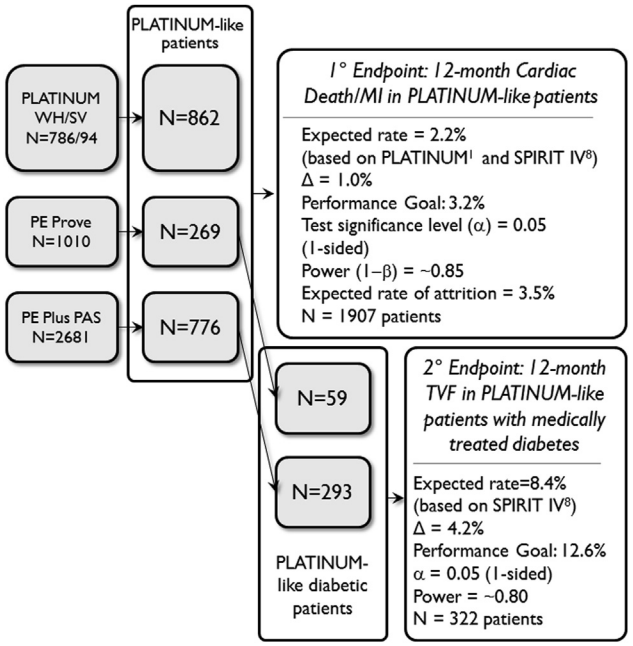

Figure 1. Study design for the primary end point and key secondary end point.

(expected rate of 2.2% plus a delta of 1.0%; based on data from the PLATINUM and the SPIRIT IV trials[1,8]). A secondary, statistically powered hypothesis was 12-month target vessel failure (TVF, defined as death, MI, or revascularization related to the target vessel) among PLATINUM-like patients with medically treated diabetes from the PE-Plus and PE-PROVE clinical trials, compared with a performance goal of 12.6% (expected rate of 8.4% + delta of 4.2%; Figure 1). The prespecified performance goal for the PLATINUM-like medically treated diabetes subset was based on the SPIRIT IV trial.[8] Additional prespecified end points for the overall PE-Plus population included the incidence of longitudinal stent deformation (LSD) and the overall and PROMUS Element Plus–related rates of cardiac and noncardiac death, MI, target vessel revascularization (TVR), TVF, major adverse cardiac events (MACE, defined as cardiac death, MI, and TVR) and Academic Research Consortium definite/probable stent thrombosis[9] (ST). MI was assessed according to the definition used in the PLATINUM study.[1] Target lesion revascularization (TLR) was defined as stent-related TVR, as assessed by the clinical events committee. For the purposes of the analysis, if it could not be determined with certainty whether MI or death was related to the target vessel, then it was considered TVF by default. Clinical procedural success was defined as post-procedure mean lesion diameter stenosis <30% in 2 near-orthogonal projections with Thrombolysis In Myocardial Infarction 3 flow, as visually assessed by the physician, without the occurrence of inhospital MACE (analyzed per patient). Technical success was defined as successful delivery and deployment of the study stent to the target lesion, without balloon rupture or embolization (analyzed per lesion).

The PE-Plus study complies with the principles of the Declaration of Helsinki and all applicable local and federal regulations. The protocol was reviewed and approved by the Institutional Review Boards/Ethics Committees at each site

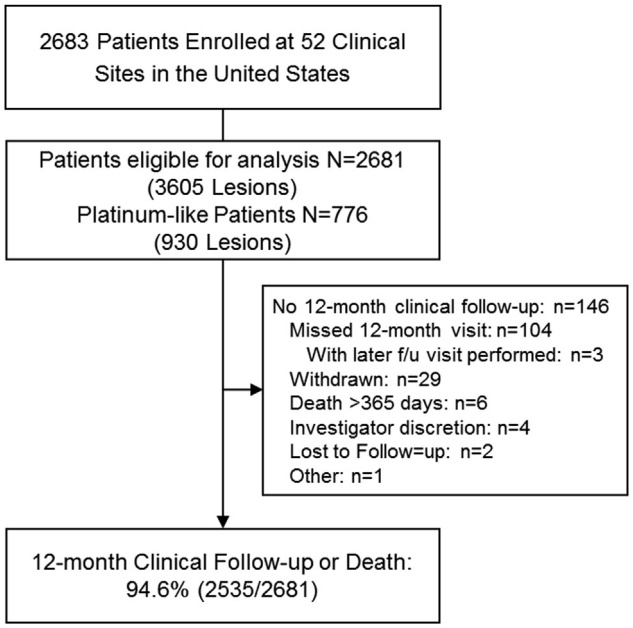

Figure 2. Patient disposition at 12 months.

before patient enrollment, and all patients or their guardians provided written informed consent. The study is registered at the *www.clinicaltrials.gov* under the identifier NCT01589978. An independent clinical events committee reviewed and adjudicated all death, MI, TVR, and target vessel ST events according to protocol definitions and for their relation to the PROMUS Element Plus stent. An independent angiographic core laboratory was used to confirm all site-reported cases of LSD; in addition, the core laboratory reviewed all reports of ST for potential LSD. Details of the Clinical Events Committee and the angiographic core laboratory are provided in Supplementary Table 1.

The statistical methods used in PE-Plus PAS are as follows: The overall sample size was driven by the TVF end point in the PLATINUM-like medically treated diabetic subset. The expected rate of TVF in the PLATINUM-like medically treated diabetic subset was 8.4%, based on results from the SPIRIT IV trial.[8] Given a performance goal of 12.6% (expected rate + delta = 8.4% + 4.2%) and a 1-sided 5% significance level, a minimum of 345 PLATINUM-like medically treated diabetic patients were required to provide ~80% power for TVF at 12 months. Per protocol, this required that the sample size comprised PLATINUM-like medically treated diabetic patients from the PE-PROVE study and the PE-Plus PAS. Assuming an attrition rate of no more than 3.5% at 12 months, 57 PLATINUM-like medically treated diabetic patients from PE-PROVE were projected to be available for TVF end point analysis. As a result, 288 PLATINUM-like medically treated diabetic patients were needed from the PE-Plus PAS to complete a total enrollment of 345 patients (n = 345 − 57 = 288). Based on the TAXUS Libertē post-approval study,[10] approximately 11.1% of those enrolled in PE-Plus were expected to be PLATINUM-like medically treated patients with diabetes; thus 2,595 total patients were required at 12 months to yield ~80% power in this prespecified diabetic subset. Assuming an attrition rate of no more than 3.5% in both the PLATINUM-like and PLATINUM-like medically treated diabetic subsets, a total enrollment of approximately 2,689 patients was required in the PE-Plus study. For the primary statistical hypothesis, the expected 12-month CD/MI rate was estimated at 2.2% based on data from the PLATINUM and the SPIRIT IV trials.[1,8] The performance goal is 3.2% using a delta of 1.0%. Given the performance goal and a 1-sided 5% significance level, approximately 1,706 PLATINUM-like patients were needed to provide at least 80% power to reject the null hypothesis.

Table 1
Baseline patient characteristics

Variable	PE-Plus − Overall (N=2,681)
Men	69.9% (1874/2,681)
Age (years)	63.7±11.1 (2,681) (28.0, 91.0)
Current Smoker	22.8% (610/2,681)
Medically Treated Diabetes Mellitus	32.9% (882/2,681)
Insulin-Requiring	13.8% (371/2,681)
Hyperlipidemia Requiring Medication	75.2% (2,016/2,681)
Hypertension Requiring Medication	77.5% (2,077/2,681)
Prior Cerebrovascular Accidents	4.2% (113/2,681)
Renal Disease	10.6% (283/2,681)
Peripheral Vascular Disease	11.2% (299/2,681)
Family History of Coronary Artery Disease	60.6% (1,625/2,681)
Prior Myocardial Infarction	52.6% (1,409/2,681)
Congestive Heart Failure	10.3% (275/2,681)
NYHA Classification	
I	2.2% (58/2,681)
II	2.9% (79/2,681)
III	1.8% (49/2,681)
IV	0.4% (12/2,681)
Stable Angina Pectoris	23.1% (620/2,681)
Unstable Angina Pectoris	50.2% (1,347/2,681)
Silent Myocardial Ischemia	5.6% (149/2,681)
Prior Percutaneous Coronary Intervention	43.2% (1,159/2,681)
Prior Coronary Artery Bypass Graft	17.0% (457/2,681)
Left ventricular ejection fraction Measured	86.9% (2,331/2,681)
Left ventricular ejection fraction (%)	53.711.2 (2,286) (5.0, 85.0)
Left ventricular ejection fraction ≤30%	5.7% (131/2,286)

Values are percent (count/sample size) or mean ± standard deviation (n) (min, max).
NYHA = New York Heart Association.

Clinical outcomes were evaluated as binary % or as Kaplan-Meier estimates with standard error from Greenwood's formula. Discrete variables were expressed as % (count/n) and continuous variables were expressed as mean ± SD (n). The primary end point and key secondary end point of TVF in PLATINUM-like medically treated patients with diabetes were assessed using a 1-sided, single binomial test to compare the observed rate against the performance goal and using the normal approximation of the test statistic. The performance goal was considered as met if the 1-sided upper 95% confidence bound for the observed binary rate was less than the performance goal. All analyses were conducted using SAS, version 9.0 or greater (SAS Institute, Cary, North Carolina).

Results

A total of 2,683 patients were enrolled at 52 clinical sites in the United States (Supplementary Table 2). Of these, 2

Table 2
Baseline angiographic characteristics

Event	N=3,605 Lesions
De Novo Lesion	90.3% (3,255/3,605)
Culprit Lesion for STEMI	11.8% (426/3,605)
In-stent Restenosis (DES)	5.1% (183/3,605)
In-stent Restenosis (BMS)	2.8% (102/3,605)
Ostial Lesion	4.6% (165/3,605)
Bifurcation Lesion	8.0% (288/3,605)
Chronic Total Occlusion	5.2% (187/3,605)
Thrombus Present	12.3% (442/3,605)
Reference Vessel Diameter (mm)	2.94 ± 0.51 (3,571)
Lesion Length (mm)	17.0 ± 10.3 (3,571)
Preprocedure %DS	86.7 ± 10.7 (3,604)
Moderate Vessel Tortuosity	10.0% (362/3,605)
Severe Vessel Tortuosity	4.1% (149/3,605)
Moderate or Severe Lesion Calcification	14.1% (509/3,605)
Location of Coronary Narrowing	
Right	32.3% (1,165/3,605)
Left Anterior Descending	37.1% (1,339/3,605)
Left Circumflex	23.5% (848/3,605)
Left Main	1.5% (54/3,605)
Bypass graft	5.5% (199/3,605)

Values are percent (count/sample size) or mean ± standard deviation (n).
%DS = percent diameter stenosis; BMS = bare metal stents; DES = drug-eluting stent; STEMI = ST-segment elevation myocardial infarction.

Table 3
Procedural characteristics

Event	N=2,681 Patients N=2,712 Procedures N=3,605 Lesions N=4,021 Stents
Emergent/Urgent Procedure	41.0% (1,113/2,712)
Number of Lesions Treated Per Patient	1.3 ± 0.6 (2,681)
≥3 Lesions	6.2% (166/2,681)
Number of Vessels Treated Per Patient	1.1 ± 0.4 (2,681)
≥3 Vessels	0.8% (21/2,681)
Stents Implanted Per Patient	1.5 ± 0.8 (2,681)
Stent Length (mm)	19.5 ± 7.7 (4,019)
Stent Diameter (mm)	2.87 ± 0.48 (4,021)
Stent Deployment Pressure (atm)	14.1 ± 3.5 (4,014)
Post-dilation Performed	55.6% (2,005/3,605)
Post-Procedure Target Lesion %DS	1.0 ± 5.6 (3,605)
Post-procedure TIMI flow 3	99.4% (3,583/3,605)
Clinical Procedural Success (Patient-based)	98.6% (2,644/2,681)
Technical Success (Lesion-based)	99.9% (3,605/3,609)

Values are percent (count/sample size) or mean ± standard deviation (n).
%DS = percent diameter stenosis.

patients did not have a stent implanted because of inability to cross the lesion and, per protocol, were ineligible for inclusion in the 12-month analysis. These 2 patients did not have any MACE through discharge.

Of the remaining 2,681 patients, 776 (29%) were considered PLATINUM like (Figure 2). At 1 year, 95% (2,535 of 2,681) of the patients had 12-month clinical follow-up available or had died; the predominant reason for lack of follow-up was a missed 12-month visit (n = 104).

Baseline patient and angiographic characteristics are listed in Tables 1 and 2, respectively; procedural characteristics are provided in Table 3. Clinical procedural success was 99%, and technical success was 99.9%. At hospital discharge, 96% of patients were on dual antiplatelet therapy, with 91% continuing dual antiplatelet therapy through 1 year (Table 4).

The primary end point of PE-Plus PAS compared clinical outcomes with a prespecified performance goal in selected patients from 3 studies. The primary end point, 12-month CD/MI tested in PLATINUM-like patients, was 2.12% for 862 patients enrolled in the PLATINUM WH/SV trials, 3.42% for 269 patients enrolled in PE-PROVE, and 0.81% for 776 patients enrolled in PE-Plus (Figure 3). In the combined analysis of 1,907 patients, CD/MI was 1.78% with an upper 1-sided 95% confidence limit of 2.28%, which was significantly less than the prespecified performance goal of 3.2%, thus meeting the criteria for noninferiority ($p < 0.001$).

For the secondary end point of 12-month TVF in PLATINUM-like patients with medically treated diabetes, 8.93% of patients from PE-PROVE (n = 59) and 3.26% of patients enrolled in PE-Plus (n = 293) experienced TVF (Figure 3). The overall rate of 12-month TVF in diabetic patients was 4.22% (upper 1-sided 95% confidence limit of 6.03%), which was significantly less than the prespecified performance goal of 12.6%, thus meeting the criteria for noninferiority ($p < 0.001$). Among PLATINUM-like patients without diabetes enrolled in the PE-Plus study, the 12-month rate of TVF was 2.6% (12 of 465; $p = 0.59$ vs PLATINUM-like patients with diabetes). To assess safety and efficacy in the broad, unselected patient population of PE-Plus PAS additional clinical end point rates at 12 months are provided in Table 5.

Two cases of LSD (0.05% [2 of 4,021]) were confirmed by the angiographic core laboratory at 12 months. In the first case, the distal end of a deployed 3.5 × 38-mm stent was longitudinally compressed on retrieval of a distal protection device. This was resolved using post-dilation angioplasty alone. In the second case, LSD occurred in the proximal end of a 2.75 × 28-mm stent on post-dilation. This was resolved by deployment of an additional stent. There were no associated adverse events with either case.

Multivariate baseline predictors of 12-month CD/MI and MACE are depicted in Figure 4. The most significant predictors of 12-month CD/MI were a history of renal disease or congestive heart failure. The most significant baseline predictors of 12-month MACE were a history of renal disease, PCI, and current smoking status (Figure 4).

Discussion

Everolimus-eluting stents (EES) have become a standard of comparison for drug-eluting stents, as evidenced in both direct and indirect (network) comparative analyses that have shown that EES are associated with the most favorable clinical outcomes among stents.[11–13] This study extends our understanding of platinum-chromium EES (PtCr-EES) to a broad, unselected patient population representative of "real-world" clinical practice, demonstrating a low incidence of CD/MI, TLR, and ST at 1 year. These low rates are confirmed by the observation that both the primary end point of 12-month CD/MI and the key secondary end point of TVF in diabetic patients were met, resulting in rates of

ARTICLE IN PRESS

Table 4
Antiplatelet medications

Medication	Discharge	6 Months	12 Months
Aspirin	97.4% (2,608/2,677)	96.7% (2,389/2,471)	95.9% (2,354/2,455)
Clopidogrel	67.5% (1,807/2,677)	70.4% (1,739/2,471)	69.4% (1,703/2,455)
Prasugrel	25.3% (676/2,677)	22.7% (561/2,471)	20.8% (510/2,455)
Ticagrelor	6.9% (185/2,677)	5.5% (136/2,471)	5.2% (127/2,455)
Ticlopidine	0.04% (1/2,677)	0.04% (1/2,471)	0.04% (0/2,455)
Dual Antiplatelet Therapy	96.1% (2,573/2,677)	95.4% (2,357/2,471)	91.3% (2,242/2,455)

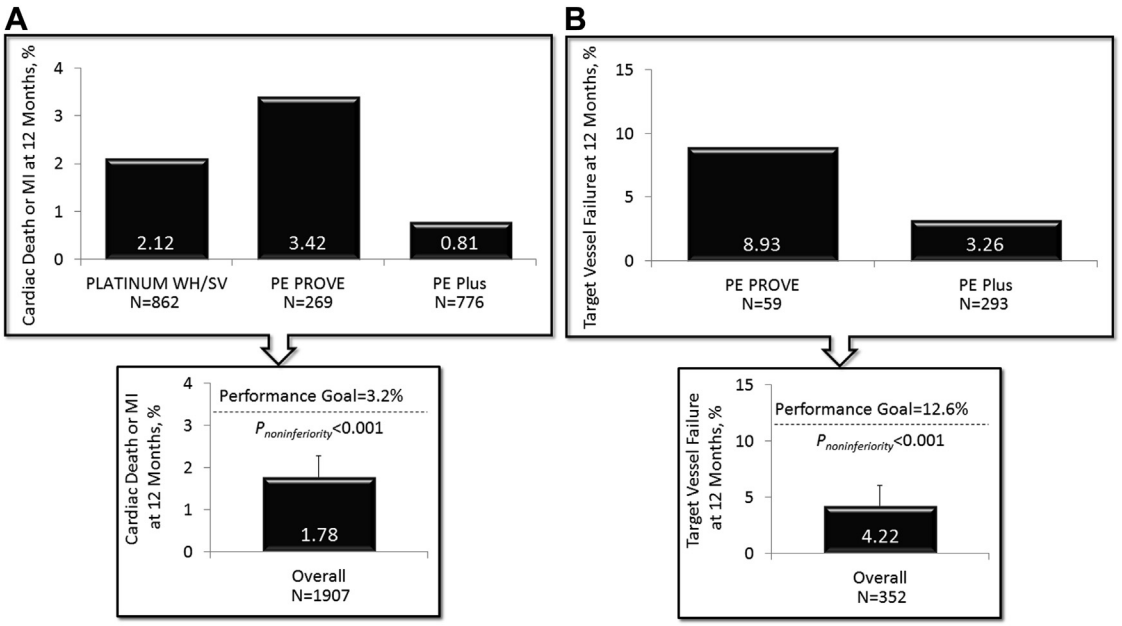

Figure 3. Primary end point and key secondary end point results at 12 months. *(A)* Cardiac death or MI at 12 months in PLATINUM-like patients; *(B)* TVF at 12 months in PLATINUM-like patients with medically treated diabetes.

1.8% and 4.2%, respectively (both p <0.001 vs the prespecified performance goals).

Despite greater clinical and lesion complexity, event rates in this post-approval registry compare well with those observed in the randomized, controlled PLATINUM Workhorse trial,[1] with approximately similar rates of MI and ST at 1 year. Compared with patients enrolled in the PLATINUM WH, the PE-Plus study did demonstrate higher rates of all-cause death, driven both by cardiovascular (1.4% PE-Plus vs 0.9% PLATINUM WH PtCr-EES arm) and noncardiovascular causes (0.9% PE-Plus vs 0.4% PLATINUM WH PtCr-EES arm) and increased TLR (3.5% for PE-Plus vs 1.9% for PLATINUM WH PtCr-EES arm). This is not unexpected given the notably higher rates of diabetes and unstable angina pectoris in the unselected PE-Plus study population (33% PE-Plus vs 22% PLATINUM WH PtCr-EES arm and 50% PE-Plus vs 24% PLATINUM WH PtCr-EES arm, respectively). The results from the PE-Plus study are also comparable with those observed in the PE-PROVE registry,[7] with very similar rates of MACE, cardiac death, and definite/probable ST. Interestingly, the PE-PROVE study reported a threefold higher rate of non-Q-wave MI (0.9% PE-Plus vs 3.2% PE-PROVE), which may be because of chance given that the PE-Plus study had an approximately twofold higher incidence of previous MI and unstable angina pectoris at baseline (53% PE-Plus vs 34% PE-PROVE and 50% PE-Plus vs 20% PE-PROVE, respectively), and both studies had similar protocol requirements for cardiac enzyme assessment.

Overall, the outcomes with PtCr-EES were favorable in patients treated across complex disease and indications. The 4.2% rate of 1-year TVF, defined in this analysis as TVR, MI, or death related to the target vessel, among PLATINUM-like patients with medically treated diabetes is difficult to place into context with other trials given a paucity of published reports of 1-year TVF in diabetic patients treated with EES. However, we note that the combined end point of all death/MI/TVR (regardless of relatedness to the target vessel) was 6.7% at 1 year in patients with medically treated diabetes in the PLATINUM WH PtCr-EES arm (Boston Scientific Corporation, data on file) and that the rate of 1-year MACE (defined as cardiac death, MI, or ischemia-driven TLR) in the SPIRIT IV randomized controlled trial was 6.4% in diabetic patients treated with EES.[14] In contrast, the combination of cardiac death, target vessel MI, and clinically indicated TLR was 11.2% in 215 patients treated with EES in the SPIRIT V Diabetic Study[15] and 11.0% among all diabetic patients

Table 5
Clinical outcomes at 12 months in the PE-Plus overall population

Event	N=2,681
Major Adverse Cardiac Events	6.9% (177/2,554)
Related to Study Stent	4.7% (119/2,554)
Cardiac Death or Myocardial Infarction	2.3% (59/2,554)
Related to Study Stent	1.8% (46/2,554)
Related to Target Vessel	2.0% (51/2,554)
Death	2.3% (60/2,554)
Cardiac Death	1.4% (37/2,554)
Related to Target Vessel	1.3% (33/2,554)
Noncardiac Death	0.9% (23/2,554)
Myocardial Infarction	1.1% (28/2,554)
Related to Study Stent	0.7% (17/2,554)
Related to Target Vessel	0.9% (23/2,554)
Q-Wave Myocardial Infarction	0.2% (5/2,554)
Non Q-Wave Myocardial Infarction	0.9% (23/2,554)
Target Vessel Revascularization	5.6% (142/2,554)
Target Lesion Revascularization	3.5% (90/2,554)
Target Vessel Failure	6.7% (170/2,554)
Target Lesion Failure	4.7% (119/2,554)
Academic Research Consortium	0.7% (19/2,554)
Stent Thrombosis (Definite/Probable)*	
0-1 Days	0.1% (2/2,681)
2-30 Days	0.3% (8/2,661)
31-365 Days	0.4% (10/2,615)
Longitudinal Stent Deformation†	0.05% (2/4,021)

Values are percent (count/sample size). Binary analysis.

Relatedness to study stent was adjudicated and determined by the Clinical Events Committee for each event.

Major Adverse Cardiac Events were defined as cardiac death, myocardial infarction, or target vessel revascularization; Target Vessel Failure was defined as target vessel revascularization, target vessel myocardial infarction, or death related to the target vessel. For the purposes of the analysis, if it could not be determined with certainty whether MI or death was related to the target vessel, then it was considered related by default.

ST = stent thrombosis.

* One patient reported 2 Stent Thrombosis events: one on day 20 and one on day 34 and is only counted once in the overall total.

† Site-reported and angiographic core lab-confirmed events; stent-based analysis.

(PLATINUM-like and non-PLATINUM like) in the PE-PROVE trial.[16]

In the PE-Plus study, we observed 2 reported incidences of LSD, neither of which was associated with adverse clinical sequelae. This is concordant with the results from the PE-PROVE registry, which also observed only 2 cases of LSD, both without clinical sequelae, among 1,679 implanted stents on independent angiographic review.[7] The incidence of LSD with the PtCr-EES stent is very low and generally not associated with adverse clinical events, as shown in a quantitative review of clinical trials of the PtCr-EES that had mandated angiographic follow-up.[17]

This study has several limitations that must be acknowledged. First, this was an open-label study with no active comparator, as is common for post-market evaluations. Second, the study was not powered for individual clinical end points at 1 year, although the similarity of the results to the randomized pivotal PLATINUM trial provides reassurance in this regard. Finally, a smaller proportion of PLATINUM-like patients with medically treated diabetes

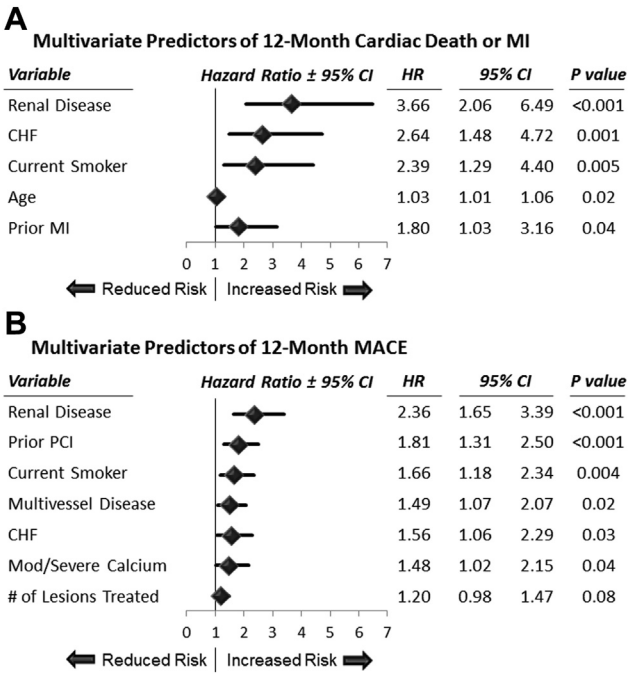

Figure 4. Multivariate predictors of *(A)* 12-month CD/MI and *(B)* 12-month MACE. mod/severe calcium = moderate or severe lesion calcification.

enrolled in PE-Plus than was anticipated in sample size calculations; however, statistical power for the diabetes subgroup comparison remains at ~80%.

Acknowledgment: The authors thank Vicki M. Houle, PhD, and Kristine Roy, PhD (Boston Scientific Corporation), for assistance in manuscript preparation and Songtao Jiang, MS (Boston Scientific Corporation), for statistical analysis.

Disclosures

Dr. Kandzari: Research/grant support: Abbott Vascular (NCT01205776, NCT01435031), Biotronik (NCT02389946), Boston Scientific Corporation (NCT01589978), Medtronic (NCT02439775, NCT02439749), and Medinol (NCT01995487); consulting/honoraria: Boston Scientific Corporation and Medtronic; Drs Christen, Allocco, and Dawkins: full-time employment and equity interest: Boston Scientific Corporation. All other authors report no conflicts of interest.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amjcard.2015.11.043.

1. Stone GW, Teirstein PS, Meredith IT, Farah B, Dubois CL, Feldman RL, Dens J, Hagiwara N, Allocco DJ, Dawkins KD; PLATINUM Trial Investigators. A prospective, randomized evaluation of a novel everolimus-eluting coronary stent: 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. *J Am Coll Cardiol* 2011;57:1700–1708.

ARTICLE IN PRESS

2. Meredith IT, Whitbourn R, Scott D, El-Jack S, Zambahari R, Stone GW, Teirstein PS, Starzyk RM, Allocco DJ, Dawkins KD. PLATINUM QCA: a prospective, multicentre study assessing clinical, angiographic, and intravascular ultrasound outcomes with the novel platinum chromium thin-strut PROMUS Element everolimus-eluting stent in de novo coronary stenoses. *EuroIntervention* 2011;7:84−90.
3. Saito S, Hagiwara N, Seki A, Igarashi K, Muramatsu T, Yajima J, Yokoi H, Nakamura M, Fujii K, Isshiki T, Stone GW, Teirstein PS, Meredith IT, Allocco DJ, Dawkins KD. Japanese and non-Japanese patient outcomes in the PLATINUM randomized trial comparing the PROMUS Element and XIENCE V everolimus-eluting stents. *J Cardiol* 2014;64:105−112.
4. Teirstein PS, Meredith IT, Feldman RL, Rabinowitz AC, Cannon LA, Lee TC, Dens J, Dubois CL, Mooney MR, Pompili VJ, Saito S, Allocco DJ, Dawkins KD, Stone GW. Two-year safety and effectiveness of the platinum chromium everolimus-eluting stent for the treatment of small vessels and longer lesions. *Catheter Cardiovasc Interv* 2014;85:207−215.
5. PROMUS Element Plus Everolimus-eluting Platinum Chromium Coronary Stent System Directions for Use, Boston Scientific, 2011.
6. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, Chambers CE, Ellis SG, Guyton RA, Hollenberg SM, Khot UN, Lange RA, Mauri L, Mehran R, Moussa ID, Mukherjee D, Nallamothu BK, Ting HH. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation* 2011;124:2574−2609.
7. Thomas MR, Birkemeyer R, Schwimmbeck P, Legrand V, Moreno R, Briguori C, Werner N, Bramucci E, Ungi I, Richardt G, Underwood PL, Dawkins KD. One-year outcomes in 1010 unselected patients treated with the PROMUS element everolimus-eluting stent: the multicentre PROMUS element European Post-Approval surveillance study. *EuroIntervention* 2015;10:1267−1271.
8. Stone GW, Rizvi A, Newman W, Mastali K, Wang JC, Caputo R, Doostzadeh J, Cao S, Simonton CA, Sudhir K, Lansky AJ, Cutlip DE, Kereiakes DJ; SPIRIT IV Investigators. Everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease. *N Engl J Med* 2010;362:1663−1674.
9. Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, McFadden E, Lansky A, Hamon M, Krucoff MW, Serruys PW; Academic Research Consortium. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007;115:2344−2351.
10. Lee DP, Paulus R, Giri K, Carr J, Baran KW, Hassel D, Winters KJ, Christen T, Dawkins KD, Garratt KN. Primary Endpoint Results of the TAXUS Libertē Post Approval Study. TCT-167. San Francisco: Transcatheter Cardiovascular Therapeutics, 2013.
11. Palmerini T, Biondi-Zoccai G, Della Riva D, Stettler C, Sangiorgi D, D'Ascenzo F, Kimura T, Briguori C, Sabate M, Kim HS, De Waha A, Kedhi E, Smits PC, Kaiser C, Sardella G, Marullo A, Kirtane AJ, Leon MB, Stone GW. Stent thrombosis with drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *Lancet* 2012;379:1393−1402.
12. Kang SH, Park KW, Kang DY, Lim WH, Park KT, Han JK, Kang HJ, Koo BK, Oh BH, Park YB, Kandzari DE, Cohen DJ, Hwang SS, Kim HS. Biodegradable-polymer drug-eluting stents vs. bare metal stents vs. durable-polymer drug-eluting stents: a systematic review and Bayesian approach network meta-analysis. *Eur Heart J* 2014;35:1147−1158.
13. Palmerini T, Benedetto U, Biondi-Zoccai G, Della Riva D, Bacchi-Reggiani L, Smits PC, Vlachojannis GJ, Jensen LO, Christiansen EH, Berencsi K, Valgimigli M, Orlandi C, Petrou M, Rapezzi C, Stone GW. Long-term safety of drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. *J Am Coll Cardiol* 2015;65:2496−2507.
14. Kereiakes DJ, Cutlip DE, Applegate RJ, Wang J, Yaqub M, Sood P, Su X, Su G, Farhat N, Rizvi A, Simonton CA, Sudhir K, Stone GW. Outcomes in diabetic and nondiabetic patients treated with everolimus- or paclitaxel-eluting stents: results from the SPIRIT IV clinical trial (Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System). *J Am Coll Cardiol* 2010;56:2084−2089.
15. Grube E, Chevalier B, Guagliumi G, Smits PC, Stuteville M, Dorange C, Papeleu P, Kaul U, Dzavik V. The SPIRIT V diabetic study: a randomized clinical evaluation of the XIENCE V everolimus-eluting stent vs the TAXUS Liberte paclitaxel-eluting stent in diabetic patients with de novo coronary artery lesions. *Am Heart J* 2012;163:867−875 e1.
16. Moreno R, Thomas MR, Birkemeyer R, Schwimmbeck P, Legrand V, Briguori C, Werner N, Bramucci E, Ungi I, Richardt G, Underwood P, Dawkins K. One-year Outcomes in 1010 Unselected Patients Treated with the PROMUS Element Everolimus-eluting Stent: The Multicenter PROMUS Element European Post-Approval Surveillance Study, EuroPCR 2013; Paris, France.
17. Kereiakes DJ, Popma J, Cannon L, Kandzari D, Kimmelstiel C, Meredith IT, Teirstein PS, Verheye S, Allocco DJ, Dawkins KD, Stone G. Longitudinal stent deformation: quantitative coronary angiographic analysis from the PERSEUS and PLATINUM randomised controlled clinical trials. *EuroIntervention* 2012;8:187−195.