International Journal of Cardiology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

# The Promus Premier everolimus-eluting platinum chromium stent with durable polymer evaluated in a real world all-comer population in Rotterdam cardiology hospital (the P-SEARCH registry)

Miguel E. Lemmert [1], Nicolas M. van Mieghem [1], Robert-Jan van Geuns [1], Roberto Diletti [1], Rutger J. van Bommel [1], Ron T. van Domburg [1], Peter P. de Jaegere [1], Evelyn Regar [1], Felix Zijlstra [1], Eric Boersma [1], Joost Daemen *[,1]

*Thoraxcenter, Erasmus Medical Center, Rotterdam, Netherlands*

ARTICLE INFO

*Article history:*
Received 23 November 2016
Accepted 13 March 2017
Available online xxxx

*Keywords:*
Drug eluting stent(s)
Platinum-chromium stent
Cobalt-chromium stent
Everolimus-eluting stent
All-comer registry

ABSTRACT

*Background:* A new-generation everolimus eluting platinum-chromium stent (EePCS), offering improved radial strength, radiopacity and conformability compared to everolimus-eluting cobalt-chromium stents (EeCCS), was evaluated with regard to safety and efficacy in an all-comer cohort.
*Methods:* A total of 1000 consecutive all-comer patients (including acute coronary syndrome, multivessel disease, calcified lesions) treated with an EePCS (Promus Premier™, Boston Scientific, Natick, Massachusetts) from May 2013 to October 2014 were compared to 1000 consecutive patients treated with an EeCCS (Xience Prime™, Abbott Vascular, Santa Clara, California) from April 2012 to May 2013. Patients were clinically followed for 1 year.
*Results:* Mean age was 66 ± 12 years with diabetes in 20.7%, previous infarction in 22.7%, and ACS as the indication in 71.2% of patients. The mean number of stents per patient was 1.8 ± 1.13. Total stented length was 35 ± 25 mm. Lesion classification was B2/C in 73.9% of patients. At 1 year the primary endpoint of major adverse cardiac events (all-cause mortality, myocardial infarction [MI], ischemia-driven target vessel revascularization [TVR]) was reached in 11.7% in the EePCS cohort and 10.9% in the EeCCS cohort (adjusted HR 1.01 [0.77–1.33]; p = 0.95). No significant differences were noted in the individual clinical endpoints all-cause mortality (6.8% versus 6.4%), MI (2.2% versus 2.3%), and TVR (4.3% versus 3.7%) in the respective EePCS and EeCCS cohorts. Stent thrombosis occurred in 0.8% and 1.0% respectively.
*Conclusions:* In all-comer patients undergoing percutaneous coronary intervention, the use of EePCS was associated with similar 1-year clinical outcome as compared to EeCCS.



## 1. Introduction

Percutaneous coronary intervention (PCI) has become increasingly safe with good peri-procedural and long-term outcomes due to continuous improvements in interventional technology. Compared to bare-metal stents, drug-eluting stents (DES) have reduced in-stent restenosis, as demonstrated by multiple randomized controlled trials and large real-world registries [1,2].

The continuous improvement of DES focuses on several aspects, including the stent platform used. The latest evolution regarding alloys is the use of platinum-chromium, offering thin struts but higher radiopacity, better deliverability and conformability and superior radial and longitudinal strength than cobalt-chromium [3–5].

Recent studies demonstrated non-inferiority of a new-generation everolimus-eluting platinum-chromium stent (EePCS) as compared to a zotarolimus-eluting cobalt-chromium stent and an everolimus-

*Abbreviations:* ACC, American College of Cardiology; ACS, Acute coronary syndrome; AHA, American Heart Association; CABG, Coronary artery bypass graft; CK-MB, Creatine kinase-MB fraction; CTO, Chronic total occlusion; DES, Drug-eluting stent; DM, Diabetes mellitus; EeCCS, Everolimus-eluting cobalt-chromium stent; EePCS, Everolimus-eluting platinum-chromium stent; HR, Hazard ratio; IDDM, Insulin-dependent diabetes mellitus; LAD, Left anterior descending coronary artery; LCx, Left circumflex coronary artery; LM, Left main coronary artery; MACE, Major adverse cardiac events; MI, Myocardial infarction; PCI, Percutaneous coronary intervention; RCA, Right coronary artery; SA, Stable angina; SD, Standard deviation; ST, Stent thrombosis; TIMI, Thrombolysis In Myocardial Infarction; TLR, Target-lesion revascularization; TVR, Target-vessel revascularization; UA, Unstable angina.

* Corresponding author at: Thoraxcenter, Ad-342, 's-Gravendijkwal 230, 3015, CE, Rotterdam, Netherlands.
*E-mail address:* j.daemen@erasmusmc.nl (J. Daemen).

[1] This author takes responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

http://dx.doi.org/10.1016/j.ijcard.2017.03.054
0167-5273/

eluting cobalt-chromium stent (EeCCS) in both simple and more complex patient cohorts [6–8]. The most commonly used EePCS in these trials was subject to concerns in terms of longitudinal stent deformation, theoretically predisposing to future adverse events [9]. Therefore, a next-generation EePCS was released with 4 connectors between stent hoops, as opposed to the earlier generation's 2 connectors.

The objective of the present study is to compare the 1-year clinical outcome of this latest-generation EePCS versus an EeCCS in an all-comer cohort, without pre-specified exclusion criteria.

## 2. Methods

### 2.1. Study design and patient cohorts

This is a single-center prospective all-comer cohort study with two periods of exclusive use of either the EePCS or the EeCCS. Without exclusion criteria, between May 2013 and October 2014, 1000 consecutive patients presenting with acute coronary syndrome (ST-elevation myocardial infarction [STEMI] or non-ST-elevation acute coronary syndrome [NSTE-ACS]) or stable angina were treated with Promus Premier® stents (Boston Scientific, Natick, MA), constituting the EePCS cohort. These patients were compared to a historical EeCCS cohort of 1000 consecutive patients treated with Xience Prime ® stents (Abbott Vascular, Santa Clara, CA) from April 2012 to May 2013. One-year clinical follow-up data were collected. This study was performed in accordance with the Declaration of Helsinki and was not subject to the Dutch Medical Research Involving Human Subjects Act. Therefore, approval from the local research ethics committee to conduct this prospective follow-up study was not required at the time of enrolment. All patients consented to participation in this study by returning the questionnaire.

### 2.2. Study stents

The Xience Prime cobalt-chromium stent platform (Abbott Vascular, Santa Clara, CA, USA) has a strut thickness of 81 μm and is coated with a formulation containing everolimus embedded in a non-erodible polymer.

The Promus Premier everolimus-eluting platinum-chromium stent platform (Boston Scientific, Natick, MA, USA) also has a strut thickness of 81 μm and a non-erodible polymer loaded with 1 μg/mm$^2$ of everolimus. Compared to the earlier-generation Promus Element stent with 2 stent hoop connectors, the Promus Premier has 2 additional connectors at the proximal and distal sides to increase the longitudinal robustness.

### 2.3. Procedures and post-intervention medication

Baseline, clinical and procedural patient characteristics were prospectively entered into a dedicated database. Procedures were performed under heparin 70–100 units/kg in order to achieve an activated clotting time of >250 s.

Patients were treated in accordance with European Society of Cardiology guidelines [10]. Patients with stable angina were prescribed aspirin plus clopidogrel 75 mg/day (after a loading dose of 600 mg before or during the coronary interventions). Patients with acute coronary syndromes, including unstable angina, were prescribed aspirin plus either prasugrel 10 mg (after a loading dose of 60 mg) or ticagrelor 90 mg b.i.d. (after a loading dose of 180 mg). All patients were advised to remain on P2Y12 inhibitors for 12 months and on aspirin indefinitely. Administration of peri-procedural glycoprotein IIb/IIIa inhibitors was at the operator's discretion, as was the choice of vascular access site, with the notion that, during the inclusion period, there was a shift towards standard radial approach in our center. There was no mandated angiographic follow-up.

### 2.4. Baseline characteristics

Hypertension was defined as a blood pressure ≥140 mm Hg systolic or ≥90 mm Hg diastolic or the current use of antihypertensive medication. Hypercholesterolemia was classified as a total serum cholesterol level ≥6.2 mmol/l or the use of lipid lowering drugs. Diabetes was defined as treatment with either an oral hypoglycemic agent, insulin, or through diet. Clinically present cardiogenic shock was defined as a systolic blood pressure of <90 mm Hg for at least 30 min or the need for positive inotropes [11].

### 2.5. Procedural characteristics

Coronary artery lesion characteristics were classified according to the American College of Cardiology/American Heart Association (ACC/AHA) lesion classification [12]. Lesion characteristics included bifurcation lesions, presence of thrombotic, aorto-ostial and calcified lesions, presence and treatment of multivessel disease and treatment of chronic total occlusions (CTOs). Procedural characteristics include femoral or radial approach, total number of stents implanted, average stent diameter and total stented length. Angiographic success was defined as the achievement of <30% diameter stenosis (visual assessment) and Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow in all lesions intended to treat.

### 2.6. Endpoint definitions and clinical follow-up

The primary endpoint consisted of major adverse cardiac events (MACE), defined as a composite of death from any cause, any myocardial infarction (MI), or ischemia-driven target vessel revascularization (TVR). Secondary endpoints were cardiac death, target lesion revascularization (TLR), MI and stent thrombosis (ST).

Survival data for all patients were obtained from the municipal civil registry. A questionnaire was sent to all living patients with specific queries on rehospitalization and MACE. As the principal regional cardiac referral center, most repeat revascularizations (percutaneous or surgical) are usually performed at our institution and recorded prospectively in our database. For patients who suffered an adverse event at another center, medical records or discharge letters from the other institutions were systematically reviewed. General practitioners and referring physicians were contacted for additional information if necessary. Any death due to a proximate cardiac cause, unwitnessed death or death of unknown cause, was classified as cardiac death [13]. TVR was defined as a re-intervention driven by any lesion located in the same epicardial vessel. TLR was defined as a re-intervention of the treated segment within 5 mm proximal or distal to the stent [13]. MI at follow-up was diagnosed by a rise in creatine kinase-MB fraction (CK-MB) of 3 times the upper limit of normal, according to American Heart Association/American College of Cardiology guidelines [13]. Information on periprocedural MI was available for patients with stable angina and was diagnosed by a rise in cardiac markers of 5 times the upper limit of normal, according to the European Society of Cardiology's third universal definition [14]. ST was defined as angiographically defined thrombosis within the stent or within 5 mm proximal or distal to the stent with TIMI grade 0 or 1 flow or the presence of a flow limiting thrombus, accompanied by acute symptoms [15]. The timing of ST was categorized as early (within 30 days after implantation) or late (between 30 days and 1 year) [13].

### 2.7. Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD). Categorical variables are expressed as percentages. For comparison of continuous variables, a Student's *t*-test for normally distributed data or a Mann-Whitney *U* test for non-normally distributed data was used. For comparison of categorical variables the Pearson's Chi-Square test was used. All statistical tests are 2-tailed. The incidence of events over time was studied with the use of the Kaplan-Meier method, whereas log-rank tests were applied to evaluate differences between the treatment groups. Patients lost to follow-up were considered at risk until the date of last contact, at which point they were censored. Cox proportional-hazards regression analyses were applied to further study treatment effects, adjusting for potential confounders. Variables with $p < 0.10$ in the univariate analyses and variables considered clinically relevant for each specific endpoint were entered in the multivariate Cox proportional hazards models. Final results are presented as adjusted hazard ratios with 95% confidence interval. Statistical analysis was performed using SPSS Statistics version 22.0 (IBM, Armonk, NY, USA). The authors take responsibility for the integrity of the data and the accuracy of the analyses.

## 3. Results

### 3.1. Baseline and procedural characteristics

Baseline and procedural characteristics are depicted in Table 1. Mean age was higher in the EePCS group than in the EeCCS group (66.9 [SD 11.8] and 64.9 [SD 12.0] years; $p < 0.001$). Patients in the EePCS group were less frequently male (68.8% and 73.2%; $p = 0.03$), with less hypercholesterolemia (43.1% and 48.0%; $p = 0.03$) and current smoking (21.4% and 27.0%; $p = 0.003$). EePCS patients less frequently had an acute STEMI as the indication for their PCI (28.9% and 33.1%; $p = 0.04$). Chronic renal failure was more prevalent among EePCS patients (respectively 25.7% and 20.4%; $p = 0.005$).

Regarding procedural characteristics, EePCS patients less often received treatment of the right coronary artery (33.8% and 38.3%; $p = 0.04$) and CTOs (4.3% and 6.3%; $p = 0.046$), but more often received treatment for bifurcation lesions (12.2% and 8.2%; $p = 0.003$). EePCS patients less often received stents with a diameter of ≤2.5 mm (15.3% and 21.6%; $p < 0.001$) and had a larger average stent diameter (3.1 [SD 0.4] and 3.0 [SD 0.5] mm; $p = 0.01$). Furthermore, EePCS patients had a lower number of implanted stents (1.7 [SD 1.0] and 1.9 [SD 1.2]; $p = 0.01$). Occurrence of periprocedural MI, known for patients with stable angina, did not differ between the EePCS and EeCCS group (3.9% and 2.0%; $p = 0.30$) (not shown in table). In the total cohort radial access was used in 1147 patients (57.4%) with a higher percentage of patients with radial access in the EePCS as compared to the EeCCS group (68.0% and 46.8% respectively; $p < 0.001$), concurrent with the shift towards a standard radial approach in our center.

Please cite this article as: M.E. Lemmert, et al., The Promus Premier everolimus-eluting platinum chromium stent with durable polymer evaluated in a real world all-comer population ..., Int J Cardiol (2017), http://dx.doi.org/10.1016/j.ijcard.2017.03.054