JACC: CARDIOVASCULAR INTERVENTIONS VOL. 11, NO. 5, 2018

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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ISSN 1936-8798 https://doi.org/10.1016/j.jcin.2017.11.031

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)

This investigator-initiated study was equally supported by Boston Scientific and Medtronic. Dr. von Birgelen has reported that the research department of Thoraxcentrum Twente has received institutional research grants provided by AstraZeneca, Biotronik, Boston Scientific, and Medtronic. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received October 13, 2017; revised manuscript received November 15, 2017, accepted November 21, 2017.