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Biodegradable Polymer Biolimus-Eluting Stents Versus Durable Polymer Everolimus-Eluting Stents in Patients With Coronary Artery Disease

Final 5-Year Report From the COMPARE II Trial (Abluminal Biodegradable Polymer Biolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Stent)

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ABSTRACT

OBJECTIVES This analysis investigates the 5-year outcomes of the biodegradable polymer biolimus-eluting stent (BP-BES) and durable polymer everolimus-eluting stent (DP-EES) in an all-comers population undergoing percutaneous coronary intervention.

BACKGROUND Recent 1- and 3-year results from randomized trials have indicated similar safety and efficacy outcomes of BP-BES and DP-EES. Whether benefits of the biodegradable polymer device arise over longer follow-up is unknown. Moreover, in-depth, prospective, long-term follow-up data on metallic drug-eluting stents with durable or biodegradable polymers are scarce.

METHODS The COMPARE II trial (Abluminal Biodegradable Polymer Biolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Stent) was a prospective, randomized, multicenter, all-comers trial in which 2,707 patients were randomly allocated (2:1) to BP-BES or DP-EES. The pre-specified endpoint at 5 years was major adverse cardiac events, a composite of cardiac death, nonfatal myocardial infarction, or target vessel revascularization.

RESULTS Five-year follow-up was available in 2,657 patients (98%). At 5 years, major adverse cardiac events occurred in 310 patients (17.3%) in the BP-BES group and 142 patients (15.6%) in the DP-EES group ($p = 0.26$). The rate of the combined safety endpoint all-cause death or myocardial infarction was 15.0% in the BP-BES group versus 14.8% in the DP-EES group ($p = 0.90$), whereas the efficacy measure target vessel revascularization was 10.6% versus 9.0% ($p = 0.18$), respectively. Interestingly, definite stent thrombosis rates did not differ between groups (1.5% for BP-BES vs. 0.9% for DP-EES; $p = 0.17$).

CONCLUSIONS The 5-year analysis comparing biodegradable polymer-coated BES and the durable polymer-coated EES confirms the initial early- and mid-term results regarding similar safety and efficacy outcomes in this all-comers percutaneous coronary intervention population. (J Am Coll Cardiol Intv 2017;■:■-■) © 2017 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

BES = biolimus-eluting stent(s)

BP-BES = biodegradable polymer biolimus-eluting stent(s)

DES = drug-eluting stent(s)

DP-EES = durable polymer everolimus-eluting stent(s)

EES = everolimus-eluting stent(s)

MACE = major adverse cardiac event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

SES = sirolimus-eluting stent(s)

STEMI = ST-segment elevation myocardial infarction

TVR = target vessel revascularization

Different approaches have been applied to address the risk of very late adverse events such as stent thrombosis in patients treated with permanent polymer drug-eluting coronary devices. One innovation was to replace the permanent polymer responsible for the drug release of the drug-eluting stent (DES) platform with a biodegradable polymer, because durable polymers of first-generation DES have been linked to enduring inflammatory response at implantation site that might lead to delayed re-endothelialization, late-acquired malapposition, and neointimal proliferation (1–3).

Early results from randomized trials have underlined the safety benefits of biodegradable polymer-coated DES when compared with first-generation DES in terms of a significant reduction in very late stent thrombosis events and associated composite clinical outcomes, including the primary endpoint cardiac death, myocardial infarction (MI), and clinically indicated target vessel revascularization (TVR) (4).

The purpose of the COMPARE II (Abluminal Biodegradable Polymer Biolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Stent; NCT01233453) trial was to compare the biodegradable polymer-coated biolimus-eluting stent (BP-BES) (Nobori, Terumo, Tokyo, Japan) to the newer-generation durable polymer-coated everolimus-eluting stent (DP-EES) (Xience V or Prime, Abbott Vascular, Santa Clara, California, or Promus, Boston Scientific, Natick, Massachusetts) in an all-comers percutaneous coronary intervention (PCI) population. Initial early- and mid-term reports from the COMPARE II and NEXT (NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-eluting Stent Trial) trials showed similar outcomes of BP-BES compared with DP-EES up to 3 years (5–7). However, potential benefits of the BP-BES are expected over a long-term period. The present analysis displays the final 5-year results of the COMPARE II trial.

METHODS

The COMPARE II trial is an investigator-initiated, multicenter, open-label, randomized, all-comers trial that assigned patients undergoing PCI in a 2:1 fashion to either biolimus-eluting stents (BES) (316L stainless steel stent with 120-μm strut thickness coated abluminally with biodegradable polymer poly-lactic acid, eluting the drug Biolimus A9/Nobori, Terumo) or everolimus-eluting stents (EES) (cobalt or platinum chromium metallic stent with a strut thickness of 81 μm coated with a durable fluoropolymer, eluting the drug everolimus/Xience V or Xience Prime, Abbot Vascular, or Promus, Boston Scientific, respectively). Patients were followed for 5 years after index procedure. A detailed description of study and procedural methodologies has been published previously (6).

The study complied with the CONSORT 2010 Statement of Declaration of Helsinki and was approved by all the institutional ethics committees of all participating centers. Patients were evaluated at 1, 6, 12, 24, 36, and 60 months at the outpatient clinic or by post, e-mail, or telephone regarding medication regime and adverse events; whenever required, general practitioners, medical specialists, or hospitals were contacted to collect further information. The study protocol-pre-specified composite endpoint at 5 years was major adverse cardiac events (MACE) defined as cardiac death, nonfatal MI, or TVR.

STATISTICAL ANALYSIS. The study was designed as a noninferiority trial at 1 year (6). The current analysis at 5-year follow-up, including subgroup analysis across clinically relevant subgroups, was pre-specified as secondary endpoint per protocol. Categorical variables are presented as numbers and percentages, and were compared with the Fisher exact test, due to the low prevalence of some baseline variables. Continuous variables were expressed as mean ± SD or medians with interquartile ranges. Continuous variables were compared using the Wilcoxon rank sum test. All analyses were performed according to the intention-to-treat principle. Time to the respective endpoint was analyzed according to the Kaplan-Meier method and the log-rank test was applied to compare the incidence of endpoints between groups. The landmark analysis used the 1-year landmark, thus patients who had experienced the event of interest during the first year following index procedure were excluded from analysis.

All p values were 2-sided, and a p value of <0.05 was regarded as statistically significant. SAS version 8.02 (SAS Institute, Cary, North Carolina) was used for analysis.

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