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Safety and Effectiveness of the Endeavor Zotarolimus-Eluting Stent in Real-World Clinical Practice

12-Month Data From the E-Five Registry

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Objectives The E-Five registry was designed to evaluate the safety and effectiveness of the Endeavor zotarolimus-eluting stent (ZES) (Medtronic CardioVascular, Santa Rosa, California) for the treatment of coronary artery stenosis across a wide range of patients treated in real-world clinical practice settings.

Background Early clinical trials with the Endeavor ZES have demonstrated low rates of target lesion revascularization with a favorable safety profile including low late stent thrombosis with up to 4 years of follow-up. A clinical registry was designed to complement controlled trial data by examining a large patient population, including high-risk patient subsets.

Methods The E-Five registry is a prospective, nonrandomized, multicenter global registry conducted at 188 centers worldwide. Adult patients (n = 8,314) with coronary artery disease who underwent single-vessel or multivessel percutaneous coronary intervention were enrolled. The primary end point was the rate of major adverse cardiac events (MACE) at 12 months. A secondary analysis stratified patients by standard versus extended-use clinical and lesion characteristics.

Results Overall 12-month outcome rates were MACE 7.5%; cardiac death 1.7%; myocardial infarction (all) 1.6%; target lesion revascularization 4.5%; and stent thrombosis (Academic Research Consortium definite and probable) 1.1%. The 12-month MACE rates were 4.3% and 8.6% for standard- and extended-use patients, respectively ($p < 0.001$).

Conclusions This large, international multicenter registry provides important information regarding the long-term safety and efficacy of the Endeavor ZES across standard and extended-use patients in the real-world setting. Rates of MACE and measures of safety including cardiac death, myocardial infarction, and stent thrombosis were low and consistent with pooled results of clinical trials.
(E-Five Registry: A World-Wide Registry With The Endeavor Zotarolimus Eluting Coronary Stent [eFive Registry]; NCT00623441) (J Am Coll Cardiol Intv 2009;2:1227–35) © 2009 by the American College of Cardiology Foundation

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Results from multiple randomized trials demonstrate that drug-eluting stents (DES) significantly reduce rates of restenosis and target lesion revascularization (TLR) in patients with symptomatic coronary artery disease when compared with bare-metal stents (BMS) (1–4). Although concerns have been raised about the safety of DES due to

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apparent increases in late stent thrombosis, the clinical benefits seem to outweigh the risks (5). Experience with DES now extends to patients outside of controlled clinical trials, allowing for the inclusion of patients with diverse characteristics and more complex clinical or angiographic presentations, such as diabetes, multivessel disease, acute myocardial infarction (MI), or long lesions, as is often seen in real-world practice settings.

Abbreviations and Acronyms

ARC = Academic Research Consortium
BMS = bare-metal stent(s)
CEC = clinical events committee
CK-MB = creatine kinase-myocardial band
DES = drug-eluting stent(s)
MACE = major adverse cardiac events
MI = myocardial infarction
PCI = percutaneous coronary intervention
PES = paclitaxel-eluting stent(s)
SES = sirolimus-eluting stent(s)
TLR = target lesion revascularization
TVF = target vessel failure
TVR = target vessel revascularization
ZES = zotarolimus-eluting stent(s)

Clinical registries are excellent complements to randomized controlled studies because they provide insight into the performance of DES in broader patient populations as well as special patient subsets. The E-Five registry is a prospective, nonrandomized, multicenter global registry conducted at 188 centers in Europe, Asia/Pacific, and Latin America designed to evaluate the safety and effectiveness of the Endeavor zotarolimus-eluting stent (ZES) (Medtronic CardioVascular, Santa Rosa, California) in routine treatment of patients with coronary artery stenosis, including patients with clinical characteristics or lesion types that are often excluded from randomized controlled trials (6). The registry includes over 8,000 adult patients who underwent single-vessel or multivessel percutaneous coronary intervention (PCI). The primary end point was the rate of major adverse cardiac events (MACE) at 12 months (6).

The Endeavor ZES received Conformité Européenne (CE) marking in August 2005 and U.S. Food and Drug Administration approval in February 2008. The safety and efficacy of the Endeavor ZES has been evaluated in a number of clinical trials, and the results consistently show low rates of angiographic restenosis and repeat revascularization as well as a favorable safety profile, with a low rate of late stent thrombosis beyond 12 months of follow-up (4,7–12).

Preliminary 30-day data for 1,989 patients enrolled in the E-Five registry were published in 2007 (6). The acute procedure success rate was 98.6%, which is comparable with procedure success rates observed in previous Endeavor ZES clinical trials. The 30-day rate of MACE in these patients was 1.7%, which is also comparable with 30-day rates of MACE observed in previous Endeavor clinical trials.

This report describes 12-month safety and clinical data from the E-Five registry for all patients in the registry and further examines the outcomes among patients with clinical and lesion characteristics similar to those enrolled in randomized clinical trials (standard-use group) compared with patients with more complex clinical (e.g., acute MI) and lesion (e.g., bifurcation, left main) characteristics (extended-use group) (Fig. 1).

Methods

Study design and objectives. The E-Five registry is a prospective, nonrandomized, multicenter registry conducted at 188 centers in Europe, Asia/Pacific, and Latin America. The registry includes 8,314 adult patients who underwent single-vessel or multivessel PCI. The primary objective of the E-Five registry was to evaluate the safety and overall clinical performance of the Endeavor ZES (Medtronic CardioVascular) in real-world patients who required stent implantation. The secondary objective was to assess the event rate in patient subgroups known to have a higher risk of MACE, such as those with diabetes mellitus, small vessels, and long lesions.

Study population and protocol. All patients with coronary artery lesions suitable for stenting were eligible for recruitment in the registry. Consecutive patients for whom implantation with an Endeavor ZES was intended were enrolled at the time of stent introduction into the guiding catheter. The registry population included a large number of patients with clinical and lesion characteristics that did not fit the standard-use criteria of previous clinical trials and thus are included in an extended-use group. The extended-use group was defined as patients with a baseline acute MI (within 72 h), left main stenting, saphenous vein grafts, in-stent restenosis, bifurcated or ostial lesions, severe tortuosity, multivessel stenting, moderate/severe calcification, reference vessel diameter <2.5 mm or >3.5 mm, lesion length >27 mm, or moderate or severe renal impairment. All other patients were classified as standard use.

Patients were permitted to have 1 or more Endeavor ZES implanted, and implantation of BMS or other DES was allowed if the investigators deemed it beneficial.

Before stent implantation, all patients received daily aspirin per their physician's usual practice and either clopidogrel 75 mg/day for 3 days before the procedure or a preprocedural loading dose of clopidogrel (at least 300 mg). The recommended maintenance regimen was clopidogrel