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1-Year Results of the REMEDEE Registry

Clinical Outcomes After Deployment of the Abluminal Sirolimus-Coated Bioengineered (Combo) Stent in a Multicenter, Prospective All-Comers Registry

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ABSTRACT

OBJECTIVES This registry evaluated the safety and clinical outcomes of the Combo stent in an all-comers population in routine clinical practice. We report 1-year results.

BACKGROUND Limitations of current generation drug-eluting stents (DES) are 3-fold: stent thrombosis, neoatherosclerosis related to impaired healing, and repeat revascularization due to (late-) in-stent restenosis. The Combo stent combines an abluminal biodegradable coating eluting sirolimus and a luminal anti-$CD34^{+}$ antibody layer to attract endothelial progenitor cells in order to promote vessel healing, thus preventing neointima formation and restenosis.

METHODS The REMEDEE (Randomized study to Evaluate the safety and effectiveness of an abluMinal sirolimus coatED bio-Engineered StEnt) post-market registry was an international, multicenter, prospective trial that evaluated clinical outcomes after deployment of the Combo stent, in an all-comers population of patients treated with a Combo stent in the setting of routine clinical care. Clinical endpoints were target lesion failure (TLF), defined as a composite of cardiac death, nonfatal myocardial infarction (MI), or target lesion revascularization (TLR).

RESULTS Between June 2013 and March 2014, a total of 1,000 patients were included in the registry, 49.9% of whom presented with acute coronary syndrome. Mean age was 65 ± 11 years old (range: 34 to 94 years of age), and 74% of patients were male; 58.9% of 1,255 lesions were American Heart Association type B2 or C lesions. The primary endpoints were 5.7% TLF, 1.7% cardiac death, 0.7% target vessel MI, and 4.4% TLR. Definite stent thrombosis occurred in 0.5% of subjects; no thrombosis occurred after 9 days post-stenting.

CONCLUSIONS This registry showed excellent 1-year results of novel Combo bioengineered stent technology in an all-comers patient population. (Prospective Registry to Assess the Long-term Safety and Performance of the Combo Stent [REMEDEE]; NCT01874002) (J Am Coll Cardiol Intv 2016;9:1127–34) © 2016 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

DAPT = dual antiplatelet therapy

DES = drug-eluting stent(s)

MI = myocardial infarction

NSTE-ACS = non-ST-segment elevation acute coronary syndrome(s)

PCI = percutaneous coronary intervention

ST = stent thrombosis

STEMI = ST-segment elevation myocardial infarction

TLF = target lesion failure

TLR = target lesion revascularization

Drug-eluting stents (DES) have been shown to be superior to bare metal stents in reducing the rate of repeat revascularization in various patient populations and lesion complexities (1-5). Vascular smooth muscle cell proliferation and neointimal hyperplasia are efficiently inhibited by current generation DES, although there is concern regarding late and very late in-stent-restenosis (6-10). In addition, a major concern in using these cytostatic or cytotoxic drugs is the healing process that is impeded in response to delayed functional endothelialization of the treated segment (11,12). Late "catch-up restenosis" resulting in the need for late repeat revascularization may be associated with an ongoing inflammatory response due to the use of durable polymers. Delayed vascular healing is associated with vasomotor dysfunction and an increased incidence in stent thrombosis (13-17).

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The Combo stent (OrbusNeich Medical BV, the Netherlands) consists of a thin (100-μm) stainless steel strut platform and a biodegradable abluminal coating containing antiproliferative sirolimus (5 μg/mm). In addition, the luminal stent surface is covered with anti-CD34$^+$ antibody that captures endothelial progenitor cells, resulting in rapid re-endothelialization of the treated segment. This anti-CD34$^+$ antibody technology has been shown in pre-clinical and clinical work to prevent thrombus formation and enhance vessel healing (18-20), thus combining the benefits from previous endothelial progenitor cell-capturing stents and modern DES technologies. In the REMEDEE (Randomized study to Evaluate the safety and effectiveness of an abluMinal sirolimus coatED bio-Engineered StEnt) first-in-man trial, the Combo stent showed rates of angiographic in-stent-restenosis similar to those of the Taxus Liberté paclitaxel-eluting stent (Boston Scientific, Marlborough, Massachusetts) in a patient population with single de novo lesions and no definite or probable stent thrombosis (21).

The aim of this registry was to evaluate the clinical performance of the Combo stent in a real-world, multicenter, multinational, all-comers patient population in routine clinical practice.

METHODS

STUDY OVERSIGHT. This REMEDEE Registry was a multicenter, prospective, clinical outcomes post-market registry of the Combo abluminal sirolimus-coated bioengineered stent. The study was investigator-initiated and coordinated by the Academic Medical Center, University of Amsterdam.

PATIENT POPULATION. A total of 1,000 patients, in whom treatment with a Combo stent in the setting of routine clinical care was attempted, were enrolled in the registry. Treatment with the Combo stent was part of clinical routine. Informed consent for participation in the registry (= upload of data into the REMEDEE Registry) was obtained either before the procedure or immediately after. Exclusion criteria were a high probability of nonadherence to the follow-up requirements (for social, psychological, or medical reasons), current participation in another investigational drug or device study with a planned routine angiographic follow-up, a life expectancy of <1 year, or explicit refusal of participation in the registry. All patients provided written informed consent for uploading of clinical data into the registry. Patients presenting with acute coronary syndrome (ST-segment elevation myocardial infarction [STEMI], non-STEMI [NSTEMI], and unstable angina)

TABLE 1 Baseline Demographics and Clinical Characteristics (N = 1,000)

Patients	
Age, yrs	65 ± 11
Males	739 (73.9)
History of diabetes	184 (18.4)
Requiring oral medication	103 (10.3)
Requiring insulin	64 (6.4)
History of hypertension	580 (58.0)
History of hyperlipidemia	562 (56.2)
Family history of CAD	455 (45.5)
Current smoker	241 (24.1)
Prior myocardial infarction	253 (25.3)
Prior percutaneous intervention	301 (30.1)
Prior CABG	68 (6.8)
Indication for PCI	
Urgent PCI for ACS	303 (30.4)
STEMI	178 (17.8)
NSTE-ACS	83 (8.3)
Unstable angina	42 (4.2)
Elective PCI	695 (69.6)
Stabilized STEMI	21 (2.1)
Stabilized NSTE-ACS	107 (10.7)
Stabilized unstable angina	67 (6.7)
Stable angina and/or documented ischemia	304 (30.4)
Angiographically driven	162 (16.2)
Other	35 (3.5)
Statin therapy	719 (71.9)

Values are mean ± SD or n (%).

CABG = coronary artery bypass graft; CAD = coronary artery disease; NSTE-ACS = non-ST-segment elevation acute coronary syndrome; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.