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A Next-Generation Bioresorbable Coronary Scaffold System: From Bench to First Clinical Evaluation

6- and 12-Month Clinical and Multimodality Imaging Results

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Objectives This study sought to perform clinical and imaging assessments of the DESolve Bioresorbable Coronary Scaffold (BCS).

Background BCS, which is drug eluting, may have potential advantages compared with conventional metallic drug-eluting stents. The DESolve system, designed to provide vessel support and neointimal suppression, combines a poly-L-lactic acid–based scaffold with the antiproliferative myolimus.

Methods The DESolve First-in-Man (A NON-RANDOMIZED, CONSECUTIVE ENROLLMENT EVALUATION OF THE DESolve MYOLIMUS ELUTING BIORESORBABLE CORONARY STENT IN THE TREATMENT OF PATIENTS WITH DE NOVO NATIVE CORONARY ARTERY LESIONS) trial was a prospective multicenter study enrolling 16 patients eligible for treatment. The principal safety endpoint was a composite of cardiac death, myocardial infarction, and clinically indicated target lesion revascularization. The principal imaging endpoint was in-scaffold late lumen loss (LLL) assessed by quantitative coronary angiography (QCA) at 6 months. Intravascular ultrasound (IVUS) and optical coherence tomography (OCT) imaging was performed at baseline and 6 months; multislice computed tomography (MSCT) was performed at 12 months.

Results Acute procedural success was achieved in 15 of 15 patients receiving a study scaffold. At 12 months, there was no scaffold thrombosis and no major adverse cardiac events directly attributable to the scaffold. At 6 months, in-scaffold LLL (by QCA) was 0.19 ± 0.19 mm; neointimal volume (by IVUS) was 7.19 ± 3.56%, with no evidence of scaffold recoil or late malapposition. Findings were confirmed with OCT and showed uniform, thin neointimal coverage (0.12 ± 0.04 mm). At 12 months, MSCT demonstrated excellent vessel patency.

Conclusions This study demonstrated the feasibility and efficacy of the DESolve BCS. Results showing low in-scaffold LLL, low % neointimal volume at 6 months, no chronic recoil, and maintenance of lumen patency at 12 months prompt further study. (DESolve First-in-Man; EudraCT number 2011-000027-32) (J Am Coll Cardiol Intv 2014;7:89–99) © 2014 by the American College of Cardiology Foundation

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Intracoronary stents support the vessel wall so that negative remodeling, the major cause of restenosis after balloon angioplasty, is prevented (1). The release of antiproliferative drugs from drug-eluting stents (DES) help prevent the excessive hyperplastic healing response seen after bare-metal stent implantation. Despite their efficacy (2–5), they have not completely eliminated late events, including ongoing inflammation, neoatheroma, and stent thrombosis (6,7). Metal stents can preclude percutaneous intervention to side branches, surgical intervention, disrupt magnetic resonance imaging and computed tomographic imaging. Furthermore by "caging" the artery, permanent implants prevent vasomotor response to physiological needs and accommodative positive remodeling (8–10).

Abbreviations and Acronyms

%DS = percent diameter stenosis

BCS = bioresorbable coronary scaffold

CK = creatine kinase

DES = drug-eluting stent(s)

IVUS = intravascular ultrasound

LLL = late lumen loss

MACE = major adverse cardiac event(s)

MI = myocardial infarction

MSCT = multislice computed tomography

OCT = optical coherence tomography

PLLA = poly-L-lactic acid

QCA = quantitative coronary angiography

TLR = target lesion revascularization

In the first clinical study using a fully bioabsorbable, non–drug-eluting, poly-L-lactic acid (PLLA) stent, the Igaki-Tamai stent (Kyoto Medical Planning Co., Ltd, Japan), was assessed for feasibility and safety in 50 patients who were followed for more than 10 years (8). The target lesion revascularization (TLR) rate was 16%, 18%, and 28% at 1, 5, and 10 years, respectively. The major adverse cardiac event (MACE) rate was 14% at 12 months and 16%, 18%, 24%, and 50% at 3, 4, 5, and 10 years, respectively (8). The high survival rate free of cardiac death (98% at 10 years) demonstrated the long-term safety of the PLLA stent.

Several PLLA-based or other polymeric bioabsorbable scaffolds have been clinically evaluated. The term *scaffold* may be a more appropriate term than *stent* because it implies temporary arterial support (11). These devices include the PLLA ABSORB BVS scaffold, versions 1.0 and 1.1 (Abbott Vascular, Santa Clara, California), a tyrosine-derived polycarbonate polymer stent (Reva Medical, San Diego, California), and a salicylate-based polymer stent (Bioabsorbable Therapeutics, Menlo Park, California) (12). Early results from the initial clinical trials were encouraging, but issues, including too rapid bioresorption leading to poor vessel support, scaffold shrinkage, or strut fracture when expanded to larger diameters, were seen (13). Newer iterations of these devices have addressed some design concerns.

The DESolve Myolimus-Eluting Bioresorbable Coronary Scaffold (BCS) System (Elixir Medical Corporation, Sunnyvale, California) is a PLLA-based scaffold and has several differentiating characteristics. These features include: bioresorption at about 1 year while maintaining adequate vessel support; the elimination of chronic recoil; the ability to expand the scaffold without strut fracture; and unique expansion capabilities, which minimize strut malapposition. We report pre-clinical, bench, clinical, and imaging (quantitative coronary angiography [QCA], intravascular ultrasound [IVUS], optical coherence tomography [OCT], and multislice computed tomography [MSCT]) results through 1 year from the DESolve First-In-Man study in 16 patients.

Methods

Study design and patient population. The DESolve First-in-Man study was a prospective, multicenter trial enrolling 16 patients at 3 sites in Belgium and New Zealand. Eligibility criteria were evidence of myocardial ischemia; a single, de novo native coronary artery lesion; reference vessel diameter ≤3.0 mm; lesion length ≤10 mm; and a target lesion percent diameter stenosis (%DS) <80%. Key exclusion criteria were recent (<3 days) myocardial infarction (MI); left ventricular ejection fraction <30%; left main coronary artery or restenotic lesions; lesions involving a side branch >2 mm; and the presence of thrombus or calcium.

The main analysis was conducted on the per protocol–modified intention-to-treat evaluable population inclusive of patients who received a DESolve scaffold. One patient was excluded because the lesion was not accessed within the protocol-allotted procedure time and was subsequently treated with a metallic DES. Clinical endpoints were assessed at 30 days, 6 months, and 1 year and will be assessed annually through 5 years. Angiography, IVUS, and OCT assessments were performed at baseline and at 6 months. MSCT assessment was performed at 12 months and will be repeated at 24 months.

The ethics committee at each participating institution approved the study protocol; all patients provided written informed consent, which complied with the Declaration of Helsinki. An independent clinical events committee adjudicated all deaths, MI, scaffold thrombosis, and revascularizations.

Study device: DESolve scaffold platform. The DESolve Myolimus-Eluting Bioresorbable Coronary Scaffold System is a PLLA-based polymer scaffold coated with the antiproliferative drug myolimus mounted on a rapid exchange balloon catheter delivery system.

The DESolve scaffold (Fig. 1) is formed using proprietary techniques from a bioresorbable polylactide-based polymer with strut thickness of 150 μm and incorporates 2 platinum-based radio-opaque markers at either end to aid in placement. The scaffold is coated with a matrix of polylactide-based polymer and myolimus at a 3 μg/mm dose; more than 85% of the drug is released over 4 weeks. The system has a crossing profile of 1.47 mm and is 6-F catheter compatible. The scaffold is designed to resorb in about 1 year. The degradation process of PLLA-based polymers occurs primarily by