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Lessons from the trials

Biocorrosible metals for coronary revascularization: Lessons from PROGRESS-AMS, BIOSOLVE-I, and BIOSOLVE-II

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ABSTRACT

The impetus for developing drug-eluting bioresorbable scaffolds (BRS) has been driven by the need for elastic and transient platforms instead of stiff and permanent metallic implants in diseased coronary anatomies. This endeavor would prevent acute recoil or occlusion, allow sealing of post-procedural dissections following acute barotrauma, provide inhibition of in-segment restenosis through efficient drug-elution and would further prepare the vessel to enter a reparative phase following scaffold resorption. Biocorrosible metallic platforms have been introduced as alternatives to bioresorbable polymeric scaffolds for the treatment of significant atherosclerosis and in view of the body of evidence derived from recent clinical trials we elaborate on the clinical safety and efficacy of these devices in interventional cardiology.

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<http://dx.doi.org/10.5339/gcsp.2015.63>

Submitted: 1 August 2015
Accepted: 29 September 2015
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INTRODUCTION

Similar to their bioresorbable scaffold (BRS) counterpart, biocorrosible metallic platforms provide a novel class device for treating coronary atherosclerosis with properties of improved tensile strength and more rapid biodegradation. The mechanical principle of biocorrosible metals is the high corrosion rate (complete biodegradation within 3 months) with end products being elemental Mg and inorganic salts. The earliest proof-of-mechanism which indicated the biocompatibility of such materials with vascular tissue was introduced by Heublein et al. who employed absorbable magnesium devices in porcine coronary arteries demonstrating rapid endothelialization and low inflammatory response.^{1,2}

Preliminary observations from prospective, non-randomized clinical trials assessing the efficacy and clinical safety of deployed biocorrosible metallic stents in selected lesions and clinical subsets have been promising. Herein we provide a comprehensive overview of the first-in-man PROGRESS-AMS study as well as the BIOSOLVE-I and BIOSOLVE-II trials indicating the clinical safety and efficacy of deployed biocorrosible metallic scaffolds for the treatment of non-complex coronary artery disease.

PROGRESS-AMS

Study design

The PROGRESS-AMS clinical trial was a non-randomized, prospective, multi-center trial that was designed to assess the efficacy and clinical safety of the absorbable magnesium stent.³ (AMS-1) (BIOTRONIK, Berlin, Germany). AMS-1 was made of 93% Mg and 7% rare earth metals, had a strut thickness of 165 μ m and carried two radiopaque markers at each proximal and distal ends as the device was radiolucent.

Sixty-three patients underwent revascularization with an AMS in vessels with reference diameters of 3 to 3.5 mm and average lesion lengths of <13 mm. Coronary angiography and intravascular ultrasound imaging was completed post-procedure and at 12-month follow-up. The primary endpoint of this feasibility study was cardiac death, non-fatal myocardial infarction, or target lesion revascularization at 4 months.

Results

The rates of major adverse cardiac events reached 24% and TLR rates reached 39.7% at 4 months. There were no events of cardiac death, myocardial infarction, or stent thrombosis. The angiographic in-stent lumen loss was 1.08 ± 0.49 mm at 4 months, and IVUS imaging suggested that most of the struts were fully resorbed with only strut remnants being visibly embedded into the intima.

Discussion

Although this study demonstrated the safety of AMS-1 with no reported death, myocardial infarction or stent thrombosis, imaging and clinical results raised concerns over the further use of this generation in coronary interventions as increased neo-intimal formation and vessel recoil became evident. Subsequently AMS-2 and AMS-3 were developed to overcome the aforementioned limitations primarily caused by the lack of drug-elution and early loss of radial strength. AMS-2 provided an improved Mg alloy with higher collapse pressure of 1.5 bar compared to 0.8 bar of AMS-1, a slower degradation rate with expected absorption after 9–12 months and reduced strut thickness of 125 μ m with rectangular shape to enhance stent integrity. The AMS-3 was designed to address the issue of previously observed intense neo-intimal hyperplasia, thus a bioresorbable matrix for controlled release of paclitaxel was added to the previous AMS-2. The new device was named drug-eluting AMS (DREAMS) 1.0 (BIOTRONIK, Bulach, Switzerland) and was evaluated for safety, feasibility and efficacy in the prospective, multicenter, FIM BIOSOLVE-1 trial. (Safety and Performance of the Drug- Eluting Absorbable Metal Scaffold (DREAMS) in Patients with de-novo Coronary Lesions).

Study design

The BIOSOLVE-I clinical trial was a prospective, non-randomized, multicenter, first-in-man trial assessing the safety and efficacy of DREAMS in non-complex coronary lesions.⁴ Forty-six patients with stable/unstable angina or silent ischemia were treated with 47 stents. Imaging follow-up included angiography and IVUS at 6 and 12 months with clinical assessment scheduled at 1, 6, 12, 24 and 36 months.

Results

The angiographic in-stent lumen loss was 0.64 ± 0.50 mm at 6-months and 0.52 ± 0.49 mm at 1 year, which represents a 61% reduction compared to the 4-month results of AMS-1. Serial IVUS imaging confirmed the angiographic observations showing in-scaffold area obstruction of only 6.24% ($p < 0.0001$) at 1 year, attributed to neo-intimal formation with extra-scaffold plaque area increase. TLR rates reached 7% with no reported episodes of stent thrombosis throughout the 3-year follow-up. The second-generation DREAMS device has been recently developed. This generation elutes sirolimus instead of paclitaxel, carries two tantalum radiopaque markers at both ends and delivers higher bending flexibility with slower resorption rate compared to the previous generation. The BIOSOLVE-II study was designed to assess the safety, efficacy and feasibility of this generation in 120 patients.

BIOSOLVE-II

Study design

The BIOSOLVE-II was a prospective, non-randomized, multicenter, first-in-man clinical trial evaluating the safety and effectiveness of the second-generation drug eluting absorbable metal scaffold (DREAMS 2).⁵ 123 patients with stable and unstable angina were enrolled and were followed up at 1, 6, 12, 24, and 36 months. Intravascular ultrasound, optical coherence tomography, and vasomotion testing were completed in a subset of patients at 6 months. Primary end points were in-segment late lumen loss at 6-months.

Results

In-segment and in-scaffold late lumen loss at 6 months was $0.27 \text{ mm} \pm 0.37 \text{ mm}$ and $0.44 \text{ mm} \pm 0.36 \text{ mm}$ respectively.

Discussion

BIOSOLVE-I and -II added to the ever-expanding evidence to support bioresorbable scaffolds by assessing the safety and efficacy of two generations of drug eluting metallic scaffolds. The first iteration of the drug eluting magnesium based metallic scaffold in BIOSOLVE-I showed similar safety findings to PROGRESS-AMS in that it could be safely and successfully implanted in patients without an associated risk for cardiac death or stent thrombosis. The addition of drug-elution with paclitaxel further improved the rates of target lesion revascularization from 26.7% to 4.7%.

The second iteration of the DREAMS platform in BIOSOLVE-II had large improvements over the previous DREAMS 1. The scaffold was more flexible, had greater radial strength, and a change in the eluted drug from paclitaxel to sirolimus. Combined, these changes showed slower rates of strut degradation compared to DREAMS 1, and completely restored vasomotion at 12-months. Compared to the DREAMS 1, DREAMS 2 showed better rates of late lumen loss both in-segment and in-scaffold.

CONCLUSION

Current evidence suggests that bio-corrodible metallic scaffolds can be safely implanted in patients with favorable clinical outcomes. Despite the encouraging preliminary observations, further randomized clinical trials with head to head comparisons with newer generation drug-eluting stents will define whether these technologies will be adopted over contemporary CAD treatments.

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