



## EDITORIAL COMMENT

# Magmaris resorbable magnesium scaffolds: *Are they here to stay?*



## Suporte vascular restaurativo transitório coronário de magnésio – Magmaris: *Veio para ficar?*

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The introduction of drug-eluting stents (DES) in 2002 was considered to be the third revolution in interventional cardiology, after the first one, balloon angioplasty and the second, bare metal stents (BMS). DES were primarily designed to overcome the main drawback of BMS: the occurrence of in-stent restenosis due to intimal hyperplasia and its proof of concept was the publication of the RAVEL trial.<sup>1</sup> Shortly afterwards, both large scale randomized trials and all-comer registries showed excellent results in terms of the need for repeat revascularization. However, after the enthusiasm that followed these initial results, later registries of all-comers treated with first generation DES showed late stent thrombosis rates of 0.53% per year, which continued increase to 3% over four years.<sup>2</sup>

Over the past decade, in efforts to improve safety and efficacy, several second and even third generation DES have been developed with different alloys, polymers, and antiproliferative drugs. These refinements have confirmed DES as superior to BMS in terms of safety and efficacy.<sup>3</sup> On the other hand, evidence suggests that permanent metallic coronary stents may alter flow dynamics, abolish vascular reactivity and limit the potential for maximal vasodilation.<sup>4</sup>

In any case, the concept of a fully resorbable stent-like device has always been very attractive to the interventional community; such a device could offer transient radial strength to resist acute vessel recoil, and at a later stage would be fully resorbed, leading to restoration of the vessel's biological properties. This would make the device one of the holy grails of interventional cardiology.

In 2008, what has been called the fourth revolution in interventional cardiology came about the advent of the first CE mark approved bioabsorbable platform, ABSORB (Abbott Vascular, Santa Clara, CA, USA). The feasibility and clinical safety of the first generation ABSORB was proven by the ABSORB Cohort A trial in 30 low risk patients with coronary artery disease. A reported incidence of major adverse cardiac events of 3.4% at four-year follow up was observed, with no episodes of stent thrombosis.<sup>5</sup>

However, the inclusion of increasingly more complex patients in studies and registries has shown a suboptimal rate of events with ABSORB, raising concerns mainly with regard to scaffold thrombosis.<sup>6</sup>

Bioabsorbable metallic scaffolds, which are intuitively an attractive option because their mechanical performance is similar to that of metal stents, are an alternative to polymeric scaffolds.<sup>7</sup> PROGRESS AMS was the first-in-man trial of an absorbable metal stent (magnesium alloy) in coronary arteries. Results showed that the device had a good safety profile, with no deaths, myocardial infarction, or scaffold thrombosis reported. In-scaffold acute gain was promising, but in-scaffold late lumen loss and ischemia-

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driven target lesion revascularization (TLR) were high at four months because of negative remodeling and neointimal proliferation, suggesting the need for slower scaffold absorption and antiproliferative drug elution.<sup>8</sup>

Several modifications were made to the original platform giving rise to DREAMS 1-G, which included a modified magnesium alloy and the addition of paclitaxel; a further evolution with sirolimus elution, DREAMS 2-G, commercially known as MAGMARIS (Biotronik, Berlin, Germany) was finally launched.

The BIOSOLVE Clinical Program was set up to assess the clinical efficacy and safety of Magmaris in four multicenter studies, totaling more than 1500 patients.

BIOSOLVE I was a prospective, multicenter, first-in-man trial designed to assess the safety and performance of the paclitaxel-eluting DREAMS scaffold.<sup>9</sup> In a population of 46 patients with simple lesions, the resorbable device showed a target lesion failure (TLF) rate of 6.6%, with no cases of scaffold thrombosis.

Data from BIOSOLVE II and BIOSOLVE-III were pooled and published together.<sup>10,11</sup> BIOSOLVE II was a prospective, international, multi-center, first-in-man trial using the second-generation drug-eluting absorbable metal scaffold Magmaris. Twelve-month in-segment late lumen loss (LLL) was  $0.39 \pm 0.27$  mm, superior to the LLL described with the previous iteration of the absorbable metal scaffold.<sup>9</sup> TLF was reported in four patients (3.4%) at 12 months, again with no cases of scaffold thrombosis. At 24 months the combined rate of TLF in both studies was 5.9% and no definite or probable scaffold thrombosis was reported.<sup>11</sup>

Finally, BIOSOLVE-IV is an international, single-arm, multicenter registry conducted at 86 centers.<sup>12</sup> Among the first 400 patients included, procedure and device success was high (98.5% and 96.1%, respectively) in this more complex population of patients. Only one case of scaffold thrombosis was found (0.3%) and TLF at 12 months was 4.3%.

In this issue of the Portuguese Journal of Cardiology, Abellas et al.<sup>13</sup> present their experience with Magmaris in a population of 42 real-world patients. In this single-center registry, the strategy of the 4Ps (patient selection, proper sizing, predilatation and post-dilatation) was followed scrupulously in all cases. At 12 months, TLF was 4.7%, corresponding to two cases of clinically driven TLR, with no cases of scaffold thrombosis. The authors emphasize the need for an adequate selection of patients, especially the absence of calcium, in order to achieve these excellent outcomes.

These results corroborate those from BIOSOLVE II, III and IV,<sup>10-12</sup> with very similar TLF rates and, more importantly, no cases of scaffold thrombosis in spite of 54.7% of patients presenting with acute coronary syndromes.

The only publication with Magmaris in an acute setting to date is the MAGSTEMI trial, which randomized 150 ST-elevation myocardial infarction patients to Magmaris or a sirolimus-eluting DES. At 12 months, a better vasomotor response was found in patients treated with Magmaris (primary endpoint), although TLR was significantly higher in the Magmaris group (16.2% vs. 5.2%,  $p=0.03$ ). Only one case of ST occurred in the Magmaris group versus two cases in the DES group.<sup>14</sup>

In summary, with an adequate selection of patients and technique, safety with Magmaris does not seem to be a major issue, while efficacy will need to be assessed in further randomized trials, probably compared with a state-of-the-art DES.

In conclusion, despite the compelling evidence of metallic DES efficacy in a large proportion of patients, important limitations remain such as hypersensitivity reactions, late stent thrombosis, and neoatherosclerotic stent failure. Further improvements in the magnesium scaffold device characteristics in newer generations could help resolve these issues.

In the meantime, it seems clear that Magmaris is here to stay.

## Conflicts of interest

The authors have no conflicts of interest to declare.

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