

One- and two-year clinical outcomes of treatment with resorbable magnesium scaffolds for coronary artery disease: the prospective, international, multicentre BIOSOLVE-IV registry

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KEYWORDS

- bioresorbable scaffolds
- diabetes
- NSTEMI
- stable angina

Abstract

Background: Bioresorbable scaffolds have been developed to overcome the limitations of drug-eluting stents and to reduce long-term adverse events.

Aims: We aimed to assess the long-term safety and efficacy of a sirolimus-eluting resorbable magnesium scaffold to ensure its safe rollout into clinical routine.

Methods: BIOSOLVE-IV is a prospective, international, multicentre registry including more than 100 centres in Europe, Asia, and Asia-Pacific. Enrolment started directly after the commercialisation of the device. Follow-up assessments are scheduled at 6 and 12 months, and annually for up to 5 years; we herein report the 24-month outcomes.

Results: Overall, 2,066 patients with 2,154 lesions were enrolled. Patients were 61.9±10.5 years old, 21.6% had diabetes, and 18.5% had non-ST-elevation myocardial infarction (NSTEMI). Lesions were 14.8±4.0 mm long with a reference vessel diameter of 3.2±0.3 mm. Device and procedure success were 97.5%, and 99.1%, respectively. The 24-month target lesion failure (TLF) rate was 6.8%, mainly consisting of clinically driven target lesion revascularisations (6.0%). Patients with NSTEMI had significantly higher TLF rates than those without (9.3% vs 6.2%; $p=0.025$), whereas there were no significant differences observed for patients with diabetes or with type B2/C lesions (a 24-month TLF rate of 7.0% and 7.9%, respectively). The 24-month rate of definite or probable scaffold thrombosis was 0.8%. Half of the scaffold thromboses occurred after premature discontinuation of antiplatelet/anticoagulation therapy, and only one scaffold thrombosis occurred beyond the 6-month follow-up, on day 391.

Conclusions: The BIOSOLVE-IV registry showed good safety and efficacy outcomes, confirming a safe rollout of the Magmaris into clinical practice.

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Abbreviations

ACS	acute coronary syndrome
BRS	bioresorbable scaffold
DAPT	dual antiplatelet therapy
DES	drug-eluting stent
DREAMS	drug-eluting absorbable magnesium scaffold
MI	myocardial infarction
NSTEMI	non-ST-elevation myocardial infarction
TLF	target lesion failure
TLR	target lesion revascularisation
TVR	target vessel revascularisation

Introduction

Second-generation drug-eluting stents (DES) have reduced restenosis rates compared to bare metal stents but have been associated with an increased risk of late events, especially late thrombotic events. These complications could be limited by prolonged dual antiplatelet therapy (DAPT) and refinements in stent designs but are still associated with a steady annual complication rate without a decline^{1,2}.

Bioresorbable scaffolds (BRS) have been developed to overcome the limitations of permanent stents, to avoid the creation of permanently caged vessel segments with inhibition of vasomotion and vessel remodelling, and to avoid chronic vessel wall inflammation or long-term stent crushing and fractures¹. The Absorb (Abbott Vascular) polymeric bioresorbable scaffold was the first European conformity (CE)-marked BRS. Initial short-term data were encouraging; however, the optimism associated with these preliminary studies was tempered by the results of the ABSORB II and III Trials. Finally, as a result of safety concerns (mainly increased rates of scaffold thrombosis), this technology was withdrawn from commercial use².

In contrast to polymeric scaffolds, magnesium-based scaffolds have the advantage of a metal stent-like behaviour with good radial strength, low acute recoil, and laser polishing for a smooth surface that facilitates embedding into the vessel wall, reducing wall shear stress and thrombogenicity^{1,3}.

The second-generation magnesium-based sirolimus-eluting scaffold Magmaris (BIOTRONIK) has shown promising outcomes in the controlled study environment of the BIOSOLVE-II and -III Studies¹. To enable the safe rollout of this device into clinical practice, the BIOSOLVE-IV registry was initiated immediately after the obtention of the CE mark to collect long-term data on a large patient population, with endpoints powered for 12-month target lesion failure (TLF) and definite or probable scaffold thrombosis, and to comply with the call for more data from the European Society of Cardiology (ESC) and the European Association of Percutaneous Cardiovascular Interventions². The 12-month outcomes of the first cohort of 1,075 patients, powered for the outcome of TLF, have been published previously³. To allow for an endpoint powered for device thrombosis, a second cohort was added, bringing the total to 2,066 patients. We herein report the 24-month outcomes of the full cohort. In addition, we assess the outcomes for the high-risk subgroups with type

B2/C lesions, diabetes, and non-ST-elevation myocardial infarction (NSTEMI)⁴⁻⁶.

Methods

STUDY DESIGN AND PATIENTS

The BIOSOLVE-IV registry has been described previously³. In brief, it is an international, multicentre, prospective registry with clinical follow-up at 6 and 12 months, and annually thereafter for 5 years. It is being conducted at 106 sites in Europe, Asia and Asia-Pacific.

Adult patients with a maximum of two single *de novo* lesions in two different major epicardial vessels ≤ 21 mm in length and between 2.7 and 3.7 mm in diameter were eligible. Patients with ST-elevation myocardial infarction, restenotic target lesion, and left main disease were excluded. The full list of in- and exclusion criteria is available at ClinicalTrials.gov: NCT02817802.

The registry was conducted according to the current version of the Declaration of Helsinki, ISO14155, where applicable, and local guidelines; it was approved by the institutional ethics committees. All patients provided informed consent prior to any study procedure. The registry was monitored, and a clinical events committee member adjudicated all events for which a device relationship could not be ruled out.

DEVICE AND PROCEDURE

The Magmaris is a scaffold system consisting of a balloon-expandable bioresorbable scaffold premounted on the balloon of a rapid exchange percutaneous transluminal coronary angioplasty catheter. The scaffold backbone is made from bioresorbable magnesium, a material with high biocompatibility. Magnesium ions have several positive effects, such as decreased thrombogenicity, vasodilatation, inhibition of arterial wall stiffening processes and attenuation of vascular calcifications⁷.

The surface of the scaffold backbone is completely coated with bioresorbable poly-L-lactic acid (PLLA), which incorporates sirolimus and which is identical to the coating of the Orsiro (BIOTRONIK) DES³.

Implantation recommendations have been described previously³ and followed the “4P” strategy⁸; the use of intravascular ultrasound (IVUS) guidance was optional and left to the discretion of the implanting physician. DAPT had to be administered for at least 6 months.

ENDPOINTS

The primary endpoint was TLF at 12 months, a composite of cardiac death, target vessel Q-wave or non-Q-wave myocardial infarction (MI), emergent coronary artery bypass graft (CABG), and clinically driven target lesion revascularisation (TLR). Procedural MI were adjudicated according to the Society for Cardiovascular Angiography and Interventions (SCAI) definition⁹, and spontaneous MI according to the extended historical definitions¹⁰. The secondary endpoints were TLF at timepoints other than 12 months and its individual components: clinically driven target vessel

revascularisation (TVR), scaffold thrombosis¹¹, procedure success and device success.

STATISTICAL ANALYSIS

The sample size calculation has been reported previously³. A minimum of 1,065 patients were included in the calculation of the first cohort (endpoints of 12-month TLF, null hypothesis $\geq 10\%$, weighted mean 6.6%, and 95% power), and 2,054 patients for the full cohort (endpoints of 12-month definite or probable scaffold thrombosis, null hypothesis $\geq 1.49\%$, weighted mean 0.65%, and 90% power), both with a normal approximation to the binomial test, significance level $\alpha=0.025$ (one-sided) and an expected drop-out rate of 20%.

The analysis was performed for the intention-to-treat population and is based on data available. For quantitative variables, the mean values and standard deviation were calculated, and for qualitative variables, absolute and relative frequencies. For individual and combined clinical outcomes, the Kaplan-Meier estimator and 95% confidence intervals (CI) were calculated. In a *post hoc* analysis, outcomes in specific high-risk groups were compared using the Chi-square test, the t-test, Fisher's exact test, and the log-rank test. No alpha-adjustment for multiple testing was performed for *post hoc* subgroup analyses, which are considered exploratory and hypothesis-generating. For exploratory analyses, a multivariable Cox regression model was performed for variables that showed an effect of $p < 0.15$ in univariable Cox regression, to evaluate the adjusted hazard ratios. All analyses were conducted using SAS version 9.4 (SAS Institute).

Results

From September 2016 until July 2020, 2,066 subjects with 2,154 lesions were enrolled. Patients were 61.9 ± 10.5 years on average, ranging from 26 to 86 years, 21.6% ($n=446$) had diabetes, 18.5% ($n=383$) had NSTEMI, and 0.4% ($n=8$) had ST-elevation myocardial infarction. The mean lesion length was 14.8 ± 4.0 mm, with a mean reference vessel diameter of 3.2 ± 0.3 mm (Table 1, for subgroups Supplementary Table 1).

Pre- and post-dilatation were performed in nearly all lesions (99.8% and 95.7%, respectively) (Table 2, for subgroups Supplementary Table 2). Nine subjects, in whom the Magmaris system entered the guiding catheter but could not be implanted at the target lesion, were only considered for device and procedural success analyses and were exempt from follow-up. When multiple scaffolds were implanted ($n=65$), they were implanted end-to-end in 61.5% of cases ($n=40$), overlapping in 32.3% ($n=21$), and "other" in 6.2% ($n=4$).

At follow-up, approximately 90% of patients were symptom-free, around 10% had stable angina, and unstable angina or documented silent ischaemia was present in less than 1% (Figure 1). In terms of antiplatelet therapy, at 12 months, 72.7% of patients were on DAPT therapy and 18.7% were on acetylsalicylic acid, whilst at 24 months, 21.3% were on DAPT and 54.6% on acetylsalicylic acid.

Table 1. Baseline characteristics.

		N=2,066 patients
Age, years		61.9±10.5 [61.4-62.3]
Male		1,539 (74.5)
Hypertension		1,370 (66.3)
Hyperlipidaemia		1,347 (65.2)
Diabetes		446 (21.6)
<i>Insulin-dependent</i>		94 (21.1)
Renal disease		126 (6.1)
History of smoking		1,224 (59.2)
<i>Current smoker</i>		513 (41.9)
Previous PCI		594 (28.8)
Coronary artery bypass graft		13 (0.6)
History of myocardial infarction		448 (21.7)
NSTEMI		383 (18.5)
STEMI		8 (0.4)*
Ischaemic status	Stable angina	998 (48.3)
	Unstable angina	358 (17.3)
	Silent ischaemia	318 (15.4)
		N=2,154 lesions
Lesion length, mm		14.8±4.0 [14.6-15.0]
Reference vessel diameter, mm		3.2±0.3 [3.2-3.2]
Diameter stenosis, %		82.2±10.6 [81.8-82.7]
Target vessel	Left anterior descending	1,067 (49.5)
	Left circumflex artery	442 (20.5)
	Right coronary artery	620 (28.8)
	Ramus intermedius	25 (1.2)
AHA/ACC classification	Type A	813 (37.7)
	Type B1	1,012 (47.0)
	Type B2	255 (11.8)
	Type C	74 (3.4)
Calcification	Moderate to severe	162 (7.5)
Tortuosity	Little tortuosity	1,886 (87.6)
	Moderate tortuosity	255 (11.8)
	Excessive tortuosity	13 (0.6)
Bifurcation involved		99 (4.6)
Thrombus present		3 (0.1)
Data are mean±SD [95% CI], or n (%). *Violation of exclusion criteria. AHA/ACC: American Heart Association/American College of Cardiology; CI: confidence interval; NSTEMI: non-ST-elevation myocardial infarction; PCI: percutaneous coronary intervention; SD: standard deviation; STEMI: ST-elevation myocardial infarction		

Follow-up data were available for 96.8% of patients at 24 months (Figure 2). The 24-month Kaplan-Meier estimate for TLF is 6.8%, predominantly consisting of clinically driven TLR (6.0%) (Table 3). The subgroup of NSTEMI patients had a significantly higher TLF rate compared with non-NSTEMI patients (9.3% vs 6.2%; $p=0.025$), based on a significantly higher rate of target vessel MI (3.7% vs 1.1%; $p=0.0002$) and a numerically higher rate of clinically driven TLR (8.0% vs 5.6%; $p=0.063$). Furthermore, clinically driven TVR occurred more often in the NSTEMI group

Table 2. Procedural characteristics.

	N=2,154 lesions
Predilatation performed	2,150 (99.8)
Maximum pressure applied, atm, N=2,874	14.6±3.4 [14.5-14.7]
Scaffold length, mm, N=2,207	19.5±3.9 [19.3-19.6]
Scaffold diameter, mm, N=2,207	3.3±0.3 [3.2-3.3]
Maximum pressure applied, atm, N=2,195	14.4±2.7 [14.2-14.5]
Post-dilatation performed	2,061 (95.7)
Maximum pressure applied, atm, N=2,295	17.1±3.4 [16.9-17.2]
Device success, N=2,231 stents	2,177 (97.5)
Procedure success, N=2,062 patients	2,047 (99.1)

Data are shown as mean±SD [95% CI] or n (%). Device success was defined as a final diameter stenosis of <30% using the assigned device only, successful delivery of the scaffold, appropriate scaffold deployment, and successful removal of the delivery system. Procedure success was defined final diameter stenosis <30% without the occurrence of death, myocardial infarction, or repeat target lesion revascularisation during the hospital stay. CI: confidence interval; SD: standard deviation

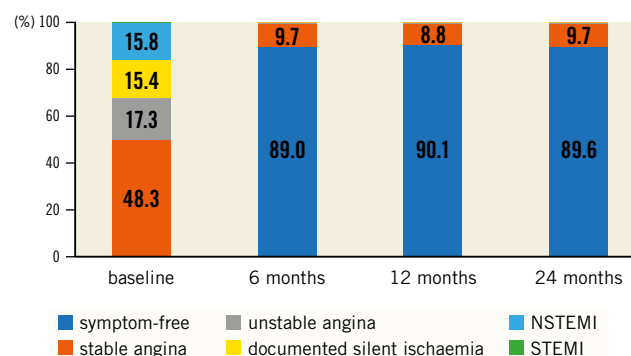


Figure 2. Patient flowchart. *One patient attended the 24-month visit, but died thereafter (resulting in 30 deaths overall). NSTEMI: non-ST-elevation myocardial infarction; STEMI: ST-elevation myocardial infarction

6-month follow-up time window, on day 391 (four scaffold thromboses were subacute, one was very late [day 391] and the remaining were late).

Discussion

In this large real-world registry with more than 2,000 patients and endpoints powered for TLF and definite or probable scaffold thrombosis, the sirolimus-eluting Magmaris resorbable scaffold achieved good safety and efficacy outcomes, meeting its pre-specified safety and performance criteria. The safety and efficacy were also confirmed in the high-risk subgroups of patients with NSTEMI, diabetes mellitus and type B2/C lesions.

The high device and procedural success rates (97.6% and 99.3%, respectively) despite a high number of first-time users is encouraging and confirms a good conformability and a DES-like behaviour of the Magmaris, which is superior to polymeric scaffolds^{12,13}. Furthermore, the high rate of pre- and post-dilatation highlights the adherence to implantation guidelines such as the “4P” strategy⁸.

Relatively simple lesions were selected, with only 15.3% type B2/C lesions and only 7.5% moderate to severely calcified lesions. However, in contrast to the precursor BIOSOLVE-II and -III studies¹⁴, patients with NSTEMI were permitted in BIOSOLVE-IV.

This might have resulted in the slightly higher rate of TLF observed in our series compared to the pooled 12-month outcomes of BIOSOLVE-II and -III (5.0%, 95% CI: 4.1-6.0 vs 3.3%, 95% CI: 1.2-7.1)¹⁴, as the NSTEMI subgroup had significantly higher TLF, target vessel MI, and clinically driven TLR rates compared to non-NSTEMI patients. However, as the confidence intervals overlap, this could be a chance finding. Moreover, BIOSOLVE-II and -III were controlled trials with a limited number of centres and with experienced users, whereas in BIOSOLVE-IV, most centres were first-time users, as the registry started immediately after gaining the CE mark. Notably, the TLF rate is still below the expected weighted mean³, and comparable to contemporary DES for which 12-month TLF rates between 4.0% and 10% are reported¹⁵⁻¹⁹. At 24 months, TLF was estimated as 6.8% compared to 5.5% in BIOSOLVE-II and -III¹,

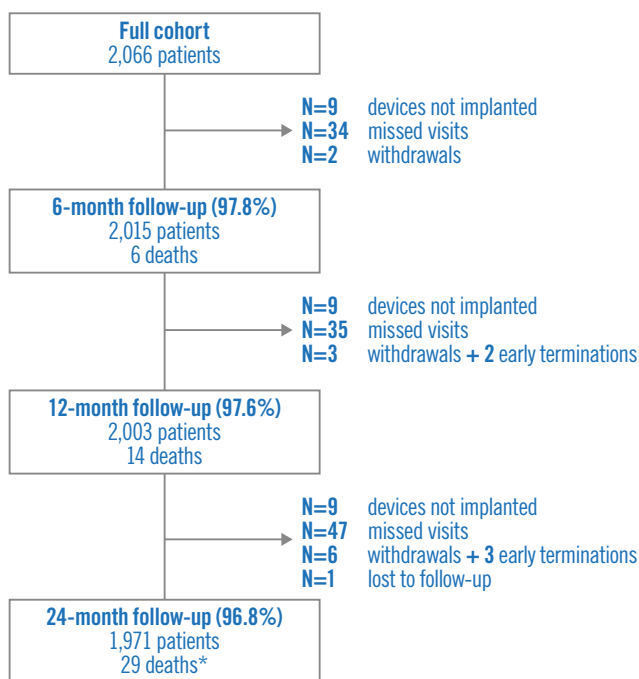


Figure 1. Ischaemic status at baseline and follow-up. Data were available for 2,066 patients at baseline, 2,015 patients at 6 months, 2,003 patients at 12 months, and 1,967 patients at 24 months.

(9.9% vs 6.1%; p=0.007). Likewise, multivariate analysis revealed NSTEMI as the only predictor for TLF (Supplementary Table 3).

There was no significant difference detected for TLF in diabetic versus non-diabetic patients (7.0% vs 6.7%; p=0.770) or for type B2/C lesions compared to type A/B1 lesions (7.9% vs 6.6%; p=0.360) (Central illustration, Table 3).

Definite or probable scaffold thrombosis occurred in 17 patients (0.8%, 0.4% excluding cases with early antiplatelet or anticoagulation interruption) and thus, the null hypothesis was rejected. Out of the 17 scaffold thromboses, only one occurred beyond the

Table 3. Kaplan-Meier failure estimate for primary and secondary endpoints.

	Full cohort N=2,057*	NSTEMI N=381	Diabetes N=444	Type B2/C lesions N=316
12 months				
TLF	103 (5.0) [4.2-6.1]	28 (7.4) [5.2-10.5]	27 (6.1) [4.2-8.8]	20 (6.3) [4.1-9.6]
Cardiac death	4 (0.2) [0.1-0.5]	0	2 (0.5) [0.1-1.8]	1 (0.3) [0.0-2.2]
Target vessel MI	28 (1.4) [0.9-2.0]	13 (3.4) [2.0-5.8]	7 (1.6) [0.8-3.3]	6 (1.9) [0.9-4.2]
Clinically driven TLR	93 (4.5) [3.7-5.5]	25 (6.6) [4.5-9.6]	24 (5.4) [3.7-8.0]	20 (6.3) [4.1-9.6]
Emergent CABG	0	0	0	0
All-cause mortality	14 (0.7) [0.4-1.2]	2 (0.5) [0.1-2.1]	4 (0.9) [0.3-2.4]	2 (0.6) [0.2-2.5]
Clinically driven TVR	102 (5.0) [4.1-6.0]	28 (7.4) [5.2-10.6]	25 (5.7) [3.9-8.3]	20 (6.3) [4.1-9.6]
Scaffold thrombosis (definite/probable)	16 (0.8) [0.5-1.3]	5 (1.3) [0.5-3.1]	4 (0.9) [0.3-2.4]	4 (1.3) [0.5-3.3]
24 months				
TLF	138 (6.8) [5.8-7.9]	35 (9.3) [6.8-12.7] p=0.025	31 (7.0) [5.0-9.8] p=0.770	25 (7.9) [5.4-11.5] p=0.359
Cardiac death	10 (0.5) [0.3-0.9]	1 (0.3) [0.0-1.9] p=0.494	2 (0.5) [0.1-1.8] p=0.901	2 (0.6) [0.2-2.5] p=0.685
Target vessel MI	32 (1.6) [1.1-2.2]	14 (3.7) [2.2-6.2] p=0.0002	8 (1.8) [0.9-3.6] p=0.633	6 (1.9) [0.9-4.2] p=0.599
Clinically driven TLR	122 (6.0) [5.0-7.1]	30 (8.0) [5.6-11.2] p=0.063	27 (6.1) [4.2-8.8] p=0.858	24 (7.6) [5.2-11.1] p=0.176
Emergent CABG	0	0	0	0
All-cause mortality	30 (1.5) [1.0-2.1]	4 (1.1) [0.4-2.8] p=0.475	7 (1.6) [0.8-3.3] p=0.821	6 (1.9) [0.9-4.2] p=0.486
Clinically driven TVR	138 (6.8) [5.8-8.0]	37 (9.9) [7.3-13.4] p=0.007	30 (6.8) [4.8-9.6] p=0.945	26 (8.3) [5.7-11.9] p=0.246
Scaffold thrombosis (definite/probable)	17 (0.8) [0.5-1.3]	5 (1.3) [0.5-3.1] p=0.242	4 (0.9) [0.3-2.4] p=0.841	4 (1.3) [0.5-3.3] p=0.351
Data are displayed as n (Kaplan-Meier failure estimates) [95% CI] log-rank. The log-rank test compared the NSTEMI to the non-NSTEMI group, the diabetes to the non-diabetes group, and Type A/B1 lesion group to Type B2/C lesions. Data are patient based. *2,066 patients – 9 patients not implanted (4 patients in the first cohort). CABG: coronary artery bypass graft; CI: confidence interval; MI: myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; TLF: target lesion failure; TLR: target lesion revascularisation; TVR: -target vessel revascularisation				

7.4% in the Magmaris Italian registry that also included NSTEMI patients, and 5 to 11.9% seen in contemporary DES trials^{16,18-20,21}.

The same applies to the outcomes in terms of definite and probable scaffold thrombosis. While it is disappointing that the “zero scaffold thrombosis” series in BIOSOLVE-II and -III could not be continued in BIOSOLVE-IV, it must be noted that 9 out of 17 scaffold thromboses occurred after the premature discontinuation of antiplatelet or anticoagulation therapy. Furthermore, all but one scaffold thrombosis in the overall cohort occurred between post-procedure days 6 and 188, hence, prior to the resorption time of the Magmaris and thus potentially influenced by Magmaris remnants, which have been observed in optical coherence tomography (OCT) studies²². Notably, the ESC guidelines provide a recommendation of at least 12-month DAPT in patients treated with resorbable scaffolds, up to the presumed time of full resorption². Another contributing factor could be – as mentioned above for TLF – the large number of operators being first-time users at the beginning of their learning curve. Nevertheless, scaffold thrombosis rates are still within the range for DES^{15-19,21} and lower than those of the Absorb BVS (12-month definite or probable scaffold thrombosis rate of 0.8% vs 1.7% observed in the European ABSORB Consortium registries²³).

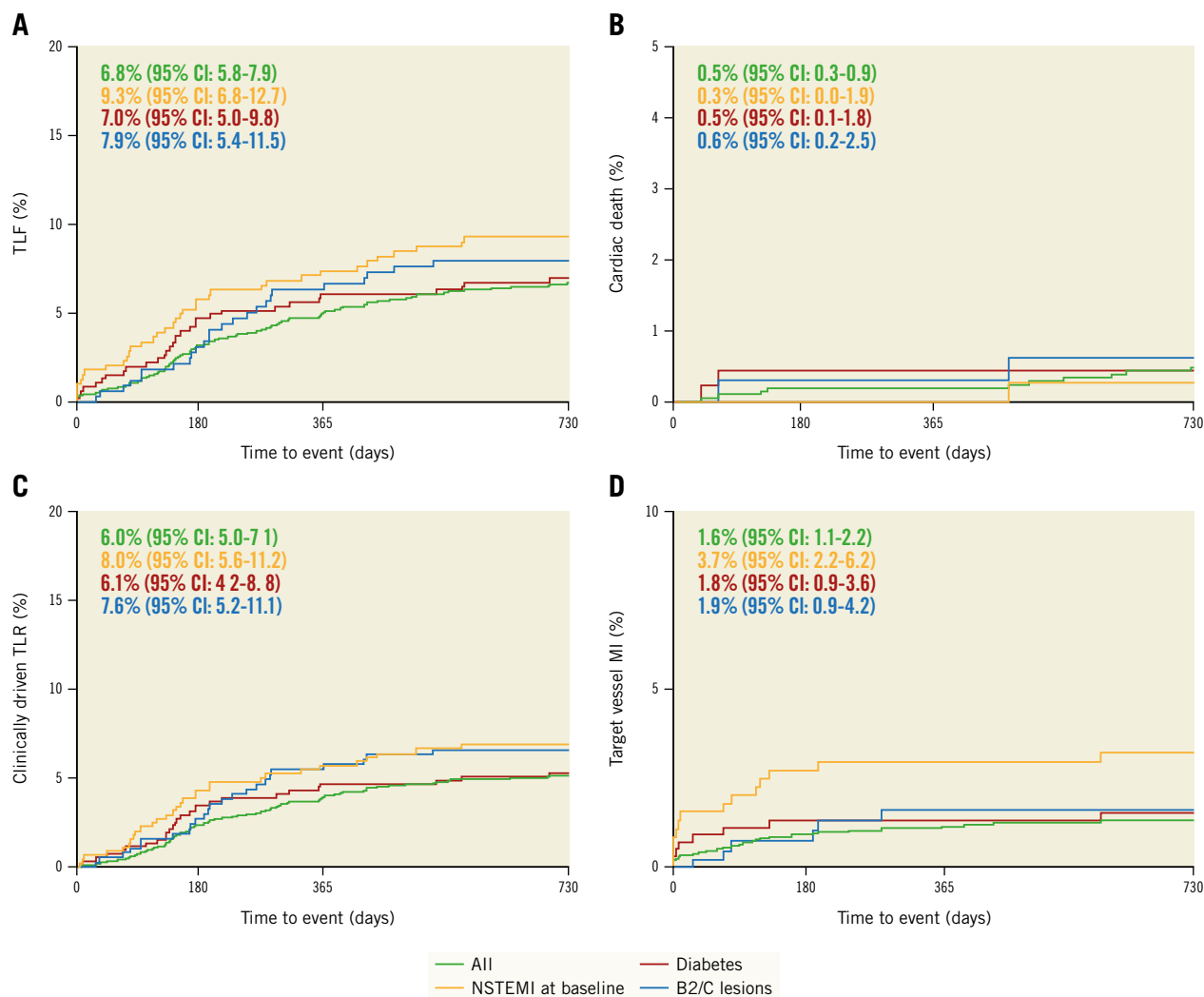
In terms of subgroups, other series with NSTEMI patients treated with the Magmaris revealed better outcomes. For example,

the Magmaris-acute coronary syndrome (ACS) Registry with 65.8% NSTEMI patients revealed a 24-month TLF rate of only 5.2% with absence of scaffold thrombosis, and Magmaris achieved similar outcomes to the Ultimaster (Terumo) DES at 12 months in diabetic patients enrolled in this registry^{24,25}. In the Italian registry with 15% NSTEMI patients, 12- and 24-month scaffold thrombosis was 0.5%²⁰; in a series of 75 NSTEMI patients, no scaffold thrombosis or target vessel MI was observed at 6 months²²; and in a series of 193 patients with 84.5% NSTEMI patients, no scaffold thrombosis occurred at 12 months²⁶. However, these series mostly involved a limited number of mostly experienced centres, which could have impacted outcomes.

It is encouraging that the clinical outcomes do not differ significantly between diabetic and non-diabetic patients or type B2/C and type A/B1 lesions, albeit these were *post hoc* analyses and might lack statistical power. Likewise, there was no relevant difference between diabetic and non-diabetic patients in other series²⁴. Furthermore, beyond 12 months, the TLF curve starts to flatten.

There are still many unknowns in terms of implantation techniques; for example, recent findings indicate that performing repetitive post-dilatation to optimise the lumen area and reduce malapposition may compromise the mechanical integrity of the scaffold²⁵. Furthermore, the late lumen loss assessed in BIOSOLVE-II and -III¹⁴ and the TLR rates observed in

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CENTRAL ILLUSTRATION 24-month target lesion failure and its composite for the overall cohort and the subgroup of patients with diabetes, NSTEMI, and type B2/C lesions.

Kaplan-Meier estimates in the overall cohort and in high-risk subgroups. A) TLF and its subcomponents cardiac death (B), clinically-driven TLR (C) and target-vessel MI (D). MI: myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; TLF: target lesion failure; TLR: target lesion revascularisation

BIOSOLVE-IV still bear room for improvement. It remains to be seen if the third-generation drug-eluting resorbable magnesium scaffolds (DREAMS 3G; BIOTRONIK) will provide improved performance outcomes while maintaining the safety profile of the Magmaris. DREAMS 3G is currently being tested in the BIOMAG-I study (ClinicalTrials.gov: NCT04157153).

Limitations

The main limitation of the BIOSOLVE-IV registry is the single-arm design, hampering comparisons to other devices. However, the aim of BIOSOLVE-IV was not to compare it against other devices, but to ensure a safe rollout of this new technology. As is inherent to the nature of an observational registry, angiographic

outcomes were not assessed. Additionally, the use of IVUS and OCT was not recorded. The strengths of BIOSOLVE-IV are the good follow-up compliance and that events were adjudicated by an independent clinical events committee.

Conclusions

The BIOSOLVE-IV registry showed good safety and performance outcomes, which were comparable to contemporary DES, confirming its safe rollout into clinical practice. In contrast to precursor studies, scaffold thromboses were observed, emphasising the need for strict antiplatelet therapy adherence. However, scaffold thrombosis rates are still low and lower than observed for first-generation resorbable polymeric scaffolds, particularly in terms of late thrombotic events.

Impact on daily practice

This is the largest series of 24-month outcomes for the second-generation drug-eluting absorbable magnesium scaffold to date (DREAMS 2G, commercial name Magmaris), powered for the endpoints of definite or probable scaffold thrombosis and TLF. The performance objectives were met, confirming the safe roll-out into clinical practice after obtaining market approval in Europe and Asia with good safety and performance outcomes comparable to state-of-the-art DES; however, the importance of strict DAPT adherence was highlighted, as half of the scaffold thromboses occurred after premature DAPT interruption. With more than 2,000 patients enrolled, BIOSOLVE-IV addresses the call for more data from the European medical societies.

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Conflict of interest statement

J. Torzewski reports speaker fees and support to attend EuroPCR 2022 from BIOTRONIK; and is an associated editor of *Frontiers in Cardiovascular Medicine*. J. Bennett has received research grants and speaking fees from Abbott Vascular and BIOTRONIK. M. Haude reports grants and/or contracts from BIOTRONIK, Cardiac Dimensions, OrbusNeich, and Philips; consulting fees from BIOTRONIK, Cardiac Dimensions, and OrbusNeich; honoraria and/or speaker fees from BIOTRONIK, Cardiac Dimensions, OrbusNeich, and Philips; support to attend meetings/travel support from BIOTRONIK; is a steering committee member of the BIOSOLVE and BIOMAG trials; and is a past president of EAPCI. M. Wiemer reports lecturer honoraria from BIOTRONIK and received support from BIOTRONIK for attending EuroPCR 2022. S. Verheye reports grants/contracts from BIOTRONIK and Elixir Medical; consulting fees from Neovasc; and speaker fees from Elixir Medical. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Table 1. Baseline characteristics per subgroups.

Supplementary Table 2. Procedural characteristics per subgroup.

Supplementary Table 3. Uni- and multivariate analysis for target lesion failure.

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Supplementary data

Supplementary Table 1. Baseline characteristics per subgroups.

	NSTEMI			Diabetes			Type B2/C lesions		
	Yes N=383	No N=1675	p-value	Yes N=446	No N=1620	p-value	Yes N=320	No N=1746	p-value
Age	59.8 ± 10.9	62.4 ± 10.4	<0.0001	63.0 ± 9.7	61.6 ± 10.7	0.007	62.6 ± 11.0	61.7 ± 10.5	0.151
Male	276 (72.1)	1258 (75.1)	0.218	355 (72.2)	1217 (75.1)	0.209	73 (72.8)	1292 (74.0)	0.229
Hypertension	231 (60.3)	1136 (67.8)	0.005	367 (82.3)	1003 (61.9)	<0.0001	218 (68.1)	1152 (66.0)	0.455
Hyperlipidemia	207 (54.0)	1135 (67.8)	<0.0001	333 (74.7)	1014 (62.6)	<0.0001	223 (69.7)	1124 (64.4)	0.067
Diabetes	79 (20.6)	365 (21.8)	0.617	446 (100.0)	0 (0.0)	-	70 (21.9)	376 (21.5)	0.892
Renal disease	25 (6.5)	100 (6.0)	0.680	46 (10.3)	79 (4.9)	<0.0001	29 (9.1)	96 (5.5)	0.014
History of smoking	257 (67.1)	961 (57.4)	0.0005	190 (42.6)	645 (39.8)	0.298	136 (42.5)	699 (40.0)	0.411
Previous PCI	69 (18.0)	522 (31.2)	<0.0001	155 (34.8)	439 (27.1)	0.002	98 (30.6)	496 (28.4)	0.421
History of MI	82 (21.4)	363 (21.7)	0.911	113 (25.3)	335 (20.7)	0.035	66 (20.6)	382 (21.9)	0.617
All lesions	N=398	N=1747		N=463	N=1691		N=345	N=1809	
Lesion length (mm)	14.9 ± 4.1	14.8 ± 4.0	0.599	14.6 ± 4.0	14.9 ± 4.0	0.692	16.5 ± 4.4	14.5 ± 3.8	<0.0001
RVD (mm)	3.23 ± 0.27	3.23 ± 0.28	0.832	3.21 ± 0.28	3.24 ± 0.28	0.037	3.25 ± 0.29	3.23 ± 0.28	0.134

Diameter stenosis (%)	87.5 ± 10.0	81.0 ± 10.4	<0.0001	8.0 ± 11.0	82.6 ± 10.5	0.004	82.7 ± 10.3	82.1 ± 10.7	0.409
Target vessel			0.753			0.361			0.908
LAD	192 (48.2)	871 (49.9)		216 (46.7)	851 (50.3)		176 (51.0)	891 (49.3)	
LCX	89 (22.4)	349 (20.0)		93 (20.1)	348 (20.6)		66 (19.1)	375 (20.7)	
RCA	113 (28.4)	505 (28.9)		148 (32.0)	472 (27.9)		99 (28.7)	521 (28.8)	
RI	4 (1.0)	22 (1.3)		6 (1.3)	20 (1.2)		4 (1.2)	22 (1.2)	
AHA/ACC classification			0.582			0.504			-
Type A	142 (35.7)	667 (38.2)		181 (39.1)	632 (37.4)		0 (0.0)	813 (44.9)	
Type B1	189 (47.5)	822 (47.1)		212 (45.8)	800 (47.3)		17 (4.9)	995 (55.0)	
Type B2	54 (13.6)	198 (11.3)		50 (10.8)	205 (12.1)		254 (73.6)	1 (0.1)*	
Type C	13 (3.3)	60 (3.4)		20 (4.3)	54 (3.2)		74 (21.4)	0 (0.0)	
Calcification			0.219			0.0009			<0.0001
None	212 (53.3)	944 (54.0)		233 (50.3)	927 (54.8)		137 (39.7)	1023 (56.6)	
Mild	160 (40.2)	668 (38.2)		176 (38.0)	656 (38.8)		137 (39.7)	695 (38.4)	
Moderate	23 (5.8)	131 (7.5)		50 (10.8)	105 (6.2)		68 (19.7)	87 (4.8)	
Severe	3 (0.8)	4 (0.2)		4 (0.9)	3 (0.2)		3 (0.9)	4 (0.2)	
Tortuosity			0.598			0.446			<0.0001
Little	349 (87.7)	1528 (87.5)		399 (86.2)	1487 (87.9)		268 (77.7)	1618 (89.4)	
Moderate	48 (12.1)			62 (13.4)	193 (11.4)		71 (20.6)	184 (10.2)	
Excessive	1 (0.3)	207 (11.8)		2 (0.4)	11 (0.7)		6 (1.7)	7 (0.4)	

Bifurcation involved	21 (5.3)	77 (4.4)	0.454	16 (3.5)	83 (4.9)	0.186	21 (6.1)	78 (4.3)	0.149
Thrombus present	2 (0.5)	1 (0.1)	0.090	0 (0.0)	3 (0.2)	>0.999	2 (0.6)	1 (0.1)	0.069

Data are mean \pm SD, or n (%). * The patient had a type B2/C lesion and a type A/B1 lesion and was hence counted to the type A/B1 lesion group. CABG-coronary artery bypass graft, LAD-left anterior descending, LCX-left circumflex artery, MI-myocardial infarction, NSTEMI-non-ST-elevation myocardial infarction, PCI-percutaneous coronary intervention, RCA-right coronary artery, RI-ramus intermedius, RVD-reference vessel diameter, STEMI-ST-elevation myocardial infarction

Supplementary Table 2. Procedural characteristics per subgroup.

	NSTEMI			Diabetes			Type B2/C lesions		
	Yes N=398	No N=1747	p- value	Yes N=463	No N=1691	p- value	Yes N=345	No N=1809	p-value
Pre-dilatation	397 (99.7)	1744 (99.8)	0.560	463 (100.0)	1687 (99.8)	0.584	345 (100.0)	1805 (99.8)	>0.999
Max. pressure, atm	14.4 ± 3.4	14.7 ± 3.5	0.226	15.0 ± 3.6	14.5 ± 3.4	0.009	15.0 ± 3.4	14.5 ± 3.4	0.013
Scaffold length, mm	19.6 ± 3.8	19.4 ± 3.9	0.457	19.4 ± 4.0	19.5 ± 3.9	0.775	21.0 ± 4.1	19.2 ± 3.8	<0.0001
Scaffold σ , mm,	3.2 ± 0.3	3.2 ± 0.3	0.648	3.22 ± 0.2	3.25 ± 0.3	0.035	3.26 ± 0.3	3.24 ± 0.3	0.300
Max. pressure, atm	14.4 ± 2.8	14.3 ± 2.7	0.581	14.5 ± 2.9	14.3 ± 2.7	0.317	14.4 ± 2.7	14.3 ± 2.7	0.898
Post-dilatation	380 (95.5)	1672 (95.7)	0.787	445 (96.1)	1616 (95.6)	0.608	336 (97.4)	1725 (95.4)	0.088
Max. pressure, atm	16.8 ± 3.3	17.1 ± 3.4	0.209	17.2 ± 3.2	17.0 ± 3.4	0.227	16.9 ± 3.4	17.1 ± 3.3	0.478
Device success, per stent	407 (98.3)	1762 (97.5)	0.374	460 (96.8)	1718 (97.8)	0.233	357 (96.5)	1821 (97.8)	0.133
Procedure success, per patient	377 (98.7)	1662 (99.4)	0.174	442 (99.3)	1605 (99.3)	>0.999	317 (99.7)	1730 (99.2)	0.492

Data are shown as mean±SD or n (%). Device success was defined as a final diameter stenosis of <30% using the assigned device only, successful delivery of the scaffold, appropriate scaffold deployment, and successful removal of the delivery system. Procedure success was defined final diameter stenosis <30% without the occurrence of death, myocardial infarction, or repeat target lesion revascularization during the hospital stay.

Supplementary Table 3. Uni- and multivariate analysis for target lesion failure.

	Univariate analysis		Multivariate analysis	
	HR	p-value	HR	p-value
Age, years	0.99 [0.97;1.00]	0.050	0.99 [0.97; 1.00]	0.088
Type B2/ C lesions	1.22 [0.79; 1.89]	0.363	-	-
Moderate/ severe calcification	1.06 [0.57; 1.96]	0.854	-	-
Diabetes	1.07 [0.71; 1.59]	0.758	-	-
Mean lesion length, mm	1.05 [1.01; 1.09]	0.027	1.04 [1.00;1.08]	0.057
NSTEMI at baseline	1.55 [1.05; 2.27]	0.026	1.49 [1.01; 2.19]	0.045
Previous coronary surgeries/ interventions	0.91 [0.62; 1.32]	0.618	-	-
Mean reference vessel diameter, mm	0.82 [0.45; 1.50]	0.514	-	-
Smoking	1.06 [0.76; 1.50]	0.727	-	-

Age is considered as integral value and the HR is assessed by increase of patients' years (i.e. an increase in one patient year has a HR of 0.99), lesion lengths and reference vessel diameter are continuous values and HR is assessed by mm. HR-hazard ratio [95%CI], NSTEMI-non ST-elevation myocardial infarction