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Safety and performance of a resorbable magnesium scaffold under real-world conditions: 12-month outcomes of the first 400 patients enrolled in the BIOSOLVE-IV registry

Short running title: BIOSOLVE-IV registry

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Conflict of Interest statement

Stefan Verheye reports speaking fees from Alvimedica, Biotronik, and Elixir Medical. Michael Haude reports study grants and personal fees from Biotronik, Abbott Vascular, Cardiac dimensions, and Philips, AA reports grants from Biotronik. Johan Bennett has received research grants and speaking fees from Abbott Vascular and Biotronik AG. All other authors reported no conflict of interest.

Classifications:
NSTEMI; Stable angina; Bioresorbable scaffolds; Myocardial infarction; Stent thrombosis

Abbreviations

DAPT	Dual Antiplatelet Therapy
DES	Drug-Eluting Stent
NSTEMI	Non-ST Elevation Myocardial Infarction
TLF	Target Lesion Failure
TLR	Target Lesion Revascularization
TV-MI	Target Vessel Myocardial Infarction

Introduction

Magmaris (Biotronik AG, Bülach, Switzerland) is a magnesium-based scaffold that has been successfully tested in 184 patients enrolled in the BIOSOLVE-II and -III studies (1,2). After gaining CE-certification in June 2016, it was paramount to test this device in clinical routine to ensure a safe roll-out of this technology.

Methods

BIOSOLVE-IV is an international, single arm, multi-center registry conducted in 86 centers. The first patient was enrolled in September 2016. In- and Exclusion criteria and endpoints are listed on ClinicalTrials.gov (NCT02817802).

Clinical follow-up was scheduled at 6 and 12 months, and annually until 5 years (telephone follow-ups were permitted). The study was performed according to the Declaration of Helsinki and ISO14155:2011, was approved by the ethics committees, and all patients provided written informed consent. Monitoring encompassed a minimum of 25% random subjects per center; an angiographic core laboratory assessed endpoint related events and device failures. All potential device-related events were adjudicated by an independent clinical events committee member. In case of disagreement with study site, the case was reviewed by a second clinical events committee member.

Magmaris has been described previously (1,2). Pre-dilatation using a non-compliant balloon with a 1:1 balloon-to-artery ratio was mandatory. The balloon should expand fully and the residual stenosis before Magmaris implantation ought to be < 20%. The scaffold implantation ought to follow the recommendation of the instructions for use and the consensus letter of Fajadet et al (3). Post-dilatation with a non-compliant balloon at high pressure (>16 atm) was recommended. Dual antiplatelet therapy (DAPT) was recommended for at least 6 months.

The sample size of 2054 patients was calculated based on the null-hypothesis that Magmaris has a 12-month probable or definite scaffold thrombosis rate of ≥1.49%. Endpoint analyses were planned after every 200 subjects reaching the primary endpoint.

Results

This publication refers to the first 400 patients with 425 lesions enrolled. Patient age ranged from 29 to 86 years (Table 1), and 63 patients (15.8%) presented with non-ST elevation myocardial infarction (NSTEMI) (Figure 1). Pre- and post-dilatation were performed in nearly all patients. Magmaris could not be implanted in 3 (0.8%) (Table 2).

At 12 months follow-up data, 2 patients had died of cancer, 6 visits were missed and one patient withdrew consent (compliance of 98.2%, 390/397); on DAPT were 76.8% (298/388). The primary endpoint, target lesion failure (TLF) at 12 months was 4.3% (n=17, Figure 2), all had clinically driven target lesion revascularization (TLR), of whom 3 (0.8%) had additional target-vessel myocardial infarction (TV-MI).

One definite scaffold thrombosis (0.3%) occurred on post-procedure day 10. The patient was admitted with NSTEMI and severe 3-vessel coronary artery disease. First, the occluded circumflex artery using a non-study stent was treated. Four days later, the index procedure with the Magmaris scaffold was performed to treat a stenosis in a heavily calcified right coronary artery. Thereafter, a minimally invasive direct coronary artery bypass graft (left internal mammary artery to ramus interventricularis anterior) was intended and hence DAPT was interrupted 5 days after the index procedure. Five days later, a scaffold thrombosis occurred that led to a TV-MI and required a TLR. The patient was alive at 12 months.

Discussion

This pre-specified interim-analysis of the first 400 patients enrolled in the BIOSOLVE-IV registry confirmed the favourable safety outcomes of the BIOSOLVE-II and -III trials with low TLF-rates at 12 months comparable to new generation permanent drug-eluting stents (DES), no cardiac death and only one scaffold thrombosis that occurred after DAPT interruption.

Comparing outcomes to the BIOSOLVE-II and -III studies, in BIOSOLVE-IV, baseline characteristics were similar with relatively simple lesions. The only relevant difference was the inclusion of 15.8% NSTEMI patients who were excluded in the precursor studies (1,2). The rate of TLF was also similar, albeit clinically driven TLR was slightly higher in BIOSOLVE-IV. One definite scaffold thrombosis occurred in our series, which is the first definite scaffold thrombosis in the 584 patients published to date (1,2). It occurred at day 10 after DAPT cessation in a patient with severe 3-vessel disease after a staged procedure, emphasizing that DAPT in the early days after Magmaris implantation is as important as after DES implantation.

Our outcomes are also within the range of the objective performance criteria for new generation stents as postulated by the ESC/EAPCI s task force, namely 2.91% TLR (IQR 1.67–5.94) and 0.47% definite stent thrombosis (IQR 0.28–0.72) at 9- to 12-month follow-up (4).

Limitations

BIOSOLVE-IV has limitations inherent to observational registries.

Conclusion

This preliminary analysis after 400 patients enrolled in the BIOSOLVE-IV real-world registry confirms the safe roll-out of a magnesium-based bioresorbable scaffold into clinical practice with low TLF rates and only one scaffold thrombosis after DAPT cessation.

Impact on daily practice

This registry represents the largest clinical experience with the sirolimus-eluting magnesium based Magmaris BRS to date. It provides additional assurance on the safety and performance of the

device with low TLF- and stent thrombosis rates. DAPT cessation prior to 6 months should be strongly discouraged.

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Figure 1 Ischemic status at baseline and follow-up

NSTEMI-non ST-elevation myocardial infarction

Figure 2 Kaplan-Meier estimates of Clinical Outcomes up to 12 months

TLF-target lesion failure, TLR- target lesion revascularization, TV-MI-target vessel myocardial infarction (periprocedural MI were adjudicated using SCAI definitions and spontaneous MI using the extended historical definitions), TVR-clinically driven target vessel revascularization

Table 1: Baseline Clinical and Lesion Characteristics

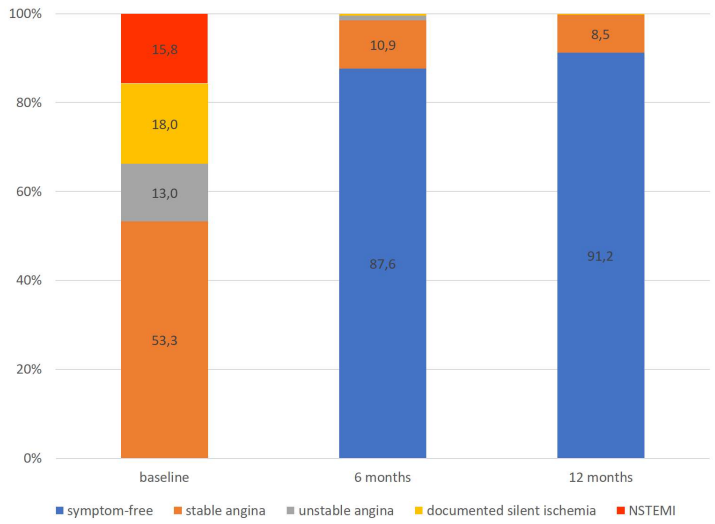
Patients	**N=400**
Mean age, years	62.0 ±11.0
Male	294 (73.5)
Hypertension	255 (63.8)
Diabetes	78 (19.5)
Insulin-dependent	*15 (19.2)*
History of myocardial infarction	73 (18.3)
Previous percutaneous coronary interventions	93 (23.3)
Lesions[a]	**N=425**
Lesion length, mm	14.5±4.1
Reference vessel diameter, mm	3.3±0.3
Diameter stenosis, %,	82.3±10.4
AHA/ACC classification type B2/C	75 (17.7)
Bifurcation lesion	24 (5.6)

Data are shown as mean±SD or n (%), [a] per site assessment

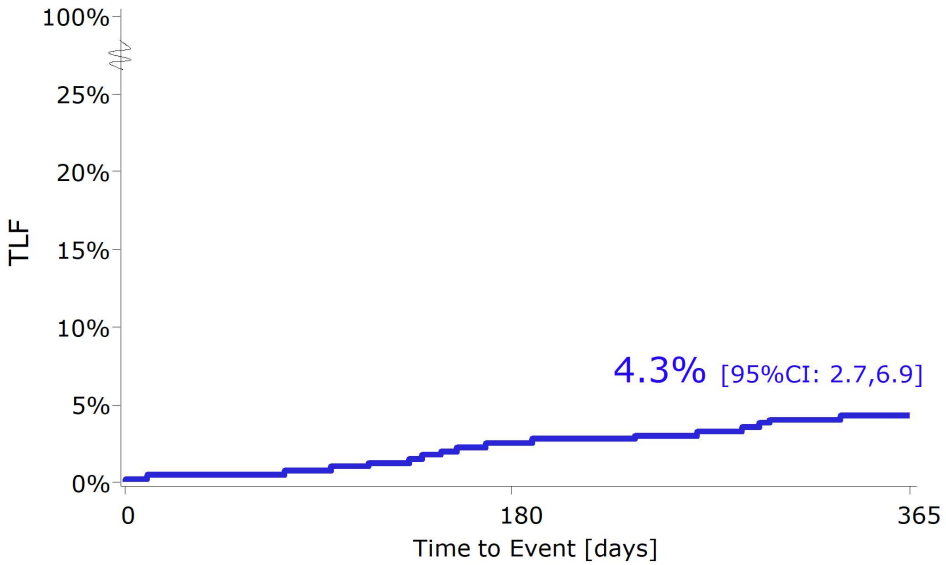
Table 2: Procedural characteristics

	N=425
Pre-dilatation performed	423 (99.5)
Maximum pressure applied, atm, N=545	13.6±3.2
Scaffold sizes	
3.0x15 mm/ x20 mm/ x25 mm	89 (20.5)/89 (20.5)/ 53 (12.2)
3.5x15mm/ x20 mm/ x25 mm	69 (15.9)/ 80 (18.4)/ 54 (12.4)
Maximum pressure applied, atm, N=431	13.9±2.8
Post-dilatation performed	403 (94.8)
Maximum pressure applied, atm, N=466	17.0±3.5
Device success, n=439 stents	422 (96.1)
Procedure success, n=400 patients	394 (98.5)

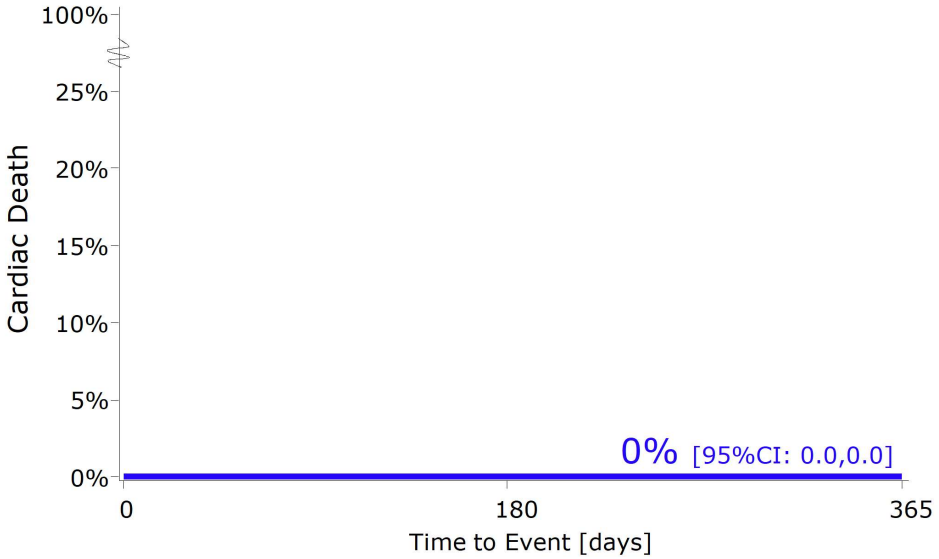
Data are shown as mean±SD or n (%). Device success was defined as a final diameter stenosis of <30% using the assigned device only, successful delivery of the scaffold, appropriate scaffold deployment, and successful removal of the device. Procedure success was defined final diameter stenosis <30% without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



TLF (MI acc to SCAI/Ext. Def.)

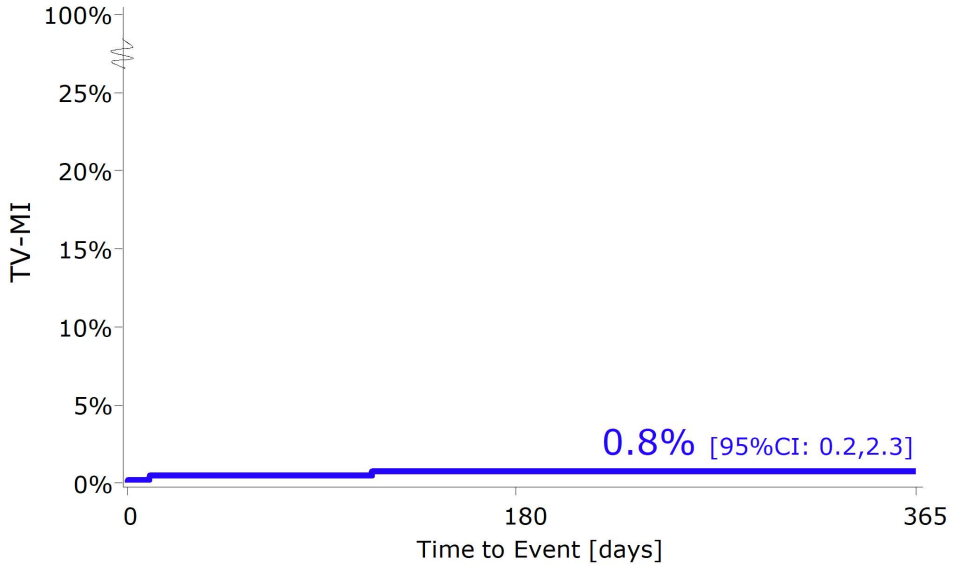


description	day 0	180 days	365 days
At risk	396	383	177
n	1	10	17
Failure (estimate)	0.3 [0.0, 1.8]	2.5 [1.4, 4.6]	4.3 [2.7, 6.9]

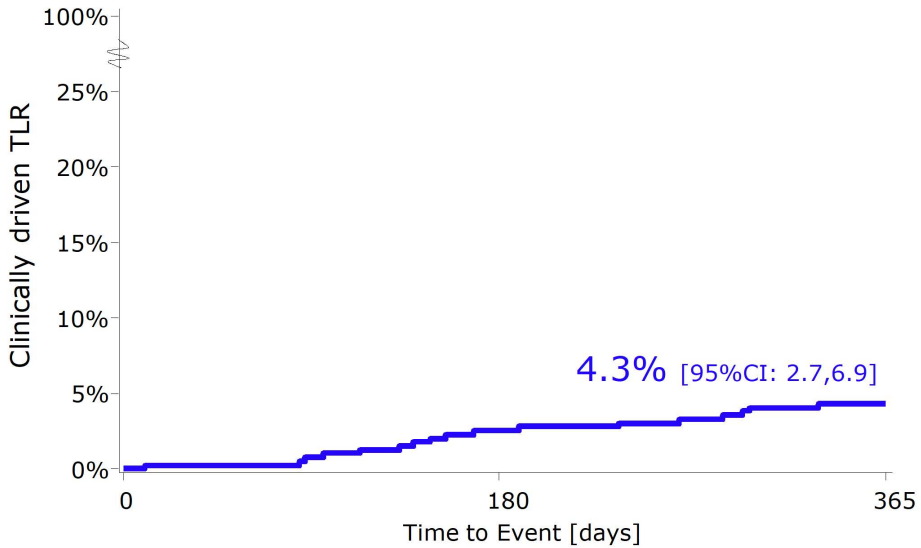


description	day 0	180 days	365 days
At risk	397	392	187
n	0	0	0
Failure (estimate)	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]

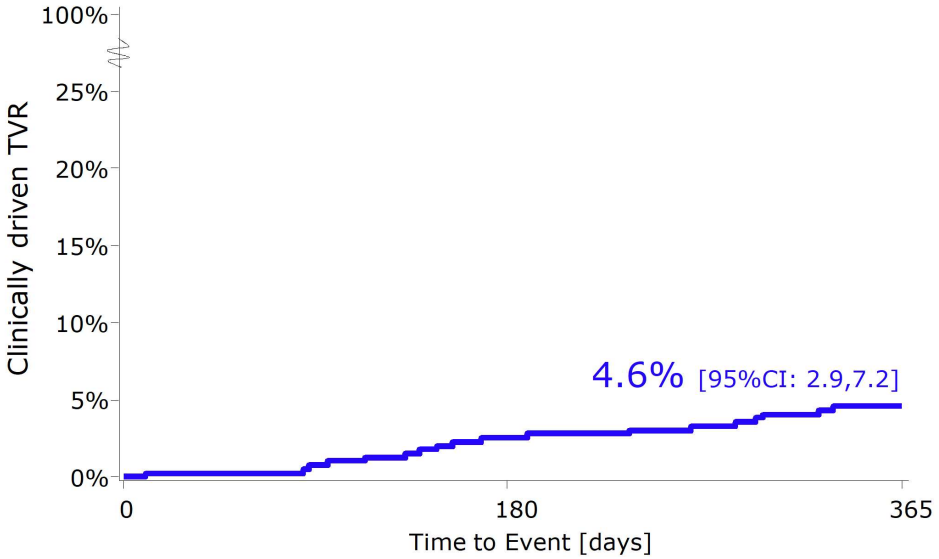
MI acc to SCAI/Ext. Def.



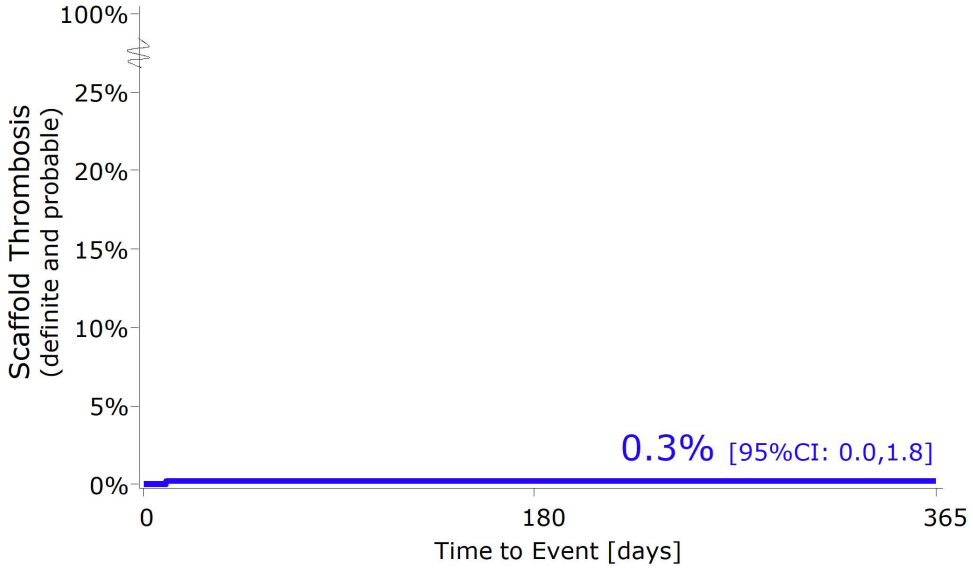
description	day 0	180 days	365 days
At risk	396	389	185
n	1	3	3
Failure (estimate)	0.3 [0.0, 1.8]	0.8 [0.2, 2.3]	0.8 [0.2, 2.3]



description	day 0	180 days	365 days
At risk	397	383	177
n	0	10	17
Failure (estimate)	0.0 [0.0, 0.0]	2.5 [1.4, 4.6]	4.3 [2.7, 6.9]



description	day 0	180 days	365 days
At risk	397	383	177
n	0	10	18
Failure (estimate)	0.0 [0.0, 0.0]	2.5 [1.4, 4.6]	4.6 [2.9, 7.2]



description	day 0	180 days	365 days
At risk	397	391	186
n	0	1	1
Failure (estimate)	0.0 [0.0, 0.0]	0.3 [0.0, 1.8]	0.3 [0.0, 1.8]