


# Safety and Efficacy Outcomes of 3rd Generation DES in an All-Comer Population of Patients Undergoing PCI: 12-Month and 24-Month Results of the e-Biomatrix French Registry

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**Objectives:** The French Ebiomatrix registry aimed to confirm the results of the Leaders trial in an all-comer population in France. **Background:** The Leaders trial showed the Biolimus-eluting-stent (BES) to be equivalent to the Cypher stent in terms of safety and efficacy at 1 year and superior regarding stent thrombosis after 1 year. **Methods:** BES recipients were enrolled in 42 French centers with up to 24-month clinical follow up. **Results:** 2365 patients were included. Mean age: 65.7 ± 11.2 years, 76.1% males, 31.8% had diabetes, 36.5% ACS (28.7% non-ST-elevation MI and 7.8% with ST-elevation MI). 1.7 ± 1.0 stents/patient were implanted and procedural success was 99.5%. 12-month follow-up was completed in 94.3% patients and 24 months in 91.4%. MACCE rates at 12 and 24 months were 5.8% and 9% (all cause-death 1.5% and 2.2%; stent thrombosis definite/probable 0.4% and 0.6%), respectively. MACCE were not significantly higher in diabetic patients compared with non-diabetics but cardiac death was higher (1.6% vs. 0.6%,  $P = 0.01$  at 1 year and 1.9% vs. 0.6%,  $P = 0.005$  at 2 years) as was stent thrombosis (0.9% vs. 0.2%,  $P = 0.009$  and 1.2 vs. 0.3%  $P = 0.008$ ). Compared with non-ACS patients, MACCE was significantly higher in the ACS subgroup (7.5% vs. 4.8%,  $P = 0.001$  at 1 year and 10.3% vs. 8.1%,  $P = 0.07$  at 2 years). **Conclusion:** In this large real-world registry, the BES with biodegradable polymer showed excellent acute and mid-term outcomes with a 5.8% and 9% rate of MACCE at one and 2 years and a very low rate of stent thrombosis between 1 and 2 years (0.2%), thus demonstrating the replicability of the LEADERS trial in a registry population. © 2017 The Authors Catheterization and Cardiovascular Interventions Published by Wiley Periodicals, Inc.

**Key words:** drug-eluting stent; biolimus-eluting stent; stent thrombosis

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## INTRODUCTION

Although 1st generation drug-eluting stents with durable polymer proved more efficient than bare-metal stents in reducing the occurrence of restenosis in patients with coronary artery disease (CAD) [1–5], the problem of late stent thrombosis remained a permanent cause for concern [6]. To address this issue, a new generation of drug-eluting stents (DES) with biodegradable polymer was developed with the purpose of decreasing the risk of stent thrombosis (ST) as well as the duration of dual anti-platelet therapy (DAPT) [7,8].

The CE marked BioMatrix™ and BioMatrix Flex™ Drug Eluting Coronary Stent Systems (BioMatrix™ and BioMatrix Flex™ DES) are combination products comprising two key components: the stent (which includes the active pharmaceutical ingredient (API) BA9™ incorporated into a polymer coating), and the delivery catheter. BA9 (Biolimus A9) is a recently discovered, proprietary semi-synthetic Sirolimus analogue. It is highly lipophilic, rapidly absorbed in tissues, and able to reversibly inhibit growth factor-stimulated cell proliferation. The biodegradable polymer is polylactic acid (PLA), which has been widely used in a variety of medical applications. Polylactic acid, its co-polymers, and mixtures have been evaluated in pre-clinical, and clinical studies. The biodegradable polymer is applied to the abluminal surface of the stent and dissolves within less than a year, thus eliminating the risk of inflammatory stimulus associated with durable polymer [9,10].

The safety and efficacy of the BioMatrix™ biolimus-eluting stent was compared with the sirolimus-eluting Cypher Select™ stent in the LEADERS Trial [11,12], a randomized, single-blinded, non-inferiority trial, in a total of 1707 patients (2472 lesions). The reported 5-year results of this trial confirmed the non-inferiority of the BES compared with the sirolimus-eluting stent in the composite endpoint of all-cause death, any MI and all-cause revascularization [13]. Indeed, the benefit of the BES was related to a significant reduction in the patient-oriented composite endpoint of all cause death, any MI and all cause revascularization (297 [35.1%] vs. 339 [40.4%], RR: 0.84 [95% CI: 0.71 to 0.98, *P* for superiority = 0.023) In addition, the BES was associated with a significant reduction in very late definite ST from 1 to 5 years (*n* = 5 [0.7%] vs. *n* = 19 [2.5%], RR: 0.26 [95% CI: 0.10 to 0.68, *P* = 0.003).

A multi-center registry was conducted in Europe [14] to investigate in a large population of all-comer patients, the reproducibility of the results achieved with the BES in the LEADERS trial.

Along the same lines, the purpose of the observational study reported here was to collect clinical data for the BioMatrix™ and the BioMatrix Flex™ Drug Eluting Coronary Stent System (Biolimus A9, BA9™-) in

normal practice in 42 French centers to find out whether the results of the LEADERS trial could be replicated in a real-world registry.

## METHODS

The e-BioMatrix France Registry is a prospective, multi-center post-market observational/non-interventional study designed to assess outcomes in a “real world, all-comer” population of patients with symptomatic coronary artery disease including patients with chronic stable angina, silent ischemia, and acute coronary syndromes, eligible for percutaneous coronary interventions with either the BioMatrix™ or the BioMatrix Flex™ stent (BioMatrix, Biosensors Europe SA, Morges, Switzerland), a DES with a biodegradable polymer polylactic acid (PLA) coating containing the BA9 drug (Biolimus A9). The BioMatrix Flex is the more recent iteration with a platform design change providing improved flexibility. The registry was conducted in 42 centers in France (Appendix A).

Baseline data were collected between January 2011 and March 2013 in eligible patients who received one or more BES. Patients were followed-up for up to 2 years until March 2015.

### Inclusion Criteria

Patients were included in the study if they had a clinical indication for percutaneous coronary intervention [PCI], with one or more coronary artery stenoses in a native coronary artery that could be covered with one or multiple BioMatrix stents. There were no restrictions regarding the clinical presentation, the number of treated vessels, or the number, type and length of treated lesions.

### Exclusion Criteria

Patients were excluded from the registry if any additional stent(s) not of the BES type were implanted during the index procedure, or if any lesions were treated solely by means of other techniques (stand-alone balloon angioplasty, atherectomy, etc.). Dual anti-platelet treatment with aspirin and a P2Y12 blocker was recommended for a duration of 12 months if possible and a minimum of 6 months in all cases.

The study complied with the declaration of Helsinki and was approved by the ethics committee (CCTIRS, Paris). All patients provided written informed consent for participation in this registry, either before or as soon as possible after the procedure.

### Data Collection and Management

The baseline data collected for the e-BioMatrix France registry included demographic information,

cardiovascular history, comorbidity, lesion and procedure characteristics and antithrombotic regimens. Follow-up intervals were scheduled at 12 months and 2 years via hospital visit or telephone contact to keep track of anginal status, medication intake and of any adverse event.

Data were collected electronically at each participating center and stored in a central database (Clinigrid, France). 100% of patient consent forms as well as all reported Major Adverse Cardiac Events (MACE), bleeding events and stent thromboses were monitored and random monitoring of an additional 15% of patients files was carried out by CERC.

### Study Organization and Supervision

The registry was conducted by an independent research organization (CERC).

All MACCE, bleeding events and stent thromboses were adjudicated by an independent Clinical Event Committee (Appendix B).

### Endpoints

The primary endpoint of the study (MACCE 1) was the occurrence of major adverse cardiac and cerebrovascular events in the overall population, defined as a composite of cardiac death, myocardial infarction (Q-wave and non-Q-wave), cerebrovascular events or clinically indicated target vessel revascularization at 12 months.

The secondary endpoints (MACCE 2) were the occurrence of stent thrombosis (definite and probable according to ARC definitions) at 12 months and 2 years and major adverse cardiac and cerebrovascular events in the overall population, defined as a Patient Oriented Composite Endpoint including all-cause mortality, MI (Q-wave and non-Q-wave), cerebrovascular events or any clinically driven target vessel revascularization at 12 months and 2 years.

### Definitions

Cardiac death was defined as any death due to an immediate cardiac cause (e.g., MI, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown causes, and all procedure-related deaths, including those related to concomitant treatment. Q-wave MI was defined as the development of new, pathological Q-waves in two or more contiguous leads (as assessed by the CEC) with or without post-procedure CK or CK-MB levels elevation above normal. Peri-procedural non-Q-wave MI was defined as the elevation of CK levels to  $> 3$  times the upper limit of normal, with CK-MB or troponin elevation if available, in the absence of pathological Q-waves. Spontaneous non-Q wave MI

was diagnosed if symptoms and/or ECG changes were associated with elevated biomarkers (CK, CKMB or troponin) above the upper limit of normal. Clinically indicated target vessel revascularization [ci-TVR] was defined as a repeat percutaneous intervention or bypass surgery of the target vessel associated with either a  $>70%$  vessel diameter reduction or a  $>50%$  diameter reduction together with angina and/or documented ischemia.

ST was classified as definite, probable and possible according to ARC definitions [15].

Bleeding was classified as major [MB] or minor according to the STEEPLE definitions [16].

Staging of the index procedure was allowed when the 2nd procedure was planned at the time of the initial procedure and scheduled for within 90 days providing that study stents alone were used. Renal failure was considered present when pre-procedure plasma creatinine was  $\geq 2.95$  mg/dl or 260  $\mu\text{mol/l}$ .

### Statistical Analysis

For all patients, standard descriptive statistics were used for baseline, lesion and procedural characteristics and for clinical results. Continuous variables are presented as mean  $\pm$  SD or median and range, and categorical variables are presented as numbers and percentages. Cumulative incidences of adverse clinical events were estimated using the Kaplan–Meier method.

All statistical analyses were performed using R 3.0.1 (R Core Team. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria, 2013).

## RESULTS

From January 2011 to December 2012, 2548 patients were enrolled in 42 French centers. A total of 183 patients were excluded, 88 of whom either did not provide or withdrew their informed consent, 78 did not receive the study stent and 17 did not fulfill the inclusion/exclusion criteria. The study population, therefore comprised 2,365 patients (Fig. 1). Baseline demographics and procedural data are shown in Tables I and II. Mean patient age was  $65.7 \pm 11.2$  years, 76.1% were males, 31.8% had diabetes and 36.5% presented with an acute coronary syndrome (28.7% non-ST-elevation MI and 7.8% with ST-elevation MI). A mean of  $1.7 \pm 1.0$  stents/patient were implanted. Procedural success including both index and staged procedures was 99.5% and complete revascularization was achieved in 81.4%.

Twelve-month and 24-month follow-up data were obtained in 94.3% and 91.4% of patients, respectively. The combined incidence of major adverse events at 12 months (MACCE 1, primary endpoints) was 5.8% and

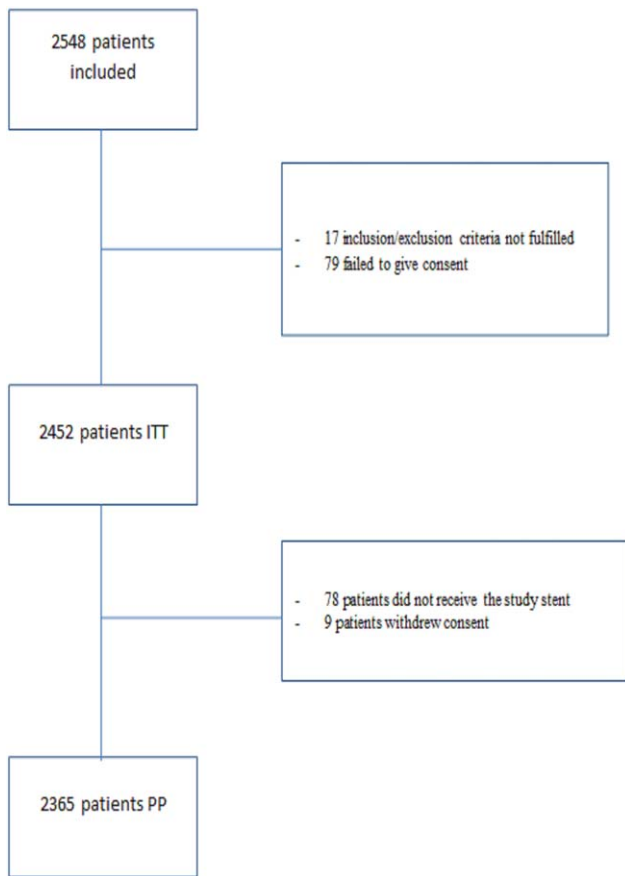


Fig. 1. Study flow chart. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE I. Baseline characteristics and clinical status of the study population

Variables	Number of patients (N = 2,365)
Age	65.7 ± 11.2
Male	1799 (76.1%)
Body mass index ≥30	571 (24.1%)
Diabetes	752 (31.8%)
Smoking	497 (21.0%)
Dyslipidemia	1511 (63.9%)
Hypertension	1437 (60.1%)
Family history	668 (28.3%)
Renal insufficiency	134 (5.7%)
History of PCI	702 (29.7%)
History of CABG	122 (5.2%)
Congestive heart failure	57 (2.4%)
ACS	863 (36.5%)
ST-elevation ACS	184 (7.8%)
Non ST-elevation ACS	679 (28.7%)
Non ACS	1502 (63.5%)
Stable angina	836 (35.3%)
Silent ischemia	666 (28.1%)
STEMI & NSTEMI	332 (14.0%)
Stroke	79 (3.3%)

PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft; ACS = acute coronary syndrome; STEMI = ST segment elevation myocardial infarction; NSTEMI = non ST segment elevation myocardial infarction.

TABLE II. Lesion and procedural characteristics and medications

Variables	Number of patients (N = 2,365)
Single vessel disease, n	1,296 (54.8%)
Multiple vessel disease, n	1,063 (45.2%)
Bifurcation lesion, n	596 (16.2%)
Chronic total occlusion, n	280 (7.6%)
Radial approach, n	2,064 (87.2%)
Sheath size ≤ 6fr	2,585 (98.8%)
Stent/patient, n	1.7 ± 1.0
Stent/lesion, n	1.14 ± 0.4
Lesion/patient, n	1.5 ± 0.8
Total stent length/patient, mm	32.4 ± 22.2
Predilatation, n	1,981 (53.9%)
Post dilatation, n	615 (16.7%)
Procedural success (index/staged)	2,353 (99.5%)
Staged procedure	252 (10.6%)
Procedural complications	21 (0.8%)
2b/3a	153 (5.8%)
Bivalirudin	45 (1.7%)
DAPT	
Clopidogrel	1,994 (78.7%)
Ticagrelor	86 (3.4%)
Prasugrel	442 (17.4%)
Thienopyridine at 12 months	67.2%
Thienopyridine after 12 months	36.9%

TABLE III. Primary endpoint and secondary endpoint composite at 12 and 24 months

	N (%)	
	12-Month	24-Month
Total MACCE 1 primary endpoint <sup>a</sup>	137 (5.8%)	–
Total MACCE 2 secondary endpoint <sup>b</sup>	151 (6.4%)	213 (9.0%)
All-cause death	35 (1.5%)	53 (2.2%)
Cardiac death	21 (0.9%)	24 (1.0%)
Myocardial infarction	34 (1.4%)	43 (1.8%)
Stroke	5 (0.2%)	9 (0.4%)
TVR	94 (4.0%)	150 (6.3%)
CABG	5 (0.2%)	7 (0.3%)
PCI	89 (3.8%)	143 (6.0%)
TLR	40 (1.7%)	32 (1.4%)
CABG	4 (0.2%)	2 (0.1%)
PCI	36 (1.5%)	30 (1.3%)
Stent thrombosis	18 (0.8%)	24 (1.0%)
Definite and probable	10 (0.4%)	14 (0.6%)
Possible	8 (0.3%)	10 (0.4%)
Major bleeding	4 (0.2%)	4 (0.2%)

<sup>a</sup>Composite of cardiac death, myocardial infarction (Q-wave and non-Q-wave), cerebrovascular events or clinically indicated target vessel revascularization at 12 months.

<sup>b</sup>Definite and probable stent thrombosis at 12 months and 2 years and major adverse cardiac and cerebrovascular events (MACCE) defined as a Composite Endpoint including all-cause mortality, MI (Q-wave and non-Q-wave), cerebrovascular events or any clinically driven target vessel revascularization at 12 months and 2 years.

TVR = target vessel revascularization; TLR = target lesion revascularization.

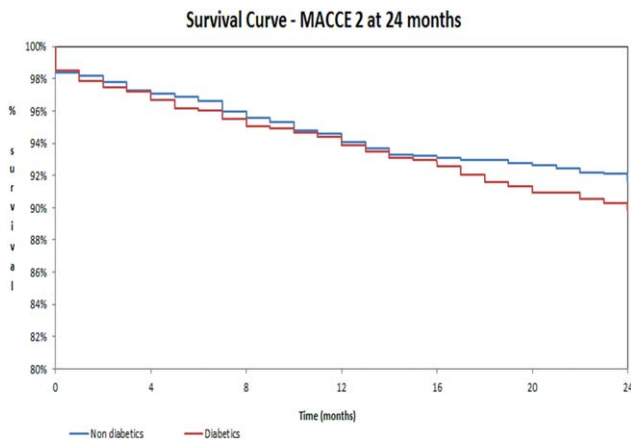
**TABLE IV. Subgroup analysis according to DM and ACS at 12 and 24 months**

	EVENTS at 12 months						EVENTS at 24 months									
	Diabetics (N=752)		Non-diabetics (N=1613)		ACS (N=863)		Non ACS (N=1502)		Diabetics (N=752)		Non-diabetics (N=1613)		ACS (N=863)		Non ACS (N=1502)	
	N (%)	N (%)	N (%)	N (%)	P	P	N (%)	N (%)	P	N (%)	N (%)	N (%)	N (%)	P	P	P
MACCE 1 <sup>a</sup>	48 (6.4%)	89 (5.5%)	65 (7.5%)	72 (4.8%)	0.40	0.001	72 (4.8%)	72 (4.8%)	0.001	76 (10.1%)	135 (8.4%)	89 (10.3%)	122 (8.1%)	0.17	0.07	0.07
Primary endpoints	46 (6.1%)	89 (5.5%)	63 (7.3%)	72 (4.8%)	0.56	0.01	72 (4.8%)	72 (4.8%)	0.01	76 (10.1%)	135 (8.4%)	89 (10.3%)	122 (8.1%)	0.17	0.07	0.07
MACCE 2 <sup>b</sup>	14 (1.9%)	21 (1.3%)	16 (1.9%)	19 (1.3%)	0.29	0.25	19 (1.3%)	19 (1.3%)	0.25	25 (3.3%)	28 (1.7%)	22 (2.5%)	31 (2.1%)	0.02	0.44	0.44
Secondary endpoints	12 (1.6%)	9 (0.6%)	11 (1.3%)	10 (0.7%)	0.01	0.13	10 (0.7%)	10 (0.7%)	0.13	14 (1.9%)	10 (0.6%)	12 (1.4%)	12 (0.8%)	0.005	0.17	0.17
All-cause death	1 (0.1%)	4 (0.2%)	1 (0.1%)	4 (0.3%)	0.17	0.30	4 (0.3%)	4 (0.3%)	0.30	2 (0.3%)	7 (0.4%)	3 (0.3%)	6 (0.4%)	0.54	0.84	0.84
Cardiac death	13 (1.7%)	21 (1.3%)	26 (3.0%)	8 (0.5%)	0.42	>0.0001	8 (0.5%)	8 (0.5%)	>0.0001	16 (2.1%)	27 (1.7%)	33 (3.8%)	10 (0.7%)	0.44	>0.0001	>0.0001
Stroke	28 (3.7%)	66 (4.1%)	33 (3.8%)	61 (4.1%)	0.67	0.78	61 (4.1%)	61 (4.1%)	0.78	49 (6.5%)	101 (6.3%)	47 (5.4%)	103 (6.9%)	0.81	0.18	0.18
MI	3 (0.4%)	2 (0.1%)	2 (0.2%)	3 (0.2%)	0.15	0.87	3 (0.2%)	3 (0.2%)	0.87	5 (0.7%)	2 (0.1%)	3 (0.3%)	4 (0.3%)	0.02	0.73	0.73
TVR	25 (3.3%)	64 (4.0%)	31 (3.6%)	58 (3.9%)	0.44	0.74	58 (3.9%)	58 (3.9%)	0.74	44 (5.9%)	99 (6.1%)	44 (5.1%)	99 (6.6%)	0.78	0.14	0.14
CABG	17 (2.3%)	23 (1.4%)	12 (1.4%)	28 (1.9%)	0.14	0.39	28 (1.9%)	28 (1.9%)	0.39	35 (4.7%)	37 (2.3%)	21 (2.4%)	51 (3.4%)	0.001	0.19	0.19
PCI	3 (0.4%)	1 (0.1%)	1 (0.1%)	3 (0.2%)	0.09	0.37	3 (0.2%)	3 (0.2%)	0.37	5 (0.7%)	1 (0.1%)	2 (0.2%)	4 (0.3%)	0.006	1	1
Stent thrombosis	14 (1.9%)	22 (1.4%)	11 (1.3%)	25 (1.7%)	0.36	0.46	25 (1.7%)	25 (1.7%)	0.46	30 (4.0%)	36 (2.2%)	19 (2.2%)	47 (3.1%)	0.015	0.19	0.19
Definite/probable	7 (0.9%)	6 (0.4%)	7 (0.8%)	11 (0.7%)	0.001	0.83	11 (0.7%)	11 (0.7%)	0.83	16 (2.1%)	8 (0.5%)	10 (1.2%)	14 (0.9%)	0.0002	0.6	0.6
Possible	5 (0.7%)	3 (0.2%)	6 (0.7%)	4 (0.5%)	0.009	0.12	4 (0.5%)	4 (0.5%)	0.12	9 (1.2%)	5 (0.3%)	9 (1.0%)	5 (0.3%)	0.008	0.03	0.03
Major bleeding <sup>a</sup>	3 (0.4%)	1 (0.1%)	1 (0.1%)	7 (0.8%)	0.06	0.16	7 (0.8%)	7 (0.8%)	0.16	7 (0.9%)	3 (0.2%)	3 (0.3%)	9 (0.6%)	0.009	0.08	0.08
Other reintervention	27 (3.6%)	36 (2.2%)	23 (2.7%)	40 (2.7%)	0.06	1	40 (2.7%)	40 (2.7%)	1	50 (6.6%)	60 (3.7%)	37 (4.3%)	73 (4.9%)	0.06	0.52	0.52
CABG	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	-	-	0 (0.0%)	0 (0.0%)	-	3 (0.4%)	1 (0.1%)	2 (0.2%)	2 (0.1%)	0.06	0.57	0.57
PCI	27 (3.6%)	36 (2.2%)	23 (2.7%)	40 (2.7%)	0.05	1	40 (2.7%)	40 (2.7%)	1	47 (6.3%)	59 (3.7%)	35 (4.1%)	71 (4.7%)	0.004	0.45	0.45

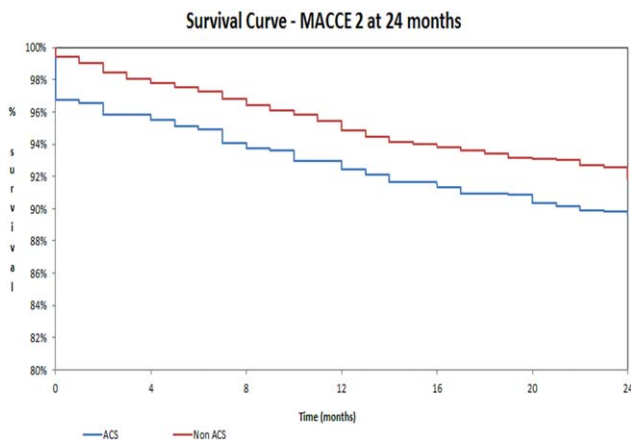
<sup>a</sup>The primary endpoint of the study was the occurrence of major adverse cardiac and cerebrovascular events (MACCE) in the overall population, defined as a composite of cardiac death, myocardial infarction (Q-wave and non-Q-wave), cerebrovascular events or clinically indicated target vessel revascularization at 12 months.

<sup>b</sup>Definite and probable stent thrombosis at 12 months and 2 years and major adverse cardiac and cerebrovascular events (MACCE) defined as a Composite Endpoint including all-cause mortality, MI (Q-wave and non-Q-wave), cerebrovascular events or any clinically driven target vessel revascularization at 12 months and 2 years.





**Fig. 2. MACCE 2 (secondary endpoints including definite and probable stent thrombosis and MACCE including all-cause mortality, MI (Q-wave and non-Q-wave), cerebrovascular events or any clinically driven target vessel revascularization at 24 years in diabetics vs. non-diabetics. [Color figure can be viewed at wileyonlinelibrary.com]**



**Fig. 3. MACCE 2 (secondary endpoints (definite and probable stent thrombosis and MACCE including all-cause mortality, MI (Q-wave and non-Q-wave), cerebrovascular events or any clinically driven target vessel revascularization at 24 years in ACS vs. non ACS. [Color figure can be viewed at wileyonlinelibrary.com]**

9% at 24 months (MACCE 2, secondary endpoints,) including 2.2% all-cause-death. ST (definite/probable) occurred in 10 (0.4%) patients at 1 year and 14 (0.6%) at 2 years. All individual components of MACCE 1 and MACCE 2 (primary and secondary endpoints) are displayed in Table III. Table IV shows the results of subgroup analyses carried out with respect to ACS vs. non ACS presentation and according to the presence of diabetes. Almost one-third of the study population (31.8%) had diabetes. The overall incidence of events (primary and secondary endpoints) was not significantly increased in diabetic patients but the rate of cardiac death was higher (1.6% vs. 0.6%,  $P = 0.01$  at 1 year; 1.9 vs. 0.6%

$P = 0.005$  at 2 years) as was the definite/probable ST rate (0.9% vs. 0.2%,  $P = 0.009$  at 1 year and 1.2 vs. 0.3%  $P = 0.008$  at 2 years) Figure 2. ACS was reported in more than one-third of the study patients (36.5%) who in turn had a significantly higher occurrence of the primary endpoint (MACCE 1): 7.5% vs. 4.8%,  $P = 0.001$  at 1 year and secondary endpoints (MACCE 2): 10.3 vs. 8.1%,  $P = 0.07$  at 2 years (Fig. 3).

Patients with renal insufficiency accounted for 5.7% of the study cohort and had a significantly higher rate of stent thrombosis (3.0% vs. 0.6%  $P = 0.002$  at 1 year, 3.7% vs. 0.9%,  $P = 0.001$  at 2 years) and major bleeding (2.2% vs. 0.04%  $P = 0.0007$  at 1 year and 2.2% vs. 0.04% at 2 years,  $P = 0.0007$ ).

At 12 months, 67.2% of the patients were still on DAPT and 36.9% at 24 months.

## DISCUSSION

The analysis of the 12-month outcomes of the all-comer population included in the E-Biomatrix French Registry confirms the safety and efficacy of the BioMatrix stents as supported by the 5.8% rate of primary endpoints (MACCE 1) at 12 months which compares favorably with the 10.6% MACE rate reported in the LEADERS trial evaluating the same stent at 1 year even if the endpoints were not strictly the same [11]. In addition, the low overall rate of major adverse events observed between one and 2 years is comparable with that recorded in the Leaders trial, supporting the biodegradable polymer concept.

Of note, although the patients enrolled in this registry had a similar incidence of diabetes and a higher rate of ACS at baseline compared with the Leaders Trial patients, their reported rate of adverse events was lower. This could be explained by the under-reporting of events and less exhaustive monitoring inherent in registry studies, as well as the fact that, as patient consent could be obtained after the index procedure, patients with serious procedural complications may have not been included.

The results reported here are also comparable with those of a randomized trial evaluating a bio-absorbable DES of similar generation (Synergy) vs. the Promus element [17], whose primary endpoint (ischemia-driven revascularization of target lesion, MI in target vessel and cardiac death) occurred in 6.7% of the Synergy recipients.

Furthermore, these results are also consistent with those of comparable registries evaluating the outcomes of the second and third generation of DES with a new fixed more biocompatible polymer (Xience and Promus stents) or biodegradable polymer in non-selected patients. Indeed, the rate of MACE reported in recipients of the Xience Stent in the SPIRIT V study [8] was 5.1%

(excluding stroke). It was 3.9% (excluding stroke) in the Nobori 2 study [7] and 4.5% in the e-BioMatrix Registry conducted in Europe [14]. In the Resolute all-comer registry [18] evaluating a zotarolimus-eluting stent with a biocompatible polymer, the primary endpoint (cardiac death and target vessel MI at 1 year) was 4.3% and TLR was 3.5%.

In addition, though not recorded in an unselected cohort, the results of a propensity score analysis of the outcomes at 12 months comparing the ABSORB BVS and the XIENCE stents [19] underlined the low MACE rate recorded in ABSORB BVS recipients (5.0% vs. 4.8% for XIENCE), which is similar to the findings of the registry reported here, albeit not in an all-comer population.

With respect to the incidence of definite and probable stent thrombosis, a very low rate (0.4%) at 1 year, was recorded in the present registry, which is again in line with the findings of SPIRIT V (0.6%) [8], the European Ebiomatrix registry (0.6%) [14] and Nobori 2 (0.8%) [7] at 1 year and with previously reported results in selected recipients of the Synergy stent (0.4%) [17], in unselected cohorts of the Resolute registry (0.9%) [18] and in patients treated with the ABSORB BVS (1.0%) [19]. In addition, the rates of very late thrombosis reported in both the French and European E-Biomatrix registries are also quite similar (0.3% and 0.2%, respectively).

These results suggest that this new generation of biodegradable stents has fulfilled its purpose and has radically reduced the risk of late stent thrombosis thanks to the complete resorption of the stent polymer after 1 year.

Of note, although more than 65% patients were still on DAPT at 12 months, the rate of major bleeding was only 0.2%. This may suggest that patients at high bleeding risk were not included in the registry.

Three sub-group analyses were conducted in the subsets of patients with renal insufficiency, diabetes and ACS who accounted for 5.7%, 31.8% and 36.5% of the study population, respectively. The excess risk associated with diabetes translated into a higher incidence of stent thrombosis and cardiac death in this population (Fig. 2).

A significantly higher rate of events in terms of stent thrombosis and major bleeding was recorded in patients with renal insufficiency.

With respect to the higher incidence of events in ACS patients, Fig. 3 (secondary endpoints, MACCE 2) shows that the differences rates between the ACS and non ACS groups were more pronounced in the early days post procedure and that the curves run parallel afterwards.

### Study Limitations

Due to the non-randomized nature of this study, the results may have been affected by a bias inherent in all

registries, namely the selective inclusion of lower-risk patients and less exhaustive monitoring compared with randomized controlled trials, which may have resulted in a potential under-reporting of events. However, the fact that the rate of monitoring of this registry was particularly high for a registry should be underlined.

### CONCLUSIONS

In this real-world post market registry of almost 2,500 patients who underwent coronary stenting in 42 French centers, the BES with biodegradable polymer was associated with excellent acute results and very good mid-term outcome with MACCE rates of 5.8% and 9% and extremely low rates of stent thrombosis, 0.4% and 0.6% at one and 2 years, respectively, thus demonstrating the replicability of the results of the LEADERS trial in a large registry population.

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