AsiaIntervention 2016;2:19-27

Late angiographic and clinical outcomes of the novel BioMime™ sirolimus-eluting coronary stent with ultra-thin cobalt-chromium platform and biodegradable polymer for the treatment of diseased coronary vessels: results from the prospective, multicentre meriT-2 clinical trial

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KEYWORDS

- angiography
- complex lesions
- sirolimus-eluting stent

Abstract

Aims: We sought to investigate the performance of the novel BioMime™ sirolimus-eluting coronary stent system (SES), with an ultra-thin cobalt-chromium platform and a biodegradable polymer, in a "real-life", minimally selected, coronary artery disease patient population.

Methods and results: A total of 250 patients (355 *de novo* lesions) were prospectively enrolled between August 2009 and January 2012 at 11 Indian sites. Mean age was 56.8±10.6 years, 36% of patients had diabetes, 32% had prior myocardial infarction, and 63.4% of lesions were classified as type B2/C. Overall, 1.4 lesions per patient were treated, and angiographic/procedural success was achieved in 99.2%. There were no major adverse cardiac events (MACE) at 30 days. At eight-month angiographic follow-up (available in 87% of patients), median in-stent late lumen loss (primary efficacy endpoint) was 0.12 mm (0.04-0.30 mm), whereas in-stent and in-segment binary restenosis rates were 4.9% and 6.2%, respectively. At 12 months (follow-up completed in 99.6% of patients), the cumulative MACE rate was 6.0%, including 0.8% cardiac death, and 5.2% target lesion revascularisation (4.8% clinically indicated target lesion revascularisation). In addition, one patient (0.4%) presented with definite/probable stent thrombosis.

Conclusions: The BioMime SES demonstrated a high procedural success rate, low late lumen loss (a surrogate of neointimal hyperplasia), and sustained safety and efficacy up to 12 months.

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SUBMITTED ON 30/06/2015 - REVISION RECEIVED ON 10/12/2015 - ACCEPTED ON 15/12/2015

DOI: 10.4244/AsiaInterv_V2I1A7

Abbreviations

DES	drug-eluting stent
DS	diameter stenosis
LLL	late lumen loss
MACE	major adverse cardiac events
MI	myocardial infarction
MLD	minimum lumen diameter
PCI	percutaneous coronary intervention
QCA	quantitative coronary angiography
RD	reference diameter
SES	sirolimus-eluting coronary stent
TLR	target lesion revascularisation

Introduction

Compared to first-generation drug-eluting coronary stents (DES), new-generation DES have attempted to improve safety, deliverability and overall performance, while maintaining efficacy by preventing neointimal hyperplasia (NIH), restenosis, and therefore the need for target lesion revascularisation (TLR) over a period of time in patients with coronary artery disease undergoing percutaneous coronary intervention (PCI)[1-3]. In general, low-profile metallic stents, polymer-based drug carriers with enhanced bio-inertness (whether durable or biodegradable), and potent yet safe pharmacological agents from the "limus" family have commonly been incorporated into novel DES technologies[4-11]. The CE (Conformité Européenne) mark-approved BioMime™ sirolimus-eluting coronary stent system (Meril Life Sciences Pvt. Ltd., Gujarat, India) is a novel DES system which incorporates an advanced ultra-thin stent platform covered with a biodegradable polymer, which releases sirolimus as the antiproliferative drug to the vessel wall. In the first clinical evaluation, the BioMime sirolimus-eluting coronary stent (SES) demonstrated safety and efficacy in inhibiting NIH in a relatively small sample of patients with single *de novo*, non-complex coronary lesions treated at a single institution[11]. However, the results of the BioMime stent in a larger "real-life" population with complex coronary lesions have not been studied. We therefore assessed the performance and late angiographic and clinical outcomes of the BioMime SES in the treatment of a relatively large series of patients with obstructive coronary artery disease with very few exclusions at multiple clinical sites.

Methods

STUDY DESIGN AND POPULATION

The meriT-2 trial was a prospective, non-randomised, single-arm, multicentre, phase II clinical evaluation of the BioMime SES in the treatment of consecutive patients with coronary artery disease. The study objective was to evaluate the overall performance, safety and efficacy of the BioMime device in inhibiting NIH in a relatively large population with minimally selected coronary lesions. Inclusion criteria were: patients ≥18 years of age, symptoms or signs of ischaemic heart disease, the presence of a single or multiple *de novo* lesion(s) ≤35 mm in length with stenosis 50-100% in native coronary vessel(s) with a reference diameter (RD) between 2.5 mm and 3.5 mm, an acceptable candidate for coronary artery bypass graft (CABG) surgery, and agreement to undergo all protocol pre-specified evaluations, including angiographic follow-up. Triple-vessel disease was not an exclusion. Exclusions were: acute myocardial infarction (MI) <48 hours from index procedure, women with childbearing potential, renal insufficiency (baseline serum creatinine >2.0 mg/dL), history of cerebral vascular accident or transient ischaemic attack <3 months previously, left main, large thrombus, saphenous vein graft, left ventricular ejection fraction <30%, contraindication to dual antiplatelet therapy, or any other known illness or clinical condition with a life expectancy of <12 months.

The study complied with the Declaration of Helsinki regarding investigation in humans, and was approved by the local ethics committee at each participating clinical institution. All patients provided written informed consent prior to enrolment. The meriT-2 trial was registered at the National Institute of Medical Statistics, Indian Council of Medical Research (Clinical Trials Registry – India, CTRI) at www.ctri.nic.in/Clinicaltrials: REFCTRI-2009000505, and at the United States National Institute of Health at www.clinicaltrials.gov: NCT02406326.

STUDY DEVICE AND PROCEDURE

The specifics of the BioMime SES have been detailed elsewhere[11]. In brief, it is built on an ultra-thin L605 cobalt-chromium platform (65 µm) with a "hybrid" cell design, including a mix of open and closed cells **(Figure 1)**. The drug carrier is a thin (~2 µm) co-polymer formulation combining two biodegradable components (poly-L-lactic and poly-lactic-co-glycolic acids), which degrades in approximately 60 days after implantation. In addition, sirolimus is coated in a dosage of 1.25 µg per mm^2 of stent surface area (total drug dose ~121 µg for a 3.0×19 mm stent), given that the complete drug release is expected to occur in approximately 30-40 days after stent implantation.

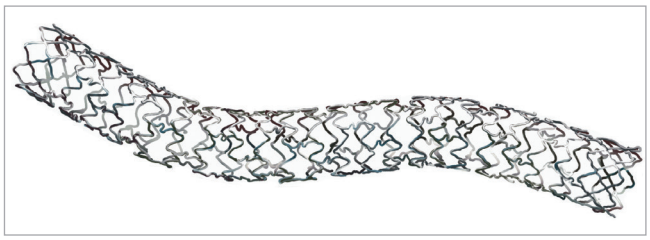

Figure 1. *The BioMime stent design showing its "hybrid" cell design with a mix of open (middle) and closed (end) cells.*

PCI procedures were performed according to current standard guidelines. Predilatation was recommended with a regular balloon catheter; post-dilatation was performed at the operator's discretion. Only one stent per lesion was allowed, even though an additional study stent could be implanted overlapping with the previous stent in case of a bail-out situation. Multiple stent implantation for multivessel PCI was allowed. The BioMime SES was available in 13, 16, 19, 24, 29, 32, 37, 40 mm lengths, and in 2.5, 3.0 and 3.5 mm

diameters. After discharge, all patients were prescribed aspirin (100-325 mg/day) indefinitely and clopidogrel 75 mg/day for at least 12 months.

ENDPOINTS, DEFINITIONS AND FOLLOW-UP

The primary safety endpoint was major adverse cardiac events (MACE) at 30 days after the procedure. The primary efficacy endpoint was in-stent late lumen loss (LLL), as determined by quantitative coronary angiography (QCA) analysis, at angiographic follow-up at eight months. Secondary endpoints were MACE and stent thrombosis (ST)[12] at all study time points up to 12 months, angiographic and procedural success, angiographic binary restenosis at eight-month angiographic follow-up, and clinically indicated TLR at 12 months. MACE was defined as the composite of cardiac death, MI or TLR. All deaths were considered cardiac unless a non-cardiac cause could be established clearly, either by clinical assessment or by pathological study. MI was classified as Q-wave or non-Q-wave, and according to its temporal and circumstantial occurrence (periprocedural, spontaneous or post-CABG), following standard definitions, as previously reported[11]. Clinically indicated TLR was considered under the following conditions at follow-up: a) stenosis ≥50% by QCA within the treated segment plus symptoms of (recurrent) angina and/or evidence of positive function test for ischaemia by either non-invasive or invasive methods, or b) the presence of stenosis ≥70% by QCA within the treated segment in the absence of the above-mentioned symptoms or signs of ischaemia. Angiographic success was defined as residual stenosis <20% plus final TIMI flow 3 after PCI with the study device. Procedural success was defined as angiographic success plus the absence of MACE during index hospitalisation. Clinical follow-up was scheduled at one, six, eight, 12, 36 and 60 months, either by medical visit or by telephone contact. All patients were assigned to angiographic re-evaluation at eight months. The study was managed by an independent clinical research organisation (SIRO Clinpharm Pvt. Ltd., Thane, India). In the current analysis, we report the baseline/index and clinical outcomes up to 12 months, and eight-month angiographic follow-up.

ANGIOGRAPHIC ANALYSIS

After intracoronary administration of nitroglycerine, serial angiographic studies were obtained in two orthogonal matching views at pre and post procedure, and eight-month follow-up. Angiographic analyses were performed off-line by experienced operators at an independent angiographic core laboratory (Cardiovascular Research Center, São Paulo, Brazil), using a validated 2D software for QCA analysis (QAngio XA® version 7.2; Medis medical imaging systems bv, Leiden, The Netherlands), as previously reported[11]. The minimum lumen diameter (MLD) and the mean RD, obtained by averaging 5 mm segments proximal and distal to the target lesion location, were used to calculate the diameter stenosis (DS=[1–MLD/RD]×100). Acute gain was the change in MLD from baseline to post-stent implantation. Late lumen loss (LLL) was the change in MLD from post-stent implantation to follow-up; the LLL index was LLL divided by acute gain. Binary restenosis was reported according to the Mehran classification[13]. QCA measurements were reported as "in-stent" within the stented segment, and "in-segment", spanning the stented segment plus the 5 mm proximal and distal peri-stent areas.

STATISTICAL ANALYSIS

Categorical data were presented as frequencies (percentages). Continuous variables were presented according to distribution pattern. In case of normal distribution, data were presented as mean values±standard deviation (SD). When non-normal distribution was evidenced, data were presented as median (interquartile). Cumulative frequency distribution (CFD) curves were used to illustrate the distribution of MLD. Time-to-event curves were reported according to the Kaplan-Meier method.

Results

A total of 250 patients with 355 *de novo* coronary lesions were enrolled between August 2009 and January 2012 at 11 sites in India. Mean age was 56.8 years, 36% of patients had diabetes, and the majority of patients presented with stable angina, followed by unstable angina **(Table 1)**. Baseline lesion characteristics are shown in **Table 2**. The left anterior descending (LAD) artery was the most prevalent target vessel, and a high complexity profile (ACC/AHA type B2/C) was found in 63.4% of patients. Overall, there were 1.4 lesions treated per patient. During the procedure, predilatation was performed in 90.1% of lesions, the study stent was implanted in all cases, 6.5% of lesions received >1 study stent, and more than half (60.8%) underwent post-dilatation. By intention-to-treat, procedural success was 98.6% (247/250). Considering only those

Table 1. Baseline demographics and clinical presentation.

Variable	n=250
Age, yrs	56.8±10.6
Female	42 (16.8)
Diabetes mellitus	91 (36.4)
Hypertension	123 (49.2)
Dyslipidaemia	26 (10.4)
Prior myocardial infarction	80 (32.0)
Prior PCI	15 (6.0)
Prior CABG	4 (1.6)
Prior CVA	2 (0.8)
History of CHF	5 (2.0)
Clinical presentation	
Asymptomatic (silent ischaemia)	28 (11.2)
Stable angina*	94 (37.6)
Unstable angina	68 (27.2)
Recent myocardial infarction¶	59 (23.6)

Values are expressed as mean±standard deviation or frequencies (percentages of the total). *According to the Canadian Cardiovascular Society classification. ¶Less than 30 days from index procedure.
CABG: coronary artery bypass graft; CHF: chronic heart failure; CVA: cerebral vascular accident; PCI: percutaneous coronary intervention

Table 2. Baseline angiographic data.

Variable		n=250 (355 lesions)
Target vessel	LAD	169 (47.6)
	LCx	76 (21.4)
	RCA	110 (31.0)
Location	Ostial	13 (3.7)
	Proximal	102 (28.7)
	Mid	200 (56.3)
	Distal	40 (11.3)
Calcium (moderate/severe)		58 (16.3)
Ulcer		19 (5.4)
Tortuosity (moderate/severe)		19 (5.4)
Bifurcation		18 (5.1)
Lesion class*	A	16 (4.5)
	B1	114 (32.1)
	B2	165 (46.5)
	C	60 (16.9)
TIMI flow grade	0 or 1	23 (6.5)
	2	23 (6.5)
	3	309 (87.0)
QCA analysis		
Lesion length, mm		12.78 (8.79-18.66)
RD, mm		2.72 (2.40-2.97)
MLD, mm		0.74 (0.47-1.03)
% DS		71.4 (61.4-83.3)

Values are expressed as frequencies (percentages of the total) or median (25-75% interquartile range). *According to the modified American College of Cardiology/American Heart Association classification. DS: diameter stenosis; LAD: left anterior descending; LCx: left circumflex; MLD: minimum lumen diameter; RCA: right coronary artery; RD: reference diameter; TIMI: Thrombolysis In Myocardial Infarction

treated with the study device (n=249) (one patient died due to a haemorrhagic complication prior to PCI), procedural success was 99.2%, as two patients did not achieve angiographic success (final TIMI flow grade 2). In addition, there was no MACE reported up to 30 days.

QCA FINDINGS

Table 3 depicts QCA results post procedure and at follow-up. At eight months (follow-up available in 87% of patients), the median in-stent late lumen loss was 0.12 (0.04-0.30) mm. CFD curves for MLD are shown in **Figure 2**. **Figure 3** shows a case with complex multivessel PCI with patent stents at follow-up re-evaluation. Angiographic binary restenosis within the stent was found in 15 lesions (4.9%), whereas the in-segment rate was 6.2% (19 lesions). The majority of recurrences were focal, including type IC in 11 cases and type IB in four cases. Conversely, types ID, II, III and IV were found in one case each. Importantly, there was neither significant acute stent recoil (balloon-artery ratio 1.10 [1.06, 1.16]; final residual stenosis within the stent 7.6% [4.8, 11.8]) nor stent fracture/longitudinal deformation as assessed both at post procedure and at follow-up angiographic evaluation.

ONE-YEAR CLINICAL OUTCOMES

A total of 15 patients (6%) experienced MACE up to 12 months, including two cases of cardiac death (0.8%). In the first case, a 72-year-old female patient with multivessel disease and multiple comorbidities (diabetes, renal insufficiency, prior MI, prior CABG, congestive heart failure, mild anaemia) underwent PCI with the study device, but a second stent had to be implanted in order to cover a distal dissection. At post procedure, there was a suboptimal angiographic result (TIMI 2). After discharge, she was re-hospitalised due to progressive congestive heart failure and died on

Table 3. QCA analyses post-procedure and at eight-month follow-up.

QCA	In-segment	In-stent	Proximal edge	Distal edge
Post-procedure (n=355)				
RD, mm	2.84 (2.51-3.05)	–	–	–
Mean diameter, mm	–	2.92 (2.54-3.07)	2.82 (2.46-3.14)	2.49 (2.20-2.81)
MLD, mm	2.30 (2.20-2.61)	2.58 (2.30-2.87)	2.65 (2.29-2.97)	2.34 (2.04-2.66)
% DS	15.4 (10.4-22.3)	7.6 (4.8-11.8)	7.5 (3.6-13.1)	8.2 (4.2-15.8)
Acute gain, mm	1.59 (1.22-1.95)	1.85 (1.48-2.21)	–	–
Eight months (n=309)				
RD, mm	2.77 (2.45-2.99)	–	–	–
Mean diameter, mm	–	2.75 (2.48-2.98)	2.63 (2.35-3.03)	2.39 (2.09-2.71)
MLD, mm	2.09 (1.79-2.43)	2.36 (2.02-2.68)	2.45 (2.10-2.81)	2.17 (1.89-2.52)
% DS	21.4 (14.1-30.8)	12.2 (7.4-19.8)	11.1 (5.5-21.1)	12.6 (6.4-19.9)
LLL, mm	0.11 (0.04-0.29)	0.12 (0.04-0.30)	0.13 (0.03-0.30)	0.07 (0.03-0.19)
LLL index	0.07 (0.03-0.20)	0.06 (0.02-0.18)	–	–

Values are expressed as median (25-75% interquartile range). DS: diameter stenosis; LLL: late lumen loss; MLD: minimum lumen diameter; RD: reference diameter

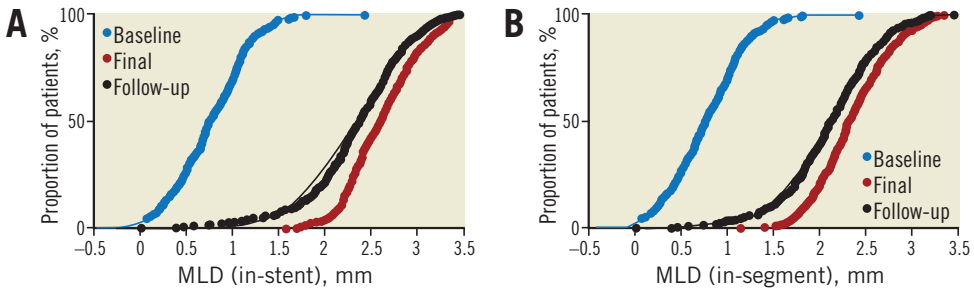

Figure 2. *Cumulative frequency distribution curves at pre-procedure, post-procedure and eight-month follow-up for in-stent MLD (A), and in-segment MLD (B).*

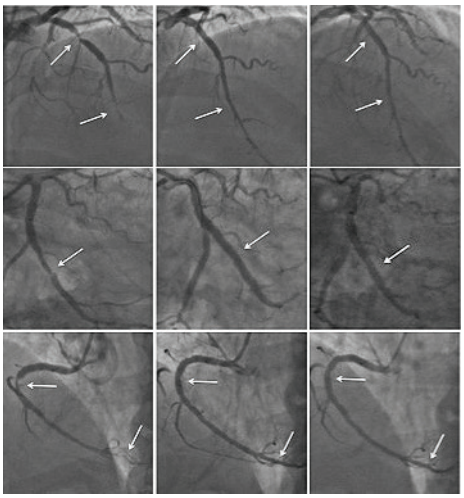

Figure 3. *Case example showing serial angiographic studies at pre-procedure (left column), post-procedure (centre column), and eight-month follow-up (right column) of a patient with multivessel disease treated with five BioMime SES in the mid and distal LAD (top row), mid LCx (centre row), and mid and distal RCA (bottom row).*

day 60. The second case was a 70-year-old patient, who had two target lesions successfully treated at the index procedure, developed cardiac heart failure and died at day 158. As for new revascularisation procedures, there were 13 cases of any TLR (5.2%), including 12 cases of clinically indicated TLR (4.8%) – 11 treated by PCI, one treated by CABG **(Table 4)**. The time-to-event curve for MACE is shown in **Figure 4**. Furthermore, there was only one case of definite/probable ST (0.4%) in a patient who presented with ST-elevation MI during the late follow-up. The angiographic study at the event evidenced occlusive thrombosis involving the study stent, which was successfully treated by PCI (also listed as MI and TLR for the individual event components).

Discussion

The results of the meriT-2 study demonstrated that the BioMime stent was associated with: a) high angiographic and procedural success among the treated population (99.2%); b) efficacy in inhibiting NIH at eight-month angiographic follow-up (median LLL 0.12 mm and binary restenosis rate <5% within the stented segment), despite

Table 4. Cumulative clinical events up to 12 months for patients receiving the study stent.

Outcome	30 days	6 months	8 months	12 months
MACE	0 (0)	6 (2.4)	8 (3.2)	15 (6.0)
All-cause death	0 (0)	2 (0.8)	2 (0.8)	2 (0.8)
Cardiac death	0 (0)	2 (0.8)	2 (0.8)	2 (0.8)
Non-cardiac death	0 (0)	0 (0)	0 (0)	0 (0)
MI	0 (0)	1 (0.4)	1 (0.4)	1 (0.4)
Any TLR	0 (0)	3 (1.2)	5 (2.0)	13 (5.2)
PCI	0 (0)	3 (1.2)	4 (1.6)	11 (4.4)
CABG	0 (0)	0 (0)	1 (0.4)	2 (0.8)
Clinically indicated TLR	0 (0)	3 (1.2)	5 (2.0)	12 (4.8)
PCI	0 (0)	3 (1.2)	4 (1.6)	11 (4.4)
CABG	0 (0)	0 (0)	1 (0.4)	1 (0.4)
Stent thrombosis (ARC)[12]				
Any	0 (0)	1 (0.4)	1 (0.4)	1 (0.4)
Definite/probable	0 (0)	1 (0.4)	1 (0.4)	1 (0.4)
Possible	0 (0)	0 (0)	0 (0)	0 (0)

Values are expressed as frequencies (percentages of the total).
ARC: Academic Research Consortium; CABG: coronary artery bypass graft; MACE: major adverse cardiac events (a composite of cardiac death, MI or any TLR); MI: myocardial infarction; PCI: percutaneous coronary intervention; TLR: target lesion revascularisation

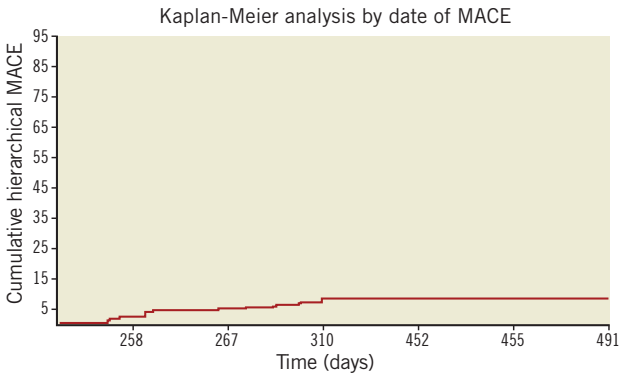

Figure 4. *Cumulative incidence of MACE up to 12-month follow-up (n=249).*

a high prevalence of small vessels (median RD <2.75 mm) and lesion complexity (63% type B2/C); and c) sustained safety and clinical efficacy (cardiac death 0.8%, ARC definite/probable ST 0.4%, clinically indicated TLR <5%) up to 12-month follow-up. Overall, these findings confirmed the results found in the first-in-human evaluation of BioMime SES (meriT-1)[11] despite the fact that the meriT-2 trial was a much larger trial involving a more complex population, with a high prevalence of diabetes and multivessel disease, enrolled at multiple sites. In addition, the performance, safety and efficacy demonstrated with the study stent appear to be comparable to those seen with the most effective new-generation low-profile DES used nowadays[5,7-10,14-16] **(Table 5)**.

Previous studies have demonstrated that strut thickness is a major determinant of local inflammation and NIH after stenting[17,18]. Moreover, thin-strut stent platforms offer enhanced flexibility and deliverability, thus facilitating PCI procedures, especially when targeting complex coronary anatomies. Still, a major concern about thinner devices may be their short- and long-term durability against axial and longitudinal stress in the coronary vessels[19,20]. In general, new advanced cobalt- or platinum-chromium DES platforms with thin struts (65-91 µm) have demonstrated the ability to preserve radial strength. They have also been associated with improved deliverability and procedural outcomes compared to DES with thicker struts[21-23]. Several reports with everolimus-eluting stents, zotarolimus-eluting stents, and other new SES systems have demonstrated high acute success and efficacy in the treatment of real-world patients, including complex subsets[21,24,25]. To our knowledge, the BioMime SES has the lowest profile among DES in current clinical use, with ultra-thin struts of 65 µm regardless of stent size. In addition, it has a thinner polymeric drug carrier (~2 µm). Interestingly, we did not observe direct evidence of mechanistic issues such as stent recoil, disruption or deformation that could be associated with acute or late stent failure in our study. This may be related to the innovative "hybrid" cell design combining open and closed cells in the BioMime **(Figure 1)**, which has been shown to preserve radial strength with minimal stent recoil (<3%) and without deformation in bench testing[11]. In fact, among 280 patients with 385 lesions (64% type B2/C) included in the combined meriT-1[11] and meriT-2 trials, there was neither unsuccessful PCI related to the study stent nor periprocedural MI. In terms of efficacy, BioMime SES demonstrated relatively low LLL at eight-month follow-up (0.12 mm), thus placing it within the range found

Table 5. Comparison of new-generation low-profile cobalt- or platinum-chromium DES trials.

Study	meriT-1[11]	meriT-2	SPIRIT I[5,14]	SPIRIT II[15,16]	RESOLUTE[7]	PLATINUM QCA[8]	EVOLVE FHU[9]	BIOFLOW-I[10]
No. (lesions)	30 (30)	250 (355)	27 (27)*	222 (260)*	139 (140)	100 (100)	94 (94)*	30 (30)
Device	BioMime™	BioMime™	XIENCE V®	XIENCE V®	Resolute®	Promus Element®	Synergy®	Orsiro®
Platform	cobalt-chromium	cobalt-chromium	cobalt-chromium	cobalt-chromium	cobalt-chromium	platinum-chromium	platinum-chromium	cobalt-chromium
Strut thickness	65 µm	65 µm	81 µm	81 µm	91 µm	81 µm	74 µm	71 µm¶
Polymer type	biodegradable	biodegradable	durable	durable	durable	durable	biodegradable	biodegradable
Polymer component(s)	PLLA/PLGA	PLLA/PLGA	acrylic/fluorinated polymers	acrylic/fluorinated polymers	C10/C19/polyvinyl pyrrolidinone	acrylic/fluorinated polymers	PLGA	PLLA
Polymer thickness	2 µm	2 µm	5-6 µm	5-6 µm	5.6 µm	5-6 µm	4 µm	7.5 µm
Drug	sirolimus	sirolimus	everolimus	everolimus	zotarolimus	everolimus	everolimus	sirolimus
Drug dose	1.25 µg/mm^2	1.25 µg/mm^2	100 µg/cm^2	100 µg/cm^2	1.6 µg/mm^2	100 µg/cm^2	100 µg/cm^2	1.4 µg/mm^2
Drug release	100% (30-40 days)	100% (30-40 days)	70-80% (30 days)	70-80% (30 days)	85% (60 days)	70-80% (30 days)	70-80% (30 days)	50% (30 days)
Diabetes mellitus	30%	36%	11%	23%	17%	19%	17%	23%
LAD	40%	48%	48%	41%	34%	–	42%	53%
Lesion class B2/C‡	77%	63%	59%	78%	81%	–	56%	47%
Lesion length, mm	15.51	12.78	10.1	13.0	15.61	15.40	13.41	11.71
RD, mm	2.94	2.72	2.61	2.70	2.81	2.72	2.60	2.75
Angio. FU (%)	8-mo. (87%)	8-mo. (87%)	6-mo. (85%)	6-mo. (91%)	9-mo. (96%)§	9-mo. (88%)	6-mo. (96%)	9-mo. (100%)
LLL, mm (in-stent)	0.15	0.12	0.10	0.12	0.22	0.20	0.10	0.05
ABR (in-segment)	0%	6.2%	0%	3.4%	2.1%	1.1%	2.3%	0%
Clinical FU (%)	1-yr (100%)	1-yr (99.6%)	1-yr (96.3%)	1-yr (99.1%)	1-yr (99.3%)	1-yr (100%)	6-mo. (100%)	1-yr (100%)
MACE◊	0%	6%	15.4%	2.7%	8.7%	1%	2.2%	10%
TLR	0%	5.2%	7.7%	2.7%	0.7%	1%	1.1%	6.7%
ST (ARC def./prob.)	0%	0.4%	0%	0%	0%	1%	0%	0%

*Number of patients (lesions) allocated in the corresponding device group in randomised trials with active control group. ¶For stents with nominal diameters ≤3.0 mm. ‡According to the modified American College of Cardiology/American Heart Association classification. §Pre-specified subset with late angiographic follow-up. ◊May also represent a similar composite endpoint. ABR: angiographic binary restenosis; ARC: Academic Research Consortium; FU: follow-up; MACE: major adverse cardiac (or clinical) events; RD: reference diameter; ST: stent thrombosis; TLR: target lesion revascularisation

with everolimus- and sirolimus-eluting stents reported in phase I and phase II studies (0.05-0.22 mm)[5,7-11,14-16] **(Table 5)**. In the first-in-human meriT-1 trial, there were no cases of binary restenosis reported at angio follow-up (26/30)[11]. However, restenosis rates were higher in meriT-2 (in-stent 4.9%, in-segment 6.2%) and directly associated with new revascularisation procedures (TLR 5.2%). A possible explanation may be found in the relatively high prevalence of diabetics in our population (36%), as TLR rates were numerically higher among this subset (8.8%). A similar trend has been demonstrated with first-generation SES and also with new-generation DES systems[26,27]. Overall, diabetes has historically been determined to be a major predictor of PCI failure, including ST[28,29].

Recent studies have suggested improved long-term safety associated with DES with a biodegradable polymer versus first-generation DES with a durable polymer[30,31]. However, whether this advantage would be superior to the newer-generation DES with durable polymers remains unclear. In the NEXT (NOBORI Biolimus-Eluting Versus XIENCE/PROMUS Everolimus-Eluting Stent Trial) trial, there were similar rates of death or MI (9.9% versus 10.3%, p=0.7) and target lesion revascularisation (7.4% versus 7.1%, p=0.8) at three years, when comparing biolimus-eluting stents with a biodegradable polymer versus everolimus-eluting stents with a durable polymer, respectively. Overall, the biocompatibility of the drug carriers used in DES systems has been demonstrated to impact significantly on their long-term performance. Polymer components, particularly those used in first-generation DES, may cause negative effects on vessel healing due to local inflammation and toxicity, which could lead to proliferative and thrombogenic responses[32]. Importantly, despite the unequivocal superiority of new-generation DES over first-generation DES in terms of biocompatibility and clinical outcomes, late and very late events may still occur[33,34]. Therefore, biodegradable polymer-based DES could offer, at least theoretically, additional advantages, such as avoiding the problems related to permanent polymeric residue (chronic inflammation and local toxicity over time), optimising vascular healing, potentially at an earlier stage, minimising the dependence on prolonged dual antiplatelet therapy and reducing bleeding events (without compromising safety, while maintaining efficacy in inhibiting NIH). Of note is the fact that a different clinical impact may be seen among the various DES systems with biodegradable polymer, as they vary greatly in terms of stent design, strut thickness, polymer type and degradation, and drug release, all components that have been shown to impact significantly on late and very late performance. In meriT-2, there were no safety concerns, and only one case of definite/probable ST reported. Nevertheless, larger comparative studies are needed to assess the impact of the BioMime SES technology with ultra-thin struts in comparison to contemporary new-generation DES with highly biocompatible durable polymers[35].

Limitations

A few limitations must be acknowledged in our study. First, the patient population mostly comprised patients with stable coronary artery disease or low-risk acute coronary syndrome. Therefore, caution should be exercised in extrapolating our results to patients with acute MI or high-risk ACS. Second, this was a non-randomised single-arm evaluation without an active control group. Therefore, even though our findings suggest favourable outcomes in terms of performance, safety and efficacy in a relatively large population with a representative prevalence of several high-risk subsets (diabetics, small vessels, complex lesions, total occlusions, etc.), no direct comparison can be drawn related to current "gold-standard" new-generation DES. In this regard, the randomised meriT-V trial comparing BioMime SES versus XIENCE EES (www.clinicaltrials.gov: NCT02112981) is currently recruiting patients. Third, one-year follow-up may be a relatively short time period for proper assessment of the long-term safety and efficacy of DES, as very late recurrences, including thrombotic events, may still occur after this time period, even with new-generation devices. Fourth, the sample size seemed appropriate for the evaluation of efficacy, using a surrogate endpoint of angiographic LLL (available in 87%), but is still limited for safety endpoints with a rare incidence, such as ST. Hence, larger trials with longer-term follow-up are warranted.

Conclusions

The novel BioMime SES with ultra-thin struts and a biodegradable polymer demonstrated a high procedural success rate, low late lumen loss (a surrogate of NIH), and sustained safety and efficacy up to 12 months in a relatively large patient population with a high prevalence of diabetes and multiple complex lesions treated at multiple clinical sites. Results from ongoing larger comparative studies are awaited.

Impact on daily practice

The BioMime SES is a novel DES technology, with ultra-thin struts and a biodegradable polymer which has demonstrated efficacy and sustained safety in the treatment of minimally selected patients with a relatively high prevalence of complex clinical and lesion characteristics. At eight-month angiographic follow-up, in-stent late lumen loss (the primary endpoint) was 0.12 mm. At 12-month clinical follow-up, cumulative rates for cardiac death and clinically indicated target lesion revascularisation were 0.8% and 4.8%, respectively. In addition, there was only one (0.4%) definite/probable stent thrombosis reported. Thus, in daily practice, the BioMime SES may offer an alternative for patients with an indication for percutaneous revascularisation procedures.

Funding

The meriT-2 clinical trial was funded by Meril Life Sciences Pvt. Ltd., Gujarat, India.

Conflict of interest statement

A. Seth is a member of the Scientific Advisory Board of Meril Life Sciences. R. Costa has received a research grant from Meril Life Sciences. The other authors have no conflicts of interest to declare.

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