



Original Article

One-year outcomes of a BioMime™ Sirolimus-Eluting Coronary Stent System with a biodegradable polymer in all-comers coronary artery disease patients: The meriT-3 study



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ABSTRACT

Objectives: The aim of the meriT-3 study was to determine the safety and performance of the BioMime Sirolimus-Eluting Coronary Stent System (SES) in all-comer patients with coronary artery disease (CAD) in one-year clinical follow-up period.

Methods: The meriT-3 was a multi-centre, observational, post-marketing study conducted in 1161 patients with CAD who were implanted with BioMime SES at 15 sites in India. The primary endpoint was major adverse cardiac event (MACE) at one year defined as the composite of cardiac death, myocardial infarction (MI) and target lesion revascularization (TLR). Clinical follow-up was performed at 1, 6, and 12 months. Major adverse cardiac event occurred at 30 days and subsequently at 6 months and at long-term follow-up of 1 year was analyzed.

Results: MACE observed at 1 and 6 months follow-up was 16 (1.38%) and 21 (1.83%) respectively. Cumulative 1 year MACE was 26 (2.35%) with 16 (1.39%) all cause death, 4 (0.35%) MI and 6 (0.52%) TLR. In addition, ST was observed in 1 (0.09%) patient.

Conclusions: The present study suggests that the BioMime SES is safe and effective in a “real-world”, all-comers CAD patients, indicating low rates of MACE.

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What this study adds?

- This study suggests that the BioMime SES is safe and effective in a “real-world”, all-comers CAD patients, indicating low rates of MACE and ST.

What is already known?

- First-generation DES was linked with late ST and was created on bulky stent platforms with questionable deliverability and polymer biocompatibility.

1. Introduction

Coronary artery disease (CAD) is the leading cause of mortality across the globe.¹ For the last few years, the drug eluting stents (DES) have become the treatment of choice for the vast majority of patients undergoing percutaneous coronary intervention (PCI).² The DES have been used in various clinical and anatomical scenarios due to their reduction in restenosis rates and the need for repeat revascularisation.^{3,4} However, the first-generation DES were associated with an increased risk of late events including stent thrombosis (ST) and late restenosis. Efforts to prevent these risks have included prolongation of antiplatelet therapy, and improvement in stent platforms, polymer carriers, and drug selection.³ Although the mechanism of thrombotic events is not completely clarified, hypersensitivity reaction to the permanent/non degradable polymer is one of the possible explanation in this composite equation.⁴ The residual polymers of DES (coated with durable polymer) have been accused of instigating inflammatory reaction, which delayed healing and re-endothelialization of the DES.^{5–10}

The use of the biodegradable polymer has the potential to reduce the sustained inflammatory responses of the arterial wall, facilitating re-endothelialization and minimizing the risk of thrombus formation and late restenosis.³ Thus, the DES such as BioMime Sirolimus-Eluting Coronary Stent System (Meril Life Sciences Pvt. Ltd., Gujarat, India) has been developed with an aim to reduce neointimal hyperplasia.

The BioMime Sirolimus-Eluting Coronary Stent System (SES) is a CE approved biodegradable polymer. The BioMime SES is comprised of poly-L-lactic and poly-lactic-co-glycolic acids. The BioMime SES is built on NexGen, an ultra-thin (65 μm) cobalt-chromium platform with a hybrid cell design with an aim to reduce intra-arterial injury.

The sirolimus formulated with the biodegradable polymer releases into the treated vessel during 30–40 days after stent implantation.¹¹ The first-in-man study of BioMime SES has demonstrated excellent performance in CAD patients including high procedural success (100%) and clinical performance.¹²

Consequently, the purpose of the present study was to determine the safety and performance of the BioMime SES in all-comer patients with CAD at one-year clinical follow-up.

2. Objective

The aim of the meriT-3 study was to determine the safety and performance of the BioMime SES in all-comer patients with CAD.

3. Material and methods

3.1. Device description

The BioMime SES (Meril Life Sciences Pvt. Ltd., Gujarat, India) is built on NexGen, an ultra-thin (65 μm) cobalt-chromium platform with a hybrid cell design. This design is a mix of close cells at the

edges and open cells in the mid segment. The SES is coated with 1.25 μg sirolimus/ mm^2 of stent surface area. The biodegradable polymer, which acts as a drug carrier, is a thin copolymer formulation combining two biodegradable components namely poly-L-lactic and poly-lactic-co-glycolic acids. The BioMime SES was available in sizes of 8, 13, 16, 19, 24, 29, 32, 37, 40, 44, 48 mm lengths and diameters of 2.00, 2.25, 2.50, 2.75, 3.00, 3.50, 4.00, 4.50 mm.

3.2. Study design and population

The meriT-3 study was conducted at 15 centres in India; with a total of 1161 patients were included in this study. This was a post-marketing study of all-comer patients who underwent stenting for the management of CAD using BioMime SES. The study was performed with the approval of the local ethics committee. Informed, written consent was obtained from all study participants. The PCI procedures were performed according to current standard guidelines.¹³ Clinical and angiographic data from all the patients who were treated with BioMime SES were observed in this study. The clinical/telephonic follow-up was performed at the following time points: 30 days, 6 months, and 12 months after discharge. All the serious adverse events were evaluated by Adjudication committee.

All patients received dual antiplatelet therapy (DAPT) including a loading dose of aspirin as per investigator's discretion. Aspirin was coupled with clopidogrel, prasugrel, or ticagrelor. The procedural anticoagulation was achieved either with heparin or bivalirudin. The intra-procedural administration of glycoprotein IIb/IIIa inhibitor was at the investigator's discretion. All patients were recommended the DAPT (aspirin; 75–300 mg daily indefinitely and clopidogrel; 75 mg daily or prasugrel; 10 mg daily or ticagrelor; 90 mg twice daily for at least 12 months) after the procedure.

3.3. Definitions and end points

Major adverse cardiac event (MACE) was defined as the composite of cardiac death, MI, target lesion revascularization (TLR). All cause of death were considered cardiac unless a non-cardiac cause could be established clearly, either by clinical assessment or by pathological study. The ST was classified according to the definitions of the Academic Research Consortium.¹⁴ Procedural success was defined as successful stent placement at the desired position with <30% residual stenosis.¹⁵ At follow-up, data were collected relating to current clinical status, any prior hospitalization and occurrence of any MACE. The primary endpoint was MACE at 1-month and 6-month follow-up and secondary endpoints were MACE at 1-year follow-up.

3.4. Statistical analysis

Categorical data were presented as counts and percentages. All clinical and angiographic continuous variables were presented as a mean \pm standard deviation. The time-to-event curve was presented as per the Kaplan–Meier method. All data were processed using the Statistical Package for Social Sciences, version 15 (SPSS, Chicago, IL, USA).

4. Results

4.1. Baseline demographics characteristics

The analysis consists of baseline clinical data and consecutive follow-up data collected at 1 month, 6 months, and 12 months. Of 1161 patients enrolled in the study, 922 (79.4%) were male, and

Table 1
Demographic and baseline characteristics.

Characteristics	BioMime Sirolimus Eluting Coronary Stent n = 1161 patients
<i>Patient demographics</i>	
Age (mean ± SD, yrs)	56.4 ± 10.3
Male, n (%)	922 (79.4%)
<i>Baseline medical history</i>	
History of diabetes mellitus, n (%)	477 (41.1%)
History of hypertension, n (%)	609 (52.5%)
History of hyperlipidemia, n (%)	66 (5.7%)
Smoker, n (%)	180 (15.5%)
Family history of coronary artery disease, n (%)	135 (11.6%)
<i>Cardiac history</i>	
Previous MI, n (%)	159 (13.7%)
Previous PCI, n (%)	38 (3.3%)
Previous CABG, n (%)	17 (1.5%)
<i>Cardiac status before index procedure</i>	
<i>Anginal status</i>	
Asymptomatic, n (%)	155 (13.4%)
MI, n (%)	295 (25.4%)
Stable angina, n (%)	124 (10.7%)
Unstable angina, n (%)	587 (50.6%)
<i>Type of PCI</i>	
PAMI, n (%)	148 (12.7%)
Facilitated, n (%)	1013 (87.3%)

CABG – coronary artery bypass grafting, MI – myocardial infarction, PCI – percutaneous coronary intervention, PAMI – primary angioplasty in myocardial infarction.

mean age was 56.4 ± 10.3 years. The baseline demographics of the patients are outlined in Table 1. There was a history of diabetes in 477 (41.1%) patients, hypertension in 609 (52.5%), hyperlipidemia in 66 (5.7%), and family history of CAD in 135 (11.6%) patients. Of 1161 patients, 50.6% (587) patients were included and treated with a diagnosis of unstable angina. Among 1161, 180 (15.5%) patients were Smoker and 159 (13.7%) patients had previous MI. Baseline lesion characteristics are mentioned in Table 2.

4.2. Clinical and angiographic outcomes

The composite of MACE rates at 30-day, 6-month, and 12-month follow-up was 1.38%, 1.83% and 2.35%, respectively. The summary of MACE during 1-year study period is presented in Table 3. Total 26 (2.35%) patients experienced MACE during 1 year. Of which, 16 (1.39%) were all cause death, 4 (0.35%) were MI and 6 (0.52%) were TLR. Furthermore, 1 (0.09%) patient had target vessel revascularization (TVR) and only 1 (0.09%) patient had an incidence of ST. The time-to-event analysis performed by Kaplan–Meier method was found to be 97.65% (Fig. 1).

Baseline lesion characteristics are mentioned in Table 2. An analysis of baseline angiography revealed that 88.6% of patients had single lesions who were treated with BioMime stent. The mean lesion length was 18.5 mm and mean pre-procedural diameter stenosis was 89.9%. The most prevalent target vessel was left anterior descending (LAD) artery (58.5%) and 71.1% of lesions were diffused. The average number of lesions was 1.1 per patient. The average stent length was 23.1 ± 8.4 mm and average stent diameter was 3.0 ± 0.4. A total of 1326 BioMime stents were implanted (ratio of 1.14 stents/patient which is a reflection of real-world population).

5. Discussion

In this retrospective study, the BioMime SES has demonstrated excellent performance in CAD patients including high procedural success and clinical performance. The patient population had high rates of diabetes (41.1%) and hypertension (52.5%). In this study we

Table 2
Lesion and procedural characteristics.

Characteristics	Patients = 1161/lesions = 1312
<i>Target vessel location</i>	
Left anterior descending, n (%)	768 (58.5%)
Right coronary artery, n (%)	324 (24.7%)
Left circumflex, n (%)	194 (14.8%)
Others, n (%)	26 (2.0%)
<i>Total number of patient treated lesions, n</i>	
Treated with 1 lesion, n (%)	1029 (88.6%)
Treated with 2 lesions, n (%)	114 (9.8%)
Treated with 3 lesions, n (%)	17 (1.5%)
Treated with 4 lesions, n (%)	1 (0.1%)
Average number of lesions per patient	1.1 ± 0.4
Reference vessel diameter (mean ± SD, mm)	3 ± 0.4
Lesion length (mean ± SD, mm)	18.5 ± 8.2
Diameter stenosis (mean ± SD, %)	89.9 ± 7.3
<i>Type of stenosis</i>	
De novo, n (%)	1300 (99.1%)
In-Stent, n (%)	9 (0.7%)
Bifurcation, n (%)	3 (0.2%)
<i>Type of lesion</i>	
Long, n (%)	166 (12.6%)
Diffused, n (%)	933 (71.1%)
Thrombus, n (%)	86 (6.6%)
CTO, n (%)	117 (8.9%)
Calcified, n (%)	10 (0.8%)
<i>Pre-procedural TIMI flow grade</i>	
0, n (%)	178 (13.5%)
I, n (%)	645 (49.2%)
II, n (%)	458 (34.9%)
III, n (%)	31 (2.4%)
Pre-dilatation, n (%)	961 (73.2%)
<i>Access site location, n</i>	
Femoral, n (%)	1161
Radial, n (%)	782 (67.4%)
Radial, n (%)	379 (32.6%)
Average number of stents per patient	1.0 ± 0.1
Average number of stents per lesion	1.0 ± 0.1
Average stent length (mean ± SD, mm)	23.1 ± 8.4
Average stent diameter (mean ± SD, mm)	3.0 ± 0.4

CTO – chronic total occlusion, TIMI – thrombolysis in myocardial infarction.

observed the BioMime SES, which is based on an ultra-thin cobalt-chromium platform with a hybrid cell design with an aim of optimizing performance of BioMime SES. The thin struts allow the production of stents with an extremely low profile that helps in device deliverability and flexibility. First-generation DES was linked with late ST^{16,17} and was created on bulky stent platforms with questionable deliverability and polymer biocompatibility.¹⁸ The ultra thin novel BioMime SES stent design allows for a morphologically-mediated expansion due to a hybrid cell design structure (open cell configuration in the centre and closed at the edges). This method of expansion eliminates the classic dog-boning observed with the conventional designs and also ensures

Table 3
Major adverse cardiac events at in-hospital stay, 1-month, 6-month and 1-year follow-up.

Events	In Hospital n = 1161	1 month n = 1152	6 month n = 1147	12 month n = 1147
All cause of death, n (%)	7 (0.60%)	12 (1.04%)	13 (1.13%)	16 (1.39%)
MI, n (%)	2 (0.17%)	3 (0.26%)	4 (0.35%)	4 (0.35%)
TLR, n (%)	0	1 (0.09%)	4 (0.35%)	6 (0.52%)
TVR, n (%)	0	0	1 (0.09%)	1 (0.09%)
Stent thrombosis, n (%)	1 (0.09%)	1 (0.09%)	1 (0.09%)	1 (0.09%)
Total MACE, n (%)	9 (0.77%)	16 (1.38%)	21 (1.83%)	26 (2.35%)

MI – myocardial infarction, TLR – target lesion revascularization, TVR – target vessel revascularization, MACE – major adverse cardiac events.

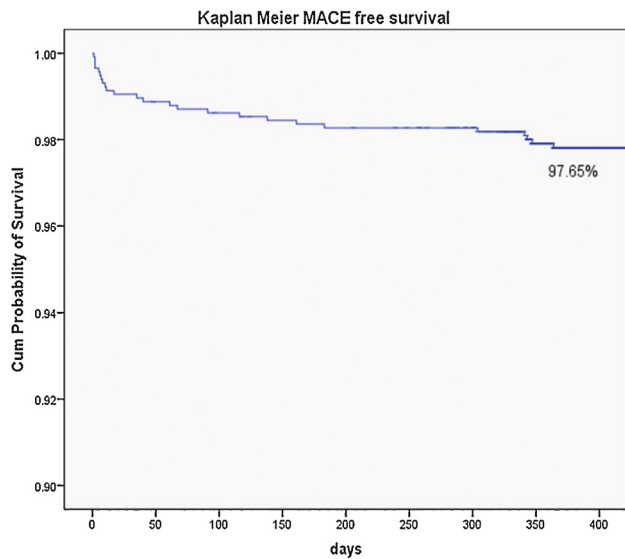


Fig. 1. Time-to-event curve at up to 1-year follow-up by Kaplan–Meier method.

minimal edge injury. We observed that the ST rate was 0.09% only. Therefore, the BioMime SES demonstrated complete wall apposition and thus lead to rapid endothelialisation. BioMime SES was designed keeping in mind that the DES should facilitate re-endothelialisation. The resultant DES has the ability to be arterially biocompatible and thus offers predictable safety and performance profile.

The drug used is sirolimus, which is an ideal choice considering that it acts on the common final pathway of cell division cycle without an exceptional risk of necrosis induction. It is a macrolide with cytostatic rather than cytotoxic properties that impedes advancement from G1 to S in the cell cycle and inhibits the vascular smooth muscle cell migration and proliferation.¹⁹

The biomimicry characteristic of the BioMime SES is maintained due to its biodegradable polymer coating of BioPolycopolymer. The biodegradable polymer is non-inflammatory and has excellent drug-release kinetics; it is also a right polymer choice because of its ability to avoid cracking, webbing, lumping or sticking to the balloon surface.

The safety and efficacy of BioMime SES owing to its biomimicry design was confirmed by the primary safety and efficacy trials meriT-1 and meriT-2 for *de novo* lesions and real-world patients, respectively.^{11,12} The meriT-1 study shown that there were no safety concerns in this preliminary evaluation including absence of MACE or ST up to 12-months. In addition, the meriT-2 study shown that the BioMime SES with ultra-thin struts and a biodegradable polymer demonstrated a high procedural success rate, low late lumen loss, and sustained safety and efficacy up to 12 months. The meriT-3 study included 1161 all-comer patients requiring stenting for the management of CAD. The MACE rate in meriT-3 was 2.35% at 1-year follow-up. However, longer follow-up of patients receiving the BioMime SES will be necessary to confirm long-term safety of this DES. The observational studies are a true representation of all-comer population, unlike prospective controlled trials which have limitations in terms of a real clinical picture and have restricted enrollment criteria. Additionally, observational studies are analyses of an homogeneous group of subjects who are prospectively followed over a defined period of time.²⁰

The ongoing concerns related to ST in implanted stents prompted us to analyze the thrombosis rates with scrutiny in the present study. Stent thrombosis incidences observed with

BioMime SES at 1-year follow-up (0.09%) were low and comparable with current industry standards like sirolimus-eluting Orsiro stent (0.4%) and biolimus-eluting Nobori stent (1.2%) at 1-year follow-up.²¹

This study has some limitations. One of the chief limitations is the nature of the study—a retrospective analysis of a post-marketing study. In addition, a 12-month follow-up period might not be long enough for the safety and performance of the BioMime SES. Consequently, further studies with longer follow-up periods, are necessary.

The present study supports conducting randomized clinical studies to evaluate the BioMime SES among the other drug-eluting stents on longer term.

6. Conclusions

The BioMime SES with biodegradable polymer is safe and effective in a real-world, all-comers CAD patients including those with high-risk and very complex lesions, indicating low rates of MACE over 1-year follow-up period.

Conflicts of interest

The authors have none to declare.

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