



Research Article

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Interim Results of Real World Randomized Clinical Trial Prism-R (Basket of Clinical Trial) for M'sure-S (Multimedics Llc) a Next Generation Sirolimus Eluting Stent vs Eliminator (Multimedics Llc) a Everolimus Eluting Stent

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Abbreviations: MACE: Major Adverse Cardiac Events; MI: Myocardial Infarction; MI TVR: Myocardial Infarction Target Vessel Revascularization; TVR: Target Vessel Revascularization; TLR: Target Lesion Revascularization; NTVR: Non-Target Vessel Revascularization; DST: Definite Stent Thrombosis.

Introduction

Drug eluting stents (DES) used for the treatment of coronary artery disease is a phenomenal achievement in the field of percutaneous coronary intervention (PCI). The use of balloon angioplasty and bare metal stents resulted in an augmented rate of reocclusions and restenosis. The incidence of restenosis and target vessel revascularizations are significantly reduced by the use of DES compared to their antecessors bare metal stents [1,2]. The second generation DES containing anti-proliferative and immunosuppressive agents are preferred over first generation DES. This is due to the increased incidences of myocardial infarction and stent thrombosis observed in first generation DES [3]. However, both the DES offer equal level of efficacy and the use of second generation DES considered being most safe among PCIs. These stents contain a cobalt chromium (L605) platform with an ultrathin struts covered with a silicon carbide layer [4]. In another study sirolimus-eluting stent (SES), the first generation DES exhibited demonstrable angiographic results compared with EES [5]. Study conducted by Han Y et al (2018) signifies the material characteristic of poly-L-lactic acid and studied the limitations of polymer based bioresorbable scaffold (BRS) in PCI. He has also compared the strut thickness in BSR and metallic drug-eluting stents [6]. PRISM basket of clinical trials is used to determine the safety and efficacy of first-generation SES (M'Sure-S) versus second generation EES (EliminatorTM). This study was sponsored by Multimedics LLC.

Thus, the present study is designed to assess multicenter trial, the procedural performance, the angiographic result, and the long-term clinical outcome obtained by a first-generation DES (i.e., SES) compared with a last-generation DES (i.e., EES). Here the safety and efficacy outcomes at the different time intervals of the PRISM trail was compared, with specific focus on long-term clinical performance of the study stents and cardiac events linked with definite stent thrombosis of SES and EES.

Materials and Methods

Study design, recruitment, enrollment and over sight

The PRISM study was a prospective, randomized, open-label all comers, single-blind, non-inferiority, multicentre trial, with clinical follow up at nine month and 18 month. In all comers' trial out of 1,174 enrolled patients, 884 patients were treated with SES and 290 were treated with EES. The multicentric study involved European & Indian populations. The patients older than 18 years, presenting symptomatic ischemic heart disease and/or objective evidence of myocardial ischemia and ready for percutaneous transluminal coronary angioplasty (PTCA), stenting, or emergency coronary artery bypass graft (CABG) were eligible for study participation. The mean age of the patients involved in all comers' trial was 68 years. Research and

Abstract

The study compares sirolimus-eluting stent (SES) with that of EES from the PRISM basket of clinical trial in coronary artery disease patients. A total of 1174 patients were enrolled in the study, 290 patients (25.28%) were assigned to receive the EES and 884 patients (74.72%) were subjected to SES. The trial (PRISM) used is a randomized multicenter, single-blind, all-comers, single arm, non-inferiority trial comparing EES and SES implanted patients with coronary artery disease. The non-inferiority criterion was a risk difference of 0.015. Intention-to-treat analysis was performed at 9 and 18-month follow-ups respectively.

The baseline characteristics were similar for both EES and SES groups. Nine month follow-up was performed on 25.28% patients treated with EES and 74.72% patients treated with the SES group, amongst them MACE occurred in 6.20% and 4.63% patients in EES and SES group respectively. At the 18-month follow up, this differential remained almost same i.e. 8.4% treated with the EES versus 9% treated with the SES group. The rate of DST at the 9 month follow up was lesser in SES group 2 (0.1%) patients compared to EES group 9 (0.7%) patients. But this difference was sustained in 3 (0.2%) patients in SES group versus 12 (0.9%) patients in EES treated group respectively (HR: 1.03; 95% CI: 0.99-1.04; p: 0.13) at the 18-month follow up. When censoring the patients at the time of stent thrombosis, we found no significant differences between the 2 stent groups. In this real-world trial, In 9 and 18-month follow-up, SES (M'Sure-S) exhibited better safety and efficacy profile when compared to EES in terms of MACE rates and Definite Stent Thrombosis. But the difference was not statistical significant and SES was found to be non-inferior to EES.

Keywords: Drug eluting stents; Sirolimus-eluting stent; Percutaneous coronary intervention; Stent thrombosis; Coronary artery disease; Angioplasty; Bioresorbable scaffold

development department of PRISM was responsible for data collection and monitoring. All the source data were verified by independent monitors on site. All the cardiac and non cardiac adverse events were reviewed and monitored by safety and data monitoring board. An independent clinical event committee adjudicated all clinical end points in a blinded fashion. The investigators involved in the study vouched for the complete and accuracy of the data and analysis. The

institutional ethical committee of each participating clinical trial site approved the study. Informed consent forms were signed and collected from the participants prior to the study. The trial was registered in clinical trial registry and conducted as per the ICH/ E6/R1 guide line. Unrestricted access to the data was given to the principal investigator post database lock and decision was taken to prepare the manuscript for publication.

Baseline Demographics	Sirolimus group (M Sure stent)	Everolimus group (Eliminator stent)	p-value
Number of patients enrolled	884	290	
Mean age in years	60±9.2	61.5±9.5	0.68
Gender: Male	716 (80.99%)	225 (77.58%)	1.00
Female	168 (19%)	65 (22.41%)	0.87
Hypertension	444 (50.22%)	154 (53.1%)	0.46
Heart rate (beats per minute)	77.14± 18.14	74.65±19.35	0.85
Previous myocardial infarction	172 (19.45%)	64 (22.06%)	0.56
stable angina	340 (38.46%)	116 (40%)	0.26
Acute Coronary Syndrome	380 (42.98%)	130 (44.83%)	1.00
Diabetes	220 (24.88%)	64 (22.07%)	0.16
Smoker	412 (46.6%)	143 (49.31%)	0.53
Hyperlipidemia	106 (11.99%)	36 (12.41%)	0.15
Family history of CAD	221 (25%)	81 (27.93%)	0.26

Table 1: Baseline Characteristics.

The most essential inclusion criterion was the presence of a de novo target lesion located in the native coronary artery suitable for conventional angioplasty, stenting and which can be covered by one stent without overlapping. More precisely the target lesion present in the native epicardial coronary artery (2.5–4.0 mm in diameter) that can be covered by a single SES with a maximum length of 40 mm. Lesions having severe calcification, tortuosity, presence of thrombus, bifurcation sites, involving left main coronary artery, saphenous vein grafts and those with left ventricular rejection fraction (LVEF)<30% were excluded from the study.

The main exclusion criteria were pregnancy, known hypersensitivity/contraindication to sirolimus or any other

mechanistic target of rapamycin (mTOR) inhibitor, hypersensitivity/contraindication to aspirin, clopidogrel or other thienopyridines. Also hypersensitivity/contraindication to cobalt, chromium, heparin or contrast media that are routinely present during stent procedures were under exclusion criteria. Other exclusion criteria included pretreatment of target lesions by stenting methods, previous brachytherapy, presence of significant non-target lesions requiring treatment within 30 days of the index procedure, prior CABG to the target vessel, acute myocardial infarction (MI) within 48 hours.

Parameters (Pre specified sub groups)	Sirolimus group (M-Sure stent)	Everolimus group (Eliminator stent)	p-value
No. of patients treated	884	290	
No. of Stents used	1326	435	
Single-vessel disease	388 (43.89 %)	184 (42.29 %)	0.84
Two-vessel disease	282 (21.9 %)	90 (20.68 %)	0.50
Triple vessel disease	214 (24.21 %)	86 (19.77 %)	0.68

TIMI flow 0	121 (13.69 %)	60 (13.79 %)	0.14
TIMI flow I	12 (1.36 %)	7 (1.60 %)	0.56
TIMI flow II	20 (2.26 %)	12 (2.75 %)	0.30
TIMI flow III	731 (82.69 %)	356 (81.83 %)	0.96
Right coronary artery	230 (17.34 %)	75 (17.24 %)	0.54
Left anterior descending artery	630 (47.51 %)	210 (48.27 %)	1.01
Left circumflex artery	334 (25.18 %)	102 (23.44 %)	0.37
Obtuse marginal artery	66(4.97 %)	25 (5.71 %)	0.18
Left Main	39 (2.9 %)	14 (3.21 %)	0.11
SVG	27 (3.19 %)	19(4.36 %)	0.29
Average stented diameter (mm)	2.93± 0.60	2.95± 0.68	0.32
Average stented length (mm)	26.4 ± 10.95	22.6 ± 9.37	0.09

Table 2: Procedural Characteristics.

Study procedure

The study subjects were treated by routine angioplasty procedure as per previously published standard protocol with slight modification [7,8]. Briefly, keeping the angiographic inclusion and exclusion criteria in mind, the stents were deployed upon receipt of visual estimation of the vessel diameter and lesion characteristics. At the end of the stent implantation, it was left to the interventional cardiologists' discretion whether or not to treat the patient further with a post-dilatation balloon catheter. Dual antiplatelet therapy (aspirin concomitantly with clopidogrel) was continued for up to one year post-procedure. Procedural success was defined as a successful device implantation with a residual stenosis of <20% of the vessel diameter, event-free sheath removal and subsequent discharge from the hospital. Angiographic follow ups were performed at nine month and 18-month. Fractional flow reserve was used in case there is intermediate target vessel stenosis <70% with or without angina or >70% in absence of angina during follow-up (Table 1) provides baseline demographics of the patients.

Quantitative coronary analysis (qca) and clinical follow-up

All the coronary angiograms were analyzed in an angiographic laboratory by automated software independently by the technicians who were unaware of the clinical information and stent allocation pertaining to this study. The quantitative measurements included the in-stent lumen loss, in segment late lumen loss, lesion length, percentage of diameter stenosis and minimal luminal diameter (MLD). The follow ups were carried out at nine and 18month, of post procedure. Follow-up information was collected either by a hospital visit or telephonic contact with the patient or the referring physician. Patients will continue to be followed up to 18 months. ECGs and cardiac biomarkers (creatinine kinase MB fraction and troponins) were to be evaluated before and after the procedure and at the time of suspected ischemic events.

Study end-points

The primary Safety endpoint is defined as Major adverse cardiac events (MACE) at 30 days, defined as a composite of death, MI (both Q-wave and Non Q-wave MI), Emergent CABG, or clinically driven target-lesion revascularization (TLR repeat PCI or CABG). The primary efficacy endpoint is the In-Stent and In-Segment late loss at nine and 18 month follow-up respectively, determined by off-line QCA at the Core Laboratory. The secondary Efficacy endpoints for PRISM were, Angiographic/Device Success, Procedural Success, QCA derived vessel parameters in-stent and 5 mm proximal and 5 mm distal from the edge of the stent (Acute gain, MLD, diameter stenosis, late loss, binary restenosis, In-stent MLD pre-, post and at angiographic follow-up). Binary restenosis was defined as a diameter stenosis ≥50%

Statistical analysis

The trial was performed for assessing non-inferiority of SES to EES with respect to the primary endpoint at 18-month. For superiority for all endpoints 2-sided 95% confidence intervals (CIs) and 2-sided p values was conducted. The primary analysis was performed according to the intention to treat principle. Distributions of continuous variables were compared between study groups using the 2-sample Student t test and Chi-Square method was utilized with a power of 95% and significance level $\alpha = 0.005$ to measure any difference in the treatment arms. CI functions were computed taking into account death (and in a sensitivity analysis also stent thrombosis) as a competing risk. The MACE per patient was ranked according to the highest category on a scale ranging from (1) death, (2) MI, (3) CABG to (4) TLR. We used Gray's test for comparing the cumulative incidence functions and Cox regression to determine the cause-specific hazard ratios (HRs). Patients treated with the SES were used as the reference group for overall and subgroup analyses. Hazard ratios were calculated for major adverse cardiac events at 18-month follow up for pre-specified patient subgroups (based on baseline demographic and clinical characteristics). The intention-to-treat principle was used in all analyses. A 2-sided p value of <0.05 was considered statistically significant. Analyses were conducted using SAS software (SAS institute, NC).

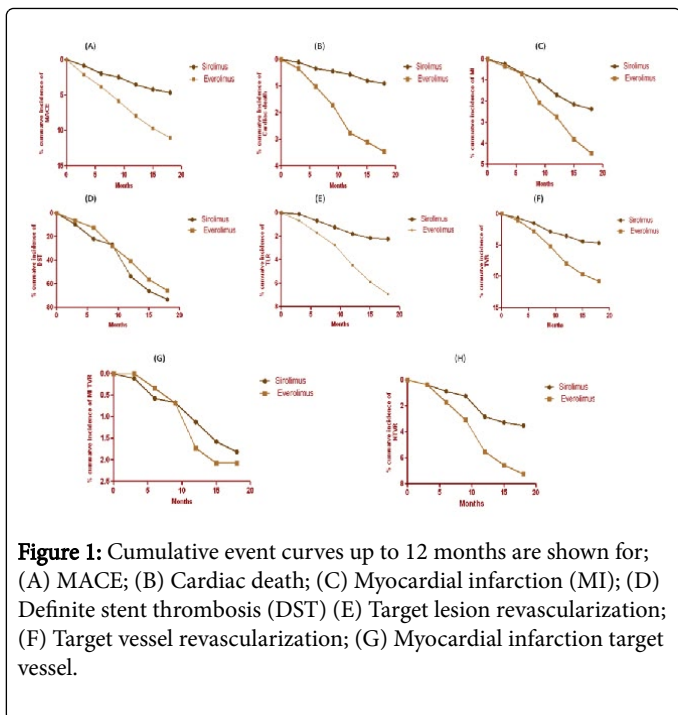


Figure 1: Cumulative event curves up to 12 months are shown for; (A) MACE; (B) Cardiac death; (C) Myocardial infarction (MI); (D) Definite stent thrombosis (DST) (E) Target lesion revascularization; (F) Target vessel revascularization; (G) Myocardial infarction target vessel.

Pre-procedure Quantitative Coronary Angiographic Data	Sirolimus group (M-Sure stent) (N=884)	Everolimus (Eliminator stent) group (N=290)	p-value
Lesion length (mm)	19.92 ± 3.4	18.41 ± 2.9	0.93
Reference vessel diameter (mm)	2.35 ± 0.52	2.2 ± 0.50	0.10
Minimum luminal diameter (mm)	0.98 ± 0.45	0.97 ± 0.43	0.82
Percentage diameter stenosis	79.29 ± 12.9	78.45 ± 11.2	0.87
Post-procedure Quantitative Coronary Angiographic Data			
Reference vessel diameter (mm)	2.67 ± 0.60	2.56 ± 0.59	0.54
In-stent			
Minimum luminal diameter (mm)	2.32 ± 0.51	2.36 ± 0.54	0.62
Percentage diameter stenosis	13.26 %	12.78 %	0.80
Acute gain (mm)	1.34 ± 0.09	1.35 ± 0.10	0.53
In-segment			
Minimum luminal diameter (mm)	2.32 ± 0.47	2.43 ± 0.50	0.57
Percentage diameter stenosis	24.56 %	25.46 %	0.26
Acute gain (mm)	1.34 ± 0.82	1.43 ± 0.90	0.65

Table 3: Pre and Post procedure Quantitative Coronary Angiographic Data.

Results

Baseline and procedural characteristics

In this clinical trial, cumulative data comprises with enrollment of 1174 patients treated with 884 SES stent and 290 patients treated with EES stent. The studies comprised mean age groups of 68 years and amongst them male and female patients were bifurcated randomly. The study population included with the larger proportion of patients suffering from diabetics, hypertension, previous MI, stable angina,

acute coronary syndrome, smoker, hyperlipidemia, and people having family history of CAD respectively. The percentages of disease cause of the SES and EES population are represented in (Table 1). From the data it was shown that there were no significant differences between the two groups.

The procedural characteristics of the patients including treated with both the groups are represented in (Table 2). Both the group achieved 100% procedural characteristics implying no significant difference between the SES and EES groups

Nine month Follow-up Quantitative Coronary Angiographic Data	Sirolimus group (M-Sure stent) (N=874)	Everolimus group (Eliminator stent) (N=282)	p-value
Reference vessel diameter (mm)	2.63 ± 0.59	2.54 ± 0.52	0.74
In-stent			
Minimum luminal diameter (mm)	2.45 ± 0.43	2.42 ± 0.41	0.29
Percentage diameter stenosis	10.26 %	10.21 %	0.65
Late lumen loss (mm)	0.05	0.04	0.53
Binary restenosis, % (n)	7.33 %	5.34 %	0.49
In-segment			
Minimum luminal diameter (mm)	3.33 ± 0.60	3.34 ± 0.62	0.20
Percentage diameter stenosis	17.14 %	17.20 %	0.81
Late lumen loss (mm)	0.05	0.04	0.77
Binary restenosis, %	13 %	5 %	0.31

Table 4: Nine-month Follow-up Quantitative Coronary Angiographic Data.

Quantitative coronary angiography

QCA were obtained at four distinct time-points pre-stenting, post-stenting, nine month and 18-month follow-up. The pre-procedure QCA result represented in (Table 3), here median lesion length (LL), median reference vessel diameter, minimum luminal diameter (MDL), percentage diameter stenosis for SES patients (19.92 mm, 2.35 mm, 0.98 mm and 79.29% respectively) were slightly higher when compared to EES 18.41mm 2.2 mm 0.97 mm 78.45% patients. These results were compared favorably with those of currently available DES studies. Here lesion length for SES showing non inferior on EES.

Post-procedure QCA details are given in (Table 4). In post-procedure in-stent residual diameter stenosis was slightly higher in SES (13.26%) group compared to EES (12.78%) group. In-stent acute gain was measured to be 1.34 mm for SES compared to EES (1.35 mm). In-segment analysis SES and EES group revealed a MLD (2.32 and 2.43 mm) and a residual diameter stenosis (24.56 and 25.46%), with an acute gain of 1.34 and 1.43 mm respectively. Hence there were no significant differences between the SES and EES groups with respect to lesion length, reference diameter, MLD, in-lesion diameter stenosis, and mean stent length, which indicated both have no complex lesion showing non inferiority. All angiographic end points data of Pre and Post Procedural QCA are summarized in (Table 3).

Nine month angiographic follow-up data from 992 and 184 patients were studied and an interesting set of values are presented in (Table 4).

Median in-stent MLD for both SES and EES group was found to be 2.30 and 2.20 mm, with a diameter stenosis of 11.26 and 11.21% and a late lumen loss (LLL) of 0.05 and 0.04 mm respectively. Interestingly, binary restenosis was not found in any patients and this remained 0% at the end of nine months, thereby indicating high efficacy of both the stents used for a trail. Likewise median in-segment MLD, LLL was calculated with no binary restenosis. (Table 4) provides nine month analyzed QCA data of PRISM Study.

There were no significant differences in angiographic measurements of lesions before and after the procedure. Angiographic follow-up at 18-months was performed in 1174 of the total patients amongst 855 in the SES group, and 264 in the EES group. The primary endpoint of the study, mean in-segment LL, was 0.07 mm in the SES group and 0.10 mm in the EES group thus the results of the in-segment LL met the criteria for non-inferiority of SES versus EES (non-inferiority margin=0.1 mm). The in-stent LL showed similar findings; the mean in-stent LL was 0.06 mm and 0.08 mm for the SES and EES groups, respectively. The angiographic results (non-inferiority of SES) were similar in the intention-to-treat population, including those who did not receive the allocated stents. Median in-stent MLD was found to be 2.17 mm, with a diameter stenosis of 14.26%, interestingly, binary restenosis was not found in any patients and this remained 0% at the end of 18-months, thereby indicating high efficacy. Likewise median in-segment MLD was 2.35 mm and thus the percentage diameter stenosis was calculated to be 21.24 mm, with no binary restenosis. The

angiographic outcomes (non-inferiority of SES) were similar in the intention-to-treat population, including those who did not receive the allocated stents. (Table 5) provides 18-month month analyzed QCA data of PRISM Study.

observed in both the treatments. At nine month follow up MACE occurred in 22 patients (2.48%) who received SES and in 17 patients who received EES (HR: 0.98; 95% CI: 1.00 – 1.06; p: 0.28). But on 18-month follow up the event got reduced to 19 (2.14%) and 15 (5.17%) in both SES and EES patients respectively (Figure 1).

Major adverse cardiac events and stent thrombosis

All patients in the trail completed primary end-point and were followed up to nine months. There were no primary events and deaths

Eighteen-month Follow-up Quantitative Coronary Angiographic Data	Sirolimus group (MSure stent) (N=855)	Everolimus group (Eliminator stent) (N=264)	p-value
Reference vessel diameter (mm)	2.63 ± 0.44	2.54 ± 0.43	0.21
In-stent			
Minimum luminal diameter (mm)	2.17 ± 0.36	2.26 ± 0.37	0.78
Percentage diameter stenosis	14.26 ± 7.4	14.21 ± 6.1	0.38
Late lumen loss (mm)	0.06	0.08	0.14
Binary restenosis, % (n)	0	0	0.45
In-segment			
Minimum luminal diameter (mm)	2.42 ± 0.40	2.34 ± 0.37	0.42
Percentage diameter stenosis	21.14 ± 4.12	21.34 ± 4.50	0.26
Late lumen loss (mm)	0.07	0.10	0.13
Binary restenosis, % (n)	0	0	

Table 5: Eighteen-month Follow-up Quantitative Coronary Angiographic Data.

Initially from 0 to nine months follow up, 4 patients and 5 patients died due to cardiac death in SES and EES treated patients (HR: 0.96 ; 95% CI: 0.97 to 1.07; p: 0.47; Figure 1) following 4 and 5 patients death was observed on nine to 18-months follow up. From the data it was observed that death rates in SES received patients were less compared to EES received patients.

Myocardial infarction was observed in 21 patients who received SES and 13 patients with EES. On nine month follow-up nine and six patients were found with MI who received SES and EES respectively (HR: 0.89; 95% CI: 0.99 -1.02; p: 0.25). The incidence of MI increased to 12 and seven on 18 month follow-up (HR: 0.95; 95% CI: 0.99-1.03; p: 0.29; Figure 1). However, SES implanted patents had lesser incidence of MI compared to EES bearers.

MI TVR was performed in 16 and six patients who received SES and EES respectively (HR: 0.89; 95%CI: 0.98-1.03; p: 0.36; Figure 1). There was need of TVR in 47 and 31 patients as a whole in SES and EES

treated patients (HR: 0.92; 95% CI: 1.01-1.10; P: 0.89). There was even need of TLR in 20 patients with SES and in 18 patients with EES (HR: 0.98; 95% CI: 0.73–1.20; P: 0.65). There were also NTVR requirement in 31 patients with SES and in 21 patients with EES (HR: 0.97; 95% CI: 0.99-1.07; p: 0.29). The number of DST was less in SES (30, 3.4%) patients compared to EES patients (21, 7.23%) (HR: 1.17., 95% CI: 0.99-1.02; p: 0.24; Figure 1). The incidence of DST did not differ significantly within zero to nine months follow-up (11 [1.24%] with SES vs. 9 [3.10%] with EES; HR: 0.97, 95% CI: 0.99-1.02; p: 0.10; Figure 1). However, on nine to 18-months follow-up, DST was significantly lower in SES group than EES group (19 [2.14%] vs. 12 [4.13%] patients, respectively; HR: 1.03; 95% CI: 0.99-1.04; p: 0.30; Figure 1). Results of the corresponding test for interaction were not significant which was deduced based on COX regression analysis [9]. Graphical representation of cumulative incidences of all the primary events of SES and EES implantation are done in (Figure 1). The data are represented in (Table 6).

Outcome	Sirolimus (N=884)	Everolimus (N=290)	Hazard ratio	95 % CI	P-value
Composite of MACE (cardiac death, MI, DST, and clinically-driven TVS)	41 (4.63 %)	21 (7.21 %)	1.05	0.9 - 1.03	0.14
0-9 months	22 (2.43 %)	17 (5.86 %)	0.98	1.00 -1.06	0.28

9-18 months	19 (2.14 %)	14 (3.17 %)	0.94	1.19- 1.58	0.36
Death	8 (0.90 %)	10 (3.44)	1.03	1.00-1.04	0.24
0-9 months	4 (0.45 %)	5 (1.72 %)	0.94	0.99 - 1.04	0.14
9-18 months	4 (0.45 %)	5 (1.72 %)	1.01	0.99 - 1.04	0.14
Cardiac Death	8 (0.95 %)	10 (3.44 %)	1.92	1.00-1.04	0.24
0-9 months	4 (0.45 %)	5 (1.72 %)	0.96	0.97 -1.07	0.47
9-18 months	4 (0.45)	5(1.72 %)	0.96	0.97-1.07	0.79
MI	21 (2.36)	13 (4.37)	1.02	0.99-1.05	0.10
0-9 months	9 (1.01 %)	6 (2.06 %)	0.89	0.99 -1.02	0.25
9-18 months	12 (1.35 %)	7 (2.41 %)	0.95	0.99-1.03	0.29
MI TVR	16 (1.80 %)	6 (2.75 %)	0.89	0.98-1.03	0.36
0-9 months	6 (0.67)	2 (0.68 %)	0.92	0.98-1.10	0.98
9-18 months	10 (1.13 %)	4 (1.37 %)	1.05	0.97-1.08	0.75
TVR	47 (5.31 %)	31 (10.68 %)	0.92	1.01-1.10	0.89
0-9 months	25 (2.82 %)	15 (5.17 %)	1.02	0.99-1.05	0.11
9-18 months	22 (2.48 %)	16 (5.51 %)	0.96	1.00-1.05	0.04
TLR	20 (2.24 %)	18 (5.45 %)	0.98	0.73–1.20	0.65
0-9 months	11 (1.24 %)	8 (2.75 %)	1.05	0.98-1.08	0.15
9-18 months	9 (1.01 %)	10 (3.44 %)	1.02	1.00-1.05	0.34
NTVR	31 (3.50 %)	21 (7.4 %)	0.97	0.99-1.07	0.29
0-9 months	11 (1.24 %)	9 (3.10 %)	1.02	0.99-1.04	0.16
9-18 months	20 (2.26 %)	12 (4.13 %)	1.01	0.96-1.05	0.14
DST	30 (3.4 %)	21 (7.23 %)	1.17	1.00-1.07	0.24
0-9 months	11 (1.24 %)	9 (3.10 %)	1.02	0.99-1.02	0.10
9-18 months	19 (2.14 %)	12 (4.13 %)	1.03	0.99-1.04	0.13

Table 6: Major Adverse Cardiac Events and Stent Thrombosis.

Discussion

In the last couple of decades stent technology has got momentum in PCI [10]. Metal surface and chemical property of the stents play a pivotal role in designing an ideal, safe and efficacious stent. In these years there has been a revolutionary change in the stent material and design. The bare-metal stents (BES) prevent negative arterial remodeling in percutaneous transluminal coronary angioplasty, prevents acute recoil and closure of vessels [11]. However, it suffers with a limitation of augmented instances of restenosis and repeat revascularization and stent thrombosis rates [12-17]. Hence newer generation DES was developed which inhibit neointimal proliferations thereby reduce repeat revascularization. Drug eluting stents primarily are of first generation which contains sirolimus and its analogues, and second generation coated with anti-proliferative and immunosuppressive agents like everolimus coated over biodegradable polymers. This is done to minimize the risk of late adverse vascular

responses to permanent stents. However, both first and second generation DES is equally efficacious but the later is safer as per recent studies [18,19].

In this arbitrary, prospective comparison of SES and EES, the efficacy of SES in suppressing neointimal growth (expressed as LL) was non-inferior to the EES. Both stents showed exceptional LL profiles at nine and 18month angiographic follow-up. Clinical outcomes, including MI, cardiac death, TLR were typically similar between the 2 stents, although this study was underpowered to demonstrate the variation in clinical outcome between the two stents. Moreover, the distinct and apparent DST rates were not statistically different between the two types of stents, although they were numerically lesser in the SES.

The research hypothesis was, significant difference exists between SES and EES treated patients. However, the statistical analysis rejects the research hypothesis and accepts the null hypothesis i.e. no

significant difference exists between SES and EES groups. Hence the paramount outcome of this investigation was the non-inferior implication of SES and EES. The trial outcome of both EES and SES was phenomenal with low rate of DST and TLR. Earlier, DES cause late Stent thrombosis, had thick struts which acted as a barrier for early endothelialization. SES has low strut thickness (59 μ m), promising early endothelialization thereby reduces the risk of stent thrombosis. SES has drug elution kinetics of 28 to 30 days and a polymer degradation that is short and well documented. SES found to be safe and efficacious in preclinical models and in the primary safety and efficacy study [20].

This study has demonstrated 2.48% MACE and 3.4% of stent thrombosis case during observation. In terms of efficacy parameters, at nine month angiographic follow-up, 0.05mm of in-stent medial LLL were observed and no binary restenosis were recorded. Analysis of data demonstrated safety and efficacy profile of SES, similar to other published randomized trials [21]. The study demonstrated a high safety profile of DESs, with 13% MACE, 10% stent thrombosis and 0% binary restenosis.

Data from other similar studies demonstrated that, in comparison to EES, SES had a better enduring safety and efficacy report [22]. Our results also revealed a 14% reduction in MACE rate that in patients treated with SES, which was largely owed to a lesser risk of very late DST. During zero to nine months, MACE rate did not differ significantly, which is the main prevalent time point considered for determining the primary endpoint in head-to-head contrasts of drug-eluting stents. However, from zero to 18-months observation the rate of MACE in SES was found to be non-inferior than EES. Throughout 18-months, the liability of DST was sporadic and alike in both groups. In a comparison of first-generation DES (EES and PES), the initial pre-eminence of the EES was lost at 18-months follow-up. DST occurred with an annual rate of 1.24% to 3.10% for both stent types [23-25]. In the PRISM trial (SES vs. EES), DST was more recurrent after implantation of EES than after SES [26], although the contradictory results were recorded between nine and 18-months follow-up. The present results from the PRISM with follow up to 18-months, in which the composite endpoint safety and efficacy factors for SES and EES were found to be non-significant. The rates of DST also presented similar results for both the DES. Results were reliable in all patients other than diabetes, where in the reports were non-significantly diverse. The SES provided long-lasting and significant decline in TLR. In PRISM trails, SES reduced MACE rates in patients with diabetes, but there was no significant interaction between treatment allocation and diabetes. Like most stent trials, the PRISM trial was designed as a single-blinded study, and we believe that the scarcity of double-blindness would not influence the results, as all endpoints were objective and determined by an event committee that was blinded to treatment group assignment during the adjudication process. Hence, we apprehend that the incident rate in the study was diplomat of the real event rate among this patient population. This registry-based randomized clinical trial design has been used in all PRISM trails and has established significant attention as a way of experimenting comprehensive, self-regulating clinical trials. Advantages of this approach include a substantial reduction in the expense associated with a randomized trial because we were able to use the established registry infrastructure. Moreover, the study design provides data that are more comparable to real-life situations because of the absence of study-related interventions.

Conclusion

At nine and 18-month follow-up, both SES and EES proven to have better safety and efficacy profile and lower MACE rates and lower rates of Definite Stent Thrombosis. But the difference was not statistically significant and SES was found to be non-inferior to EES.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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