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A prospective, multicenter, post marketing surveillance study to evaluate the safety and effectiveness of the Superia-Sirolimus Eluting Coronary Stent System (SSECSS) implanted during routine clinical practice in India

Praveen Chandra[*], *Tarun Kumar*

Department of Intervention Cardiology, Medanta the Medicity, Gurgaon, India

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ABSTRACT

Aim: A prospective, multicenter, post marketing surveillance study to evaluate the safety and effectiveness of the Superia-Sirolimus Eluting Coronary Stent System (SSECSS) implanted during routine clinical practice in India.

Objectives: Primary objective:

1. To study the MACE and in stent and In-segment Loss at Six Months (in a pre selected group of 50 patients).

Secondary objective:

1. Clinical and procedural success.

Materials and methods: This is a prospective, open label, single-arm, multicenter (16 sites), post marketing observational study enrolling patients implanted with Superia-Sirolimus Eluting Coronary Stent (SSECS) in routine clinical practice in India. A total of 200 Patients of coronary Artery Disease (CAD) implanted with Superia-Sirolimus Eluting Coronary Stent (SSECS) were enrolled. Clinical assessments were done at 30 days, 180 days and at 1, 2 years either telephonically or office visit. A cohort of 50 pre-selected patients were followed up for angiographic evaluation at 180 days.

Results: MACE at 12 month of follow up was 1.71%.Late lumen loss, in segment was 0.14 and in stent was 0.10 mm at 6 month of follow-up. TLR was required only in 2 patients.

Conclusion: Superia stent is as safe as other biodegradable polymer stent in the market and time has come for biodegradable polymer stent with thin struts.

Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; BMS, bare metal stent; CHD, coronary heart disease; CK-MB, creatinine kinase in myocardial band; FDA, food& drug administration; HF, heart failure; ICH, international conference on harmonization; IEC, independent ethics committee; IRB, institutional review board; LVEF, left ventricular ejection fraction; MACE, major cardiac adverse events; MI, myocardial infarction; NSTEMI, non- ST segment elevation myocardial infarction; PCI, percutaneous coronary intervention; QTc, QT interval corrected for heart rate; SSECSS, superia-sirolimus eluting coronary stent system; TIMI, thrombolysis in myocardial infarction; STEMI, ST elevation myocardial infarction.

* *Corresponding author.*
E-mail address: praveen.chandra@medanta.org (P. Chandra).

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1. Introduction

Drug-eluting stents continue to represent a major medical advance for angioplasty (Serruyes et al, 2006).[1] The findings of large randomized clinical trials showing the re-stenosis reduction efficacy of these stents have led to their approval and use in India.[2–5] Although rate of restenosis was lesser in DES as compared to BMS,[6] Sirolimus DES versus Paclitaxel DES,[7–10] still there was a scope of improvement.

The first generation DES initially demonstrated a good promise in terms of reducing restosis. But over a period of time, the polymeric degradation byproducts failed to bring about endothelisation. Failure to endothelisation gave rise to problem of nonhealing and restenosis.[11–13] Currently DES technology are targeted to minimize vascular injury during stenting using ultra low strut thickness stent.[14]

Biodegradable polymer DES offer controlled elution of active drug from the stent backbone by means of a biocompatible polymer coating, which after completion of its useful function, slowly degrades to inert organic monomers, thereby dissipating the risk associated with the long-term presence of durable polymer in the coronary vessel wall.

Biodegradable polymer coatings are gaining popularity and are in use to eliminate inflammation, stent thrombosis and MACE while preserving the efficacy of DES. Superia-Sirolimus-Eluting Coronary Stent System (SSECSS) is a device/drug combination product comprised of four components: Stent platform: Flexia L605Cobalt Chromium stent with most recent coronary stent designs with thin 65 micron struts, delivery system, active drug component-sirolimus and biodegradable polymers. This study was undertaken to study clinical and procedural outcomes in patients implanted with Superia-Sirolimus Eluting Coronary Stent (SSECS) in routine clinical practice in India.

2. Methods and materials

This was prospective, open label, single-arm, multicenter (16 sites), post marketing observational study enrolling patients implanted with Superia-Sirolimus Eluting Coronary Stent (SSECS) in routine clinical practice in India.

2.1. *General inclusion criteria were*

1. Patient with age >18 years.
2. The patient who agrees to participate in the study.
3. Patients whose coronary anatomy were suitable for implantation of one or more Superia-Sirolimus Eluting Coronary Stent.

2.2. *Angiographic inclusion criteria*

1. Target lesion must be located in native coronary artery (2.5–3.5 mm)
2. Treatment of two de novo lesions, each located in a separate native epicardial vessel.
3. Target lesion(s) must measure < 28 mm by length by visual estimation
4. The target lesion must be a major artery or branch with a visually estimated stenosis of >70% and <100% with a timi flow of >1

2.3. *General exclusion criteria were-*

1. Patient currently experiencing clinical symptoms consistent with AMI or with acute myocardial infarction (AMI) preceding the index procedure (CK-MB >2 times of upper limit of normal) and CK and CK-MB not have returned to the upper limit of normal at the time of procedure.
2. Patient with left ventricular ejection fraction (LVEF) of <30%
3. Patient with heart transplant or any other organ transplant or in waiting list of any organ transplant
4. Female patients with known pregnancy or who are lactating.
5. Patients with known hypersensitivity or allergies to aspirin, heparin, clopidogrel, ticlopidine, Sirolimus or similar drugs, or any other analog or derivative, cobalt, chromium, nickel, molybdenum or contrast media
6. Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon
7. Current medical condition with a life expectancy of less than 12 months
8. Patients who are receiving immunosuppressive therapy or have known serious immunosuppressive disease (eg HIV) or have severe autoimmune disease that requires chronic immunosuppressive therapy (eg SLE etc)
9. Patients who are receiving or plan to receive the chronic anticoagulation therapy (eg heparin or coumadin)
10. Subject has received brachytherapy in any epicardial vessel (including side branches)
11. Drug eluting stent treatment if done within 90 days prior to the index procedure
12. Subject has known renal insufficiency (eg. Serum creatinine level of >2.5 mg/dL or subject is under dialysis)
13. Platelet count <1,00,000 cells/mm^3 or >7,00,000 cells/mm^3, WBC of <3000 cells/mm^3

2.4. *Angiographic exclusion criteria*

1. Patients with Chronic Total Occlusions (TIMI flow 0).
2. Patient with ostial left coronary artery and left main ostial lesion (RCA-aorto ostial lesion are not excluded)
3. Patients with extreme angulation (≥90°).
4. Patients with heavy calcification of target vessel
5. Patients with instent re-stenosis.
6. Patient with target vessel containing thrombus
7. Patient with arterial or saphenous vein graft lesion.
8. Patient with target lesion involving a bifurcation in which side branch is ≥ 2 mm in diameter and the ostium of the side branch is ≥50% stenosed by visual estimation

Treatment and procedures were done as per discretion of the investigator. Safety data (death, MI, revascularization,

stent thrombosis, major bleeding complications as per ARC definitions and unexpected adverse device effects) were reviewed by independent safety monitoring board (personnel's not associated in any terms with the study organization and conduct). A total of 200 Patients of coronary Artery Disease (CAD) implanted with Superia-Sirolimus Eluting Coronary Stent (SSECS) were enrolled. Clinical assessments was done at 30 days, 180 days and at 1, 2 years either telephonically or office visit.

The following data were collected at the each follow up visit-

1. Clinical events that occur during the procedure including death, MI, revascularization and stent thrombosis
2. Adverse events (AE) data including laboratory test results, ECG and subsequent repeat coronary angiogram
3. Patient compliance to anti-platelet therapy and any interruption of therapy
4. Major bleeding complications.
5. Patient health status (symptoms physical function, and quality of life) using the Seattle angina Questionnaire.

3. Results

A total of 200 patients enrolled across 16 centers in India. First patients was enrolled in May 2012 and last patient in November 2013 and study completed in April 2014. Demographic profile of 200 patients is shown in Table 1. Mean age of patients were 56 yr, 82% were male, 38.5% were diabetic, 46% were hypertensive and 27% were having previous MI.

Procedural success was achieved in all patients. At 1 year of follow up TLR was required only in 2 patients and there was only 1 cardiac death and MACE was seen in 3 (1.71%) patients (Table 2). Angiographic follow was done in 50 patients. As shown in Table 3 late lumen loss studied at 6 month of follow up. In stent lumen loss was 0.10 mm and in segment lumen loss was 0.014 mm at 6 month of follow up.

4. Discussion

First generation DES were better than BMS, sirolimus DES fare better than Paclitaxel DES, thin struts designed stent better than thicker profile stents. When the data from present study compared with other studies, Superia-Sirolimus Eluting Coronary Stent System seems better or equivalent to other in term of MACE and TLR. As shown in SPIRIT-11 study.[15] Xience-v stent was having MACE of 2.7%, TLR of 1.8% as compared to MACE of 1.71% and TLR OF 1.14% WITH SUPERIA stent. Similarly superia stent fared better than endeavor resolute[16] in term of MACE (8.5% vs 1.7%) but TVR was slightly more (0.8% vs 1.14%).

When compared with stents with biodegradable polymer like Biomatrix stent[17] (unique abluminal biodegradable polymer) MACE was lower (5.1 vs 1.71%) and TVR was almost equal (0.8 vs 1.14%).Similarly when compared with BIOMIME stent,[18] a sirolimus DES with thin struts (65 micron) and biodegradable polymer poly l lactic acid and poly l glycolic acid, SUPERIA stent showed better MACE and TLR as shown in Table 4.

The results of meta analysis published in BMJ,[19] with data derived from 126 randomized trials and more than a quarter million patient years of follow up, showed that biodegradable polymer drug eluting stents are not superior to newer generation durable polymer drug eluting stents for either efficacy or safety outcomes. Further randomized trials are required to show the superiority of biodegradable polymer stents over newer generation durable polymer DES and one biodegradable polymer stent over other.

Thus we can conclude safely that Superia stent is as safe as other stent system in the market or even slightly better in term of MACE and finally time has come for thin struts design stents with biodegradable stent.

Table 1 – Demographics profile (200 patients).

Mean age, years	56 years
Male patients	164 (82 %)
Female patients	36 (18%)
Smokers	56 (28%)
Diabetic patients	77 (38.5%)
Hyperlipidemia	18 (9%)
Hypertension	92 (46%)
Previous MI	54 (27%)
History of previous stroke	4 (2%)
History of TIA	3 (1.5%)

Table 2 – Mortality, morbidity and MACE.

	1 Month FU ($n = 200$) (%)	6 Month FU ($n = 200$) (%)	1 Year ($n = 175$) (%)
Non cardiac death	0	1 (0.50%)	1 (0.57%)
Cardiac death	1 (0.50%)	1 (0.50%)	1 (0.57%)
Myocardial infarction	0	0	0
TVR	0	0	0
TLR	1 (0.50%)	2 (1%)	2 (1.14%)
Non – TVR	0	0	0
CABG	0	1 (0.50%)	1 (0.57%)
Device malfunction	0	0	0
Procedural success	–(100%)	–(100%)	–(100%)
Stent thrombosis	0	0	0
MACE %	2 (1.00%)	3 (1.5%)	3 (1.71%)

Table 3 – Angiographic follow up (50 patients).

		In stent	In segment
MLD	Pre procedure	0.99	0.99
	Post procedure	2.5	2.5
	180 days follow up	2.39	2.36
% Stenosis	Pre procedure	57.59%	57.59%
	Post procedure	12.04%	11.71%
	180 days follow up	15.14%	15.50%
% Area stenosis	Pre procedure	80.66%	80.66%
	Post procedure	22.42%	22.42%
	180 days follow up	26.67%	27.88%
Late lumen loss (at 180 days follow up visit)		0.10 mm	0.14 mm
% Area loss (at 180 days follow up visit)		0%	5.45%

Table 4 – Comparison between Superia PMS and other DES.

Stent name	MACE	Late loss	Cardiac death	TLR
Superia PMS (6 month) ($n = 200$)	1.50%	0.10 mm (at 6 month)	0.50%	1.00%
Superia PMS (1 year) ($n = 175$)	1.71%	0.10 mm (at 6 month)	0.57%	1.14%
Xience V, spirit II (n = 223) (1 year)[15]	2.7%	0.19 mm (at 6 months)	0%	1.8%
Xience V, spirit II (n = 223) (2 year)[15]	6.4%	0.19 mm (at 6 months)	0.5%	3.7%
Endeavour resolute ($n = 130$) (1 year)[16]	8.5%	0.22 mm (at 9 months)	0.80%	0.8%
Biomatrix (80 biomatrix subjects) (6 month)[17]	3.8%	0.19 mm (at 6 months)	0%	1.3%
Biomatrix (80 biomatrix subjects) (1 year)[17]	5.1%	0.19 mm (at 6 months)	NA	0.8%
Biomime ($n = 242$) (1 year)[18]	5.7%	0.15 mm (at 8 months)	0.50%	4.7%

Disclosures

Writers have no conflict of interest to state. Medanta, the medicity was one of the 16 centers who participated in the study. Other Investigators and centers involved in the study were, Dr. Prabhakar Shetty Columbia Asia, Bangalore, Dr. Sanjay Mehrotra Narayan Hrudalaya, Bangalore, Dr. C. N. Manjunath Sree Jayadeva Institute, Bangalore, Dr. Y.P. Raju Poulomi Hospital, Secunderabad, Dr. Milind Gadkari KEM Hospital, Pune, Dr. N.S. Rama Raju Bollineni Hospital, Rajahmundry, Dr. Ranjan KMC, Manipal, Dr. Rishi Gupta Asian Hospital, Faridabad, Dr. G.S Wander DMC, Ludhiana, Dr. Satish Roplekar Ruby Heart Care Centre, Aurangabad, Dr. G.L.Sharma Jaipur Heart Institute, Dr. P Chandwani Heart & General Hospital, Jaipur, Dr. Ajit MMM, Chennai, Dr. R.R Mantri Sir Gangaram Hospital, Dr Milind Kharche Manik Hospital and Research Centre, Aurangabad.

Conflicts of interest

All authors have none to declare.

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