Original Article

Evaluation of prolonged safety and efficacy of biodegradable polymer coated sirolimus-eluting coronary stent system: 1-year outcomes of the INDOLIMUS Registry

Durgaprasad Rajasekhar[1], Velam Vanajakshamma[1], Akula Vidyasagar[1], Kummaraganti Paramatma Ranganayakulu[1], Mannuva Boochi Babu[1], Chakali Sivasankara[1], Shivani Kothari[2], Ashok Thakkar[2]

[1]Department of Cardiology, Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati, Andhra Pradesh, India; [2]Department of Clinical Trials, Sahajanand Medical Technologies Pvt. Ltd., Surat, Gujarat, India

Contributions: (I) Conception and design: All authors; (II) Administrative support: D Rajasekhar, V Vanajakshamma, A Vidyasagar, KP Ranganayakulu, M Boochi Babu, C Sivasankara; (III) Provision of study materials or patients: D Rajasekhar, V Vanajakshamma, A Vidyasagar, KP Ranganayakulu, M Boochi Babu, C Sivasankara; (IV) Collection and assembly of data: D Rajasekhar, V Vanajakshamma, A Vidyasagar, KP Ranganayakulu, M Boochi Babu, C Sivasankara; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Dr. Durgaprasad Rajasekhar, MD, DM, FACC, FSCAI. Department of Cardiology, Sri Venkateswara Institute of Medical Sciences (SVIMS), Tirupati, Andhra Pradesh-517507, India. Email: drdrsekhar@yahoo.co.in.

Background: The main aim is to evaluate prolonged safety and efficacy of the Indolimus (Sahajanand Medical Technologies Pvt. Ltd.) sirolimus-eluting coronary stent system.

Methods: It was a single center, non randomized, retrospective registry. Out of total 530 patients involved in the INDOLIMUS Registry, follow-up of 523 patients were obtained at 1-year The primary end-point of this was major adverse cardiac events, which is a composite of cardiac death, target lesion revascularization, target vessel revascularization, myocardial infarction and stent thrombosis, at 1-year follow-up.

Results: Cardiac death, target lesion revascularization and myocardial infarction at 1-year were reported in 19 (3.6%), 2 (0.4%), and 2 (0.4%) patients respectively, while stent thrombosis was reported in 1 (0.2%) patient. The resultant major adverse cardiac events at 1-year were reported to be 24 (4.5%).

Conclusions: The lower incidence of MACE in uncontrolled and more complex cohorts at 1-year follow-up clearly depicts the prolonged safety and efficacy of the Indolimus sirolimus-eluting stent (SES) system.

Keywords: Coronary artery disease; sirolimus-eluting stents (SESs); biodegradable polymer

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Introduction

The drug eluting stents (DES) are more efficient than bare metal stents (BMS), and it has been proven erstwhile in numerous studies (1-3). DES is associated with irrefutably lower risk of restenosis and revascularization as compared to BMS (4). The first generation DES constitutes of durable polymers, and reduces the risk of target lesion revascularization (TLR) (5). But, its usage suffers from detrimental inflammatory reaction, thereby prolonging healing process of vessel wall and restoration of endothelium (6,7). The chances of late thrombotic risk is also increased several folds (8-10). DES with biodegradable polymers can overcome the pros and cons associated with durable polymers. Biodegradable polymers can be absorbed after the drug has been eluted. Thus, only a metal stent is left over ensuring that there is no further damage of the arterial wall. The polymer material used in the study stent undergoes degradation within 9-12 months of stent implantation. While, the short-term safety and efficacy of the Indolimus SES is known (11), the prolonged safety

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Table 1 Baseline demographic characteristics

Characteristics	Indolimus SES n=530 patients
Age, mean ± SD (years)	54.9±10.8
Male, n (%)	415 (78.3)
Diabetes mellitus, n (%)	169 (31.9)
Hypertension, n (%)	215 (40.6)
Smoker, n (%)	273 (51.5)
Tobacco chewer, n (%)	17 (3.2)
Alcoholism, n (%)	130 (24.5)
Renal insufficiency at screening, n (%)	25 (4.7)
Previous stroke, n (%)	12 (2.3)
Previous MI, n (%)	56 (10.6)
Primary PCI, n (%)	114 (21.5)
Unstable angina, n (%)	77 (14.5)
Left ventricular ejection fraction, (%)	49.9±9.9

SES, sirolimus-eluting stent; MI, myocardial infarction; PCI, percutaneous coronary intervention.

and efficacy of the Indolimus SES at 1-year, after the degradation of polymer material, is unknown, although an important outcome to ponder.

Thus, our main aim is to evaluate prolonged safety and efficacy of the Indolimus coronary stent system in high risk patients with complex coronary lesions.

Methods

Study design and clinical end-points

The INDOLIMUS registry is a single center, non randomized, retrospective registry with the main aim of evaluating safety and efficacy of the Indolimus SES. The study was approved by the Institutional review board and was conducted in accordance with the principles of good clinical practice (GCP) and Declaration of Helsinki. The protocol and in-hospital, 30 days and 6-months results of the registry have been described elsewhere (11). The primary end-point of this follow-up is to determine 1-year incidence of major adverse cardiac events (MACEs). MACE includes cardiac death, TLR, target vessel revascularization (TVR), myocardial infarction (MI) and stent thrombosis (ST).

Stent description

The Indolimus stent consisted of L605 cobalt chromium alloy (Co-Cr) as its stent platform having strut thickness of 60 µm and drug load of 1.4 µg/mm^2 coated with biodegradable polymer. The biodegradable polymer matrix consists of poly L-lactide, 50/50 poly DL lactide-co-glycolide and polyvinyl pyrrolidone to control the drug elution from stent coating. After unloading the drug within 48 days, the polymeric matrix undergoes hydrolysis. This process takes 9-12 months after which all the polymer gets degraded and gets excreted from the body in the form of metabolites.

Statistical analysis

Continuous variables are presented as mean ± standard deviation and categorical variables as counts and percentages. The event free survival curve was calculated according to the Kaplan-Meier method. All data were analysed using the Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 15.

Results

A total of 626 Indolimus stents were implanted in 617 lesions in 530 patients during the enrollment period. Out of 530 patients, 1-year follow-up was obtained for 523 (98.7%) patients. The patients retained the same baseline demographics (*Table 1*), and lesion and procedural characteristics (*Table 2*). At 1-year, cardiac death, TLR, and MI were reported in 19 (3.6%), 2 (0.4%), and 2 (0.4%) patients respectively, while ST was reported in 1 (0.2%) patients. The resultant MACE at 1-year was found to be 24 (4.5%) (*Table 3*). The event-free survival at 1-year follow-up by Kaplan-Meir method was found to be 94.7% (*Figure 1*).

Discussion

In the world of clinical trials, randomized controlled trial is considered as a "gold standard" for any intervention to establish its safety and efficacy. It enrolls clinically stable and straightforward lesions in contrast to real-life high-risk cohorts, involved in post-marketing surveillance registry. The INDOLIMUS registry was an "all-comers" registry, which means it also included high risk patients with complex lesions (21.5% primary PCI and 22.5% chronic total occlusions), and not ideal recruited lesions that gives an idea about the actual potential of the study stent in real-life setting. The in-hospital, 30-day and 6-month clinical outcomes have already established short-term safety and

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Table 2 Lesion and procedural characteristics

Characteristics	Patients =530/lesions =617
Lesion location, n (%)	
Left anterior descending	334 (54.1)
Right coronary artery	173 (28.0)
Left circumflex	110 (17.8)
ACC/AHA lesion classification, n (%)	
A	73 (11.9)
B1	153 (24.8)
B2	264 (42.7)
C	127 (20.6)
No. of diseased vessels, n (%)	
Single vessel disease	371 (70.0)
Double vessel disease	154 (29.1)
Triple vessel disease	6 (1.1)
Chronic total occlusion	139 (22.5)
Total no. of stent (N=626), mean ± SD, (mm)	
No. of stents per patient	1.18±0.40
Average stent length	18.8±6.0
Average stent diameter	2.9±0.3

Table 3 Clinical outcomes at 1-year follow-up

Outcomes	1-year follow-up (n=523)
Death, n (%)	23 (4.3)
Cardiac death	19 (3.6)
Non-cardiac death	4 (0.8)
MI, n (%)	2 (0.4)
TLR, n (%)	2 (0.4)
TVR, n (%)	0
ST, n (%)	1 (0.2)
Definite	0
Probable	1 (0.2)
MACE, n (%)	24 (4.5)

MI, myocardial infarction; TVR, target vessel revascularization; TLR, target lesion revascularization; ST, stent thrombosis.

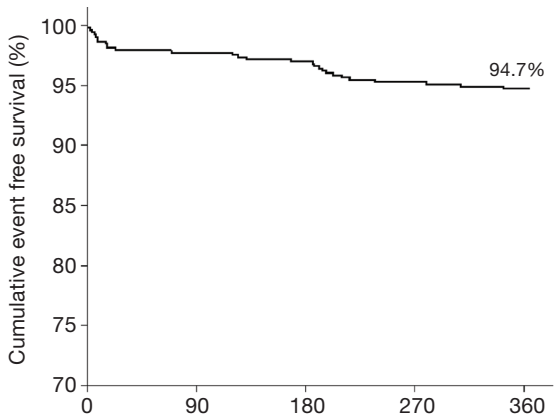

Figure 1 Event-free survival curve at 1-year follow-up.

efficacy of the Indolimus stent (11).

Indolimus, a biodegradable polymer coated sirolimus-eluting stent (SES) has been envisioned to reduce the long term sequelae associated with durable polymer DES, due to its persistence beyond the period of controlled drug release. So, the perceptible potential of biodegradable polymer DES can be acclaimed only if prolonged safety and efficacy outcomes, after the degradation of polymer, are evaluated.

Giving a quick rundown, at 1-year, MACE was found to be 24 (4.5%), which consisted of 19 (3.6%) case of cardiac death, 2 (0.4%) cases of TLR and 2 (0.4%) cases of MI. There was only 1 (0.2%) case of ST, as defined by ARC. Such promising results of biodegradable polymer coated SES were observed in a study by Han *et al.*, in which, MACE at 1-year follow-up was found to be 4% (12).

The high prevalence of cardiac death after percutaneous coronary intervention, as observed in our clinical outcomes, can be attributed to higher burden of cardiac risk factors among the patients, especially in low-income-patients. Poor are intuitively less able to afford presciption drugs, leading to suboptimal compliance with discharge medications. Moreover, reduced access to medical care or delayed presentation to tertiary care hospital after primary consultation also possibly had an impact on the outcomes. The supporting evidence by Alter *et al.* suggests an inverse relationship between socioeconomic status and mortality from acute MI (13).

Many randomized trials and meta-analysis have demonstrated conflicting results regarding the advantage of biodegradable polymer coated DES in reducing restenosis. The ISAR-TEST 3 trial, which is a non-inferiority trial, demonstrates that biodegradable polymer DES is non-inferior to durable polymer in terms of anti-restenotic effects at 1-year (14). The results of ISAR-TEST 4 trial are in concomitant with ISAR-TEST 3 and retrieves no added advantage of biodegradable polymer DES over durable polymer DES (15). In contrast, pooled analysis of three large randomized trials (ISAR-TEST 3, ISAR-TEST 4

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and LEADERS) has shown the advantage of biodegradable polymer DES over durable polymer DES and revealed clinically indicated TLR to be 7.6% at 1-year follow-up (16).

In our study, TLR was reported to be 0.4% and MI to be 0.4%. This gives an idea about the outstanding potential of the Indolimus in reducing restenosis and revascularization. Also, the lower strut thickness of Indolimus (60 μm) reduces the thrombogenic potential (17), which is evident from ST rate as low as 0.2%.

Thus, the prolonged clinical findings of the Indolimus registry satiate safety and efficacy needed for continued use of the Indolimus SES system.

Conclusions

At 1-year follow-up, there was substantially reduced rate of re-vascularization and only one case of ST. Thus, the lower incidence of MACE at 1-year follow-up clearly depicts the prolonged safety and efficacy of the Indolimus SES system. The major limitation of this registry is its observational design. It suffers the disadvantages of a nonrandomized/ single-arm investigation.

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None

Footnote

Conflicts of Interest: Dr. Ashok Thakkar and Shivani Kothari are employees of Sahajanand Medical Technologies Pvt. Ltd. and have provided detailed assistance in literature search and manuscript writing. Other authors declare that they have no conflict of interest.

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