

## Original Research Article

# Real world experience of GenXSync™ sirolimus eluting coronary stent system in patients with long coronary lesions: outcome of the GEL registry

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## ABSTRACT

**Background:** The study aimed to assess the immediate (procedural outcome) and long-term clinical (Cumulative hierarchical MACE up to 2 years) and angiographic outcomes (late lumen loss at 8 months) in the patients undergoing angioplasty with at least one 40 mm GenXSync™ SES. (Indian Study Regulatory ID CTRI/2014/07/004783).

**Methods:** This single centre prospective study included 26 real-world coronary artery disease (CAD) patients with long and very long lesions (38 lesions, 48 stents). All patients were treated with one or more 40 mm GenXSync™ sirolimus eluting stent (SES). All the subjects were followed up for 2 years including angiographic follow-up at 8 months. Angiography data was evaluated and reported by an independent angiographic core-lab. Subset analyses were performed for all 40mm long stents and 40mm with small diameter stents.

**Results:** The procedural success was observed in 94%. The acute gain was  $2.25 \pm 0.53$ mm in stent and  $2.09 \pm 0.71$ mm in segment despite of long and complex lesions including CTO. At 2 years, there was only 1 (3.84%) MACE (binary restenosis at 8 months) and stent thrombosis. At 8 months late lumen loss was in-segment  $0.15 \pm 0.30$ mm and in-stent  $0.14 \pm 0.17$ mm ( $p = 0.06$ ).

The 40mm stents subset, revealed acute gain of  $2.21 \pm 0.58$ mm in-stent and  $2.01 \pm 0.74$ mm in-segment. The late loss was  $0.16 \pm 0.31$ mm and  $0.13 \pm 0.17$ mm in-stent and in-segment respectively. In 40mm stent with small diameter subset, the acute gain was  $2.19 \pm 0.42$ mm in-stent and  $1.69 \pm 0.59$ mm in-segment and late lumen loss was  $0.10 \pm 0.18$ mm in-segment and  $0.13 \pm 0.33$ mm in-stent.

**Conclusions:** The results of real world long lesions PCI revealed efficacy, safety and procedural success observed with GenXSync™ stent comparable to other reported studies.

**Keywords:** Angioplasty, Complex PCI, Genxsync, Long stent, Long lesion PCI, MIV therapeutics, Hybrid design stent, Percutaneous coronary intervention, PCI, Sirolimus eluting stent, Tata consultancy services

## INTRODUCTION

Percutaneous coronary intervention (PCI) plays a key role in the management of patients with coronary artery disease (CAD).<sup>1</sup> Since the introduction of balloon angioplasty in 1970s, PCI has undergone significant advancement with the introduction of bare-metal stents and now, the drug-eluting stents (DES). Though the first generation DES drastically reduced restenosis, concerns with their long-term safety persist. As a result, DES has continuously undergone improvements in terms of new designs, thinner struts; novel drugs especially Sirolimus and its derivatives, and biodegradable polymer.<sup>2,3</sup> These techniques have effectively enhanced efficacy and safety of the DES as reported in the SPIRIT group of studies LEADERS, STEALTH, NOBORI 1 trial and Meri T- I studies.<sup>4-10</sup> Late lumen loss is considered as the surrogate of neo-intimal hyperplasia; the latter being an indicator of DES efficacy.<sup>11</sup> Whereas drug and its dose on the stent remains an important factor influencing neo-endothelial growth, the most important among mechanical factors is the strut thickness of the stent.<sup>12</sup> Lesion length and used stent length are among two important factors that adversely influence the outcomes after PCI as well as in long term.<sup>12</sup>

GenXSync™ is a novel platform cobalt chromium stent with hybrid cell design comprising of an intelligent mix of open and close cells. This design enables the stent to be more flexible, trackable and deliverable even in the long lesions. The platform uses a blend of biodegradable lactate derivative polymers and the proven advantage of Sirolimus. The concentration of drug on each stent is maintained to 1.0 µg/mm<sup>2</sup>. The current study evaluated the safety and efficacy of GenXSync™ stent system in real-world CAD patients with at least 1 long lesion requiring the implantation of a 40 mm stent.

## METHODS

This was a prospective, real-world study at a single centre in India, and included CAD patients with at least one lesion having angiographic evidence of >50% stenosis and requiring a stent of 40 mm length. Patients with impaired renal function; suspected liver disease; candidates of heart transplant; scheduled for major non-cardiac surgery within 6 months of PCI or with terminal diseases were excluded from the study. The study protocol was reviewed and approved by the Institutional Ethics committee. All patients underwent an angiographic follow-up at 8 months after the PCI. The core-lab evaluation was performed by an independent core laboratory. Clinical follow-up was done at 1, 6, 8, 12 and up to 24 months post-procedure. The study monitoring, data management and report including statistical analysis was performed by and Independent Contract Research Organization.

The primary clinical endpoint of the study included major adverse cardiac events (MACE) with 6 months post-

procedure as a composite of death, myocardial infarction, any target vessel revascularization (TVR) and stent thrombosis.

The primary angiographic endpoint was defined as late lumen loss (LLL) by quantitative coronary angiography (QCA) at 8 months. Two post-hoc analyses were performed to evaluate MACE, LLL and diameter stenosis percent in the two subsets: (1) Long stent use length 40 mm and (2) Long stent and small vessel length 40 mm, diameter that can be covered by a 2.75 mm stent. Post hoc power for MACE at 6 months was 90% (Hypothesized proportion 3% Vs. Actual Proportion 3.6%) and Confidence interval was 95%, Margin of Error 3% The post-hoc calculation of power for the LL in-stent was performed on basis of hypothesized mean of 0.2 – the adjusted late lumen loss of the SPIRIT Study, to obtain effect of long lengths. The post-hoc power was approximately 70% with 95% CI with one same Z test for sample size 36 (Mean late loss 0.16 mm, standard deviation 0.91mm). Data is reported as frequency (percentage of patients), mean ± standard deviation.

## RESULTS

A total of 26 CAD patients were prospectively enrolled in the study. The mean age of the patients at the time of consent was 60.26±8.09 years, and majority 19 (73.08%) patients were males. All patients had at least one significant medical risk factor; including hypertension 11 (42.30%) patients and diabetes mellitus 10 (38.6%).

**Table 1: Summary of demographic and baseline clinical characteristics of the patients.**

| Characteristics   | n = 26           |
|---|------------------|
| Age   | 60.26±8.09 years |
| Males   | 19 (73.08 %)     |
| Females   | 7 (26.92 %)      |
| Smokers   | 3 (11.54%)       |
| History of diabetes                                     | 10 (38.6 %)      |
| History of hypertension                                 | 11(42.30%)       |
| <b>Baseline lesion dimensions</b>                       |                  |
| Lesion length   | 32.20±11.23 mm   |
| Reference vessel diameter                               | 2.91±0.54 mm     |
| Minimum lumen diameter (mm)                             | 0.71±0.49        |
| Diameter stenosis percent (%)                           | 78.60±12.06      |
| <b>Subset 1: 40 mm stents - baseline QCA</b>            |                  |
| Minimum lumen diameter (mm)                             | 0.6±0.36         |
| Diameter stenosis percent                               | 78.32±12.31      |
| <b>Subset 2: 40 mm with small diameter-baseline QCA</b> |                  |
| Reference vessel diameter                               | 2.48±0.17        |
| Minimum lumen diameter (mm)                             | 0.64±0.21        |
| Diameter stenosis percent (%)                           | 74.47 ±7.73      |
| Lesion length   | 32.85 ± 5.49     |

Data presented as mean±standard deviation; number of patients (percentage).

**Table 2: Quantitative coronary angiography (QCA) analysis at post procedure and follow-up for all evaluable patients.**

| Parameters                                   | In stent      | In segment    |
|--|---------------|---------------|
| <b>Post procedure</b>                        | <b>n = 38</b> | <b>n = 38</b> |
| Minimum lumen diameter(mm)                   | 2.79 ±0.43    | 2.80±0.42     |
| Diameter stenosis percent (%)                | 3.55±8.98     | 2.41±13.85    |
| Acute gain (mm)                              | 2.25±0.53     | 2.09±0.71     |
| <b>Follow-up (n = 36)</b>                    | <b>n = 36</b> | <b>n = 36</b> |
| Minimum lumen diameter (mm)                  | 2.89±0.45     | 2.66±0.43     |
| Diameter stenosis percent (%)                | 2.79±32.87    | 3.61±23.97    |
| Late lumen loss (mm)                         | 0.15±0.30     | 0.14±0.17     |
| P <0.01 (reference spirit iii values-ci 95%) |               |               |

Data presented as mean±standard deviation.

**Table 3: Quantitative coronary angiography (QCA) analysis at post procedure and follow-up: subset wise.**

| Parameters   | In stent      | In segment    |
|--|---------------|---------------|
| <b>Subset 1: Patients with at least one 40 mm stent</b>                    |               |               |
| <b>Post Procedure</b>  | <b>n = 27</b> | <b>n = 27</b> |
| Minimum lumen diameter(mm)   | 2.75±0.43     | 2.91±0.47     |
| Diameter stenosis percent (%)  | 4.19±9.49     | 4.19±9.49     |
| Acute gain   | 2.21±0.58     | 2.01±0.74     |
| <b>Follow-up (n = 26)</b>  |               |               |
| Minimum lumen diameter   | 2.8±0.42      | 2.75±0.42     |
| Diameter stenosis percent  | 2.41±13.85    | 3.64±14.57    |
| <b>Late loss</b>   | 0.16±0.31     | 0.13±0.17     |
| <b>Subset 2: Patients with at least one 40 mm stent and small diameter</b> |               |               |
| <b>Post procedure</b>  | <b>n = 17</b> | <b>n = 17</b> |
| Minimum lumen diameter(mm)   | 2.46±0.15     | 2.94±0.37     |
| Diameter stenosis percent (%)  | 2.04±5.54     | 2.56±0.37     |
| Acute gain   | 2.19±0.42     | 1.69±0.59     |
| <b>Follow-up n = 17</b>  |               |               |
| Minimum lumen diameter   | 2.7±0.34      | 2.74±0.42     |
| Diameter stenosis percent  | 5.65±32.25    | (11.08)±18.22 |
| <b>Late loss</b>   | 0.13±0.33     | 0.10±0.18     |

The baseline characteristics have been presented in Table 1. Of the 26 enrolled patients, 16 patients (61.54%) were asymptomatic, 1 (3.84%) patient had myocardial infarction while 4 (15.38%) and 5 (19.23%) patients had stable and unstable angina, respectively. Diagnosis was

established or confirmed by ECG in 14 (53.85%) patients.

### QCA analysis

QCA analysis is an important evaluation in coronary intervention. Outcomes of QCA analysis viz. acute gain and late loss are considered to be objective parameters for performance of the device and operative skills. The acute procedural success and high acute gain highly depends upon the operative strategies.

Hence, good procedural outcomes and high acute gain results despite of long and complex lesions including CTOs pertain to very high operative standards, strategies and skills. Low late lumen loss is indicate success of the stent in controlling neo-intimal hyperplasia.

### Baseline analysis and acute gain

A total of 48 stents were implanted to treat 38 lesions in 26 patients. At baseline, the QCA based analysis revealed an average diameter stenosis of 78.6±12.06%, which included subjects with even total occlusions. After the procedure, the residual stenosis was 2.79±0.43 % in stent and 2.8±0.42% in segment. The mean Reference vessel diameter was 2.91±0.54 mm. Acute gain, surrogate of procedural success at the post procedure analysis, was evaluated in-stent and in-segment. In-stent acute gain of 2.25±0.53 and in segment 2.09±0.71 was obtained (p= 0.069).

### Late lumen loss (LLL) at 8 months

The QCA follow-up report included 40 stents in 36 lesions in 25 patients. Lesion wise QCA analysis is presented in Table 2. Of the 38 treated lesions, 36 lesions were evaluable at 8 months follow-up. The analysis was performed as in-stent - from stent margin to stent margin and in-segment - 5 mm on either side of the stent. The in-segment LLL was reported as 0.14 ±0.17 mm and in stent late lumen loss was reported as 0.15 ±0.30 mm (p= 0.06). The acute procedural success and high acute gain highly depends upon the operative strategies. Good procedural outcomes and high acute gain results despite of long and complex lesions including CTOs pertain to very high operative standards, strategies and skills. Low late lumen loss is indicate success of the stent in controlling neo-intimal hyperplasia.

### Major adverse cardiac events (MACE)

Major adverse cardiac events (MACE), defined as, cardiac death, myocardial infarction, and target lesion revascularization (repeat PTCA or coronary bypass surgery for recurrent symptoms related target-lesion re-narrowing), is the composite of safety and efficacy. The efficacy of the device was mainly assessed from Target Vessel Revascularization (TVR) at 1, 6, and 12 months. In this study no TVR was reported until 24 months.

No MACE was reported at 30 days. At the end of 12 months, a cumulative total of one (3.84%) MACE was reported and there was no further addition at 24 months. This contributed to the secondary endpoints of the study. There were no events between 1 and 2 years. No TLR was reported until 24 months.

### Safety

There was no event of acute, sub-acute or late stent thrombosis up to 24 months post procedure. No event of myocardial infarction was reported in the course of the study.

### Subset analysis - long lengths and long lengths in small

This study was conducted with a specific design that included subjects with minimum one stent of 40mm length in any diameter. Total 27 stents 40 mm long stents were implanted in 26 subjects. All the subjects essentially were the part of this subset considering the fact that all subjects included in the study, had to meet a criterion of having minimum one 40 mm stent implanted. Hence the MACE was the same. The QCA analysis revealed Reference Vessel Diameter at baseline was  $2.91 \pm 0.54$  mm with a mean diameter stenosis of 60%. At the end of procedure, the residual stenosis was 2.41% in stent and 3.64% in segment with an acute gain of  $2.21 \pm 0.58$  mm in stent and  $2.01 \pm 0.74$  mm in segment. The late lumen loss analysis in this subset with evaluation of Diameter stenosis at 8 months were very similar results to the whole study outcomes as this subset was the major contributor to the study population. The late lumen loss was  $0.16 \pm 0.31$  mm  $0.13 \pm 0.17$  mm in stent and in segment respectively, indicative of high efficacy in spite of difficult to treat lesions.

The second subset further refining of subset of long lesions subset to a small diameter. There were total 17 stents which qualified the criterion for inclusion for this subset: 40 mm long stents diameter less than 2.75 mm diameter. This subset is considered as the most difficult to treat subset. The Analysis performed analysis revealed that the GenXSync™ Stent performed extremely well even in this subset. There was no MACE in this subset for 24 months. QCA analysis revealed reference vessel diameter as  $2.48 \pm 0.17$  mm. The procedural success with TIMI III flow was observed in all the cases. Acute gain in stent and in segment was  $2.19 \pm 0.42$  and  $1.69 \pm 0.59$  respectively. The mean diameter stenosis at baseline was 74.48% and post procedure was 2.03% in stent as well as in segment. The late lumen loss was at similar to the total population revealed as  $0.10 \pm 0.18$  mm in segment and  $0.13 \pm 0.33$  mm in stent.

### DISCUSSION

Long length stents have always been a point of discussion among the cardiovascular interventionists.<sup>13</sup> The major worry being the effort required for tracking and

delivering the stent resulting into higher vessel injury and thereby a poor clinical and angiographic outcome at follow-up. This real-world data provides a strong evidence of the comparable outcomes of GenXSync™ stent systems with that of other commercially available DESs. The study patients comprised a group of real-time CAD patients, predominantly males with significant proportion of diabetic and hypertensive patients, and current smokers. The degree of stenosis also was high, including patients with totally occluded coronaries.

The TLR rate at 6 months was 0% in our study, which was even lower than that reported with Landmark clinical trials like SIRIUS and ENDEAVOR II which have reported TLR rates of ~ 4% and stent thrombosis rates of 0.4% to 0.5%.<sup>14,15</sup> The overall event free survival at 6 months in SERIES I was 95% while in other studies - SIRIUS, ENDEAVOR II and TAXUS IV - it was 92.9%, 92.6% and 91.5% respectively.<sup>16</sup> In this study, despite complex patient and lesion characteristics (i.e. 29% diabetics, 17% CTO, 5 % multi vessel disease, 56 % LAD), the safety and efficacy outcome of GenXSync™ was comparable to other approved DES.

The safety and performance of GenXSync™ stent is comparable to CYHPER™ (Cordis, USA) and SupralimusCore™ (Sahajanand Medical, India). Based on the statistical comparison, noninferiority of GenXSync™ stent (compared to CYHPER) can be assumed with a confidence of 95 %.

The eight month results of GenXSync™ also proves the safety of GenXSync™, as incidence of aneurysms, incomplete opposition and stent thrombosis was not reported. At 24 months the GenXSync™ was seen to be efficacious and safe with only 3.84% MACE, and acceptable angiographic outcomes. For interventional cardiologists PCI of long lesions is still a challenge due to its complexity. However, from this study we can understand that long stents with hybrid designs (GenXSync) and correctly used operative strategies can overcome the challenge significantly.

### CONCLUSION

Real-world experience provides valuable insights into the treatment patterns and outcome profiles of patients in actual clinical scenario. The use of GenXSync™ sirolimus eluting coronary stent system is safe and effective in a broad range of clinical conditions and lesions morphologies as represented in this study. Future studies can be directed to evaluate its efficacy in preventing a range of clinical re-stenosis in a larger population.

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