

# **DES-BTK: A Prospective, Double-Blind Randomized Trial of Polymer-Free Sirolimus-Eluting Stents Compared to Bare Metal Stents in Patients with Infrapopliteal Disease**

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# Potential Conflicts of Interest

Speaker's name: Thomas Zeller

My Disclosures:

- Consulting Fees/Honoraria:

Sanofi-Aventis, C.R. Bard, Cordis, ev3, Pathway Medical, Straub Medical, Invatec, Biotronik, Optimed, SquareOne

- Research Grants:

Cook, Krauth Medical, Pathway Medical, Abbott Vascular, Invatec, Angioslide, Novostent, IDEV, Biotronik, Atheromed, ev3, C.R. Bard, Cordis

# Sponsorship and Data Management

- Investigator initiated study
- 4 German sites
- Stent devices provided for free by Translumina, Germany
- Logistical support for data acquisition including eCRF design by Translumina
- Independant duplex and angiographic corelab analysis



# Study Background & Methods

- Preliminary reports indicate that sirolimus-eluting stents (SES) reduce the risk of restenosis after percutaneous infrapopliteal artery revascularization.
- Patient enrolment: 4/2006 to 4/2008
- Prospective, randomized, multi-centre, double blind trial
- Comparison of a polymer-free SES with a placebo coated BMS
- ClinicalTrials.gov number, NCT00664963



# Study Endpoints

- Primary Endpoint:
  - 1-year primary patency rate, defined as freedom from in-stent-restenosis ( $\geq 50\%$ ) detected with angiography or if appropriate with duplex ultrasound.
- Major secondary endpoints:
  - 6-month primary patency rate
  - secondary patency rates
  - TLR rates
  - Changes in Rutherford-Becker classification
  - Ankle-brachial index
  - MAE



# Major Inclusion Criteria

- At least 21 years old
- PAOD Rutherford-Becker class of 2 to 5
- Single de novo infrapopliteal lesion
- Vessel diameter 2.0 mm to 3.5 mm
- Lesion length 10 to 45 mm
- Diameter stenosis of at least 70%



# Major Exclusion Criteria

- PAOD Rutherford class 0, 1 & 6
- Visible thrombus within target lesion
- Known systemic coagulopathy
- Buerger's disease
- Acute limb ischemia
- Life expectancy less than 1 year
- Intolerance of aspirin, clopidogrel, and heparin



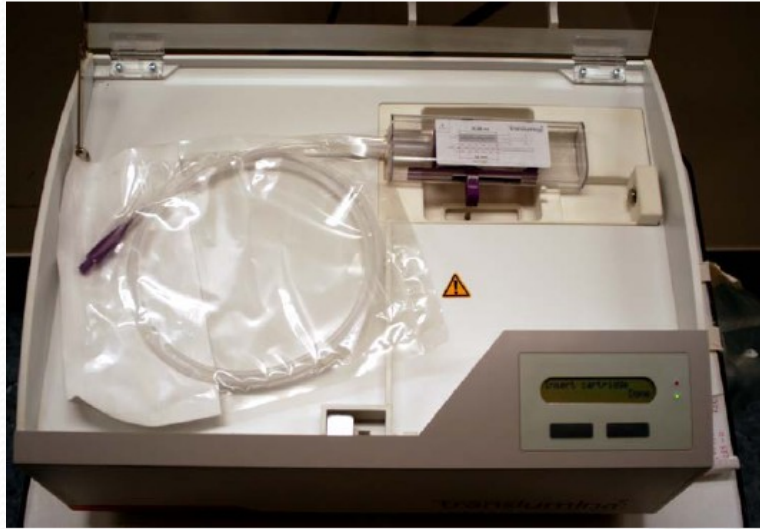
# Study Design & Drug Regimen

- 2 treatment groups using a computer generated random sequence, set in blocks for each participating centre. Patients were randomly assigned to the groups in a 1:1 ratio.
- Antiplatelet regimen:
  - Oral aspirin (100 mg daily) for life
  - Oral clopidogrel (a loading dose of 600 mg 24 hours before the procedure) 75 mg daily for six months
- Stent dimensions:
  - 1 or 2 stents
  - Length: 25mm
  - Diameter: 2.5 / 3.0 / 3.5mm



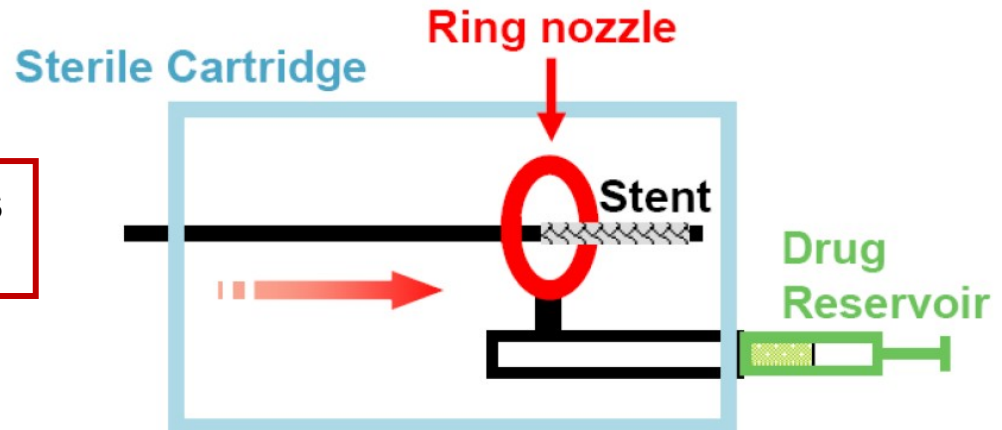
# Study Device: Yukon Stent System

## The Stent Coating Machines - inside



Current T-SCM2003

Warning: The Yukon stent device is not approved for peripheral use.



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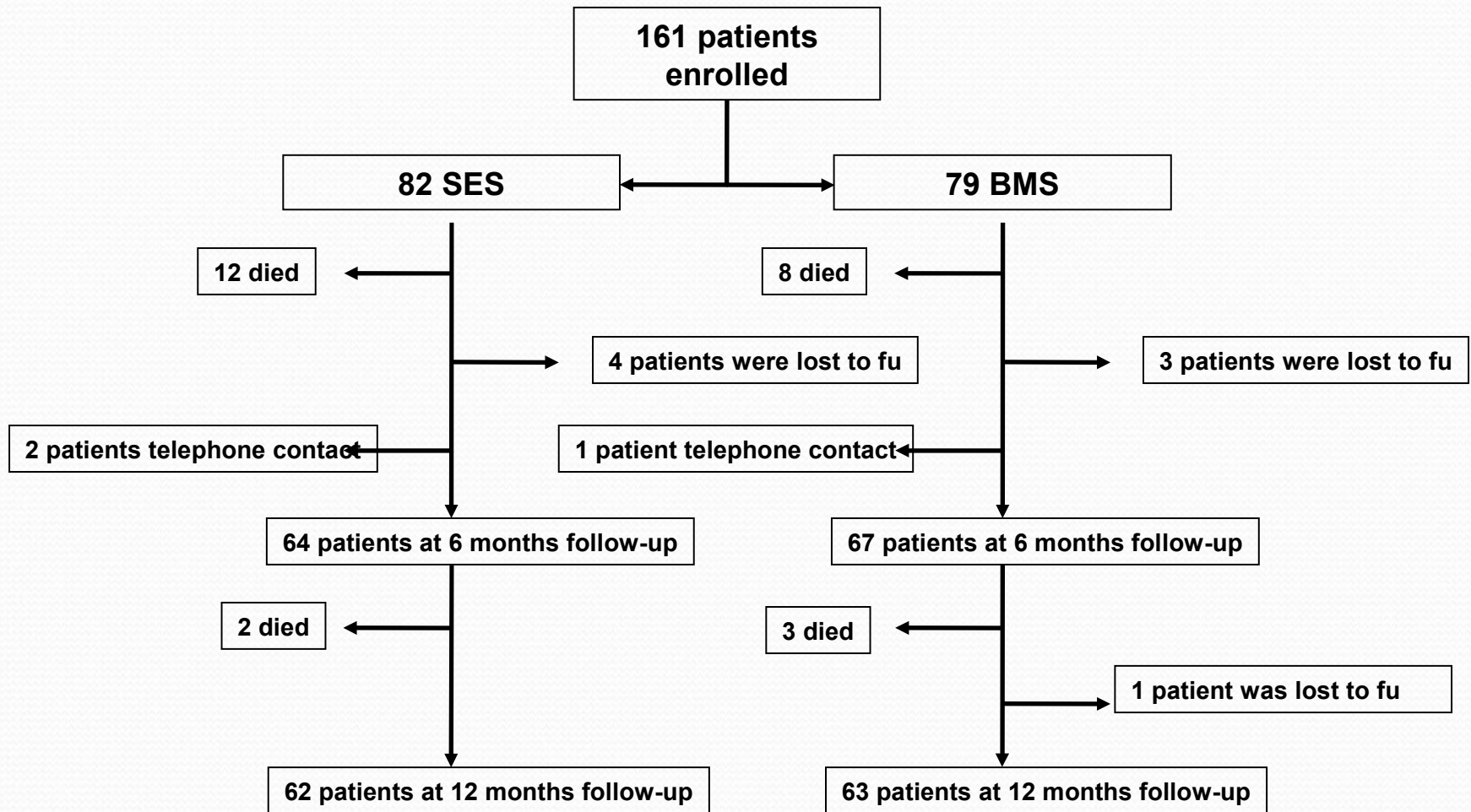
# Yukon Stent System

## Advantages of the Coating Technology

1. Late catch-up of the polymer-based DES, indicating pro-inflammatory processes still ongoing after 2 years.
2. The polymer-free Yukon DES with stable and low late-loss and less delayed restenosis after 2 years.
3. Commentary article of Virmani-group shows that polymer-based DES have late catch-up in the pig trials and late TLR up to 5 years.



# Study Profile



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# Baseline Patient Characteristics\*

	All Patients (N=161)	Sirolimus Stent (N=82)	Bare Metal Stent (N=79)
Age (years)	72.9±9	73.4±8	72.3±9
Male sex (%)	66.5	67.9	64.9
Body-mass-Index	27±4	28±5	27±4
Diabetes mellitus (%)	53.8	56.8	50.6
Dyslipidemia (%)	76.6	76.5	76.6
Hypertension (%)	89.9	91.4	88.3
Current smoker (%)	28.5	28.4	28.6
Renal insufficiency (%)	35.4	35.8	35.1
Critical Limb ischemia (%) †	46.6	51.2	41.8
Target lesion (%)			
Anterior tibial artery	27	22	31
Tibioperoneal trunk	37	42	33
Peroneal artery	21	19	23
Posterior tibial artery	15	17	13

\*Plus-minus values are means ±SD.

**There were no significant differences between the treatment groups except for body-mass-index (P=0.044).**

†Critical limb ischemia was defined according to the Rutherford-Becker classification.

# Target Lesion Characteristics and Acute Results\*

	All Patients (N=161)	Sirolimus Stent (N=82)	Bare Metal Stent (N=79)
Reference vessel diameter (mm)	3±0.4	3±0.4	3±0.4
Length of the lesion (mm)	30±9	30±8	31±9
Occlusion (%)	22.4	23.2	21.5
Target lesion diameter stenosis (%)			
Pre intervention	88±9	87±9	88±9
Post intervention	3±5	3±5	3±5
Number of stents/target lesion (%)			
1	69.6	52.7	47.3
2	28.5	48.9	51.1
3	1.9	1.2	2.6
Procedural success (%)	100	100	100
ABI pre intervention	0.48±0.16	0.47±0.18	0.49±0.14
ABI post intervention	0.84±0.17	0.86±0.15	0.83±0.19

\*Plus-minus values are means ±SD. **There were no significant differences between the treatment groups**

# Rutherford-Becker Classification at Baseline

	All Patients (N=161)	Sirolimus Stent (N=82)	Bare Metal Stent (N=79)	P
<b>Rutherford-Becker Classification at Baseline</b>				
2	10 (6.2%)	4 (4.9%)	6 (7.6%)	
3	76 (41.8%)	36 (43.9%)	40 (50.6%)	
4	9 (5.6%)	7 (8.5%)	2 (2.5%)	
5	66 (41%)	35 (42.7%)	31 (39.3%)	
Median (IQR)*	3 (3 to 5)	4 (3 to 5)	3 (3 to 5)	0.4

\*IQR = interquartile range

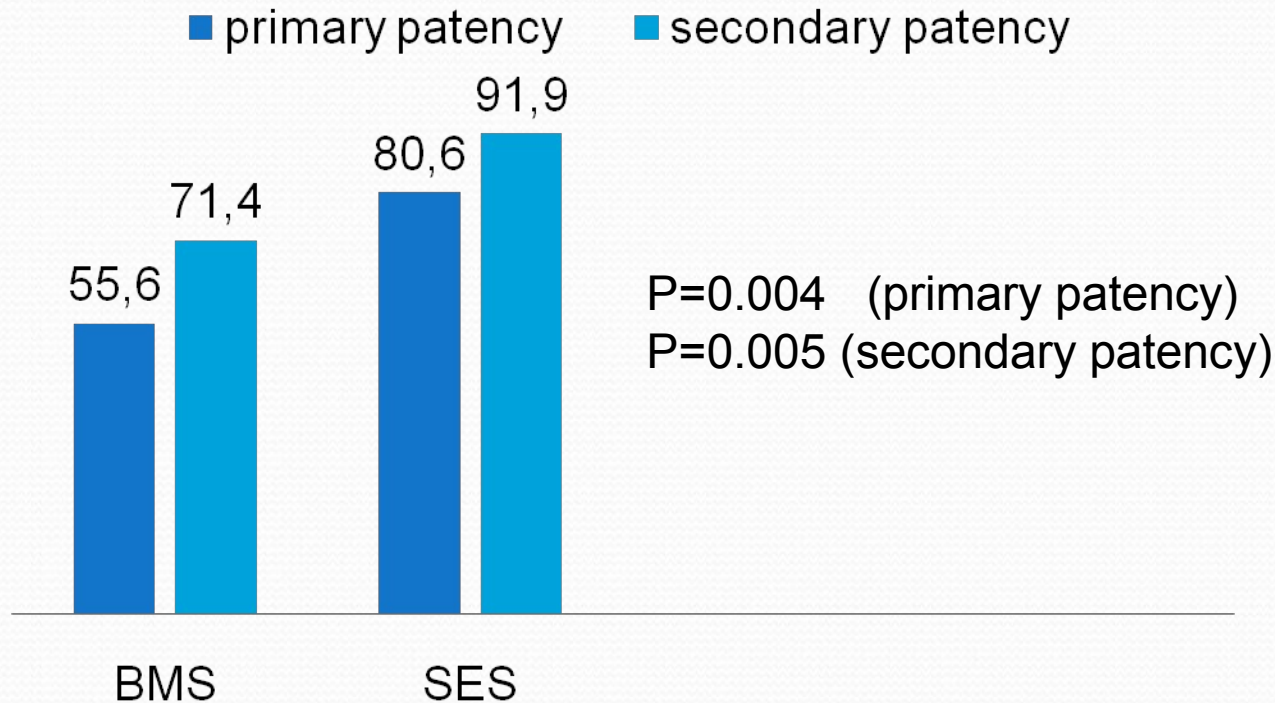


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# Primary Endpoint Primary & Secondary 1-Year Patency

## 1-Year Patency Rates



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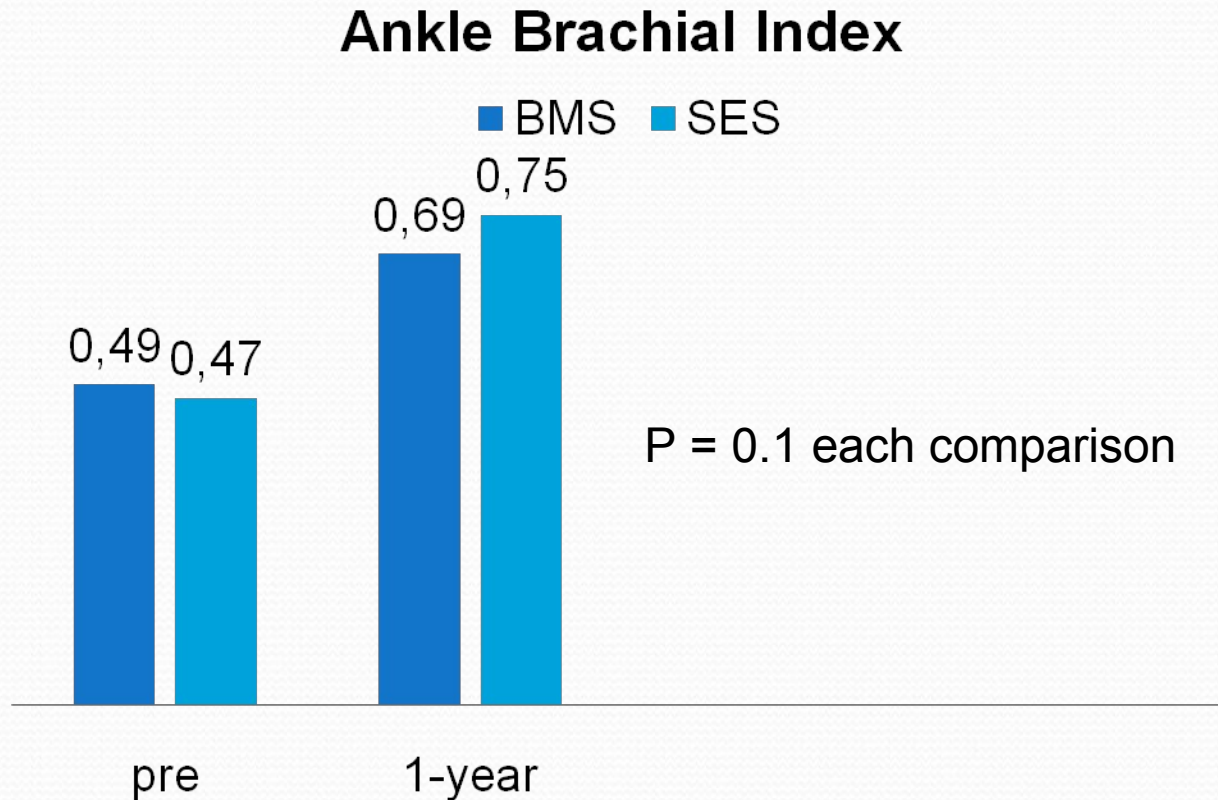
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# Cox Regression Analysis

- Hazard ratio (HR) for restenosis for BMS vs. SES:  
3.2 (95% CI 1.5 to 6.7;  $P = 0.003$ )
- Adjusted HR (diabetes mellitus, smoking status and body-mass-index) for BMS vs. SES:  
3.0 (95% CI 1.4 to 6.4;  $P = 0.005$ )
- No significant interaction between stent type and stage of disease (critical limb ischemia or intermittent claudication,  $P = 0.5$ ).



# Secondary Endpoint Ankle Brachial Index Baseline & 1-Year



# Secondary Clinical Endpoint

## Rutherford-Becker Classification at 6 Months & 1 Year

### 6 months

	N=131	N=64 (SES)	N=67 (BMS)	P-Value
Median (IQR)*	2 (1 to 3)	1 (1 to 3)	2 (1 to 3)	0.3
Improvement by $\geq 1$ Class	93 (70.9%)	49 (76.5%)	44 (65.7%)	
No Change	35 (26.9%)	14 (21.9%)	21 (31.3%)	
Worse by $\geq 1$ Class	3 (2.3%)	1 (1.6%)	2 (3.0%)	
Median Change (IQR)*	-1.5 (-3 to 0)	-2 (-3 to -1)	-1 (-2 to 0)	0.09

### 12 months

	N=131	N=64 (SES)	N=67 (BMS)	P-Value
Median (IQR)*	2 (1 to 3)	1 (1 to 3)	2 (1 to 3)	0.3
Improvement by $\geq 1$ Class	93 (70.9%)	49 (76.5%)	44 (65.7%)	
No Change	35 (26.9%)	14 (21.9%)	21 (31.3%)	
Worse by $\geq 1$ Class	3 (2.3%)	1 (1.6%)	2 (3.0%)	
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\*IQR = interquartile

# Rutherford-Becker Classification at 6 Months & 1 Year

## 6 months

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Median (IQR)*	2 (1 to 3)	1 (1 to 3)	2 (1 to 3)	0.3
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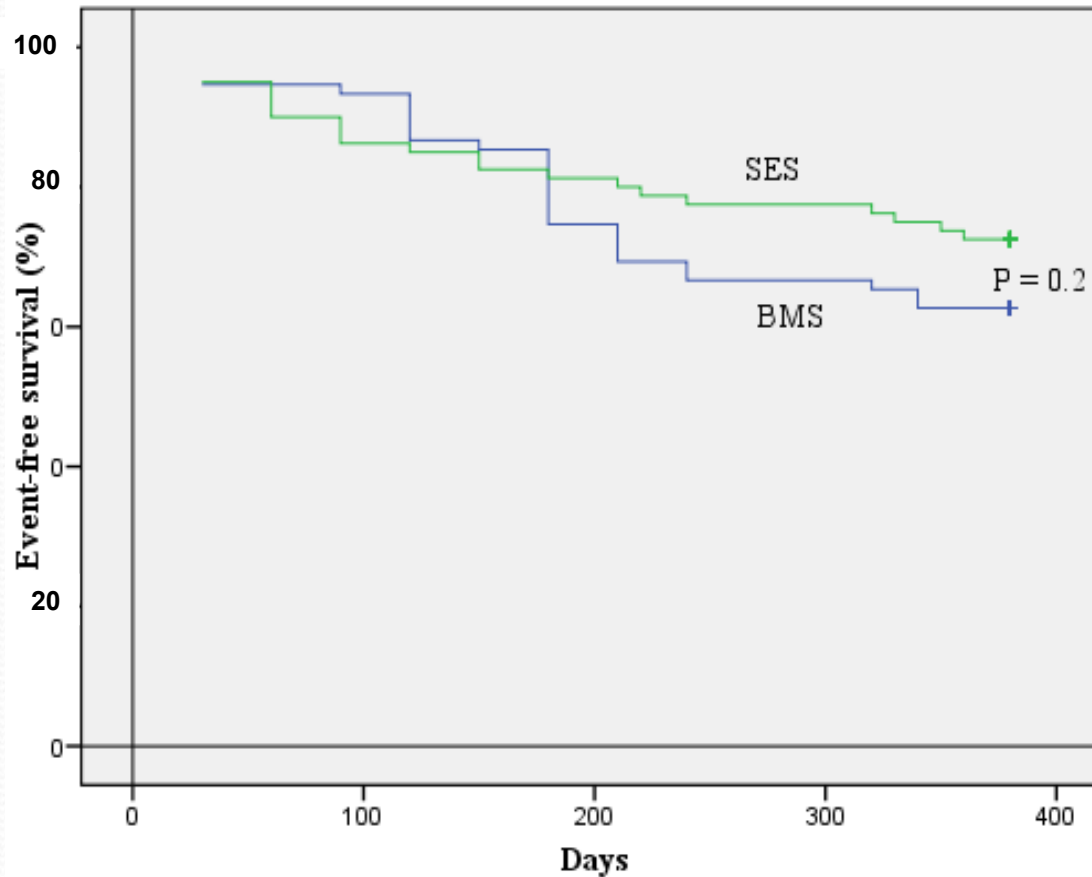
## 12 months

	N=125	N=62 (SES)	N=63 (BMS)	
Median (IQR)*	2 (1 to 3)	2 (0.75 to 3)	2 (1 to 3)	0.01
Improvement by $\geq 1$ Class	91 (72.8%)	52 (83.9%)	39 (61.9%)	
No Change	30 (24%)	8 (12.9%)	22 (34.9%)	
Worse by $\geq 1$ Class	4 (3.2%)	2 (3.2%)	2 (3.2%)	
Median Change (IQR)*	-2 (-3 to 0)	-2 (-3 to -1)	-1 (-2 to 0)	0.004

\*IQR = interquartile

# Event-free Survival at 12 months

Survival free from target lesion revascularisation, major and minor amputation, myocardial infarction and death was compared by Kaplan-Meier analysis with the use of the Mantel-Cox log-rank test.



No. at risk

	0	100	200	300	400
<b>Sirolimus Stent</b>	<b>82</b>	<b>71</b>	<b>64</b>	<b>63</b>	<b>62</b>
<b>Bare-metal Stent</b>	<b>79</b>	<b>72</b>	<b>67</b>	<b>64</b>	<b>63</b>



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# Summary

- SES achieve significantly higher primary and secondary patency rates at 1 year as compared with BMS in the treatment of infrapopliteal lesions.
- The improvement in Rutherford-Becker class at 1 year was significantly better in the SES group.
- In the long run, the superior patency of SES may also improve limb salvage rates in patients with CLI Rutherford class 5 & 6 and an appropriate life expectancy.

