A RANDOMIZED COMPARISON OF NOBORI BIOLIMUS A9 ELUTING STENT WITH CYPHER SIROLIMUS ELUTING STENT FOR CORONARY REVASCULARIZATION IN JAPANESE POPULATION

TCTAP2010

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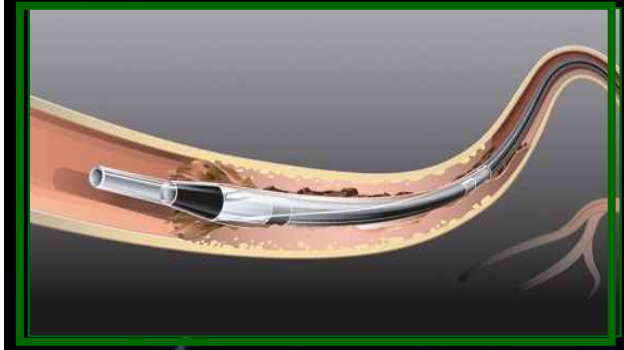
Biolimus A9™ eluting stent (BES) (Nobori, Terumo, Tokyo, Japan)

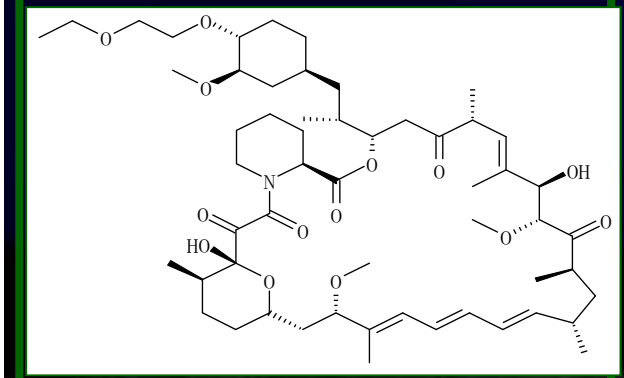


BMS Platform

- Excellent Flexibility and Scaffolding
- Optimal Side Branch Access
- Innovative Delivery System with Hydrophilic M-coating

PLA Biodegradable Polymer

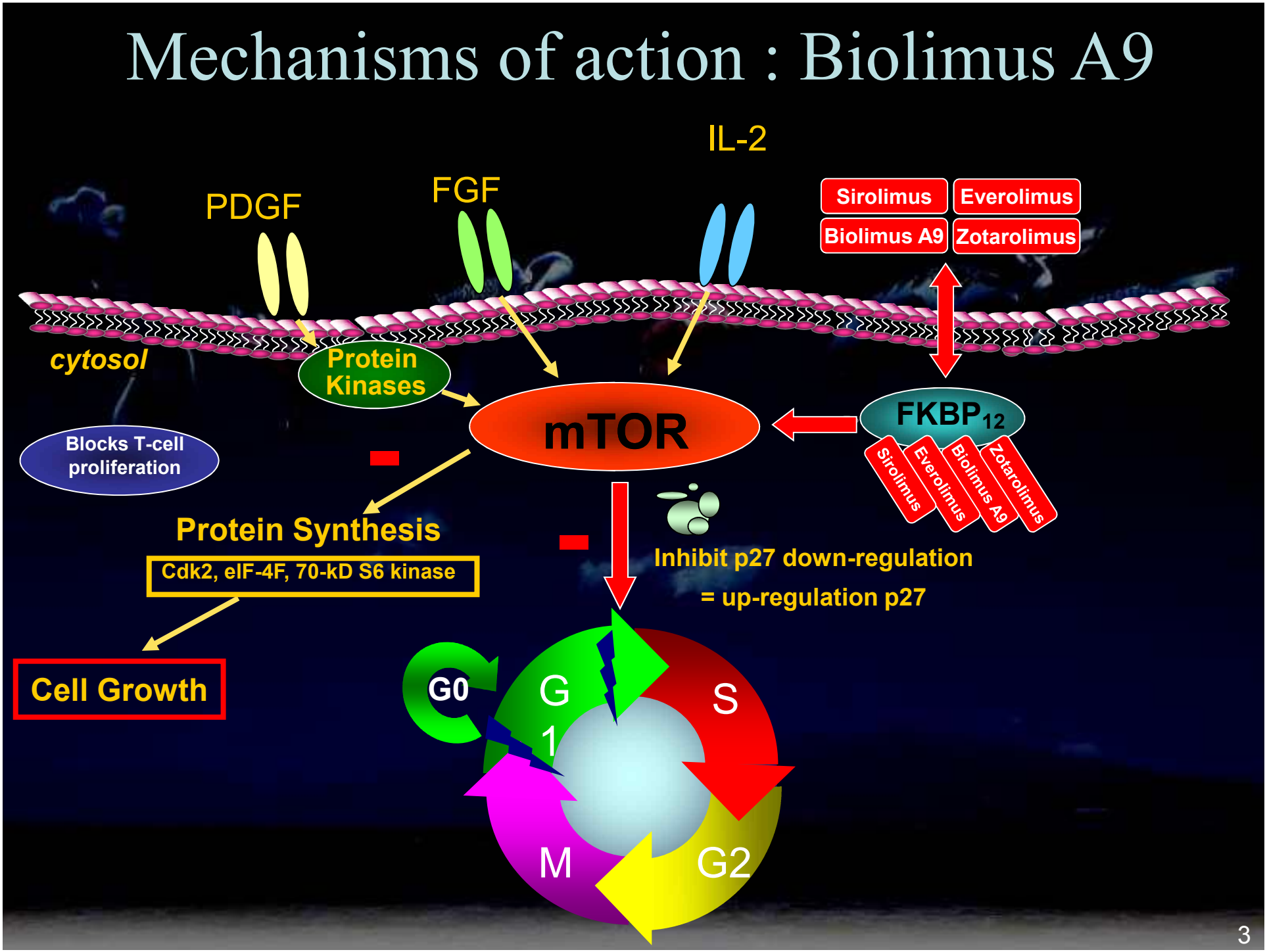
- Abluminal Coating
- Controlled Biodegradability
- Precise Drug Release Kinetics
- Simultaneous Polymer Degradation and Drug Release



Biolimus A9™ (rapamycin derivative)

- A Potent New “Limus” Designed for Stent Applications
- Powerful Anti-proliferative and Anti-inflammatory properties Prevents Smooth Muscle Cell Proliferation
- Highly Lipophilic with Optimal Local Tissue Uptake

Mechanisms of action : Biolimus A9



Trial Design

3:2 randomization （Single blind) – up to two vessels

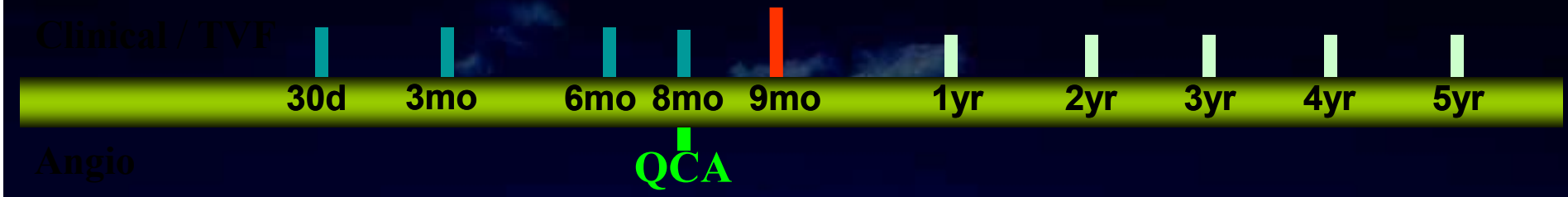
Single de novo native coronary lesion
Vessel diameter: 2.5-3.5 mm
Lesion length: ≤ 30 mm
Pre-dilatation required

BES (Nobori)
(n= 200)

PIs: Dr Kazuaki Mitsudo
Dr Hidehiko Honda
N = 335 patients (15 sites: Japan)

SES (Cypher)
(n= 135)

Primary endpoint （ TVF ）



Primary endpoint : Target Vessel Failure（TVF）at 9months

Secondary endpoint: Procedural results, Acute Gain,
Late Loss, Restenosis rate, %DS at 8months,
TLR, TVR at 9months
Major Adverse Cardiac Event（MACE）at 9months

TRE956 (Nobori Terumo Co., Japan) Investigators

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Masashi Iwabuchi	Kokura Memorial Hospital
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Yasuhiko Hayashi	Tsuchiya General Hospital
Yuji Ikari	Tokai University Hospital
Kenji Fujii	Sakurabashi Watanabe Hospital
Shinsuke Nanto	Kansai Rosai Hospital
Naoto Inoue	Sendai Kousei Hospital
Takeshi Kimura	Kyoto University Hospital
Atsuo Namiki	Kanto Rosai Hospital
Haruo Hirayama	Nagoya Daini Red Cross Hospital
Osamu Doi	Shizuoka General Hospital
Mitsuo Kashida	International Medical Center of Japan
Junji Yajima	The Cardiovascular Institute Hospital
Kazuaki Mitsudo	Kurashiki Central Hospital

Key Exclusion Criteria

- Creatinine ≥ 2.0 mg/dl
- LVEF < 30%
- AMI within 72 hours of the intended treatment
- Stroke or TIA within the prior 90 days
- Target vessel which has evidence of thrombus
- Ostial lesion
- Target lesion involves a > 2.0mm side branch.
- Unprotected Left main disease (stenosis >50%)
- More than 50% stenosis proximal or distal to the target lesion
- Within 30 days prior PCI
- Within 90 days planned PCI
- Within 1 years previous drug-eluting stenting in any vessel

Power Calculation for Primary Endpoint (Target Vessel Failure at 9months)

- Assumed Non-TVF at 9month :
  90% for BES / 90% for SES
- Significance level :
  5% (one-sided)
- Delta non-inferiority margin :
  9%
- Calculated sample size :
  287 patients (172+115)
- Sample increased to 335 patients in order to account for patients lost during follow-up

Baseline Demographics

	BES n=194	SES n=132	p
Age (years ±SD)	67.1±10.3	67.7±9.3	0.59
Male (%)	71.6	72.0	0.95
Prior MI (%)	20.6	21.2	0.90
Unstable angina (%)	16.5	11.4	0.20
Diabetes (%)	38.7	39.4	0.89
Insulin dependent (%)	5.7	6.8	0.81
Hypertension (%)	76.8	84.1	0.11
Hypercholesterolemia (%)	77.3	81.8	0.33
Smoking（past 6mo）(%)	25.8	18.2	0.11

Procedural Characteristics

	BES n=194	SES n=132	p
Nº of lesions	218	150	-
Nº of lesions per patients	1.13	1.14	0.69
Nº of stents	234	163	-
1 stent (%)	92.7	91.3	0.64
2 stents (%)	7.3	8.7	
Nº of stents per patients	1.22	1.24	0.66
Stent diameter (mm)	3.0±0.38	3.0±0.37	0.95
Stent length (mm)	21.0±6.7	21.0±7.8	0.99
Overlap (%)	7.3	8.7	0.64
Maximum inflation pressure (atm)	12.8±2.5	14.8±1.9	<0.0001

Lesion Location, Classification

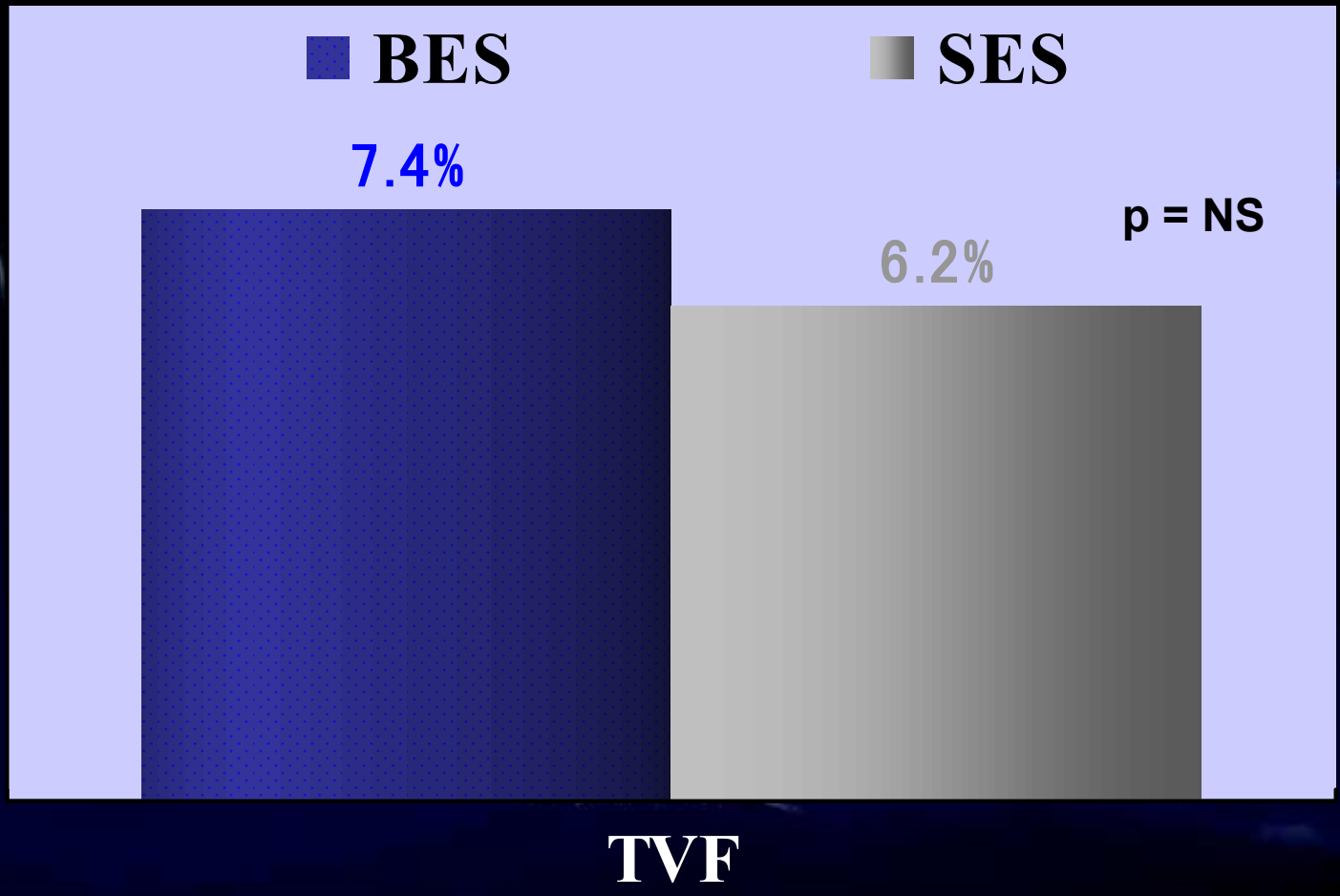
		BES n=194	SES n=132	p
Lesion (%)	LAD	39.9	44.7	0.64
	LCX	27.1	24.0	
	RCA	33.0	31.3	

ACC-AHA (%)	A	9.2	11.3	0.32
	B1	21.1	26.7	
	B2	59.2	49.3	
	C	10.6	12.7	

Base line QCA data

	BES n=194	SES n=132	p
Lesion length (mm)	12.6±5.5	12.8±6.8	0.77
MLD (mm)	0.9±0.4	0.9±0.3	0.65
RVD (mm)	2.7±0.6	2.7±0.5	0.99
% DS	66.5±12.2	65.6±11.3	0.49

Primary Endpoint
TVF at 9months



Primary endpoint Result :
BES TVF = NON-INFERIOR to SES (p = 0.0007)

TVF : Cardiac death, MI, TVR (include Non-TL TVR), CABG

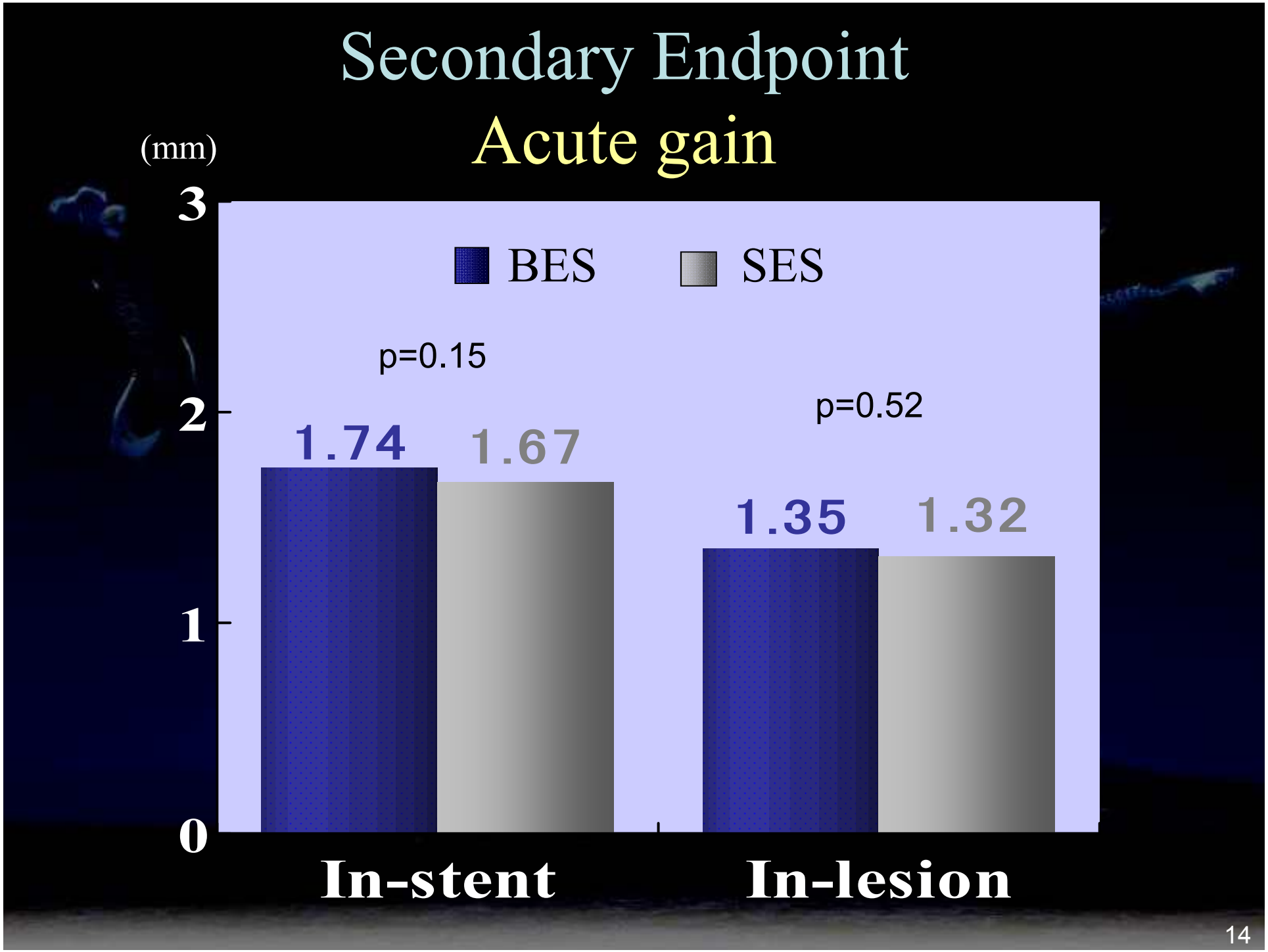
Secondary Endpoint
Procedural results

	BES	SES	p
Delivery Success (%)	98.7	100.0	0.28
Angiographic Success (%) (Cases)	100.0	99.2	0.40
Angiographic Success (%) (Lesions)	100.0	99.3	0.40
Procedure Success (%)	96.3	97.7	0.75

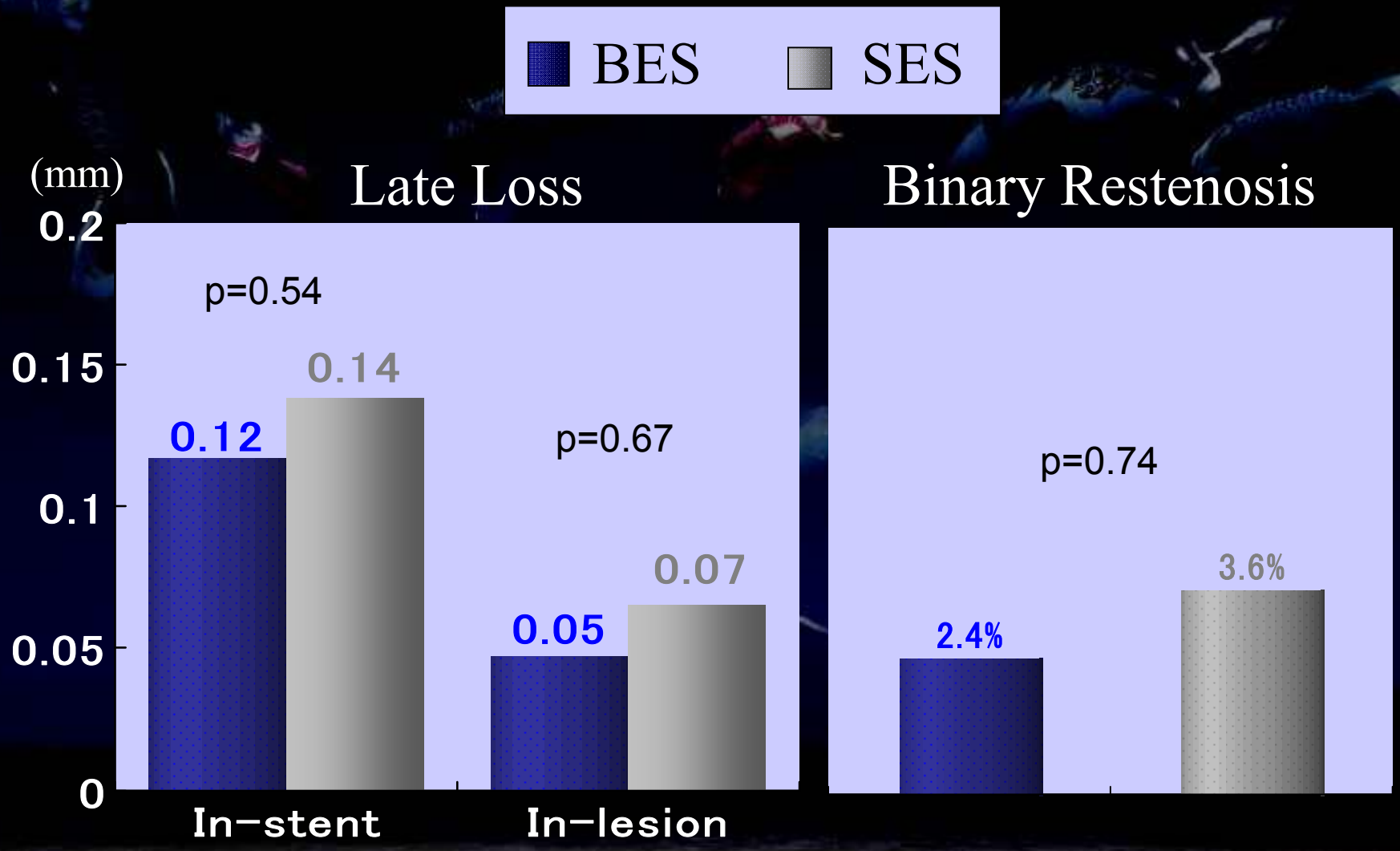
Angiographic Success:
Successful delivery of assigned stent and final diameter of stenosis of < 50% by QCA.

Procedure Success:
Angiographic success without in-hospital MACE

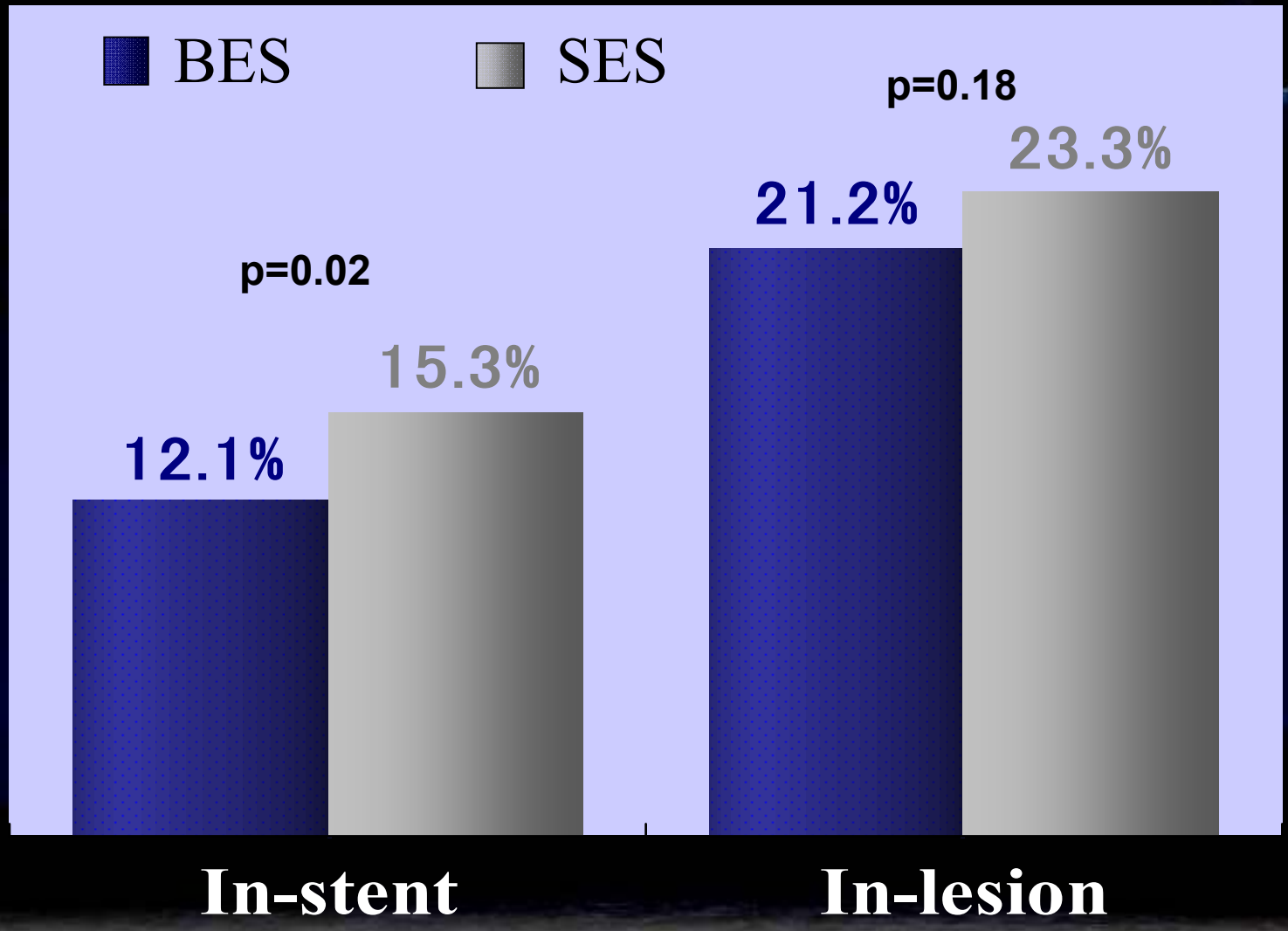
Secondary Endpoint
Acute gain



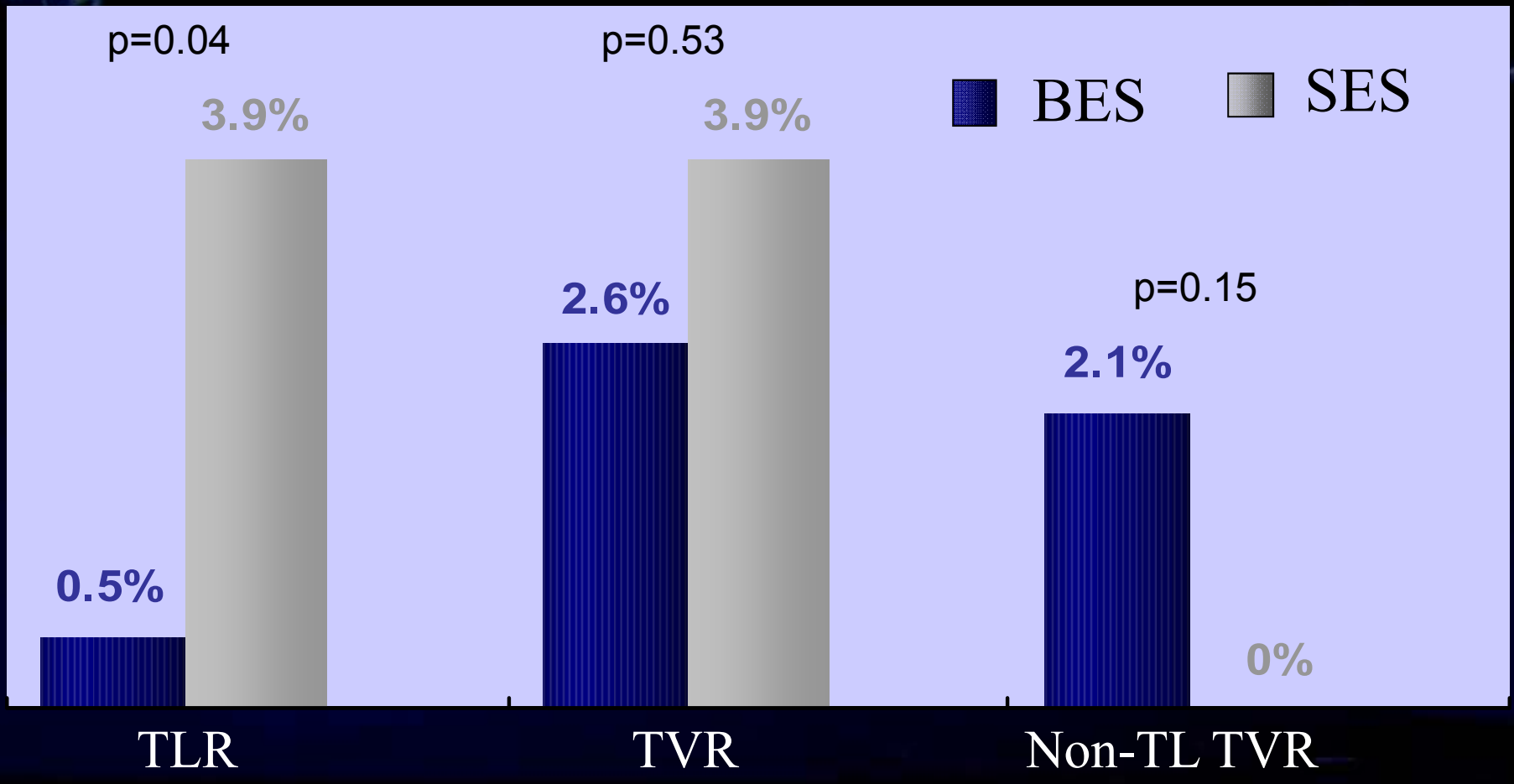
Secondary Endpoint
Late Loss, Binary Restenosis at 8months



Secondary Endpoint
% DS at 8months

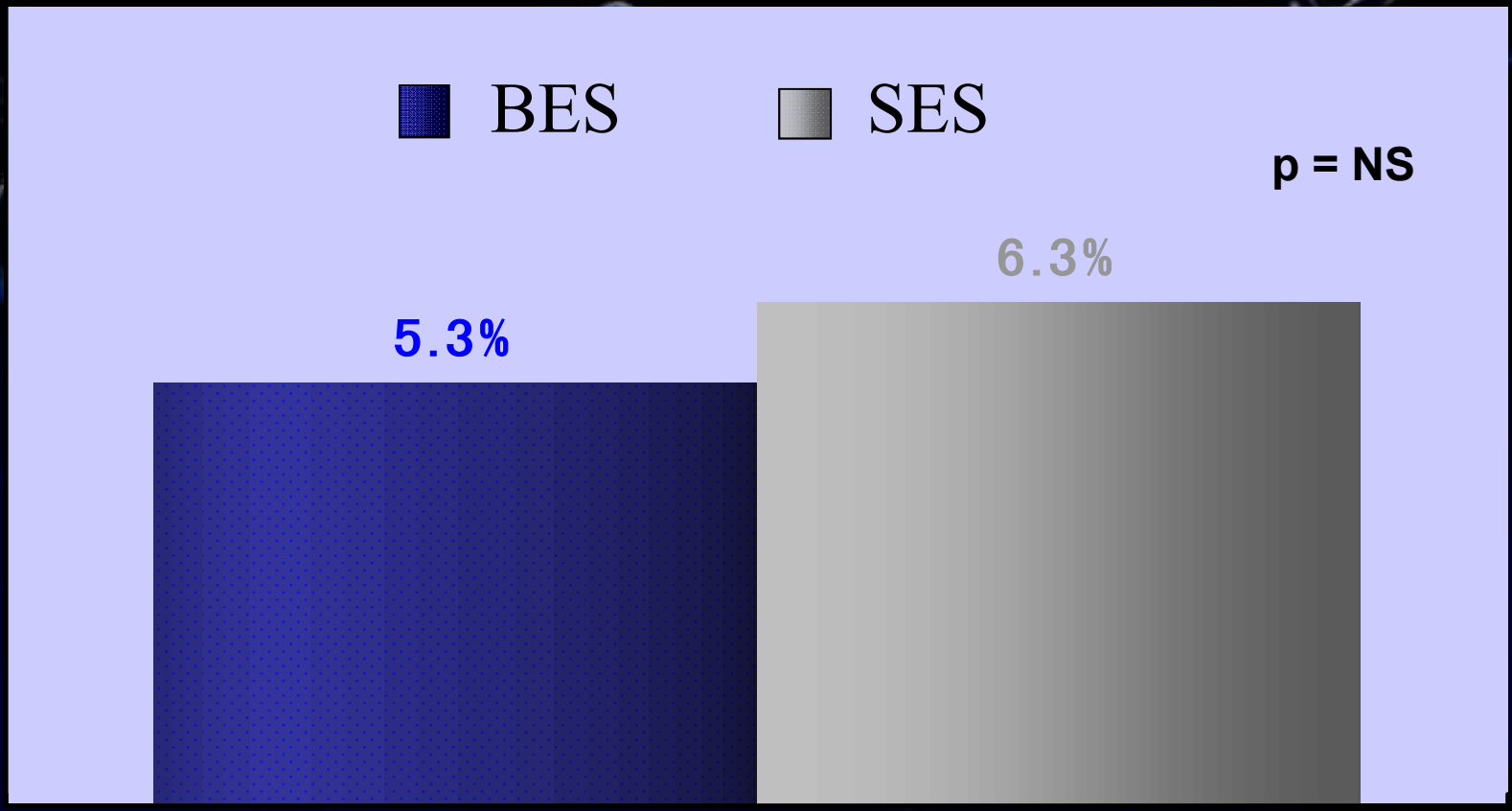


Secondary Endpoint
TLR, TVR at 9months



Revascularization after 9months which was <50% non significant lesion at enrolment (Non-TL TVR 2.1%) generates TVR of BES group.

Secondary Endpoint
MACE at 9months



MACE

MACE : Cardiac death, MI, TLR, CABG

Summary

Clinical Results at 9months

Event		BES	SES	P
Cardiac death		**0.5 (1/190)**	**0.0 (0/128)**	**1.0**
MI	**Q wave MI**	**0.5 (1/190)**	**0.0 (0/128)**	**1.0**
	Non-Q wave MI	**3.7 (7/190)**	**2.3 (3/128)**	**0.75**
TVR	**TTL**	**2.6 (5/190)**	**3.9 (5/128)**	**0.53**
	TLR	0.5 (1/190)	3.9 (5/128)	0.04
	Non-TL TVR	2.1 (4/190)	0.0 (0/128)	0.15

Conclusions

- By this first Japanese Good Clinical Practice regulated RCT, this newly developed Biolimus A9 eluting stent (Nobori, Terumo Japan) showed non inferiority versus Cypher in the primary end point TVF.
- The clinical evidence available to date for both stents shows excellent safety and efficacy confirmed by:
  - Low rate of Late loss, Binary restenosis, %DS, TLR, TVR, and MACE.
  - No stent thrombosis defined as definite or probable in ARC definition