Nobori™
The Next Generation Drug Eluting Stent

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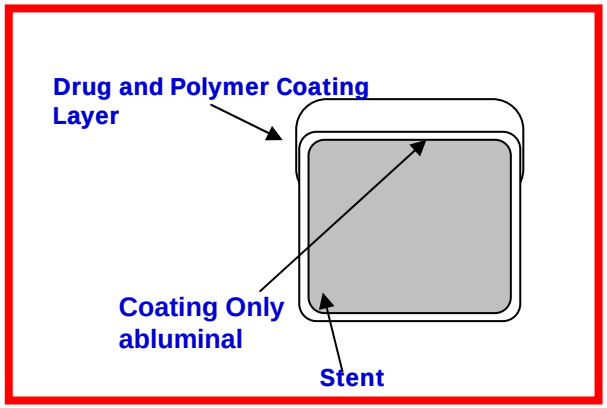
on behalf of
NOBORI 1 Clinical Trial Investigators

Nobori DES Components

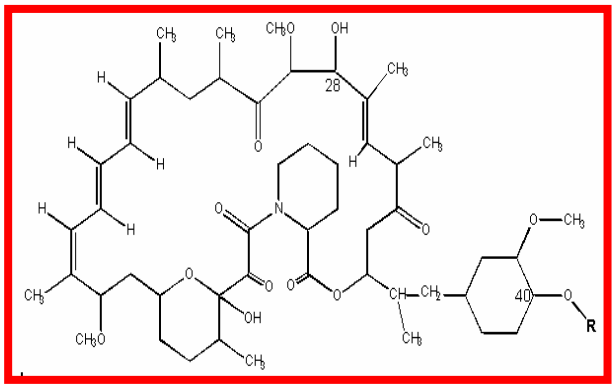
S-Stent™ (stainless steel)

- Quadrature-link design
- Excellent flexibility and scaffolding
- Reduced turbulence and wall injury



PLA bioabsorbable Polymer

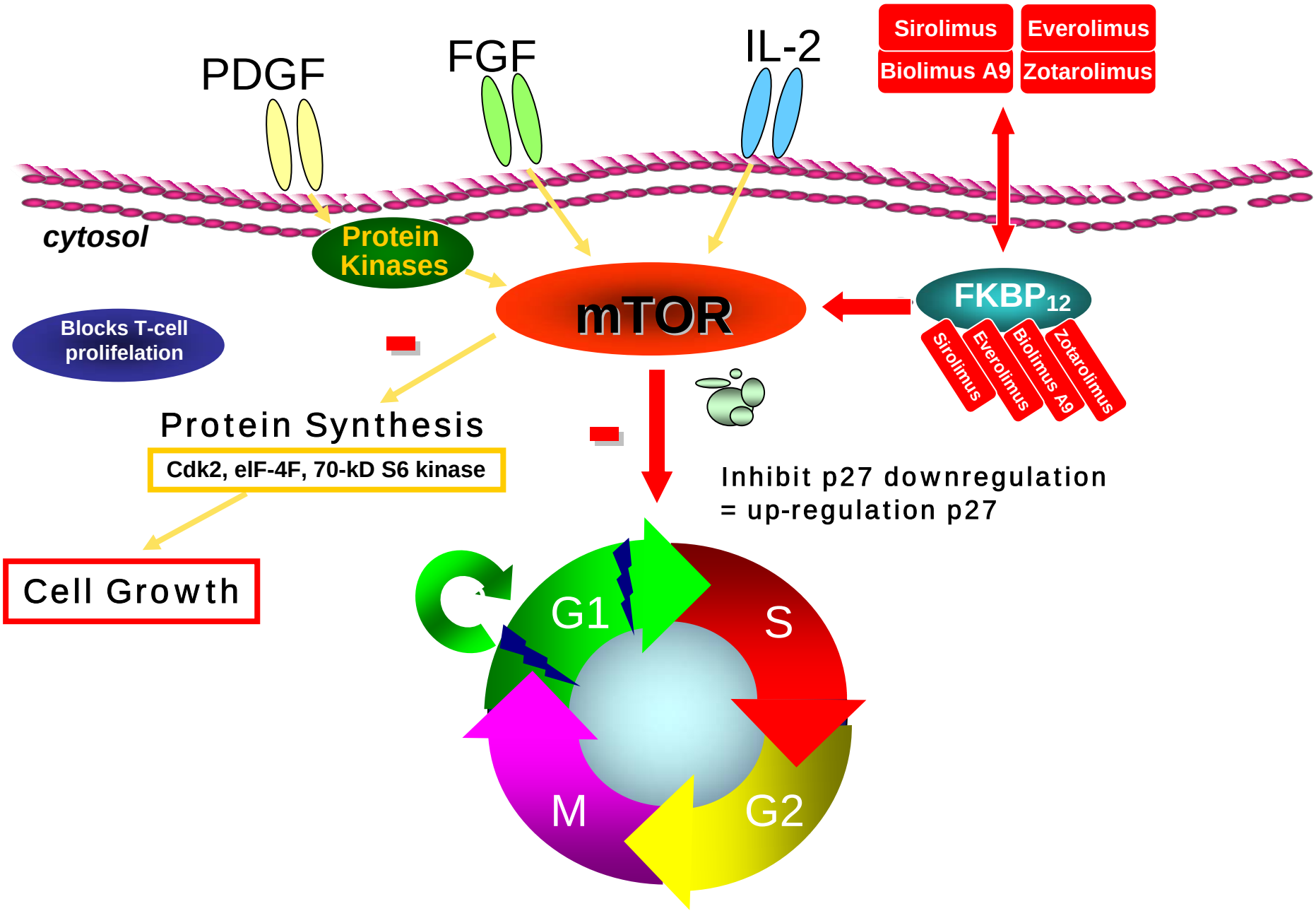
- High drug-carrying capacity
- Controlled **biodegradability**
- Simultaneous polymer degradation and release of drug into tissue
- Abluminal Coating



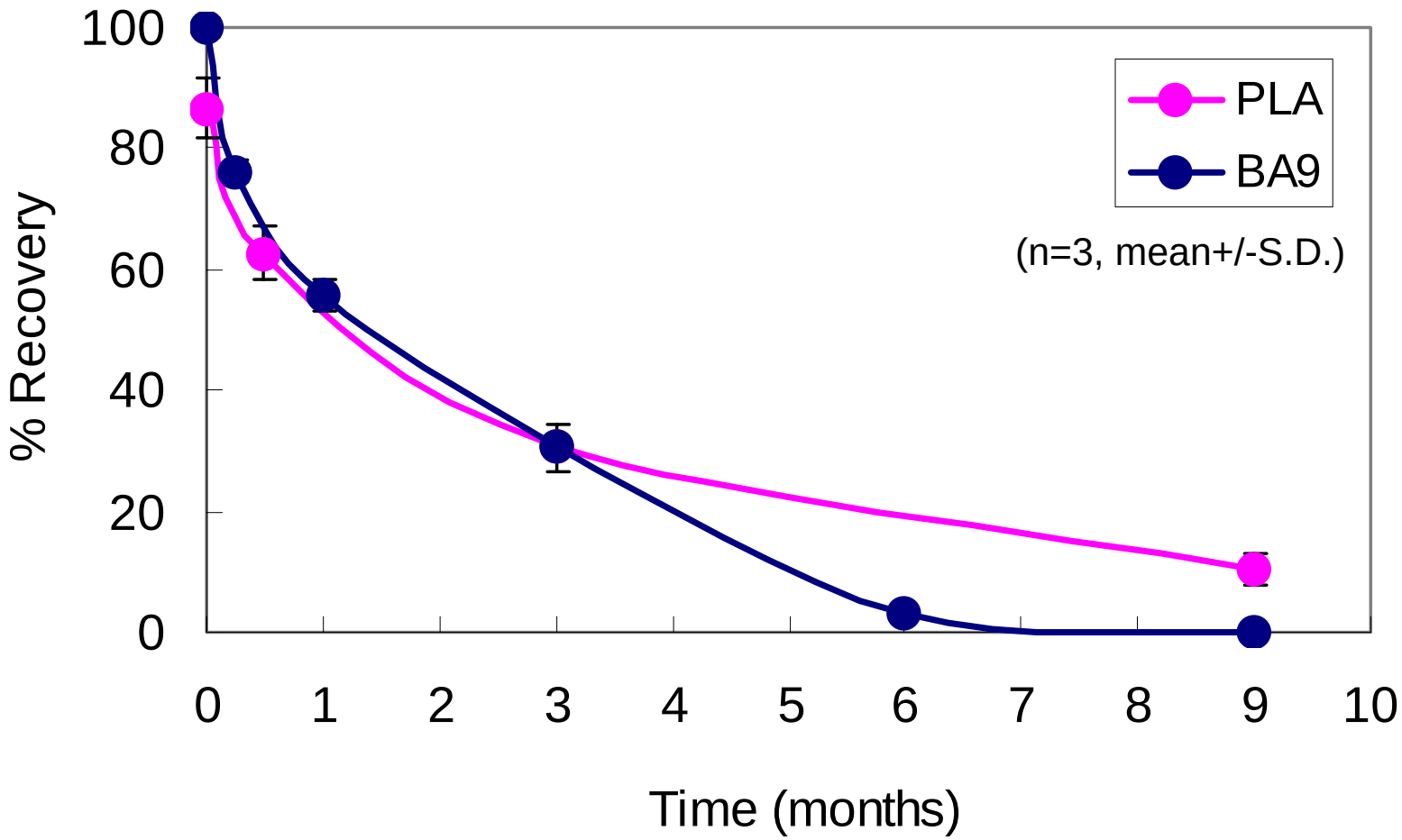
Biolimus A9™ (rapamycin derivative)

- A potent new “Limus” designed for stent applications
- Powerful immunosuppressant, anti-inflammatory compound
- Prevents smooth muscle cell proliferation
- Highly lipophylic; elutes fast from stent

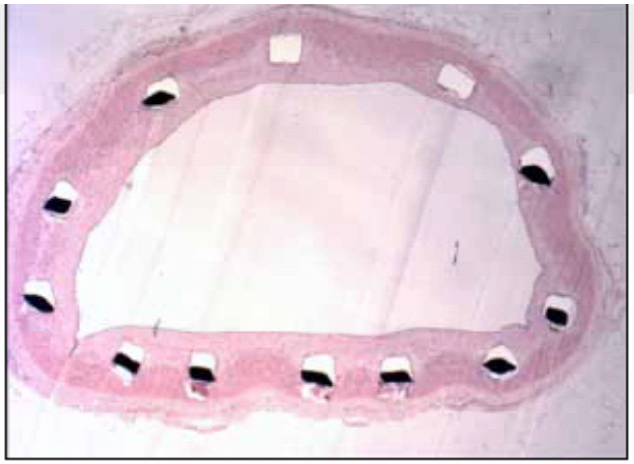
The limus drugs: mechanisms of action



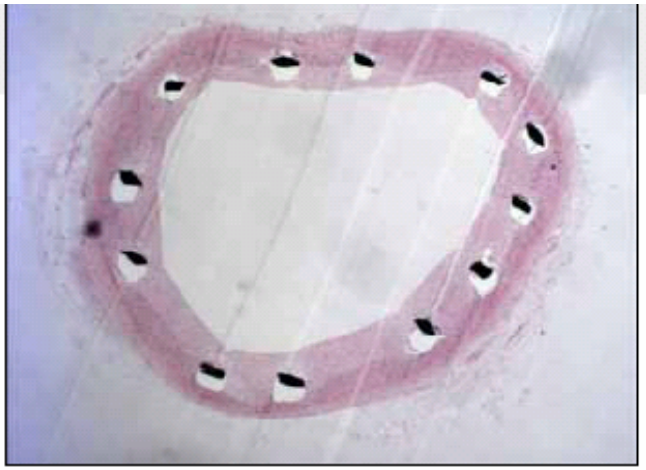
Biolimus A9 and PLA recovery over time on stents implanted in pig arteries



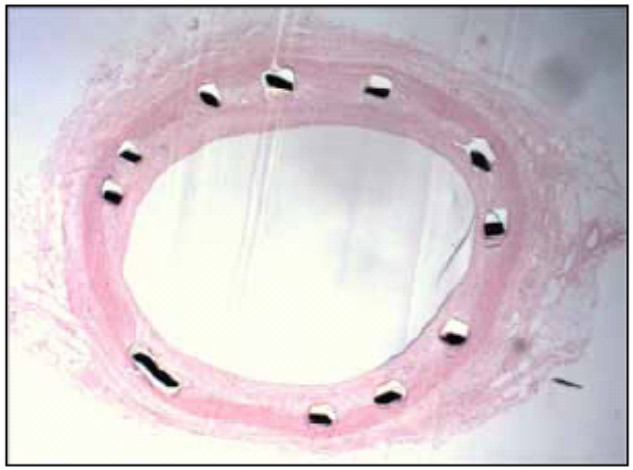
Representative Histopathology ~ 90 days



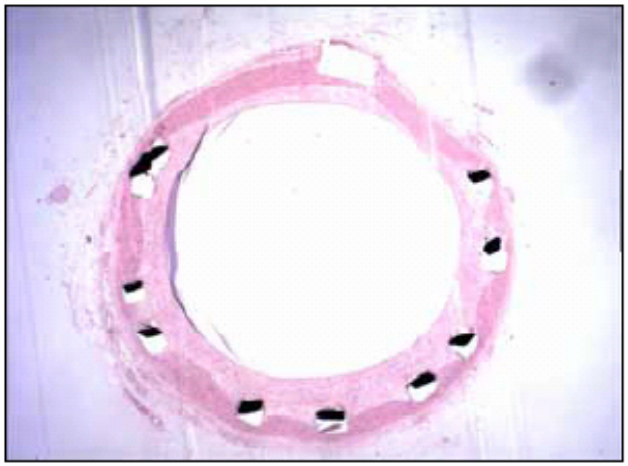
Bare (MP4-238 LCX)
Proximal 0% Overstretch



Polymer (MP4-238 RCA)
Proximal 0% Overstretch



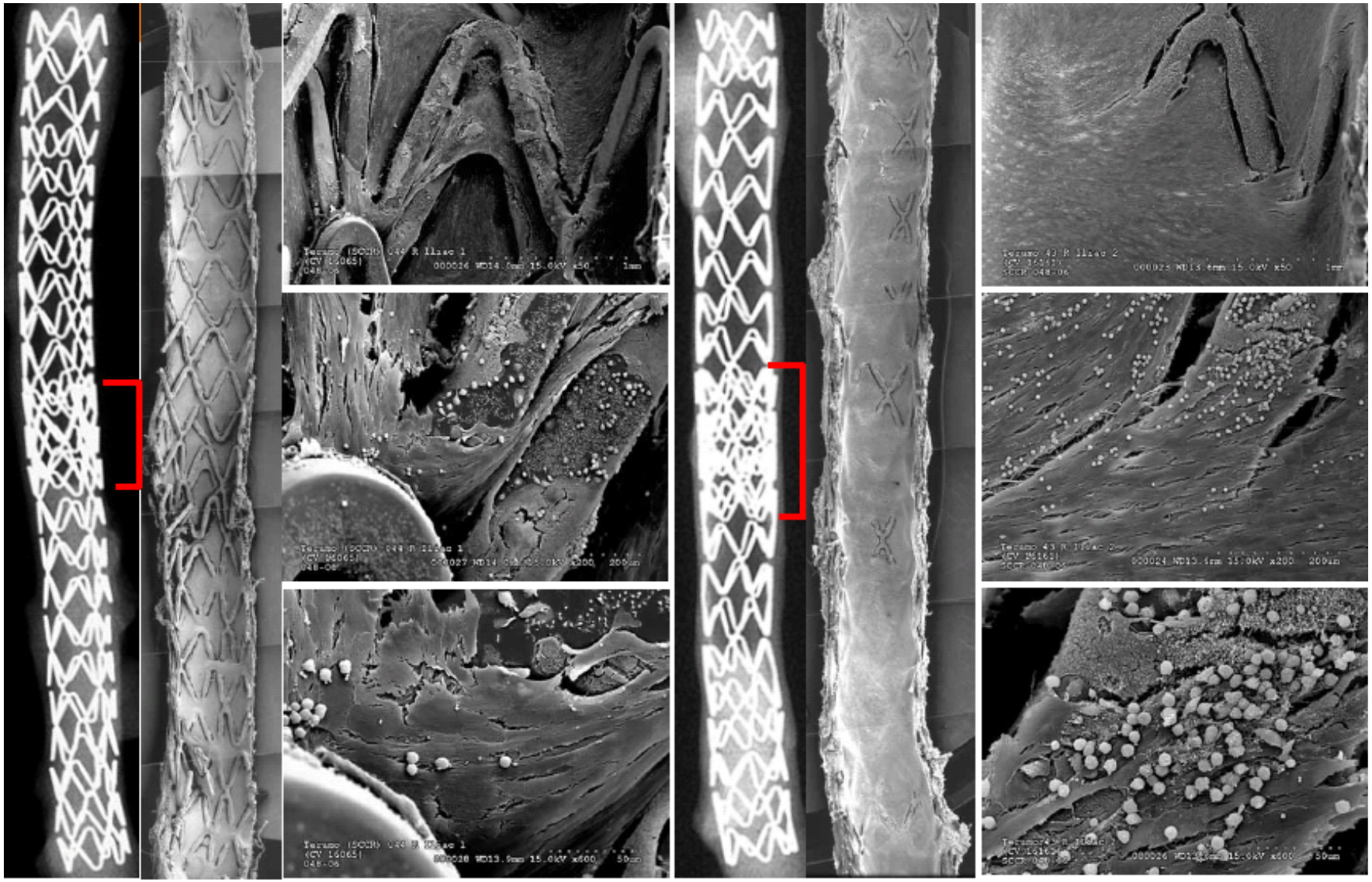
Parylene (MP4-220 LAD)
Distal 5% Overstretch



Biolimus A9 (MP4-217 LAD)
Distal 0% Overstretch

Data from company files
Virmani at Euro PCR06

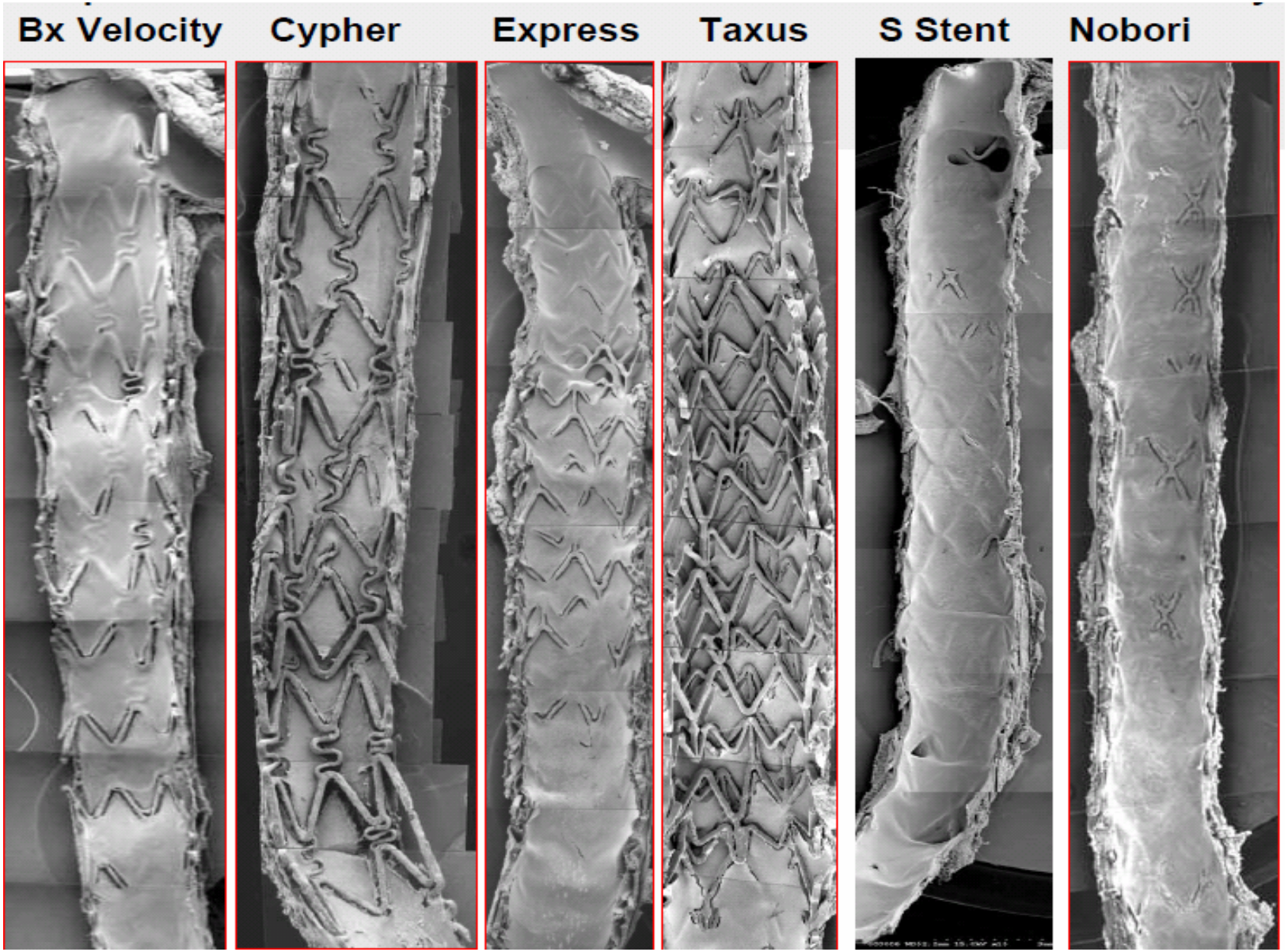
Overlapping Nobori Biolimus A9-Eluting Coronary Stent



14 days | 28 days

Virmani at Euro PCR06

Comparison of Various BMS and DES
in Rabbit Illiac Arteries at 28 days



Virmani at Euro PCR06

NOBORI 1 Phase 1
Final 9 Months Results

on behalf of NOBORI 1 investigators

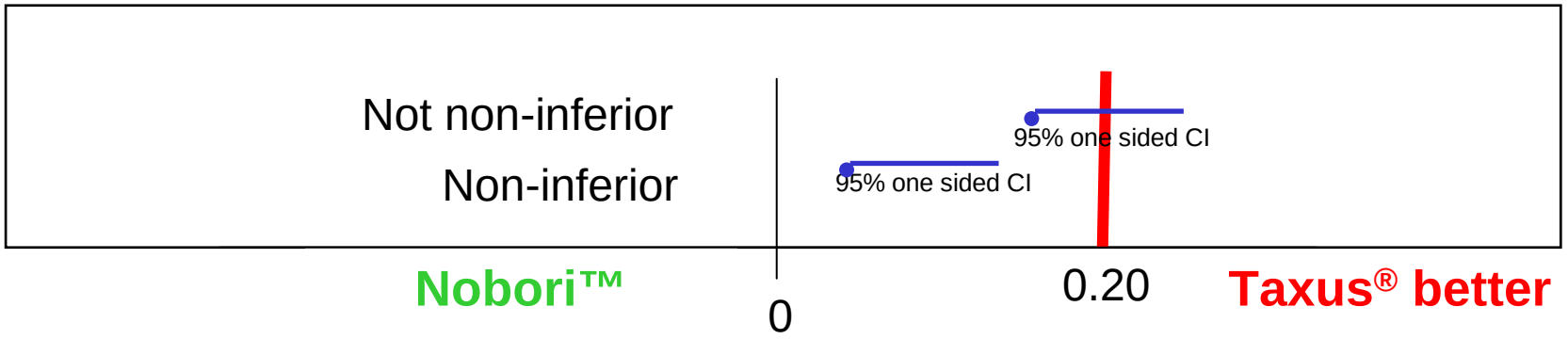
NOBORI 1 Study Organization and Design

- Prospective, randomized (2:1), non-inferiority to TAXUS® in respect to in-stent late loss
- Clinical follow-up: 30, 120, 270 days, 1, 2, 3, 4 and 5 years
- Angiographic (100%) and IVUS (40%) baseline, follow-up at 270 days
- 29 sites (EU, Korea, Australia)

- **PI: Dr. Bernard Chevalier**
- **Steering Committee: B. Chevalier, P. Serruys, E Garcia, S. Silber, H. Suryapranata**
- **DSMB: E. Boersma , B. Rensing, P. Smits**
- **CEC: GB. Danzi, P. Urban, B. Reimers, C. Hanet**
- **Study management, Data analysis, Angiographic and IVUS Corelab: Cardialysis (Rotterdam, NL)**
- **Sponsor: Terumo Europe**

Non – Inferiority Assumptions

- Assumed in-stent late loss:
  - 0.39 mm Nobori™
  - 0.39 mm TAXUS®
- **Assumed SD: 0.50 mm**



- **Delta non-inferiority margin: 0.20 mm**
- 2:1 randomization provides more precision for the Nobori™ group without loss of power
- Power: 90%; α error: 2.5%; β error: 10%
- **Primary endpoint analysis based on ITT on all lesions**

NOBORI 1 Study Design

Up to two *de novo* lesions

→

2.5 – 3.5 mm
n = 360

→

2 : 1

→

Nobori™
n = 240

TAXUS® Express
n = 120

3 dislodgments in Nobori™ arm and phasing out the Taxus Express®,
Study was split into two phases

NOBORI 1 New Study Design

Phase 1

Up to two *de novo* lesions

→ **2.5 – 3.5 mm**
n = 120

→ **2 : 1**

- **Nobori™**
  n = 85
- **TAXUS® Express**
  n = 35

Phase 2

Up to two *de novo* lesions

→ **2.5 – 3.5 mm**
n = 240

→ **2 : 1**

- **Nobori™**
  n = 160
- **TAXUS® Liberte**
  n = 80

Patient population

- Main Inclusion Criteria
  - Up to two *de-novo* lesions located in two epicardial vessels
  - Target lesion length <25 mm, RVD: 2.5-3.5 mm
- Main Exclusion Criteria
  - Allergy to major PCI associated medications, or limus like drugs
  - Left main CAD,
  - Bifurcation
  - Target lesion contains visible thrombus
  - Stenosis >50% proximally or distally to the target lesion
  - Totally occluded lesions (TIMI: 0, or I)
  - Planned major surgery within 6 m post procedure

NOBORI 1Trial Endpoints

Primary Endpoint:

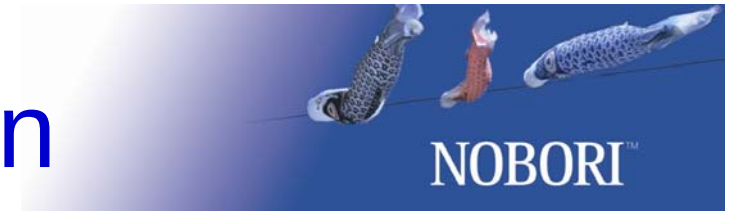
- In-stent Late Loss (LL) at 270 days

  Hypothesis – Non-Inferiority (expected difference = 0.20 mm, Power 90%)

Secondary Endpoints:

- **Major Adverse Cardiac Events (MACE) defined as cardiac death, MI (Q wave and non-Q wave), emergent coronary artery bypass surgery, or target vessel revascularization (TVR) at 30 days and 4, 9, and 12 months, and annually, thereafter, through 5 years**
- **Angiographic in-stent and in-segment binary restenosis rate (≥50% diameter stenosis) at 9 months post-procedure.**
- **In-stent, in-segment, proximal, and distal minimum lumen diameter (MLD) at 9 months post-procedure.**
- **Stent thrombosis at 30 days (acute and subacute) and 9 months (late).**
- **Neointimal hyperplasia volume at 9 months post-procedure as measured by intravascular ultrasound (IVUS).**

MACE Endpoint Definition



Cardiac Death: Any death unless proven non-cardiac

Myocardial Infarction:

- Q wave MI: development of new, pathological Q-wave on the ECG.
- Non-Q wave MI: CK level above 2xUNL with CK-MB increase (WHO definition)

Target Vessel Revascularization:

- Revascularization of any segment of the index coronary artery, which was in physical contact with any component (guiding catheter, guidewire, balloon catheter, etc.) of the angioplasty hardware during the initial procedure

All MACE reviewed and adjudicated by the Clinical Events Committee

Baseline Demographics

	Nobori N=85	Taxus N=35
Male %	69	66
Mean Age (years ± SD)	65 ± 11	63 ± 11
Previous MI (%)	31	29
Prior PCI (%)	19	9
Diabetes Mellitus (%)	18	26
Insulin – dependent (%)	8	6
Hyperlipidemia (%)	75	80
Hypertension (%)	71	77
Current Smoker (%)	21	26

No significant difference between the two treatment groups

Lesion Characteristics

	Nobori ™ 95 Lesions	Taxus® 42 Lesions
Location of lesion (%)		
LAD	55	55
RCA	23	26
LCX	22	19
Lesion classification (%)		
Types A/B1	44	31
Types B2/C	56	69

No Significant difference between the two treatment groups

Baseline and post procedure matched QCA

	Nobori ™ 95 Lesions	Taxus® 42 Lesions
Pre Procedure		
Lesion length (mm) RVD (mm) DS (%) MLD (mm)	11.4 ± 4.5 2.70 ± 0.44 60 ± 9 1.06 ± 0.24	11.0 ± 4.8 2.71 ± 0.52 59 ± 10 1.12 ± 0.38
Acute Gain	1.48 ± 0.33	1.41 ± 0.36
Post Procedure		
MLD (mm) RVD (mm) DS%	2.54 ± 0.36 2.90 ± 0.38 12 ± 6	2.54 ± 0.42 2.87 ± 0.47 11 ± 5

No Significant difference between the two treatment groups

Procedure Characteristics and Acute Success

	Nobori ™ 85 Patients 95 Lesions	Taxus® 35 Patients 42 Lesions
Lesion per patient (n ± SD)	1.1 ± 0.3	1.2 ± 0.4
Stents per lesion (n ± SD)	1.1 ± 0.3	1.2 ± 0.5
Stent Diameter (mm ± SD)	3.1 ± 0.3	3.1 ± 0.4
Stent Length (mm ± SD	18.2 ± 4.9	19.2 ± 5.8
Lesions with multiple stents (%)	14	19
Lesion Success (%)	100	100
Device Success (%)	97.9	97.6
Procedure Success (%)	95.2	88.2

No Significant difference between the two treatment groups

Primary End Point Result

Late Loss

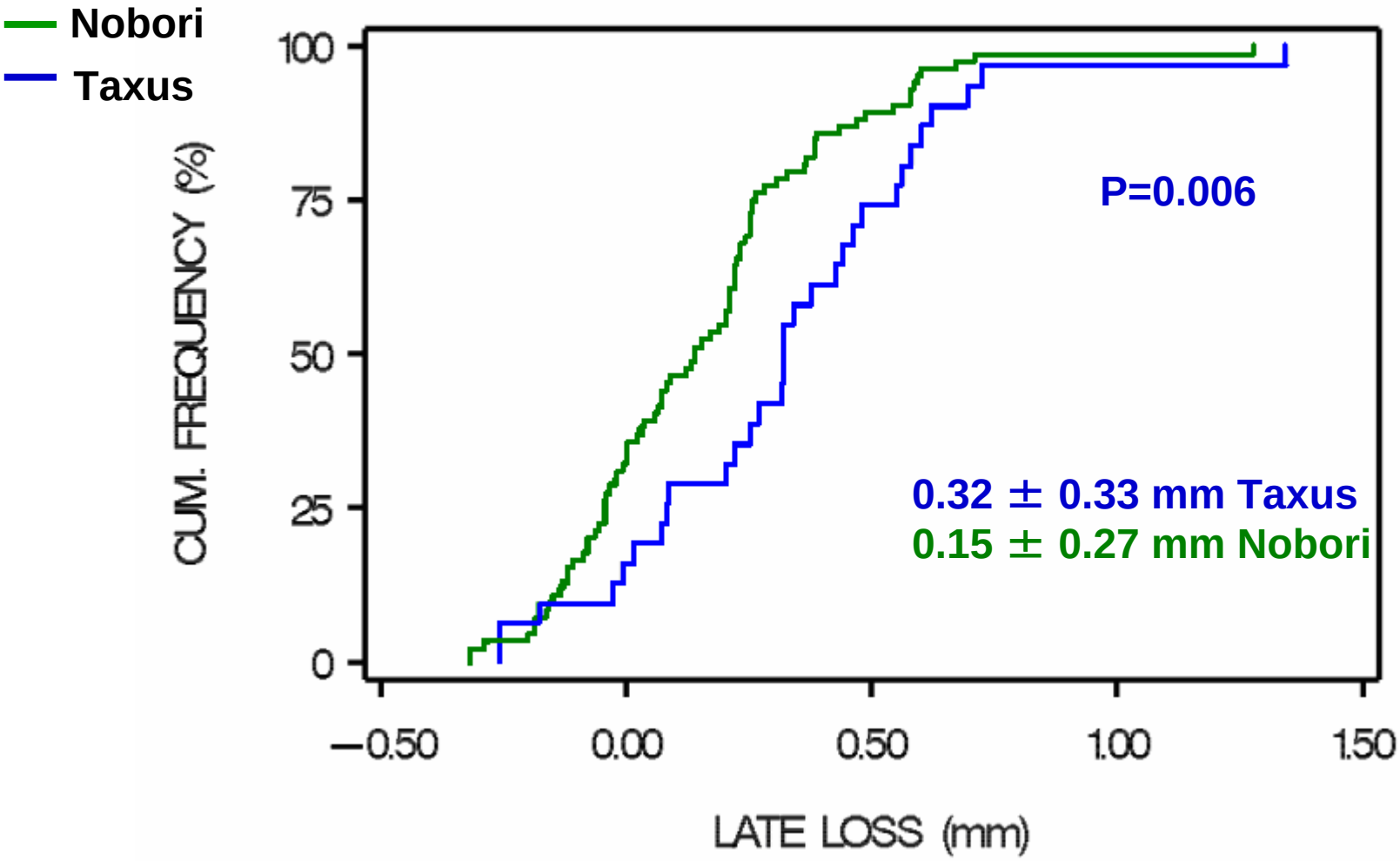
0.15 ± 0.27 mm Nobori

0.32 ± 0.33 mm Taxus™

P=0.006

* Superiority was not included in initial assumptions

Late Loss (mm) at 9 Months

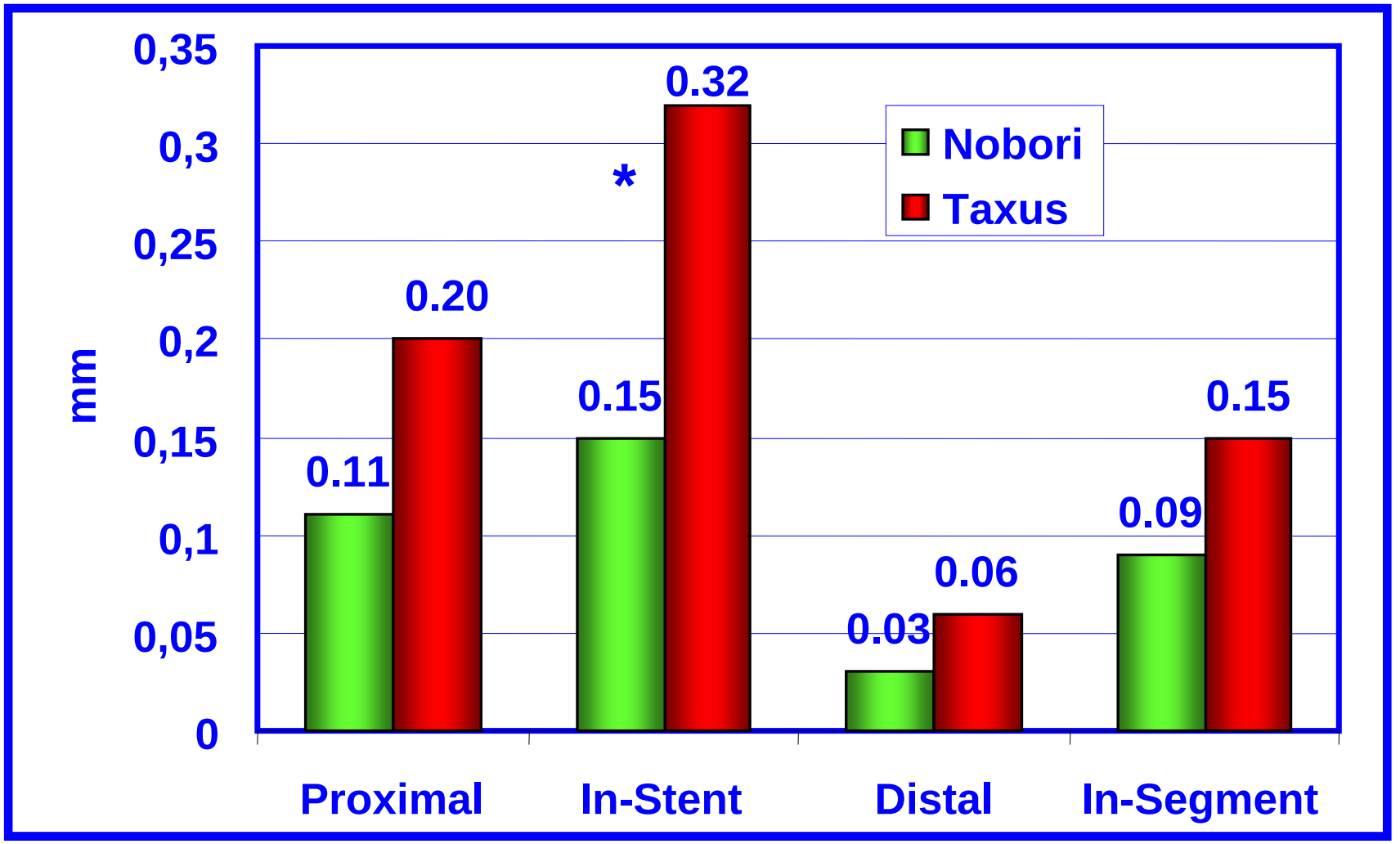


QCA Findings up to 9 Months

	Nobori ™ 84 Lesions	Taxus® 31 Lesions
RVD (mm) MLD (mm) DS (%)	2.81 ± 0.39 2.40 ± 0.39 14 ± 8	2.70 ± 0.50 2.23 ± 0.53 18 ± 10
Binary Restenosis %	0	0

No Significant difference between the two treatment groups

Late loss Distribution



* P=0.006

Main Intravascular Ultrasound Findings

Statistically significant difference between the two in all variables	Nobori ™ 36 Lesions	Taxus® 15 Lesions
Mean Lumen Area (mm^2) *	7.74 ± 1.7	6.36 ± 1.5
Minimum Luminal Area (mm^2) †	5.95 ± 1.6	4.97 ± 1.5
Mean Plaque Area (mm^2) §	0.18 ± 0.6	0.67 ± 0.7
Neointima Volume (mm^3) ‡	3.8 ± 10.9	14.6 ± 15.0
In-stent Volume obstruction (%) **	2.2 ± 6.0	8.9 ± 9.2

* p=0.010 † p=0.046 § p=0.014 ** p= 0.017 ‡ p= 0.006

Compliance with Dual Antiplatelet Therapy

	Nobori ™ 85 Patients	Taxus® 35 Patients
Dual antiplatelet therapy up to 6 months*	100%	90.6%
Ongoing dual antiplatelet therapy at 9 months follow-up	48.2%	56.5%
Average duration of dual antiplatelet therapy (days)	236 ± 45	243 ± 45

***P=0.021**

MACE Rate up to 1 year 1st Phase

	UP TO 9 MONTHS		UP TO 1 YEAR	
All Events	Nobori ™ 85 Patients	Taxus® 35 Patients	Nobori ™ 85 Patients	Taxus® 35 Patients
Cardiac and Non-Cardiac Death (%)	0	0	0	0
Myocardial Infarction (/%)	4.7	8.6	4.7	8.6
• Q-Wave	0.0	0.0	0.0	0.0
• Non-Q-Wave	4.7	8.6	4.7	8.6
– CK>2UNL<3UNL	4.7	5.7	4.7	5.7
– CK>3UNL	0.0	2.9	0.0	2.9
Clinically and Non-Clinically Driven Target vessel revascularization (%)	7.0	11.4	7.0	14.3
• CABG	0.0	2.9	0.0	2.9
• PCI	7.0	8.6	7.0	11.4
TOTAL MACE (all events)	11.7	20.0	11.7	22.9
Stent Thrombosis (%)	0	0	0	0

Clinically Driven Revascularizations up to 1 Year 1st Phase

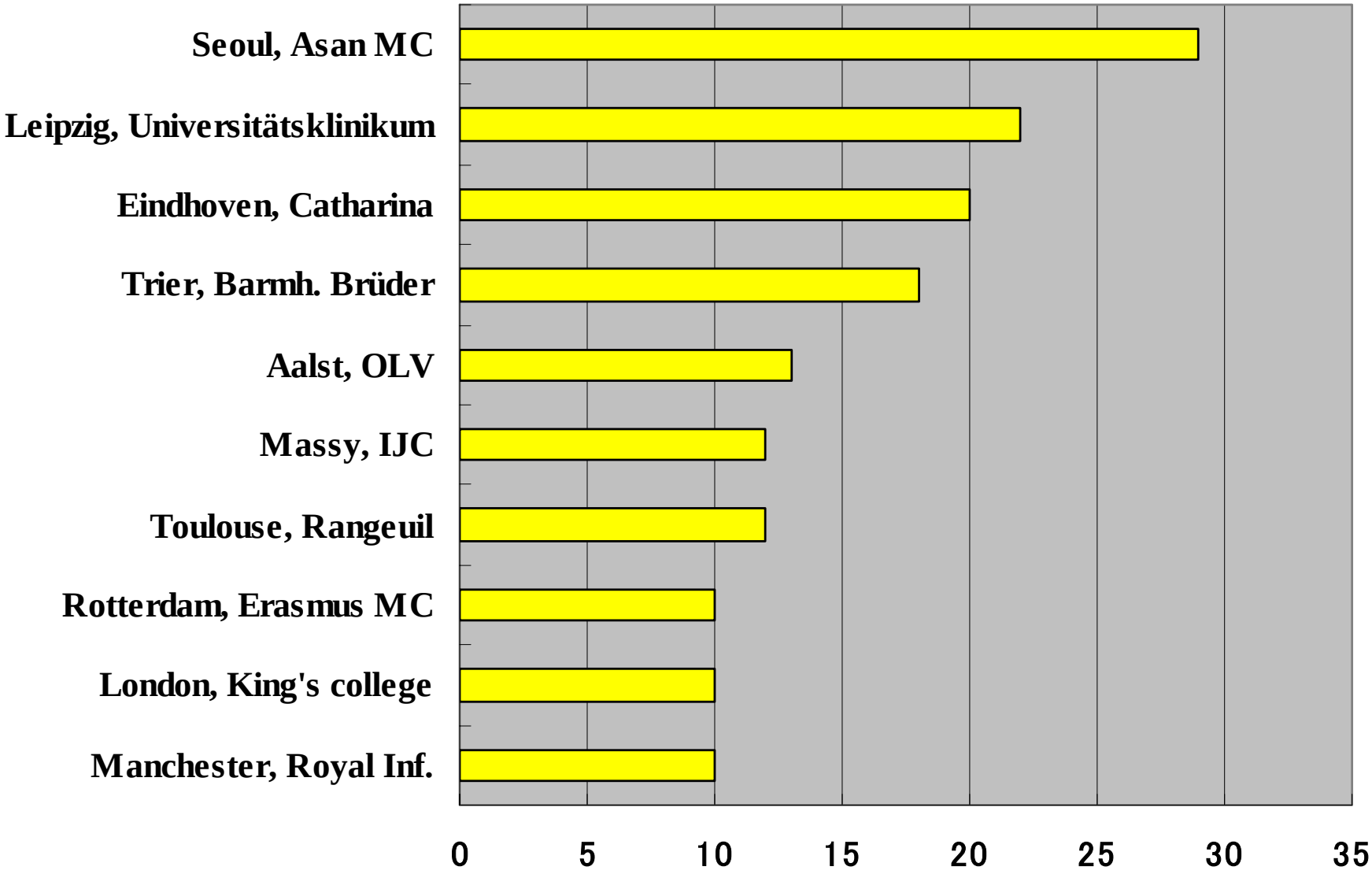
	Nobori ™ 85 Patients	Taxus® 35 Patients
TLR - Clinically Driven %	0	2.9*
TVR – non-TLR - Clinically Driven %	1.2	2.9
Total Clinically Driven TVR %	1.2	5.7
TOTAL MACE with Clinically Driven Revascularizations %	5.9	14.3

* Emergent CABG during procedure

NOBORI 1
Baseline data Phase 2

Top 10 Enrollers

Phase 2



Baseline Demographics (2nd Phase)

	Cohort A	Cohort B
Male %	75	68
Mean Age (years ± SD)	63 ± 11	63 ± 10
Previous MI (%)	20	28
Prior PCI (%)	19	9
Diabetes Mellitus (%)#	16	28
Insulin – dependent (%)*	7	2
Hyperlipidemia (%)	67	72
Hypertension (%)	63	64
Current Smoker (%)	21	20

*#: P=0.048, *: P=0.008, Others: No significant difference*

Lesion Characteristics
(2nd Phase)

	Cohort A	Cohort B
Location of lesion (%)		
LAD	36	47
RCA	40	34
LCX	24	19
Lesion classification (%)		
Types A/B1	51	55
Types B2/C	49	45

No Significant difference between the two treatment groups

Baseline and post procedure QCA (2nd Phase)

	Cohort A	Cohort B
Pre Procedure		
Lesion length (mm) RVD (mm) DS (%) MLD (mm)	10.8 ± 4.6 2.71 ± 0.51 59 ± 10 1.11 ± 0.33	11.5 ± 4.1 2.73 ± 0.55 62 ± 11 1.03 ± 0.35
Acute Gain	1.47 ± 0.34	1.52 ± 0.43
Post Procedure		
MLD (mm) RVD (mm) DS%	2.57 ± 0.41 2.92 ± 0.47 12 ± 6	2.55 ± 0.44 2.93 ± 0.50 13 ± 8

No Significant difference between the two treatment groups

Procedure Characteristics and Acute Success (2nd Phase)

	Cohort A	Cohort B
Lesion per patient (n ± SD)	1.1 ± 0.3	1.1 ± 0.3
Stents per lesion (n ± SD)	1.2 ± 0.5	1.2 ± 0.5
Stent Diameter (mm ± SD)	3.1 ± 0.4	3.1 ± 0.4
Stent Length (mm ± SD)	18.6 ± 5.2	19.1 ± 5.7
Lesions with multiple stents (%)	20	18
Lesion Success (%)	100	100
Procedure Success (%)	97.4	95.6

No Significant difference between the two treatment groups

MACE Rate up to discharge 2nd Phase

All Events	Cohort A	Cohort B
Cardiac and Non-Cardiac Death (%)	0	0
Myocardial Infarction (/%)	2.6	4.4
• Q-Wave	0.0	3.3
• Non-Q-Wave	2.6	1.1
Clinically and Non-Clinically Driven Target vessel revascularization (%)	0.0	0.0
• CABG	0.0	0.0
• PCI	0.0	0.0
TOTAL MACE (all events)	2.6	4.4
Stent Thrombosis (%)	0	0

CONCLUSIONS

1. NOBORI 1 Phase 1 met its Primary Endpoint:
   - Nobori™ stent is non-inferior to TAXUS® (in-stent late loss 0.15 mm vs 0.32 mm; p=0.006)

2. IVUS shows Nobori™ stent reducing more than TAXUS® intra-stent neointimal hyperplasia, as assessed by volume obstruction (2.2%vs 8.9%; p:0.017)

3. Confirmed good safety profile of Nobori™ up to 12 m
   - No Acute, Sub-acute nor Late Stent Thrombosis
   - No Angiographic Restenosis
   - No Clinically Driven TLR

4. Initial results in the second phase indicate good safety profile of both stents