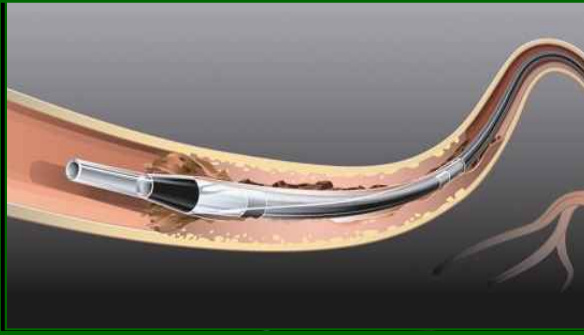


# **Nobori -New Generation DES NOBORI 1 and Early Clinical Trials Update**

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**Bernard Chevalier  
ICPS, Massy France**

# Nobori DES Components



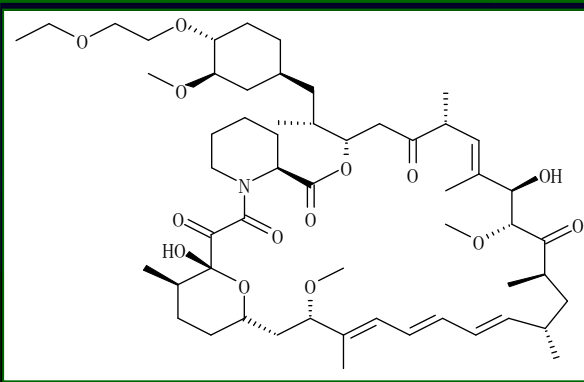
## BMS Platform

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



# Design Hypothesis

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- ***Biodegradable polymer***
  - Controlled drug release
  - Long term safety
- ***Abluminal coating***
  - Optimal drug uptake
  - Minimal systemic exposure
  - Enhanced endothelialization
- ***Drug from limus family***
  - High efficacy

# Design Supported by Extensive Clinical Program (>20.000pt)

## Foundation

### Status

NOBORI PK	Single arm – FU 4Y	N=20
NOBORI 1 Phase 1	Randomized-Taxus – FU 3Y	N=120
NOBORI 1 Phase 2	Ranomized -Taxus – FU 2Y	N=243
NOBORI CORE	Comparative Cypher – FU 2Y	N=107
NOBORI Japan	Randomized Cypher – FU 9M	N=323

## Expansion

### All comers

<b>NOBORI 2</b>	<b>Single Arm FU 6 M</b>	<b>N=3074</b>
NOBORI 2 – Off label	FU 6M	N=2090
NOBORI 2 – Diabetics	FU 6M	N=888
NOBORI 2 – Bifurcation	FU 6M	N=510
NOBORI 2 – Female	FU 6M	N=560
NOBORI 2 - ACS	FU 6M	N=802
<b>e-NOBORI</b>	<b>Enrollment June 2010</b>	<b>N=8000</b>

## Real Life

### Randomized

COMPARE 2	Nobori vs Xience V-enrolling	N=2700
BASKET PROVE 2	Nobori vs Xience vs BMS – Jan.10	N=2400
SORT-OUT IV	Nobori vs Cypher Select-enrolling	N=2400
SECURITY	6 vs 12 m DAT-enrolling	N=4000



**NOBORI PK, NOBORI 1  
NOBORI CORE, - Update**

# NOBORI PK – Pharmacokinetics Study Design

PI: M. Ostojic

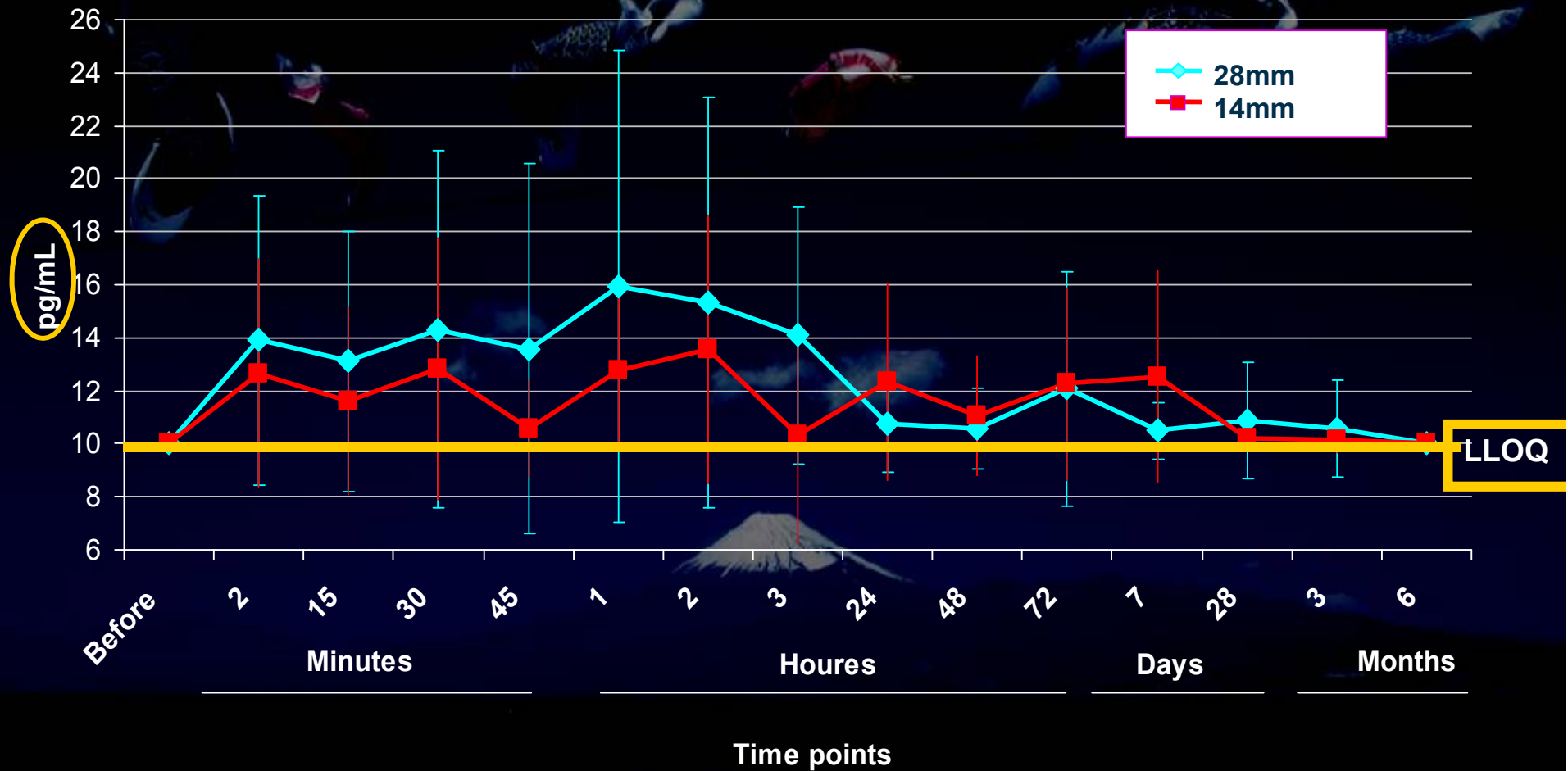
## BA9 Blood Collection Time Points

Trial	Sample Size (n)	Pre-Procedure	TIME POINTS													
			Mins / Hours / Days / Months													
			2	15	30	1	2	4	8	24	48	72	7	28	3	6
PK Study	20	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Biochemistry/Haematology Blood Collection Time Points

\* t=1 defined as deployment balloon inflation/ stent implantation

# NOBORI PK Biolimus A9 concentration



# Pharmacokinetics

Maximum blood concentration of Biolimus A9 is 52 times LOWER than Sirolimus and 87 times lower than Everolimus

## Systemic concentration of drugs (ng/mL) eluted from different DES

	Biolimus A9 <sup>1</sup>	Sirolimus <sup>2</sup>	Everolimus <sup>3</sup>
Mean	0,020	0,80	NR
SD	0,007	0,37	NR
Minimum	0,010	0,43	0,14
Maximum	0,032	1,66	2.79
n	20	19	37

NR= Not reported

<sup>1</sup>Ostojic et al. CCI 2008

<sup>2</sup>Vetrovec et al. CCI 2006

<sup>3</sup>Wiemer et al. AHJ 2008



# NOBORI 1 – Pivotal Trial

2:1 randomization  
Single blind - two vessel – staging allowed

*De novo* native coronary lesion  
Vessel diameter: 2.5-3.5 mm  
Lesion length: <25 mm  
Predilatation required

Nobori stent  
n = 85 phase 1  
153 phase 2

PI: Dr B. Chevalier  
N = 363 patients  
29 sites  
Europe, Asia, Australia

Control Taxus stent  
n = 35 Express Ph 1  
90 Liberte Ph 2

Clinical  
endpoints

Clinical/MACE

30d

4mo

9mo

12mo

2yr

3yr

4yr

5yr

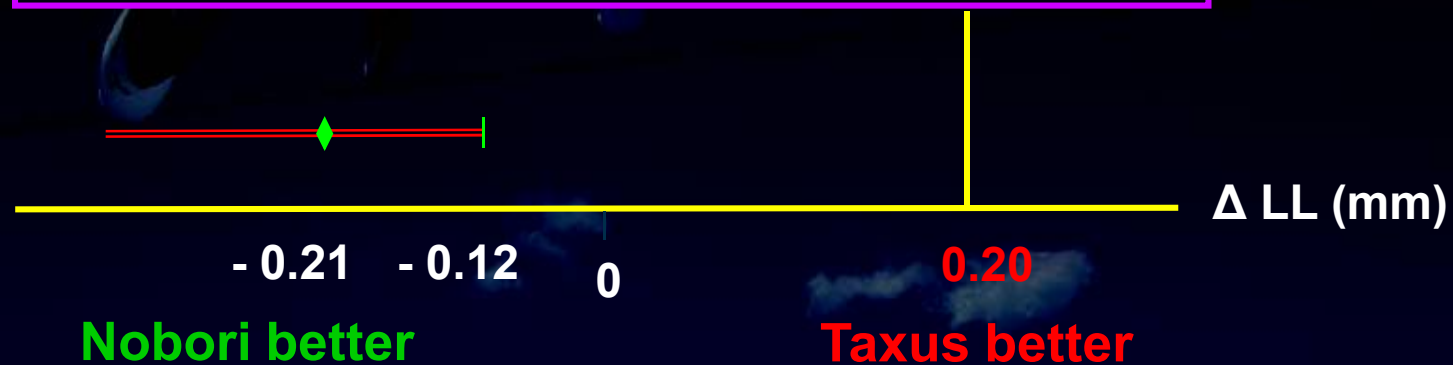
Angio/IVUS

QCA  
IVUS

Primary endpoint: In-stent late lumen loss by QCA at 9 months  
Secondary endpoints: MACE (Death, MI, TVR) TLR, TVF at 9 months and ABR at 9 months, Procedure, Lesion success, In-segment late loss, ST at 9m and up to 5 years  
Drug therapy: ASA and clopidogrel 6 months

# NOBORI 1 - Primary Endpoint Result

- Assumed in-stent Late Loss (LL)
  - ✓ 0.39 mm for Taxus® / 0.34 mm Nobori
  - ✓ Assumed SD: 0.50 mm
- Delta non-inferiority margin: 0.20 mm



## Late Loss result

- ✓  $0.32 \pm 0.50$  mm Taxus
- ✓  $0.11 \pm 0.30$  mm Nobori

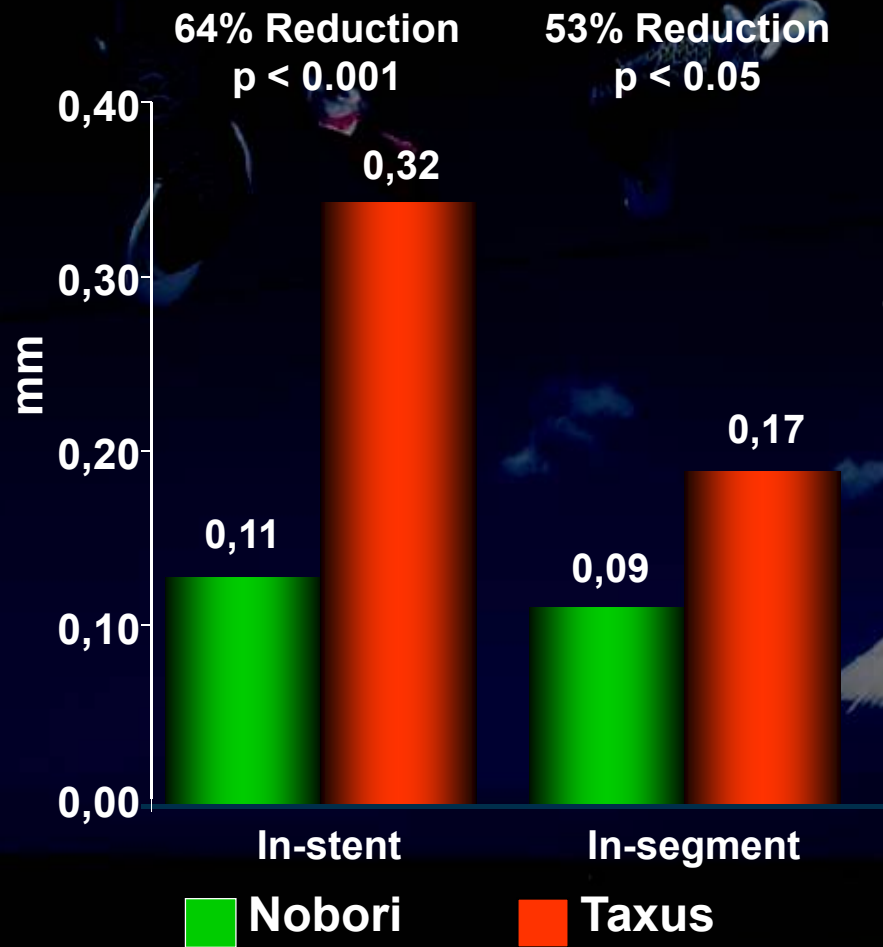
## Result:

**Nobori = NON-INFERIOR**  $p < 0.001$

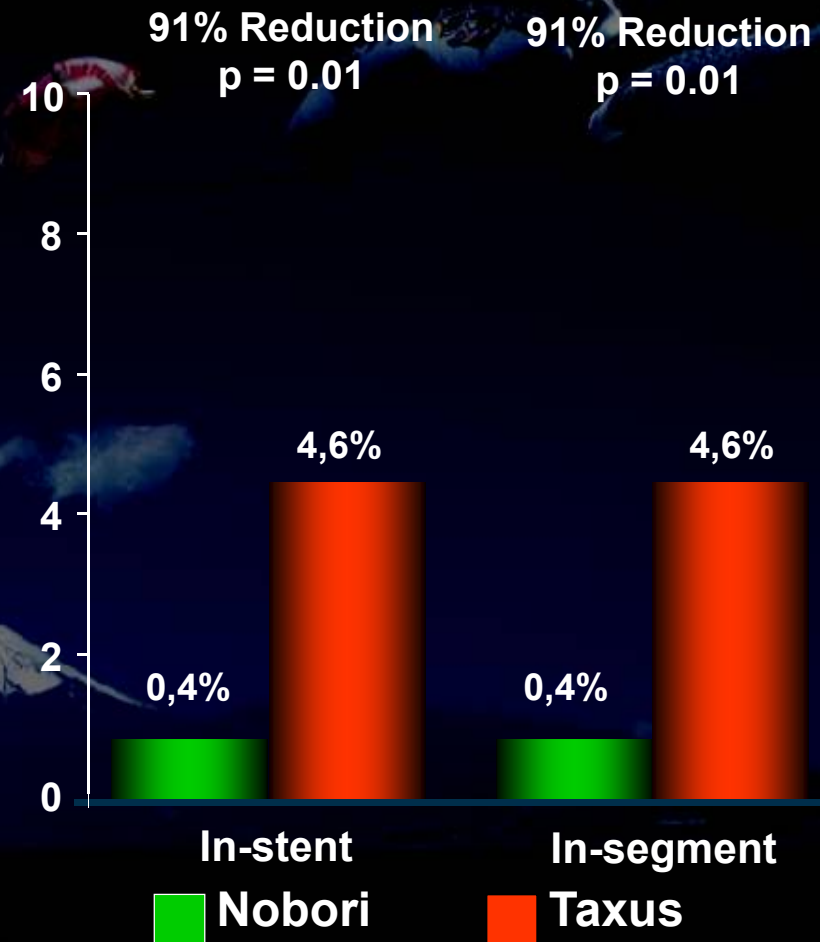
**Nobori = SUPERIOR**  $p = 0.001$

# Angiographic Findings in NOBORI 1 trial at 9 Months

## Late Loss



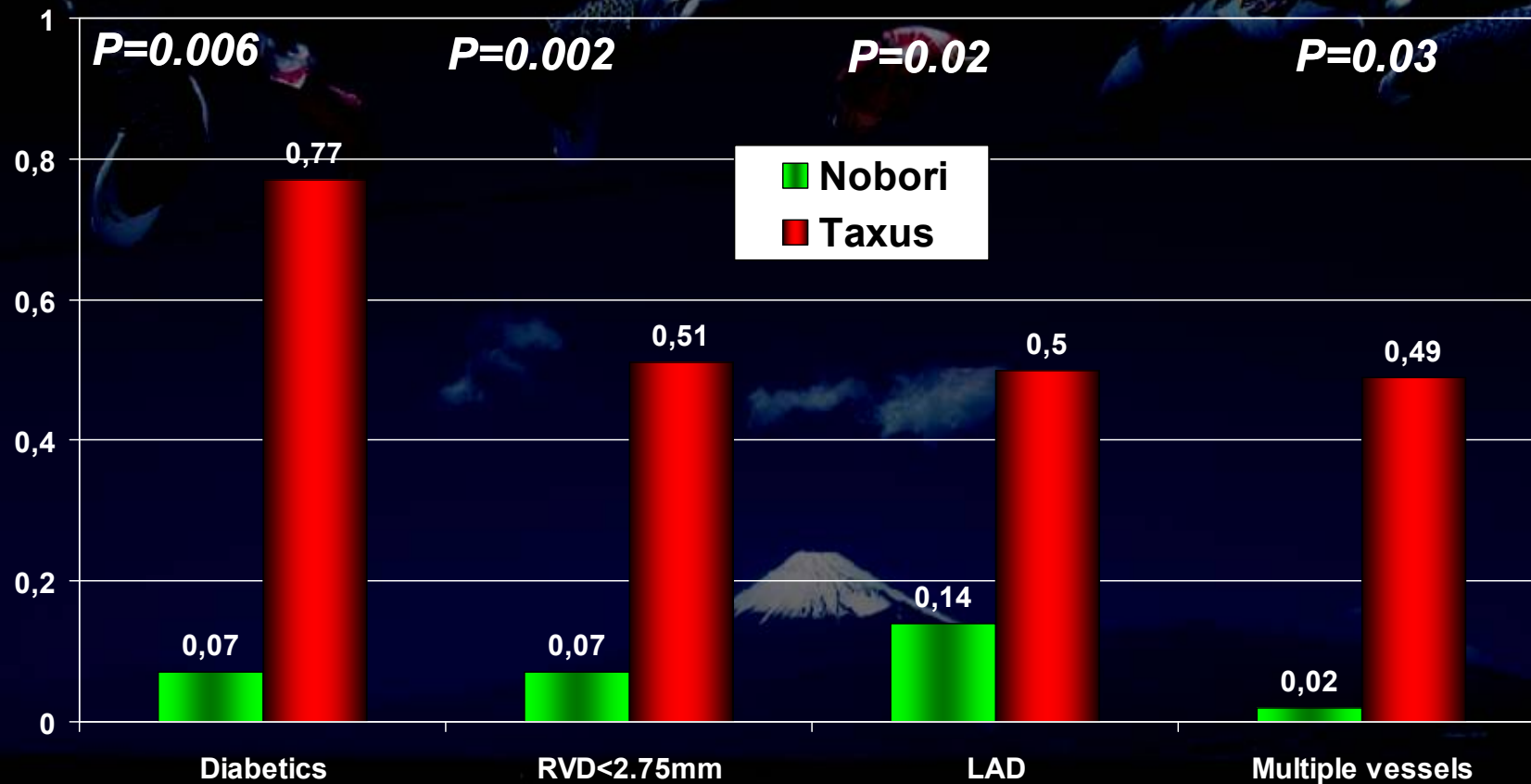
## Binary Restenosis



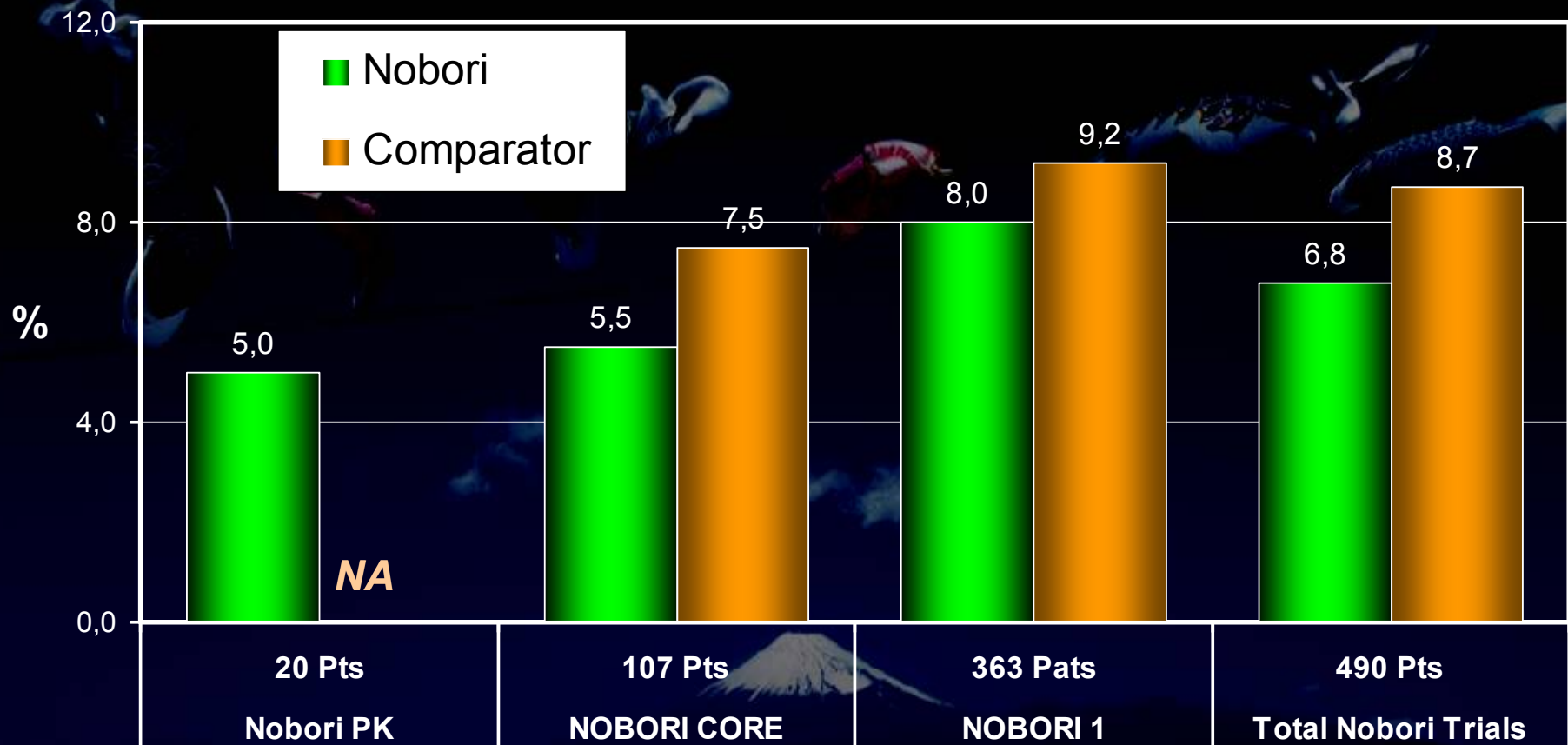
# NOBORI 1 - Main IVUS Findings at 9 months

IVUS	Nobori N =101	Taxus N =53	P value
Volume obstruction (%)	1.93±5.54	6.76±8.04	<0.001
Neointimal hyperplasia (mm <sup>3</sup> )	3.11±8.84	13.50±20.4	0.003
Mean plaque area (mm <sup>2</sup> )	0.15±0.48	0.52±0.64	<0.001

# Subgroup Analysis – NOBORI 1 IVUS - Mean Plaque Area (mm<sup>2</sup>)

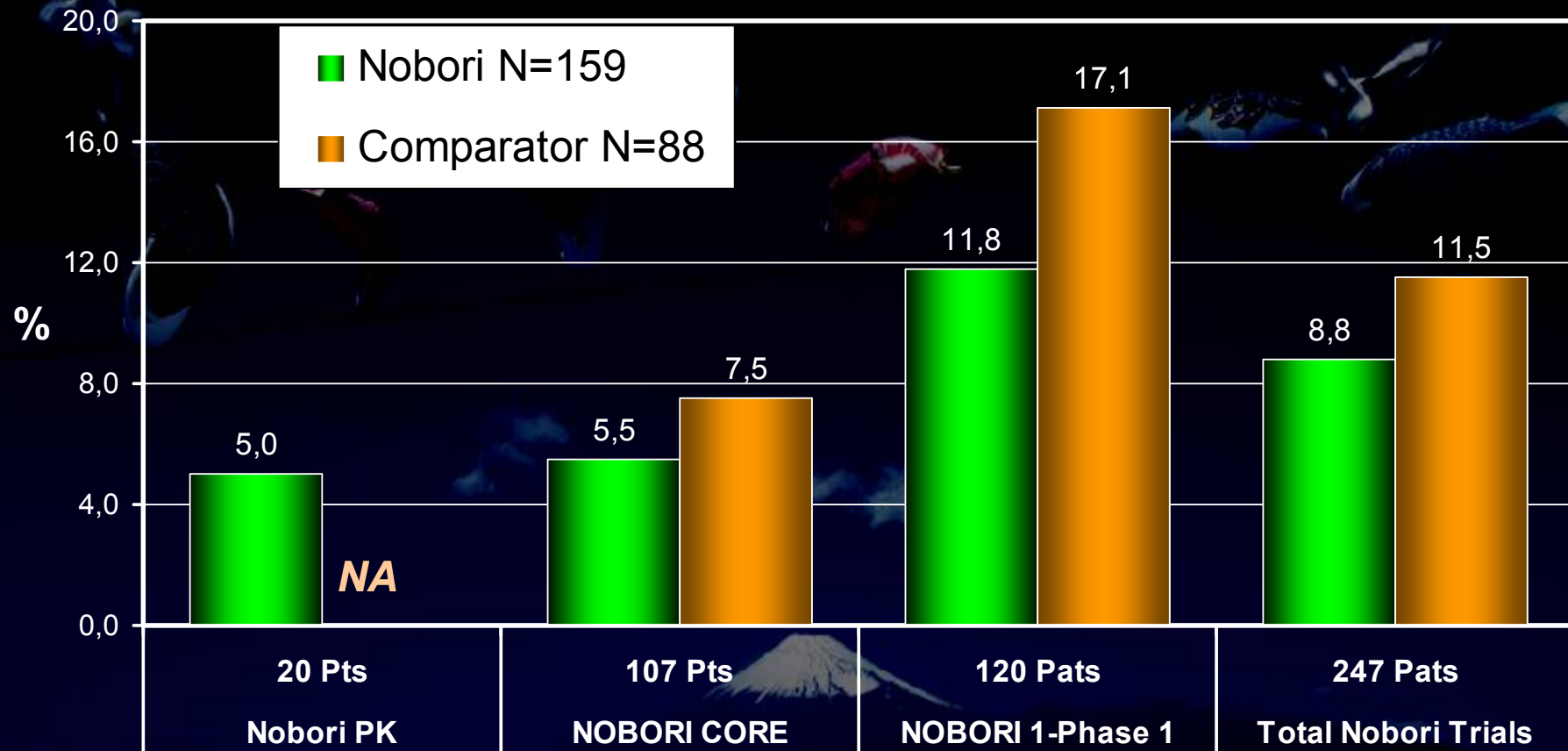


# MACE Rate in NOBORI Trials at 2 Years



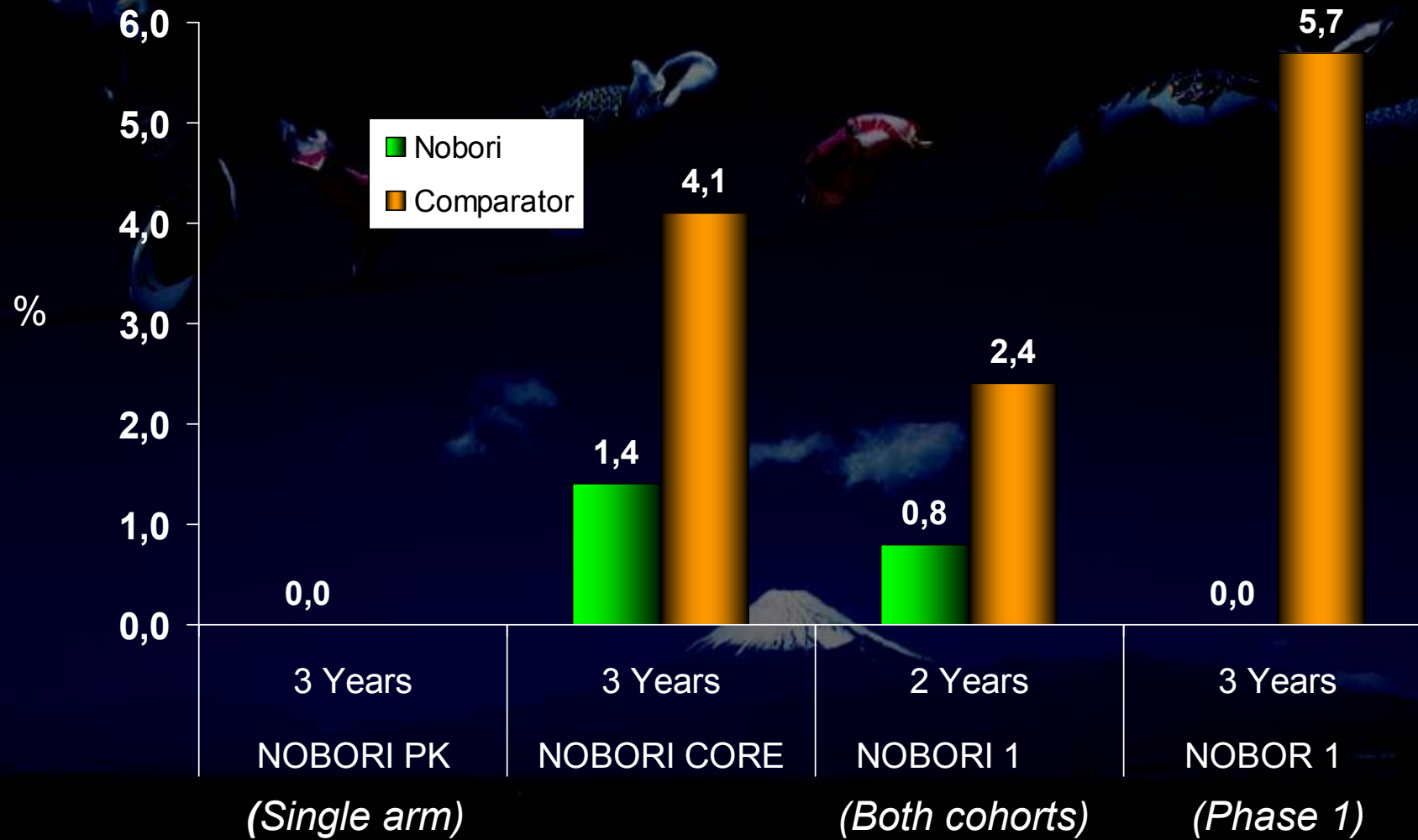
**MACE = Cardiac Death, MI, Clinically Driven Target Vessel Revascularization**

# MACE Rate in NOBORI Trials at 3 Years



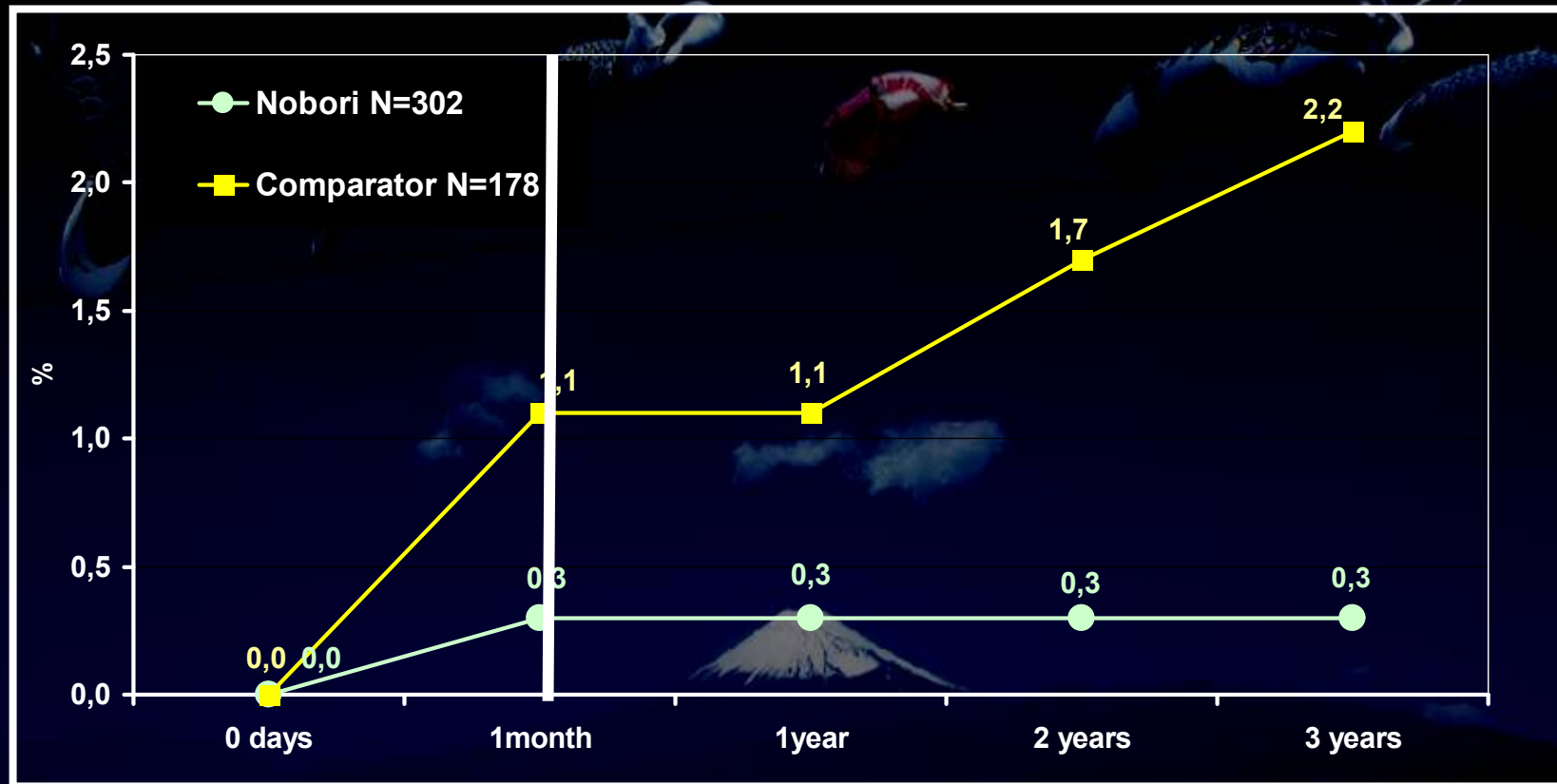
**MACE = Cardiac Death, MI, Clinically Driven Target Vessel Revascularization**

# TLR – Rate in NOBORI Trials





# Stent Thrombosis at 3 years



Stent thrombosis = Definite and Probable according to ARC definition  
*At 3 years calculation done for the entire studied population.*

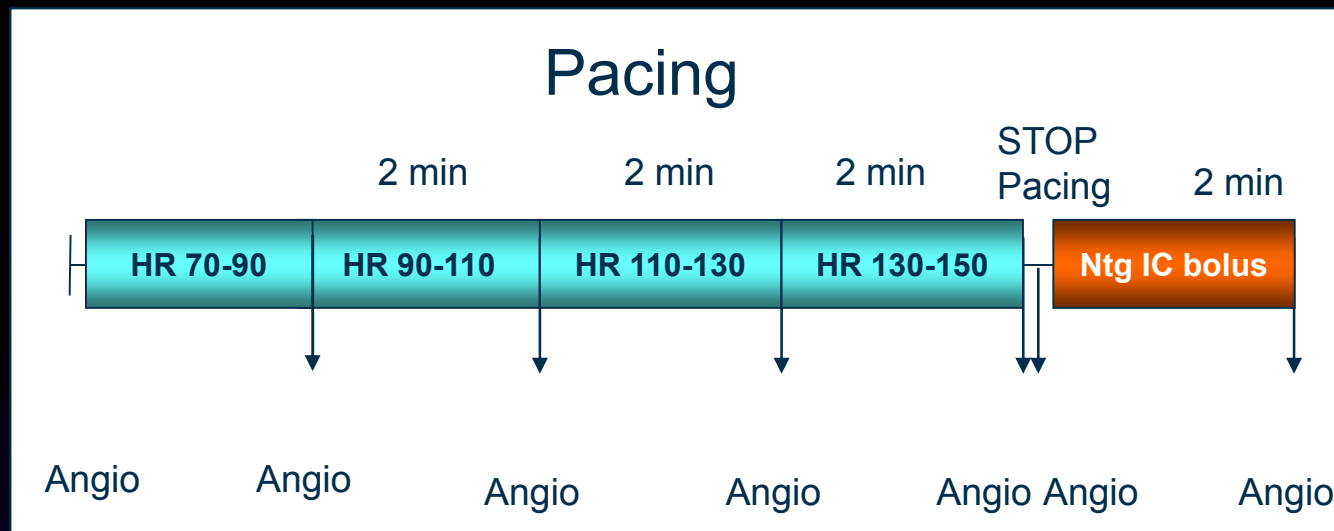
The background of the slide is a dark, atmospheric photograph. In the upper half, a traditional Japanese festival float (danjiri) is visible, featuring a crane and other figures. In the lower half, a snow-capped mountain, likely Mount Fuji, is silhouetted against a dark sky. The overall color palette is dark with some highlights from the float and the mountain's snow.

# **NOBORI CORE**

## **Endothelial Function Assessment**

**Comparative analysis of  
Nobori DES vs Cypher DES**

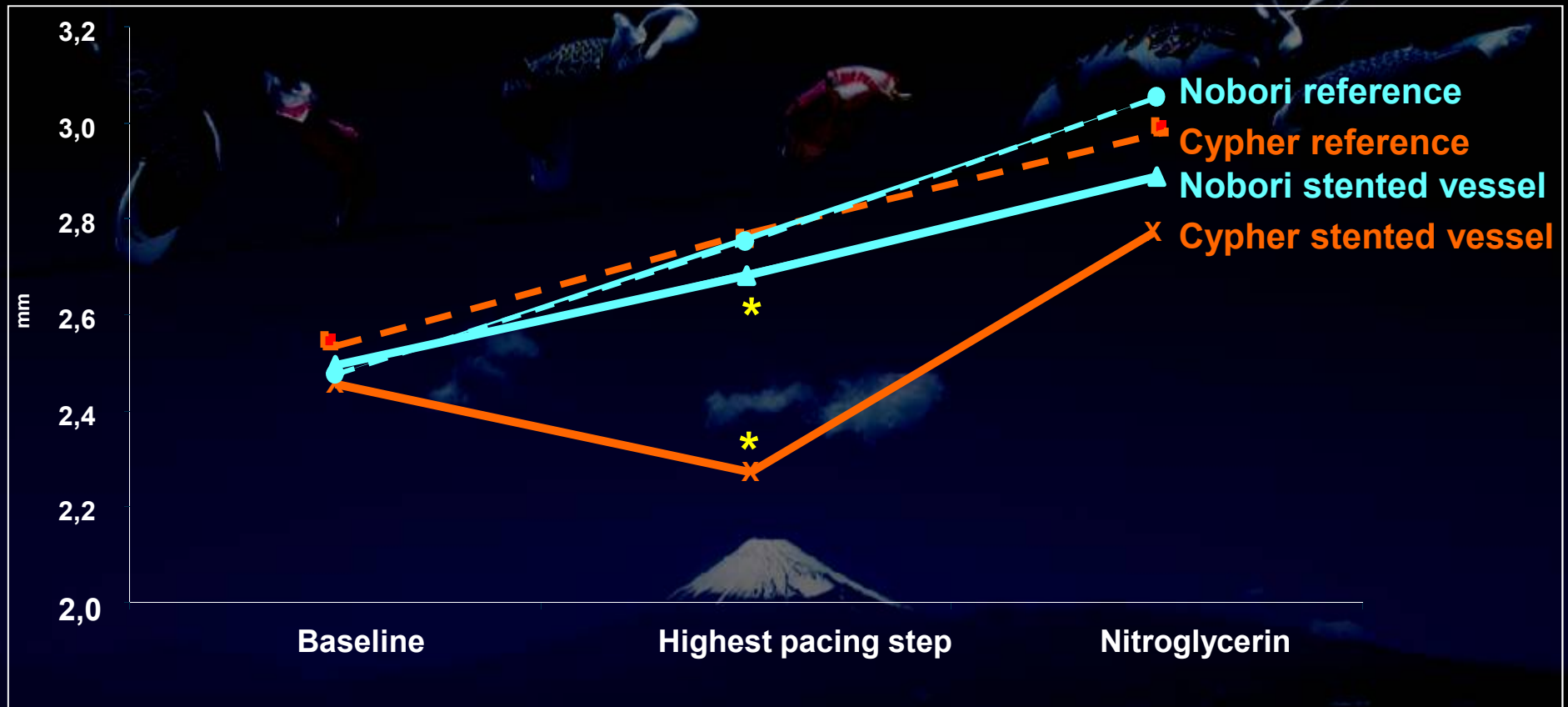
# Protocol of atrial pacing for endothelial function assessment



## METHODS

- Baseline conditions were established and angiography performed
- Rapid Atrial pacing with 20 bpm higher than baseline for 2 min
- Angiographic images taken followed by 2 minutes rest
- Repeat procedure with increasing pacing rate by 20 bpm up to 150
- Intra-arterial nitroglycerin injection
- Angiographic image taken
- Off line QCA analysis of proximal, in-stent, distal segments and reference vessel performed

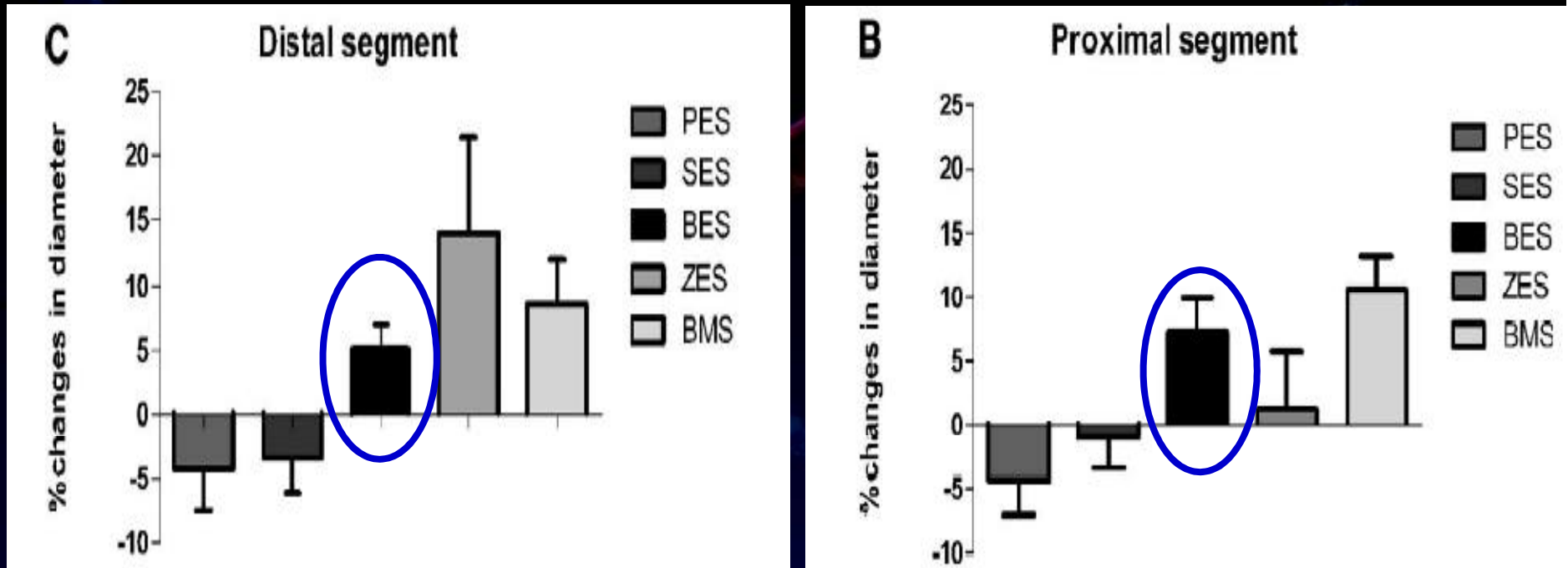
# Distal vessel: change in diameter after pacing



\*p=0.001 for percentage change

Hamilos et al. JACC 2008

# Different endothelium dependent vasomotion with different stents



- Paradoxical vasoconstriction with first generation DES
- Normal vasodilatation with second generation DES and BMS

# Conclusions

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Long term results of early clinical trials with Nobori DES are very encouraging

**No late stent thrombosis have been observed up to 3 years with very low frequency of Target Lesion Revascularization.**

**Endothelial function appears better preserved with Nobori as compared to first generation DES**

**These results give further indication of potential benefit that Nobori with biodegradable polymer and abluminal coating, could bring for treatment of patients with CAD**

**Further extensive Clinical program will help to fully explore the value of this new concept**