Nobori DES – Clinical Program

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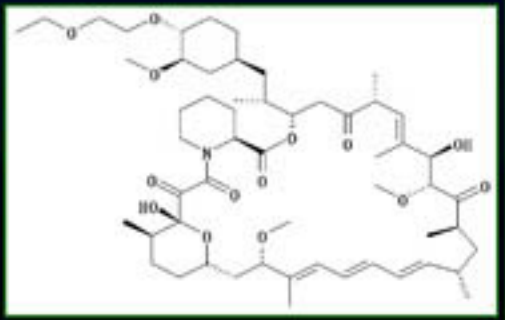
Nobori DES Design

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

Design Hypothesis

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

Design Supported by Extensive Clinical Program (>20.000pt)

		Status	
Foundation	NOBORI PK	Single arm – FU 5Y	N=20
	NOBORI 1 Phase 1	Randomized-Taxus – FU 5Y	N=120
	NOBORI 1 Phase 2	Ranomized -Taxus – FU 4Y	N=243
	NOBORI CORE	Comparative Cypher – FU 4Y	N=107
	NOBORI Japan	Randomized Cypher – FU 2Y	N=323
Expansion All comers	NOBORI 2	Single Arm FU 2Y	N=3067
	NOBORI 2 – Off label	FU 2Y	N=2090
	NOBORI 2 – Diabetics	FU 2Y	N=888
	NOBORI 2 – Bifurcation	FU 2Y	N=510
	NOBORI 2 – Female	FU 2Y	N=560
	NOBORI 2 - ACS	FU 2Y	N=802
	e-NOBORI	Enrolling	N=8000
Real Life Randomized	COMPARE 2	Nobori vs Xience V- FU	N=2700
	BASKET PROVE 2	Nobori vs Xience vs BMS -enroling	N=2400
	SORT-OUT IV	Nobori vs Cypher Select- FU	N=2400
	SECURITY	6 vs 12 m DAT-enrolling	N=4000
	ISAR-TEST 6	Nobori vs ISAR G2 vs Xience V-enrolling	N=2100

NOBORI – Pivotal Trials

NOBORI 1

NOBORI Japan

NOBORI 1

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

De novo lesions in native coronary arteries
Vessel diameter: 2.5-3.5 mm
Lesion length: <25 mm
Predilatation required

Nobori stent
n = 238

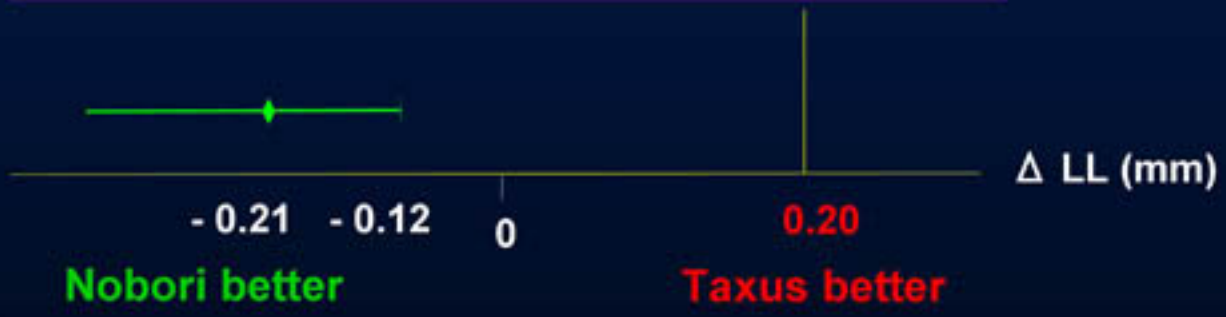
PI: Dr B. Chevalier
N = 363 patients
29 sites
Europe, Asia, Australia

Control Taxus stent
n = 125

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
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 ± 0.50 mm Taxus
- ✓ 0.11 ± 0.30 mm Nobori

Result:
Nobori = NON-INFERIOR p<0.001
Nobori = SUPERIOR p=0.001

NOBORI Japan Trial Design

3:2 randomization, single blind – up to two vessels

De novo lesions in native coronary arteries
Vessel diameter: 2.5-3.5 mm
Lesion length: ≤ 30 mm
Predilatation required

Nobori BES
(n=200)

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

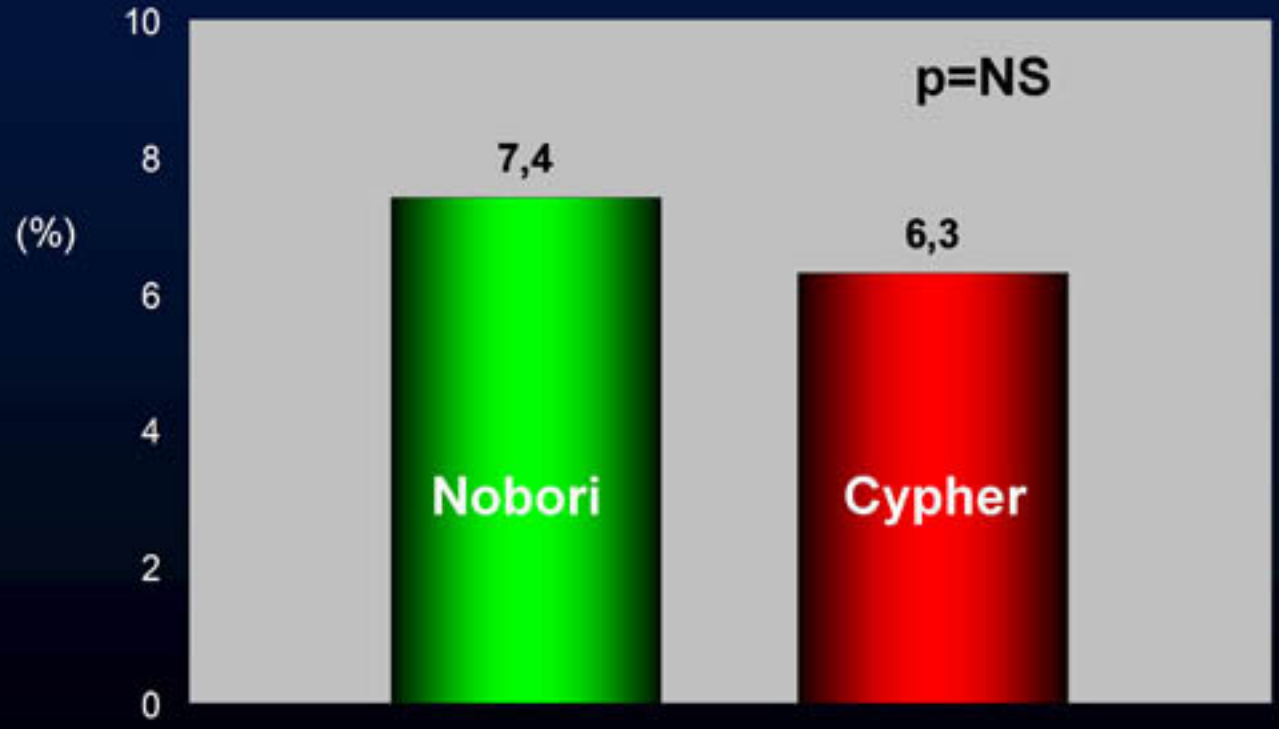
Cypher SES
(n=135)

Primary endpoint: Target Vessel Failure（TVR, Cardiac death, MI）at 9months
Secondary endpoints:

- Acute gain after PCI
- Late loss / Restenosis rate / %DS at 8 months
- MACE (Cardiac Death, MI, TLR) /TLR/TVR/TVF/Stent thrombosis at 9 months & 1,2,3,4,5Y

Primary Endpoint
TVF at 9-month

Nobori (BES) was NOT Inferior to Cypher (SES)



NOBORI – Pivotal Trials Summary

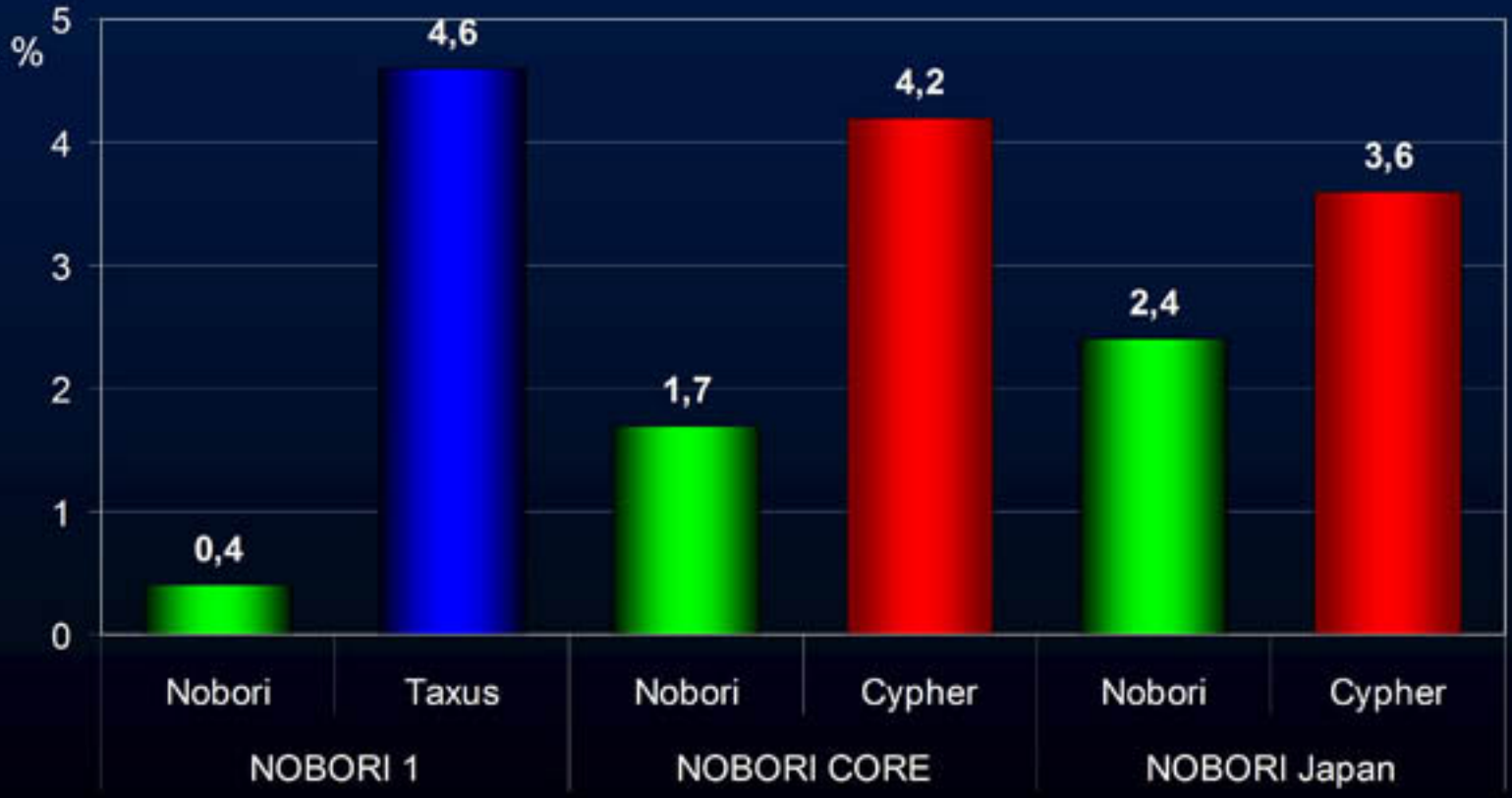
Nobori DES Efficacy

Late Loss in NOBORI Pivotal Trials

Angiographic FU at 9 mts except NOBORI JAPAN at 8 mts

Nobori DES Efficacy

Binary Restenosis in NOBORI Pivotal Trials

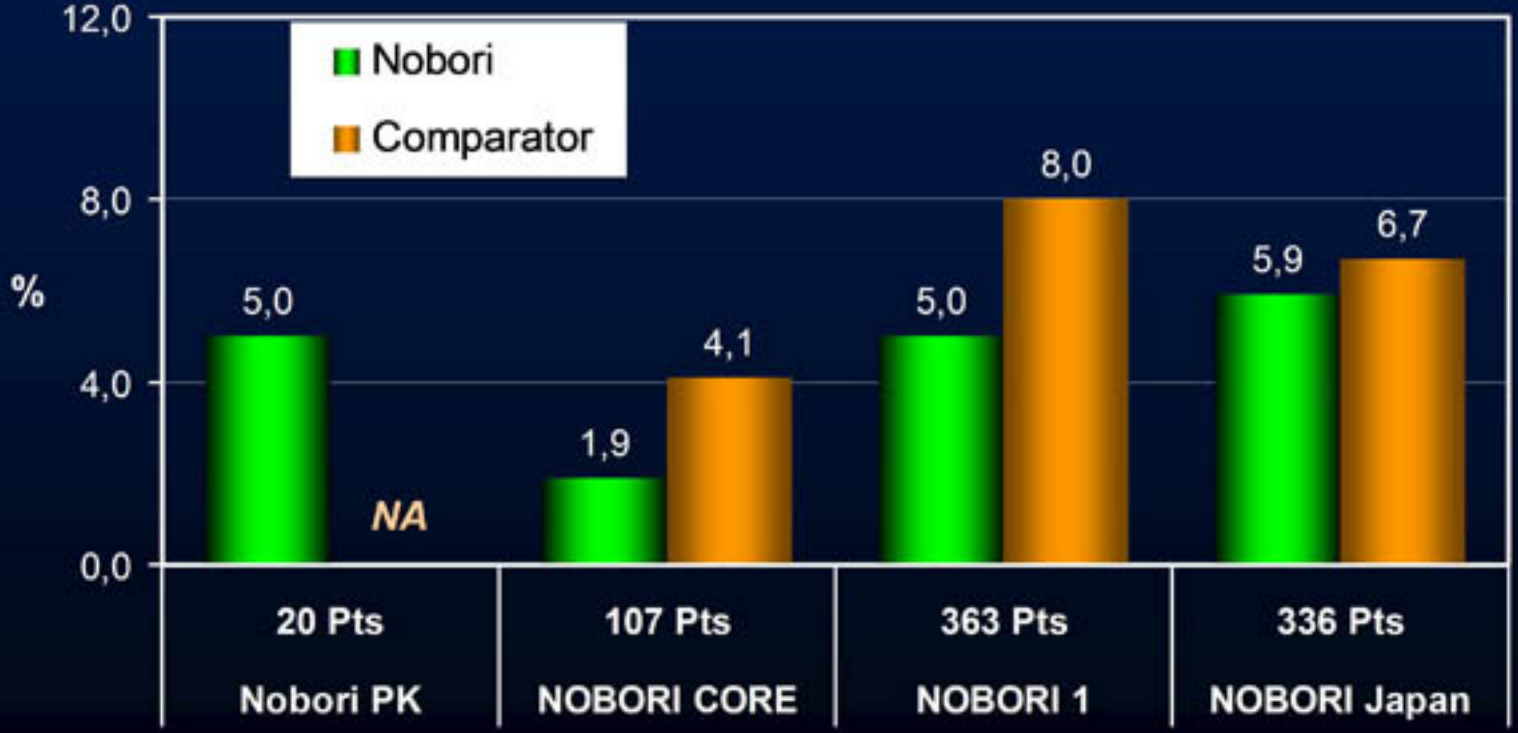


Angiographic FU at 9 mts except NOBORI JAPAN at 8 mts

Nobori DES Efficacy

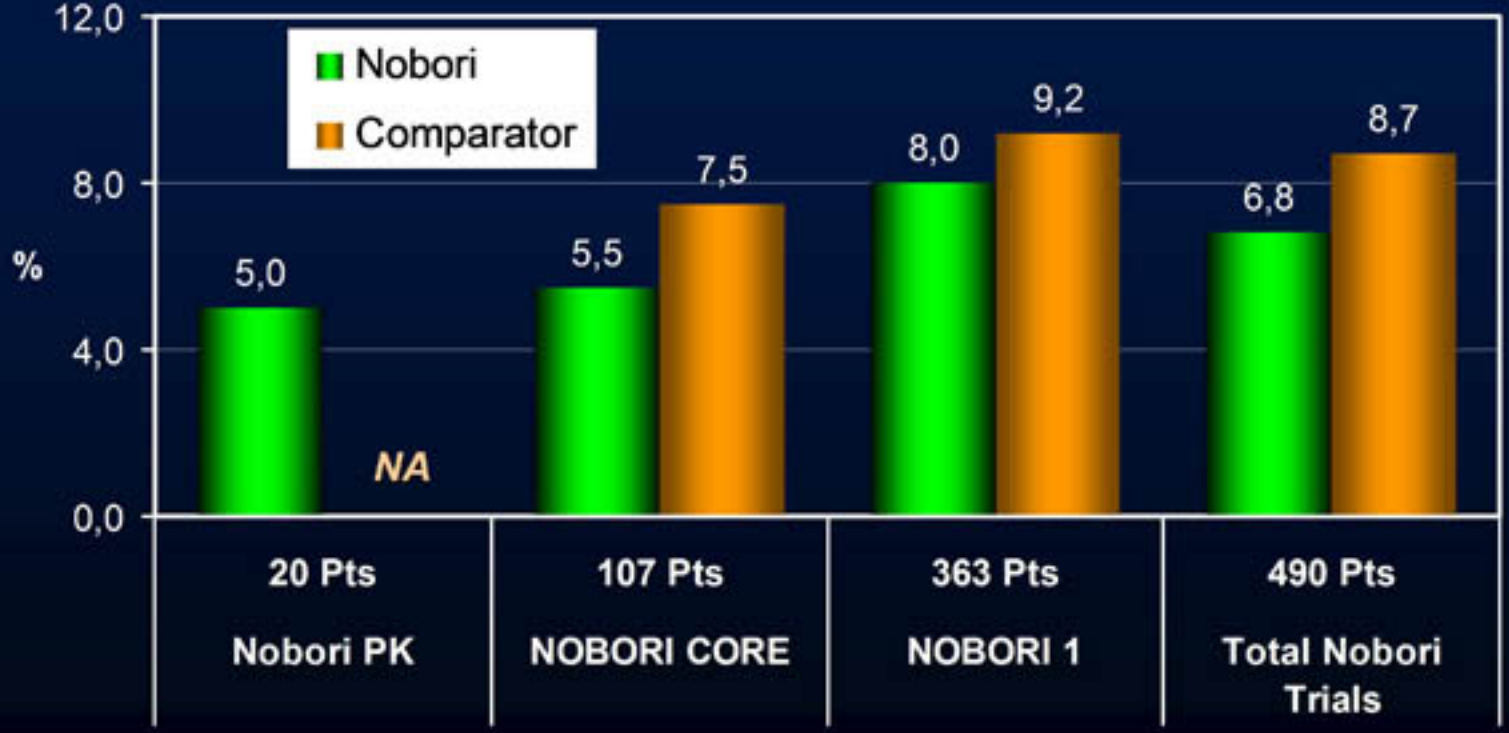
TLR at 1 year in NOBORI Pivotal Trials

MACE Rate in NOBORI Trials at 1 Year



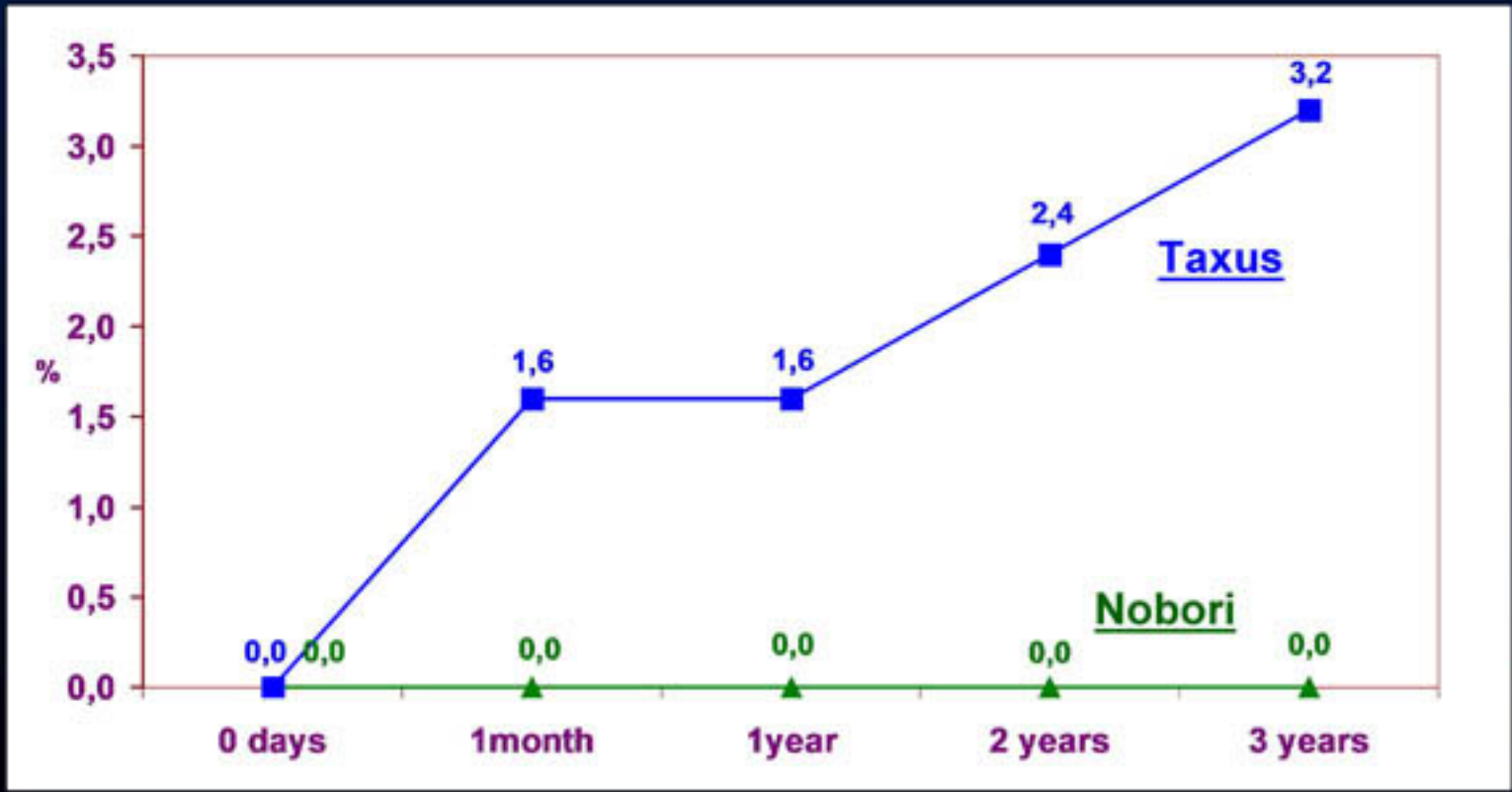
MACE = Cardiac Death, MI, Clinically Driven Target Vessel Revascularization

MACE Rate in NOBORI Trials at 3 Years

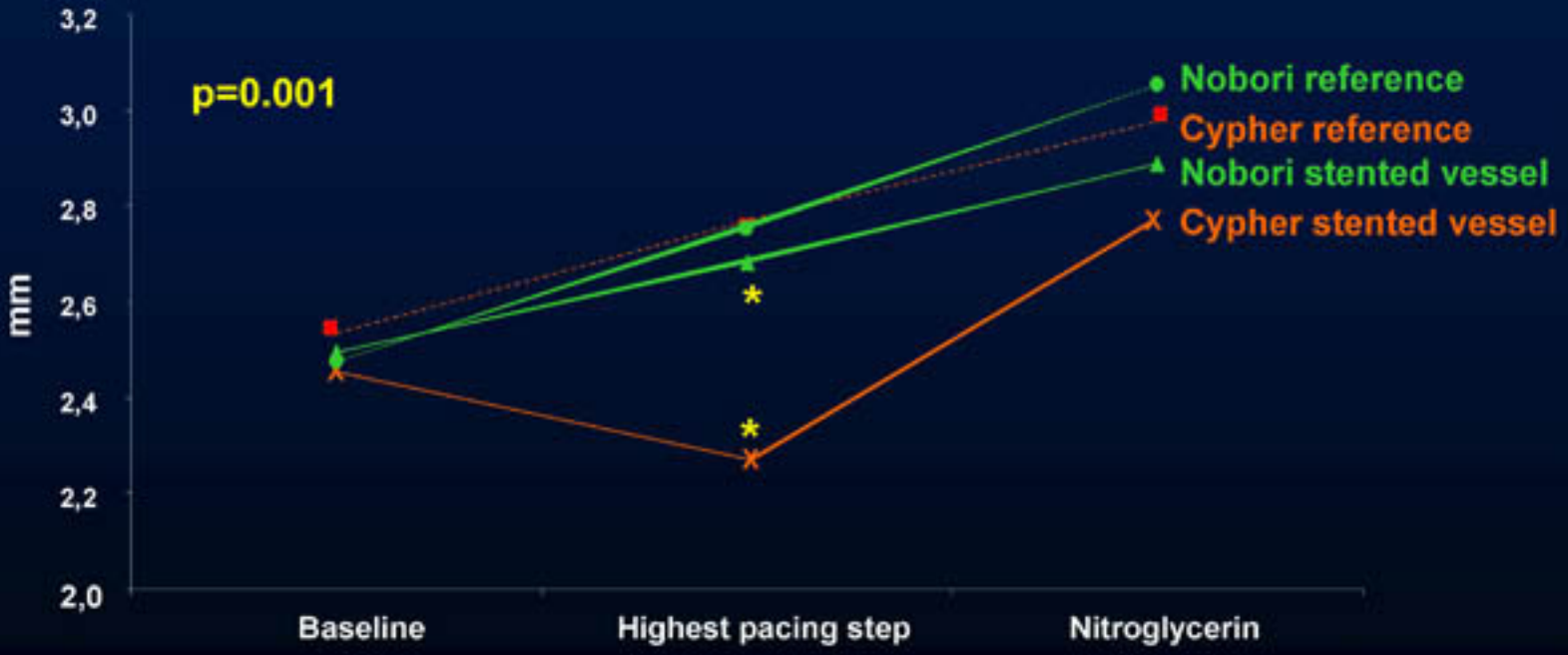


MACE = Cardiac Death, MI, Clinically Driven Target Vessel Revascularization

Long Term Stent Thrombosis in NOBORI 1 Pivotal Trial



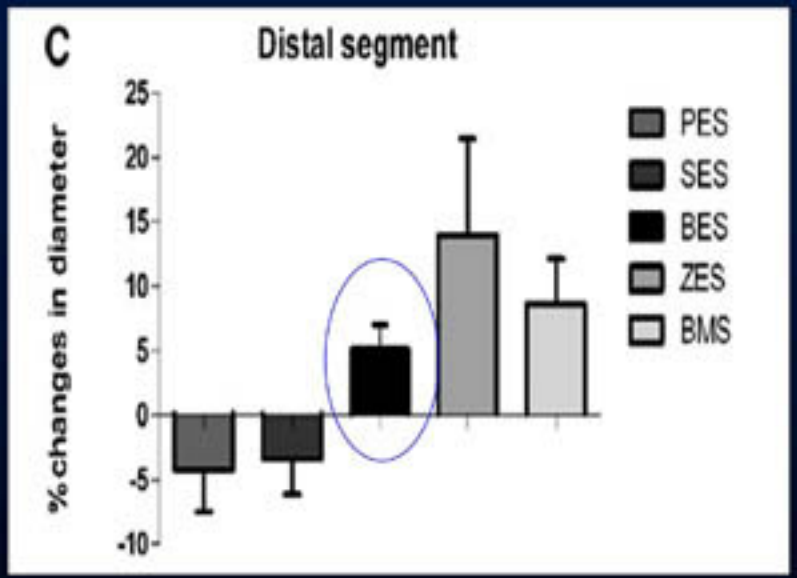
Endothelial Function
Nobori vs Cypher

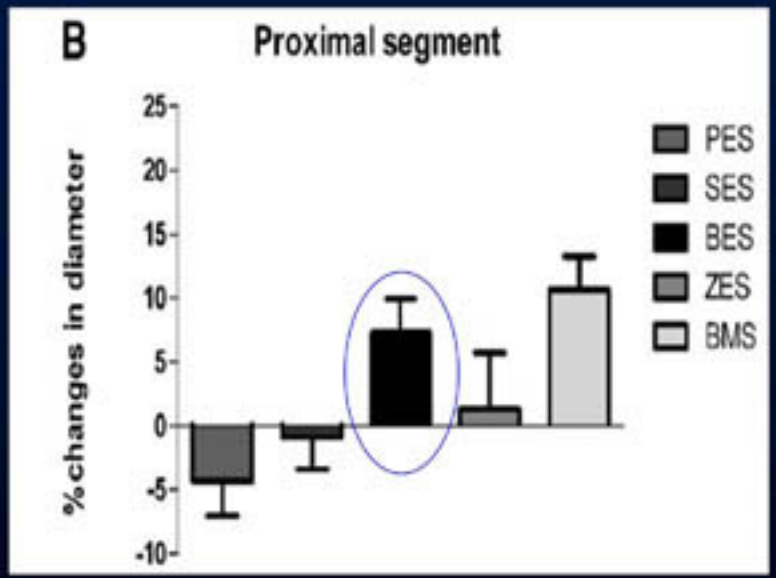


Unlike Cypher, endothelium-dependent vasomotion at adjacent stent segments seems to be preserved after Nobori implantation,

Hamilos M. et al. JACC 2008

Endothelial Function
Nobori versus other DES



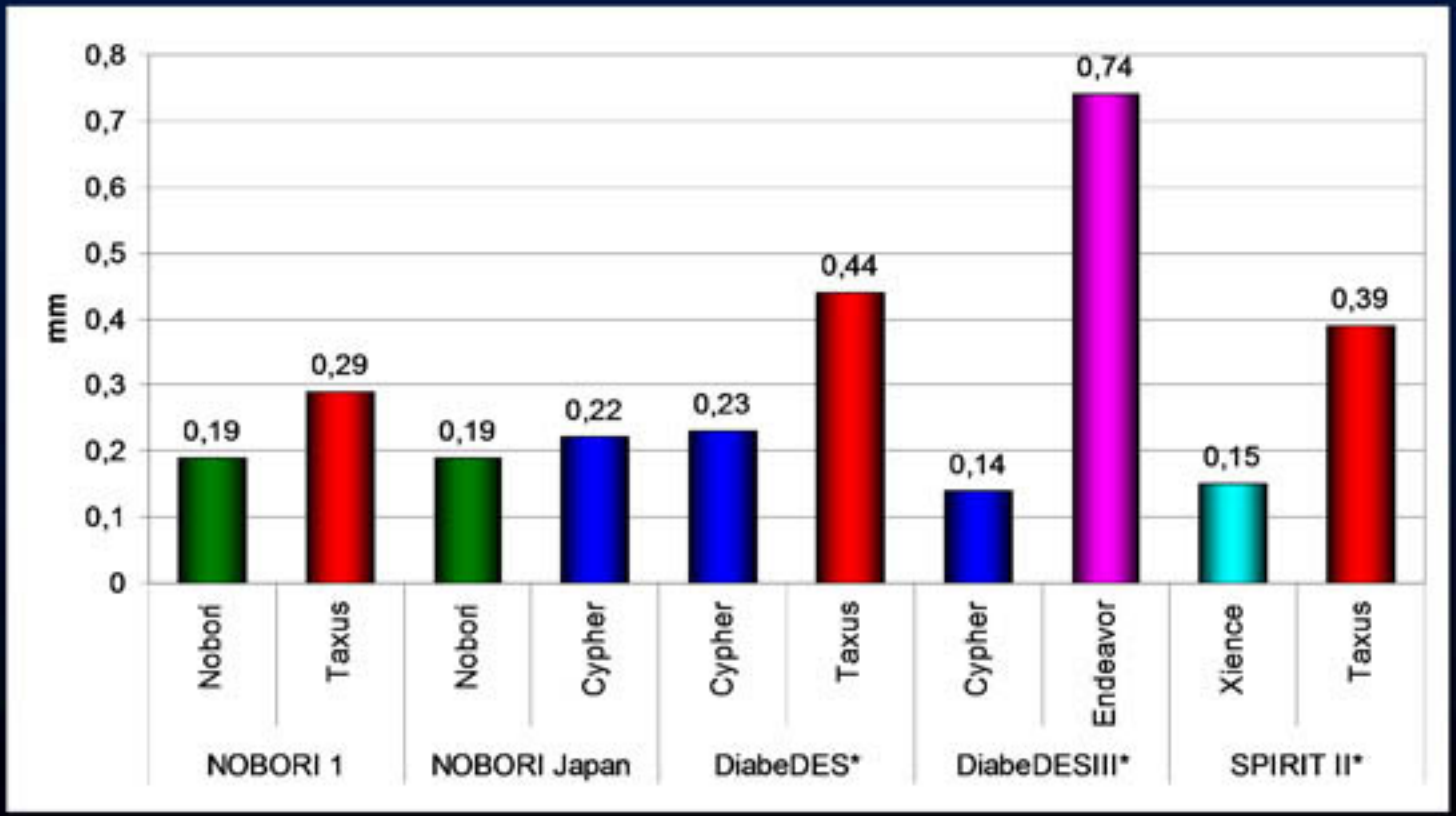


- Paradoxycal vasoconstriction with first generation DES
- Normal vasodilatation with second generation DES and BMS

Hamilos et al, Circulation CV Intervention 2008

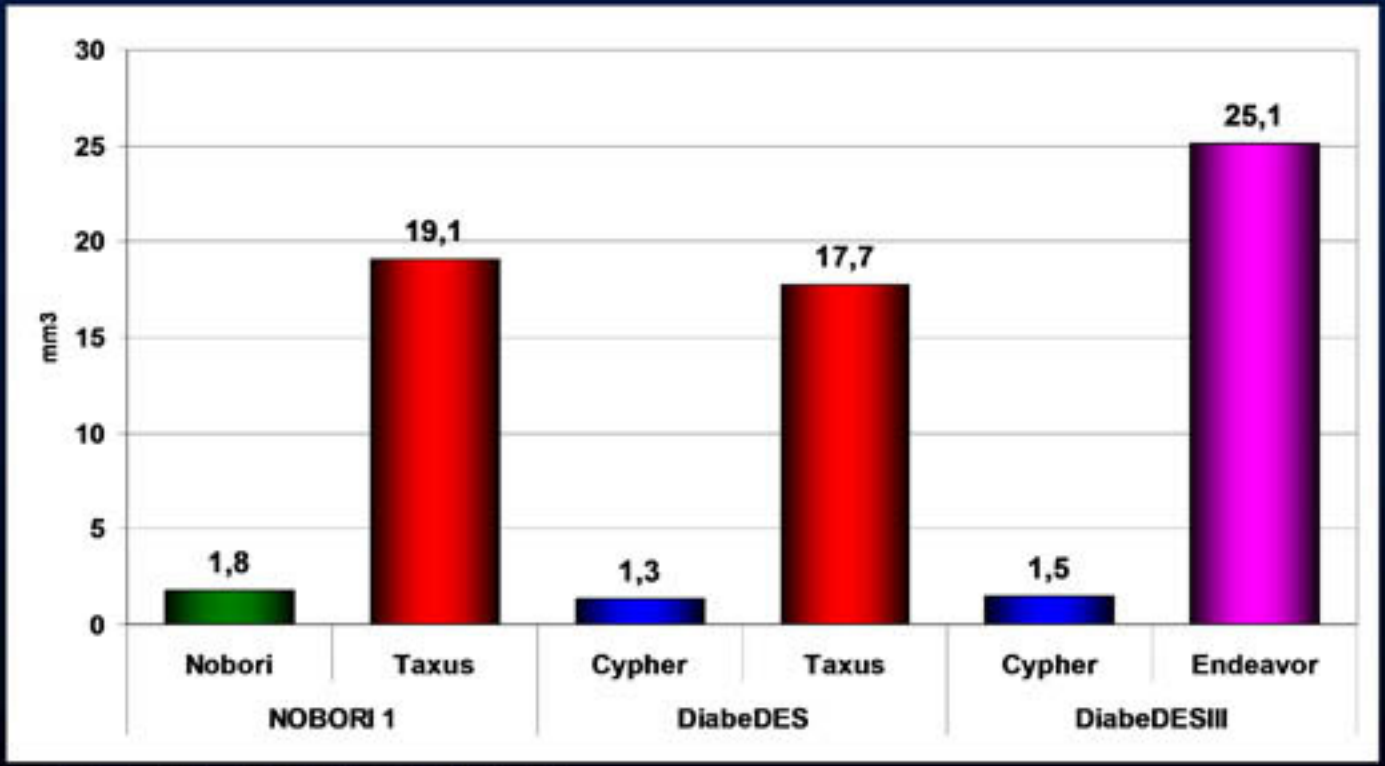
Nobori vs other DES in different patient subsets

Efficacy Patients with Diabetes
Late Loss at 6-9 Months



* 6 Months

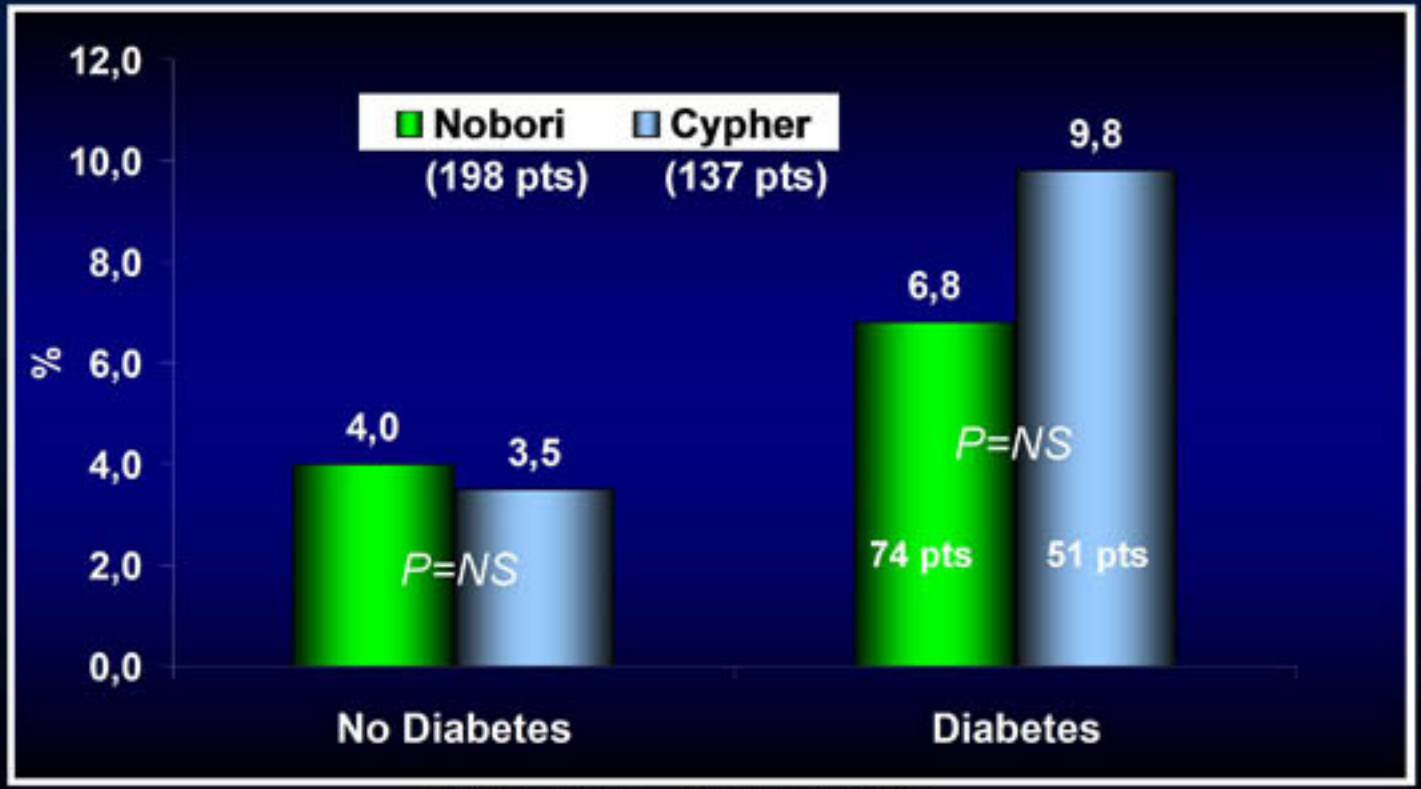
Efficacy –Patients with Diabetes Neointimal Hyperplasia Volume



Jensen L., et al. *Eur Heart J* 2008;
Jensen L. ESC 2009
Chevalier B. TCT 2009

No data for Xience/Promus available

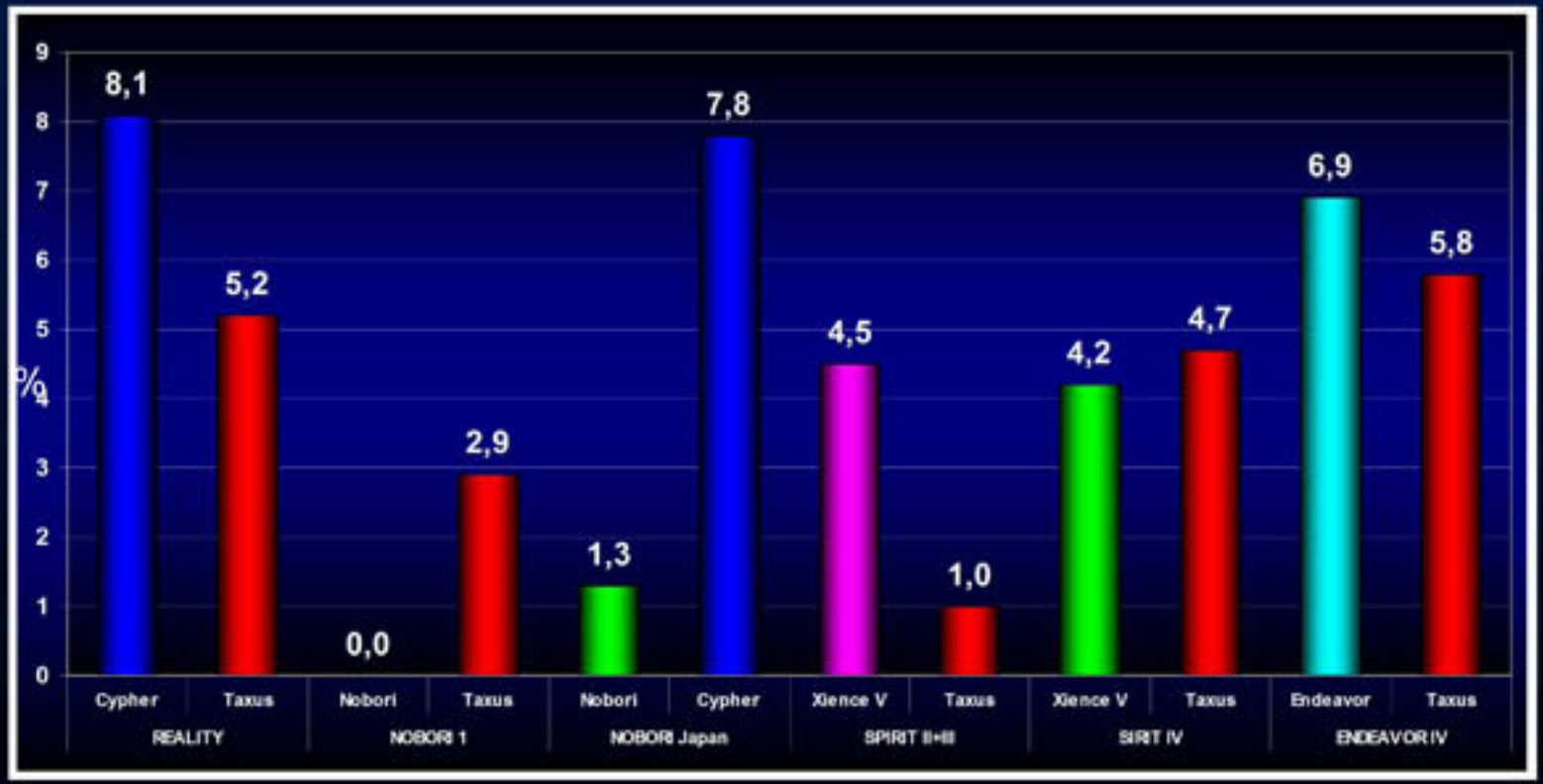
NOBORI Japan: 1 Year Impact of DM on MACE



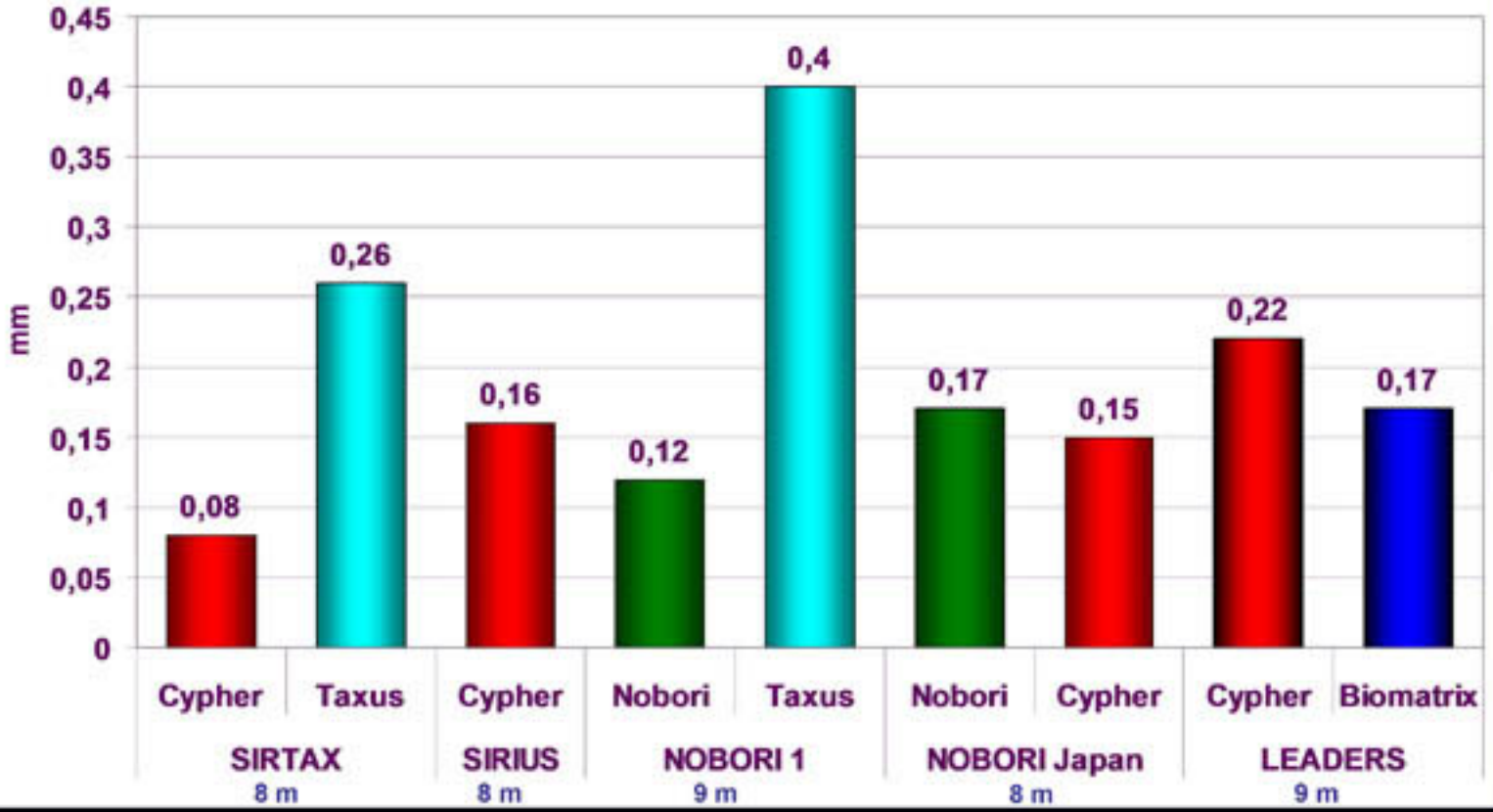
MACE=Cardiac Death, MI, TLR

S. Saito; PCR 2010

TLR in Patients with Diabetes Randomized Trials Different DES

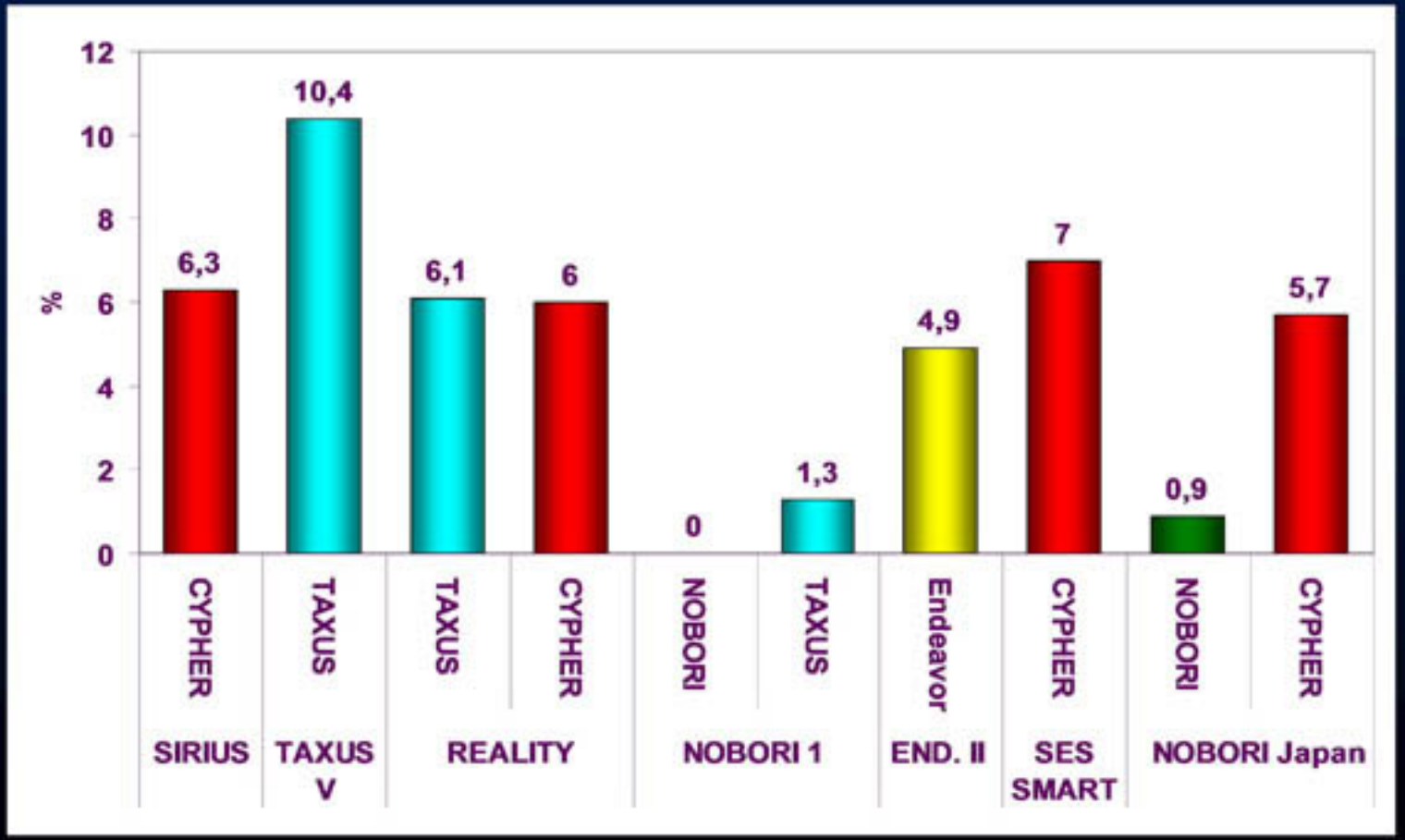


Late Loss (mm) in vessels ≤ 2.75mm DES RCT



Ref:Togni et al. JACC Vol. 50, No. 12, 2006; Moses J et al. N Engl J Med. 2003 Oct 2;349(14):1315-23
S. Saitou PCR 2010; Joanna J. Wykrzykowska, JACC vol 2 861-870

Clinical Efficacy in RCT
TLR up to 1 year in Vessels ≤ 2.75mm



ref S. Moses J et al. N Engl J Med. 2003 Oct 2;349(14):1315-2, G Stone, TCT 2005; M-C Maurice JAMA, February 22, 2006Vol 295, Saitou PCR 2010;

NOBORI Clinical Outcomes Conclusions

- Long term clinical evidence for Nobori stent from early trials shows sustained efficacy and excellent safety confirmed by:
  - ⇒ **Very Low Late Loss**
  - ⇒ **Low rate of:**
    - Restenosis
    - TLR
    - Overall MACE
  - ⇒**No late or Very Late stent thrombosis**
  - ⇒**Nobori DES also showed excellent performance in diabetics patients & small vessel lesions**