Safety and Efficacy of Latest Generation Drug-Eluting Stents and Balloons

Results from Clinical Trials

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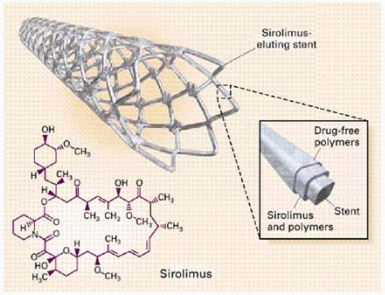
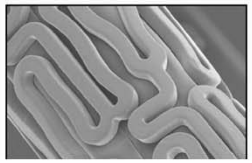
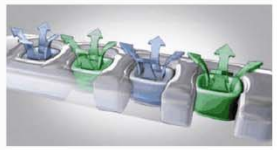
Latest Generation

Drug-Eluting Stents

2002	2004	2006	2008	2010
Cypher	Taxus (Liberte)	Pico Elite	Xience V /	Xience Prime LL, SV
Taxus (Express)	Endeavor	Coroflex Please	Promus	Promus Element
			Endeavor	Biomatrix
			Resolute	Nobori
				Nevo
				Genous







Categories of Latest DES

I. New Metallic DES with durable polymers
II. DES with biodegradable polymers
III. Non-polymeric DES
IV. Stents with novel coatings
V. Biodegradable stents
* Drug-cated balloons

Garg S, Serruys PW. *JACC 2010;56(10 Suppl):S43-78*.

New Metallic DES with durable polymers

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1. New polymer technology: Endeavor Resolute
2. New antiproliferative agents: Elixir DESyne novolimus-eluting stent (NES)
3. New metal stent platforms: platinum chromium Element stent platform

Stent	Drug (Dosage)	Stent Platform	Study (No. of Patients)	In-Stent Late Loss, mm (vs. Control)	Binary Restenosis, % (vs. Control)
Endeavor ESOLUTE	Zotarolimus (10 g/mm)	Cobalt chromium	All-Comers (n=2300)	0.22	1.0
Elixir DESyne	Novolimus (5 g/mm)	Cobalt chromium	FIM (n=15)	0.31	0.0
TAXUS Element	Paclitaxel (1 g/mm2)	Platinum chromium	RCT (Element PES=942) vs. (Express PES=320)	0.34 vs. 0.26*	—
PROMUS Element	Everolimus (1 g/mm2)	Platinum chromium	PLATINUM	—	—

Garg S, Serruys PW. *JACC 2010;56(10 Suppl):S43-78.*

Endeavor Resolute

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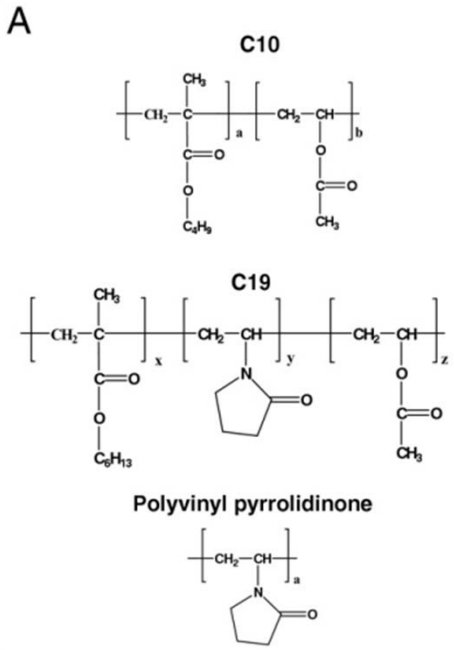
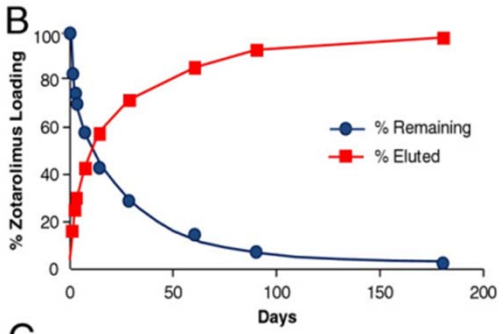
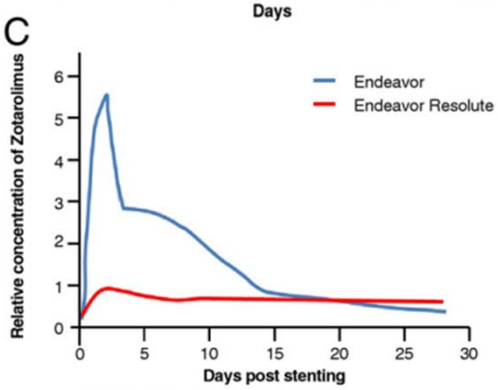
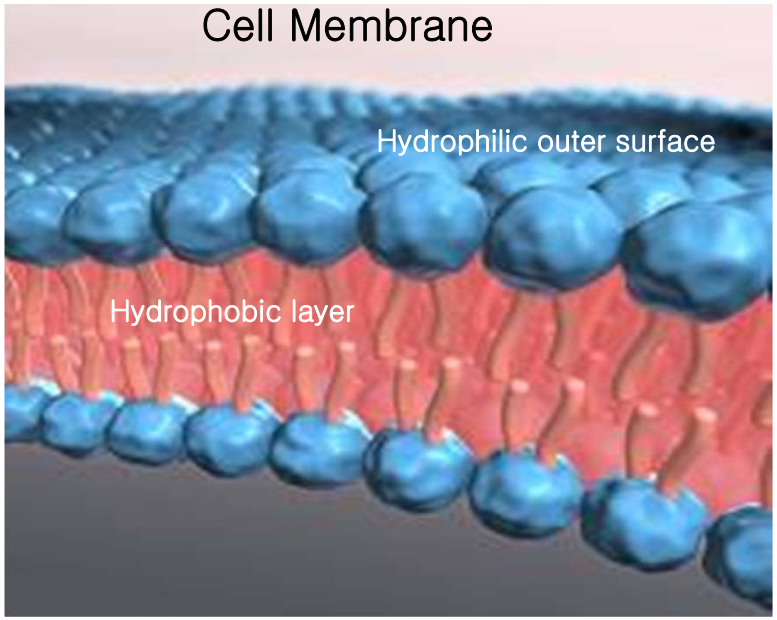




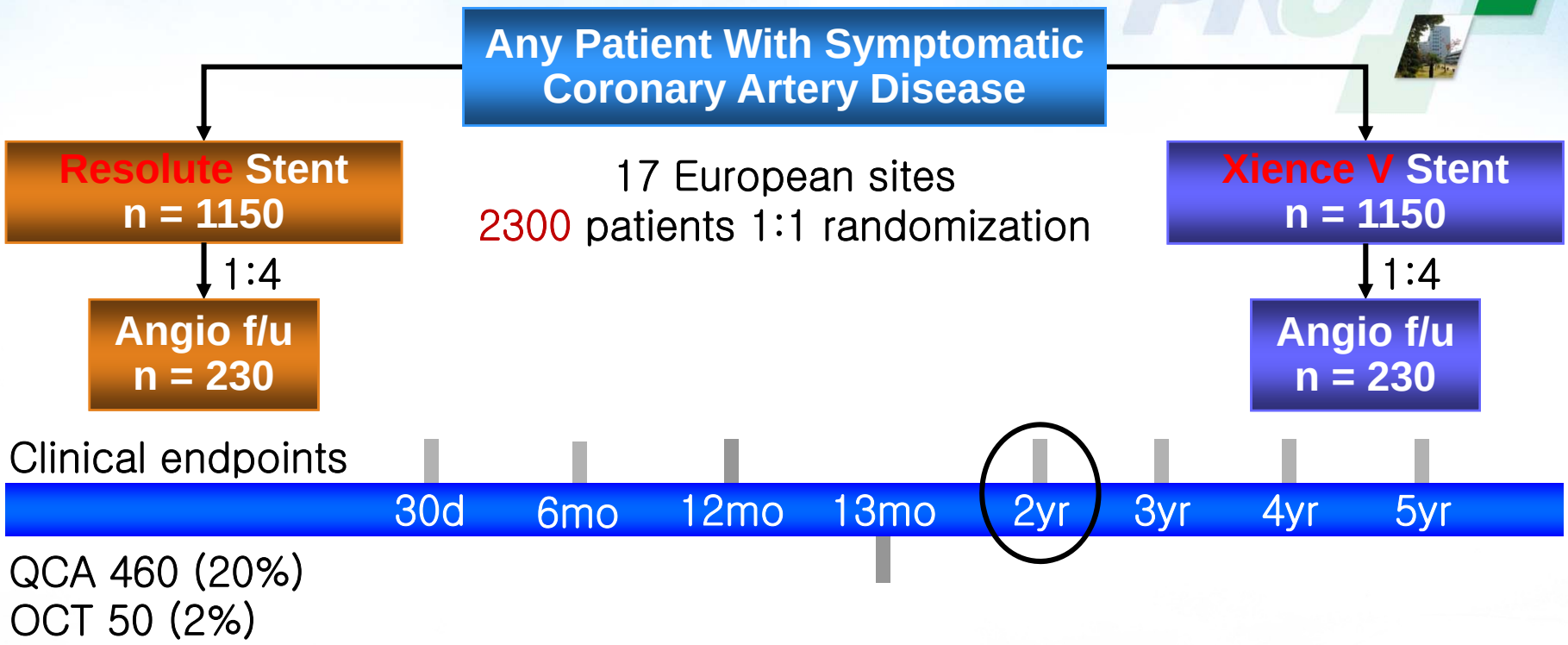




- BioLinx polymer → delayed drug release
  - 85% of the zotarolimus is released within 60 days
  - The remainder being released within 180 days

New Polymer

RESOLUTE All Comers Trial Design



Primary Endpoint:

- Target Lesion Failure (composite of cardiac death, target vessel MI & clinically driven TLR) at 12mo

Secondary Endpoints:

- Clinical: Patient composite of any death, any MI, & any repeat revascularisation
- QCA (powered): 13-month in-stent % diameter stenosis
- QCA: % diameter stenosis, late loss, and binary restenosis

Drug Therapy: ASA and clopidogrel/ticlopidine ≥ 6mo (per guidelines)

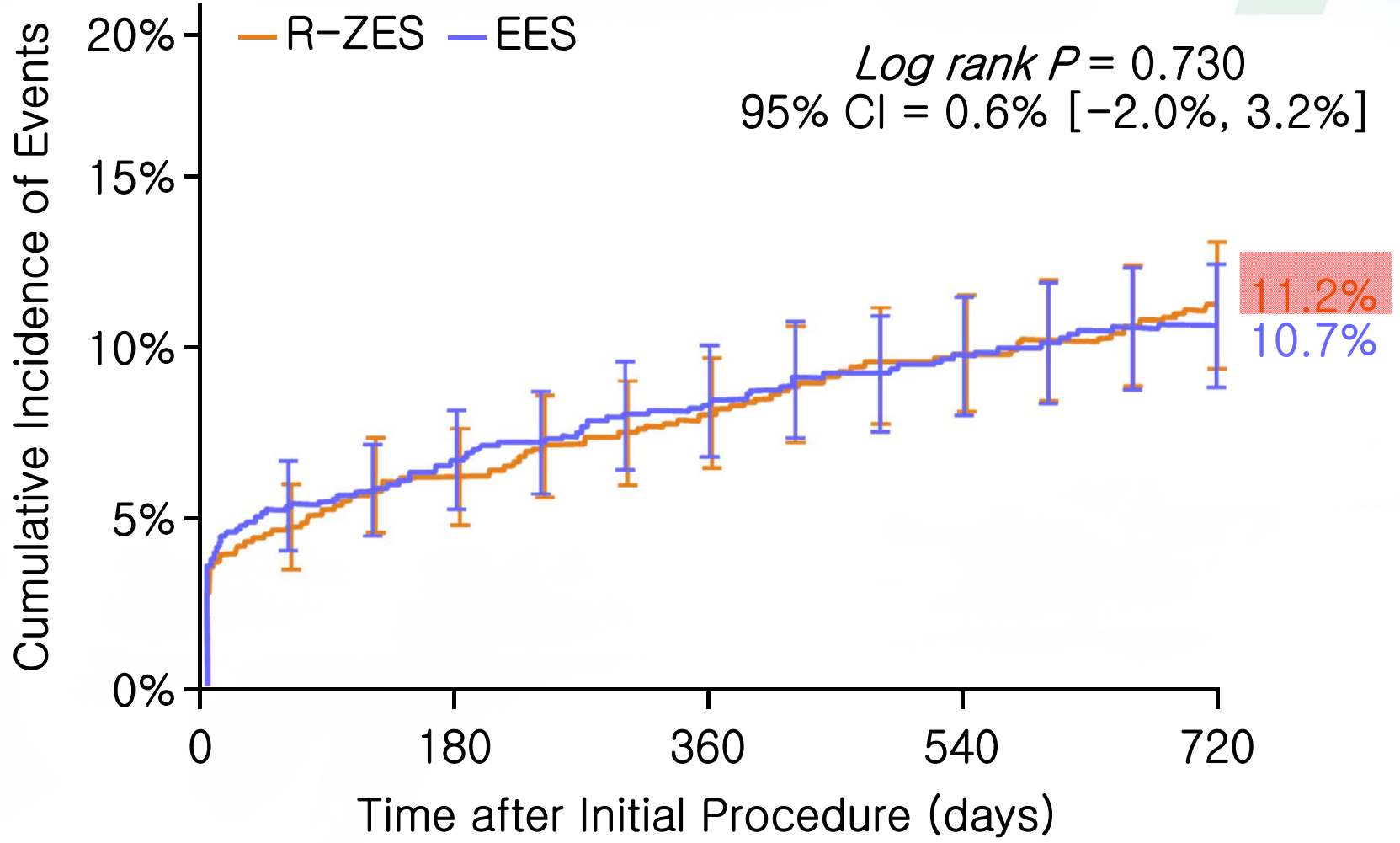
Presented at ACC 2011

RESOLUTE All Comers Trial

New Polymer

Target Lesion Failure through 2 Years

(Cardiac Death, TV MI and Clinically Driven TLR)



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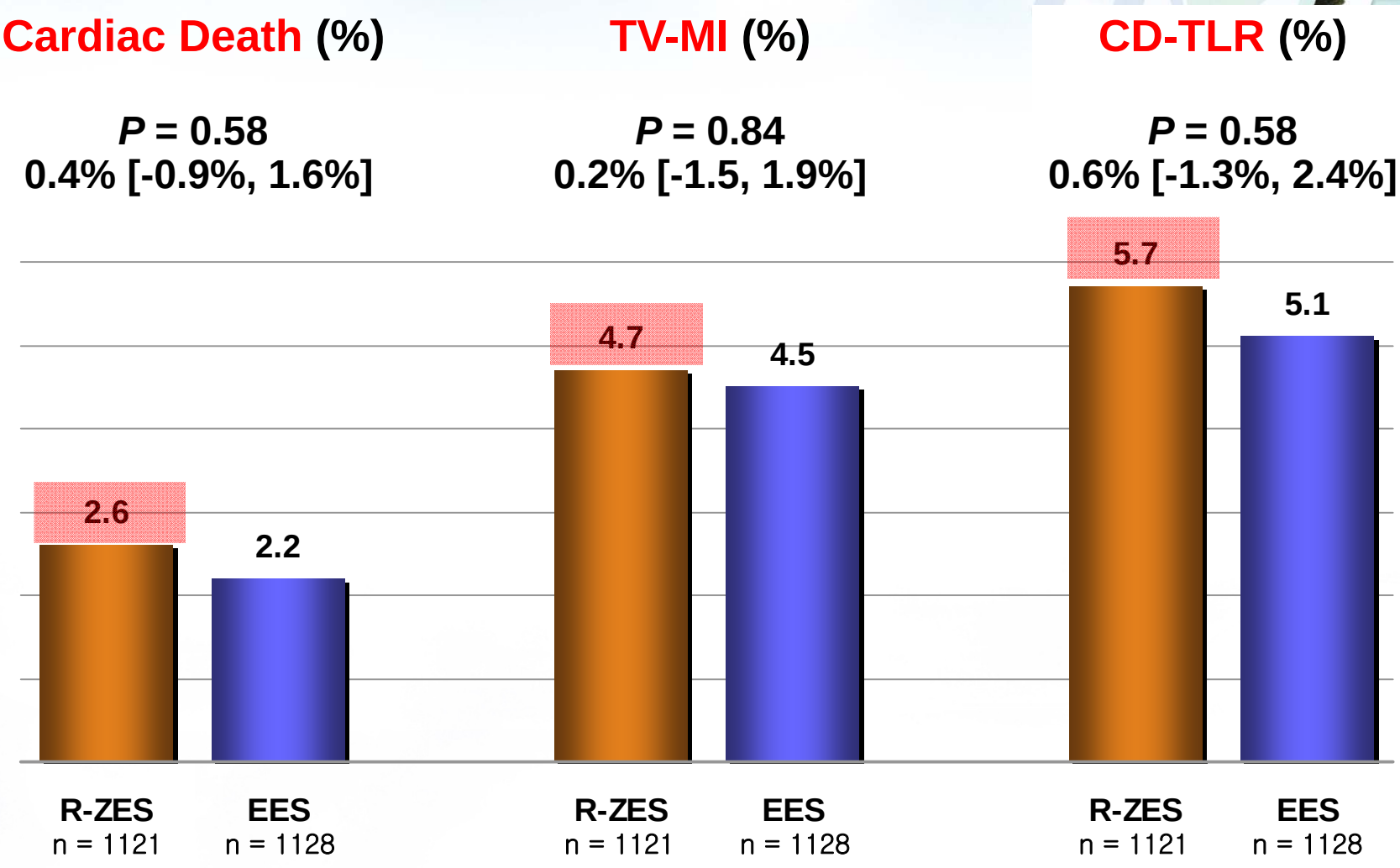
RESOLUTE All Comers Trial

New Polymer

Components of TLF



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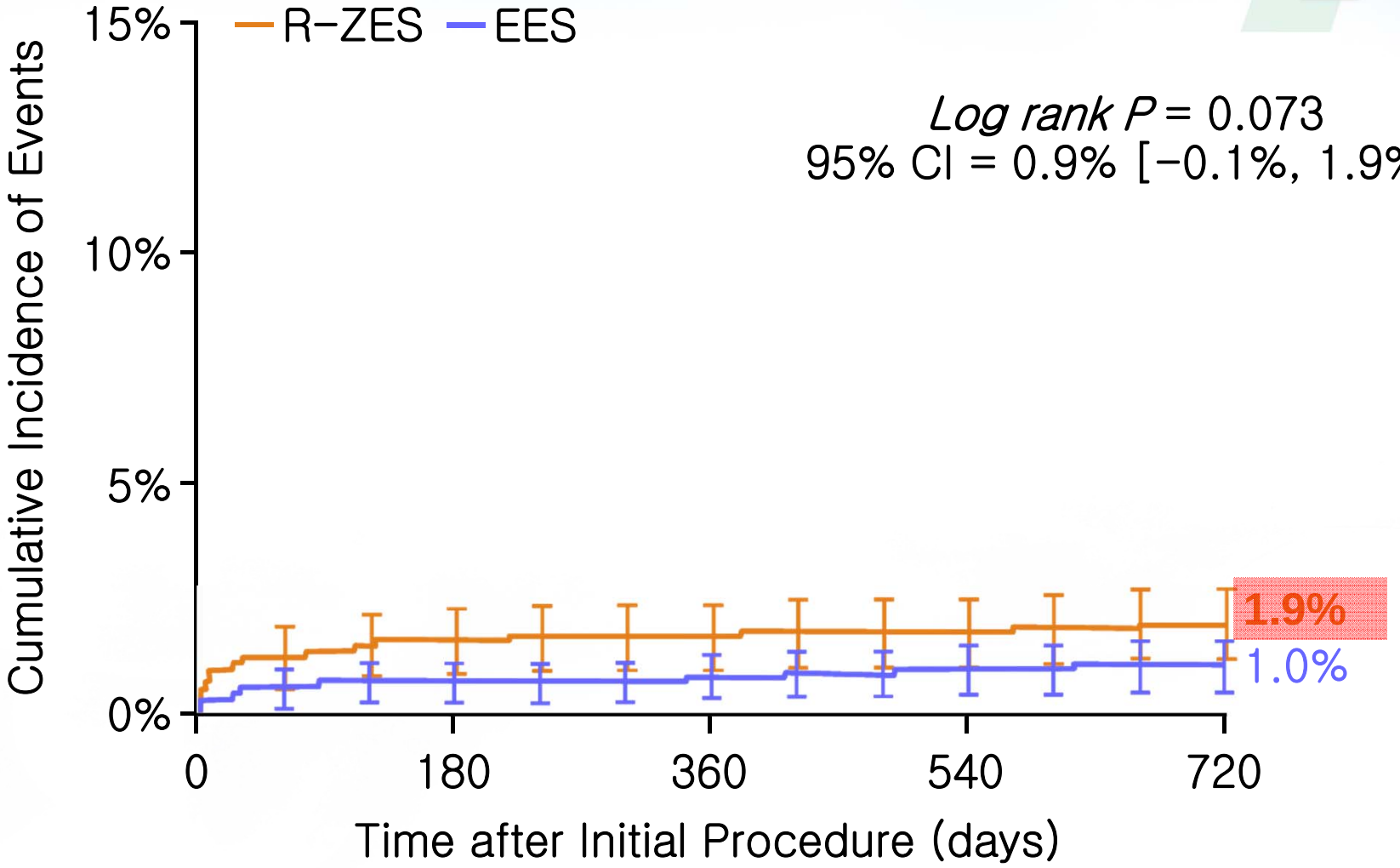
RESOLUTE All Comers Trial

Stent Thrombosis (ARC Def/Prob) through 2 Years

New Polymer



Presented at ACC 2011

New Polymer

Conclusion

- Both the Resolute ZES and the Xience V EES were associated with a relatively low frequency of adverse events even in this complex, all-comers patient population through 2 years

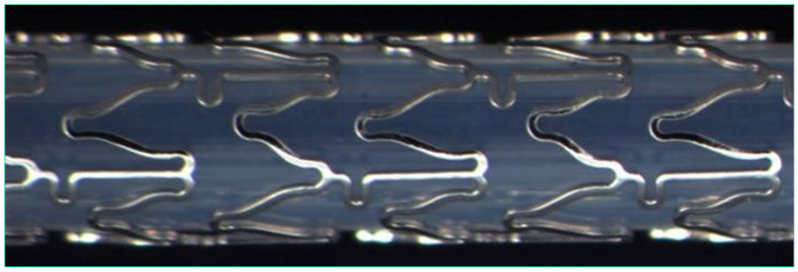
- The new generation Resolute ZES remained clinically equivalent to the Xience V EES in this predominantly complex patient population through 2 years

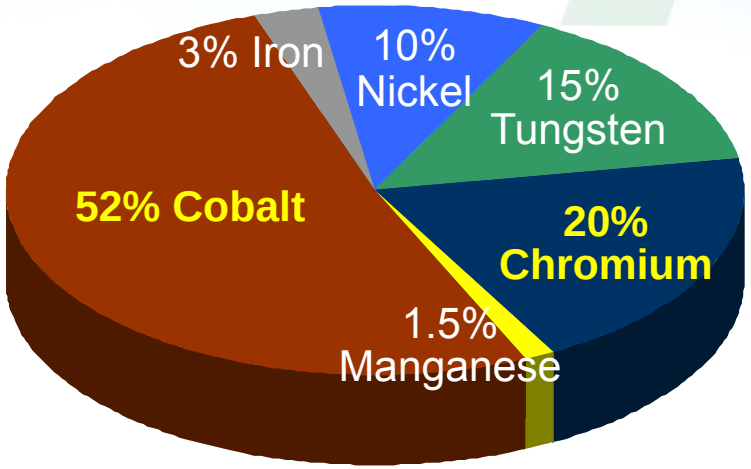
New metal stent platforms: platinum chromium Element stent platform

Platinum Chromium Element Platform

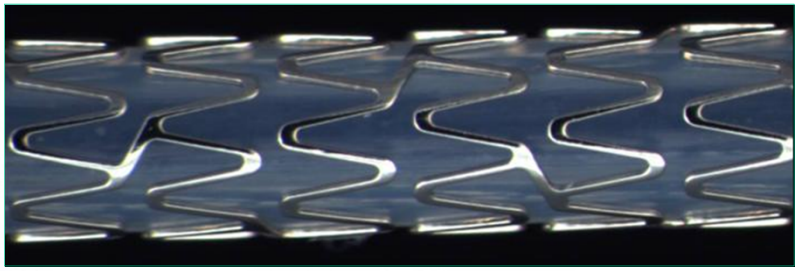
Everolimus concentration: 100 ug/cm^2
Polymer: PBMA & PVDF-HFP (7μm thickness)

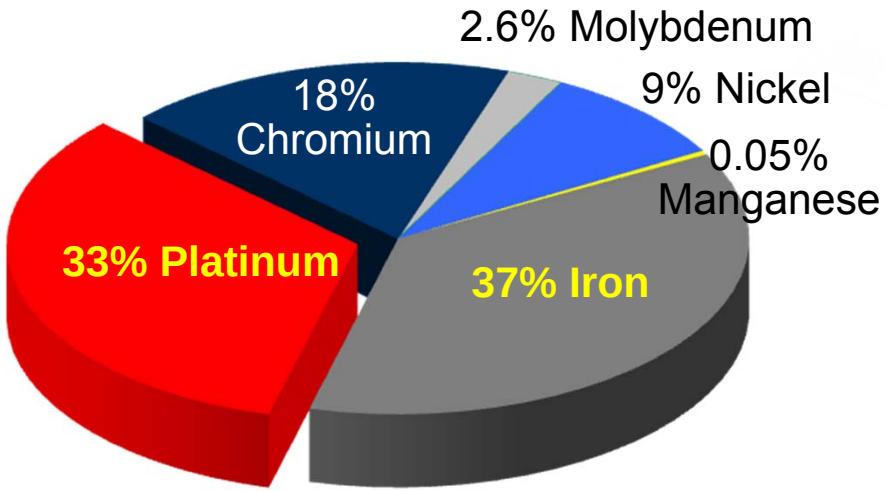
XIENCE V / PROMUS (CoCr-EES)





PROMUS Element (PtCr-EES)



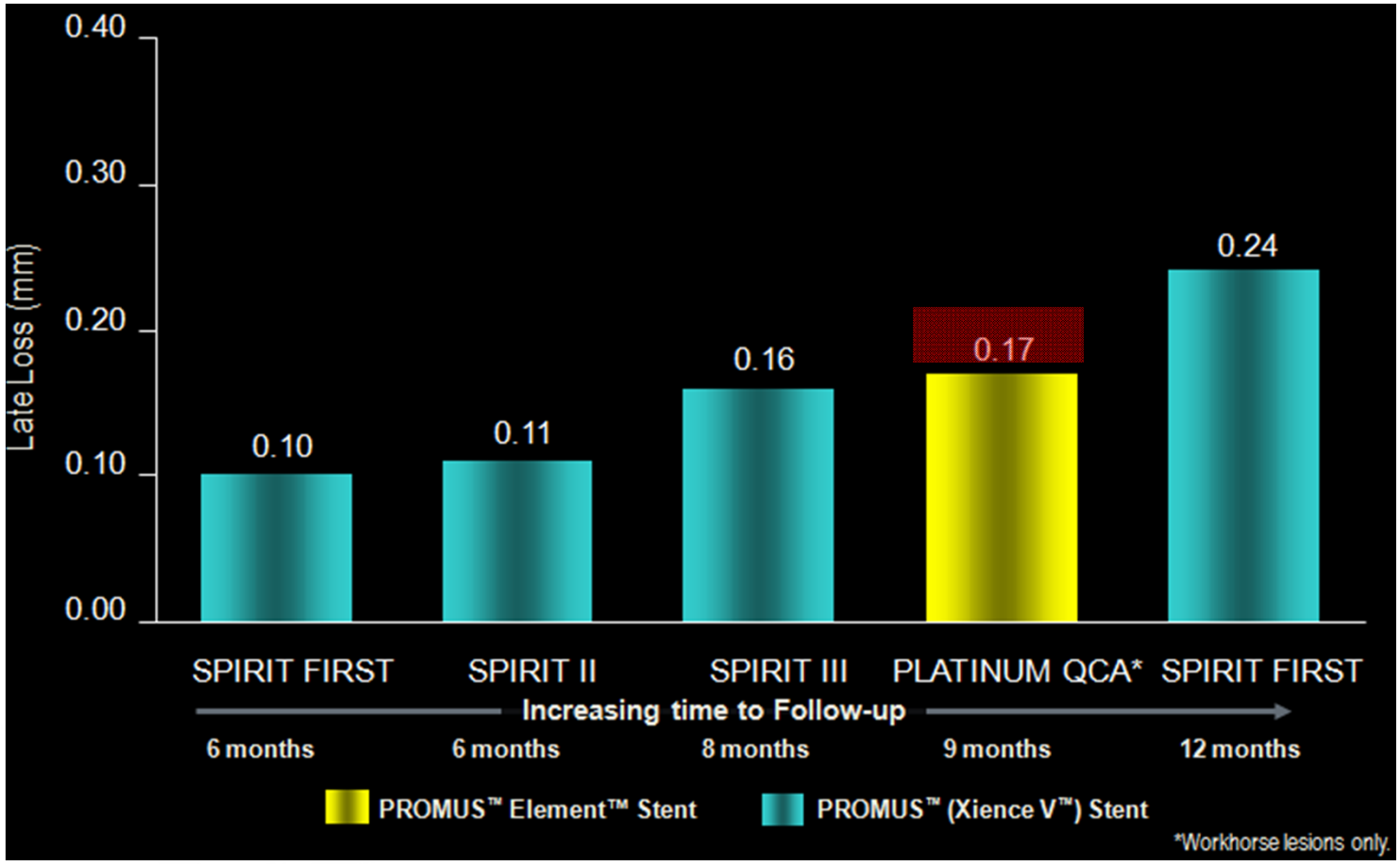


PBMA=poly (n-butyl methacrylate) (primer layer); PVDF-HFP=poly (vinylidene fluoride-co-hexafluoropropylene) (drug matrix layer)

PLATINUM QCA – in perspective

PROMUS Element EES

In-Stent Late Loss in PLATINUM and SPIRIT Trials



PLATINUM Clinical program

PROMUS Element Stent in de novo lesions

	PLATINUM WH, SV, LL			PLATINUM QCA
Trial/Subtrial	Workhorse	Small Vessel	Long Lesion	
# of Patients	1,531	94	102	100
# of Sites	160 (Worldwide)	20 (US & Japan)	20 (US & Japan)	10 (IC)
Trial Design	1:1 Randomized Single Blind	Single Arm	Single Arm	Single Arm
Success Criteria	Non-inferiority	Non-inferiority	Non-inferiority	N/A
Test Stent	PROMUS Element Stent			PROMUS Element Stent
Control Stent	PROMUS Stent	Historical PROMUS Stent Data from SPIRIT Trials		N/A
Primary Endpoint	12mo TLF	12mo TLF	12mo TLF	30 day cardiac events

PLATINUM Study Algorithm

Patients with 1 or 2 *de novo* native coronary artery target lesions

RVD ≥2.5 to ≤4.25; Lesion length ≤24 mm

Peri-proc: ASA ≥300 mg, clopidogrel ≥300 mg load unless on chronic Rx

Randomized 1:1

Stratified by diabetes, intention to treat 1 vs. 2 target lesions, & study site

CoCr-EES (N=762)	PtCr-EES (N=768)

ASA indefinitely, thienopyridine ≥6 mos (≥12 mos if not high risk for bleeding)

Clinical f/u only: 1, 6, 12, 18 months then yearly for 2-5 years

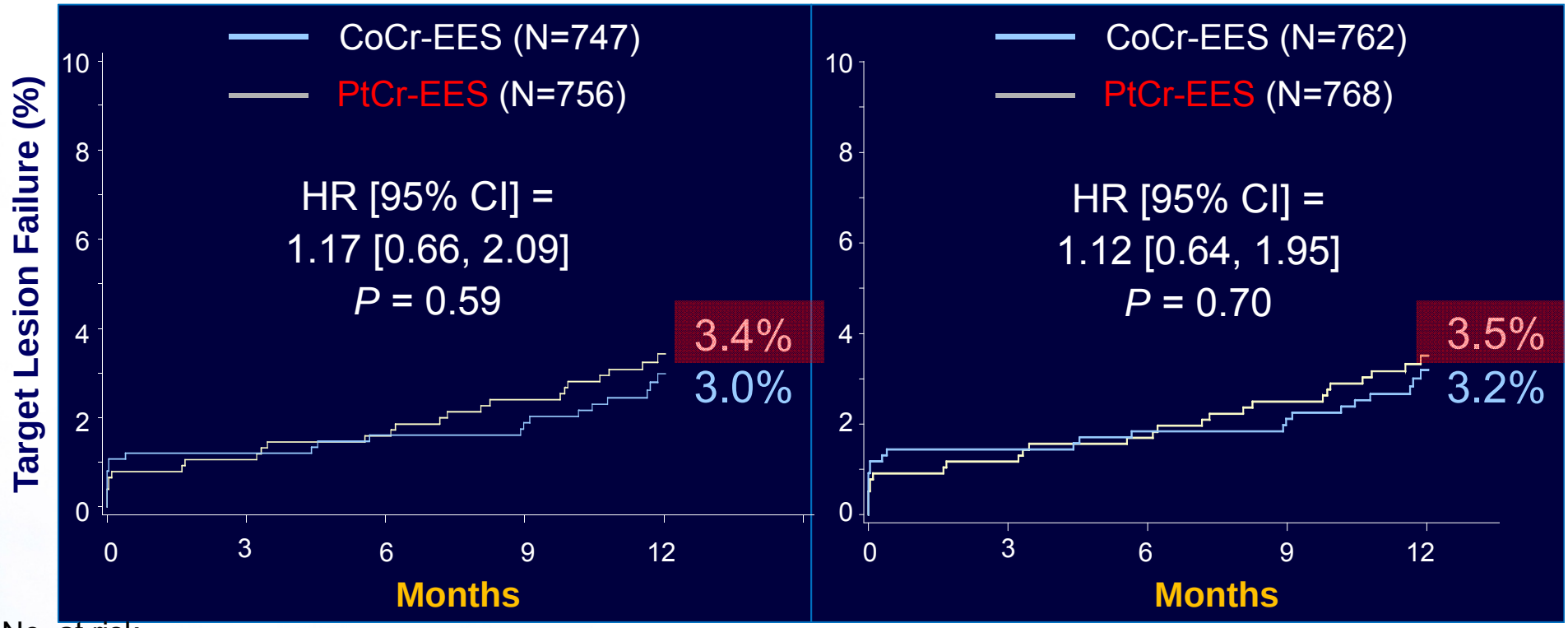
Presented at ACC 2011

PLATINUM Study

Platinum Chromium Element

Target Lesion Failure

Time-to-event analysis



No. at risk

CoCr EES	747	735	731	723	707	762	747	743	735	718
PtCr EES	756	745	740	734	719	768	756	751	745	730

Presented at ACC 2011

PLATINUM Study

Platinum Chromium Element

TLF Components

12 Months

	Per Protocol			Intention-to-Treat		
	CoCr-EES (N=747)	PtCr-EES (N=756)	*P* value	CoCr-EES (N=762)	PtCr-EES (N=768)	*P* value
TLF	2.9%	3.4%	0.60	3.2%	3.5%	0.72
Cardiac death -TV	0.4%	0.8%	0.51	0.4%	0.8%	0.51
MI - TV	1.4%	0.7%	0.18	1.6%	0.8%	0.14
ID-TLR	1.8%	1.9%	0.89	1.9%	1.9%	0.96

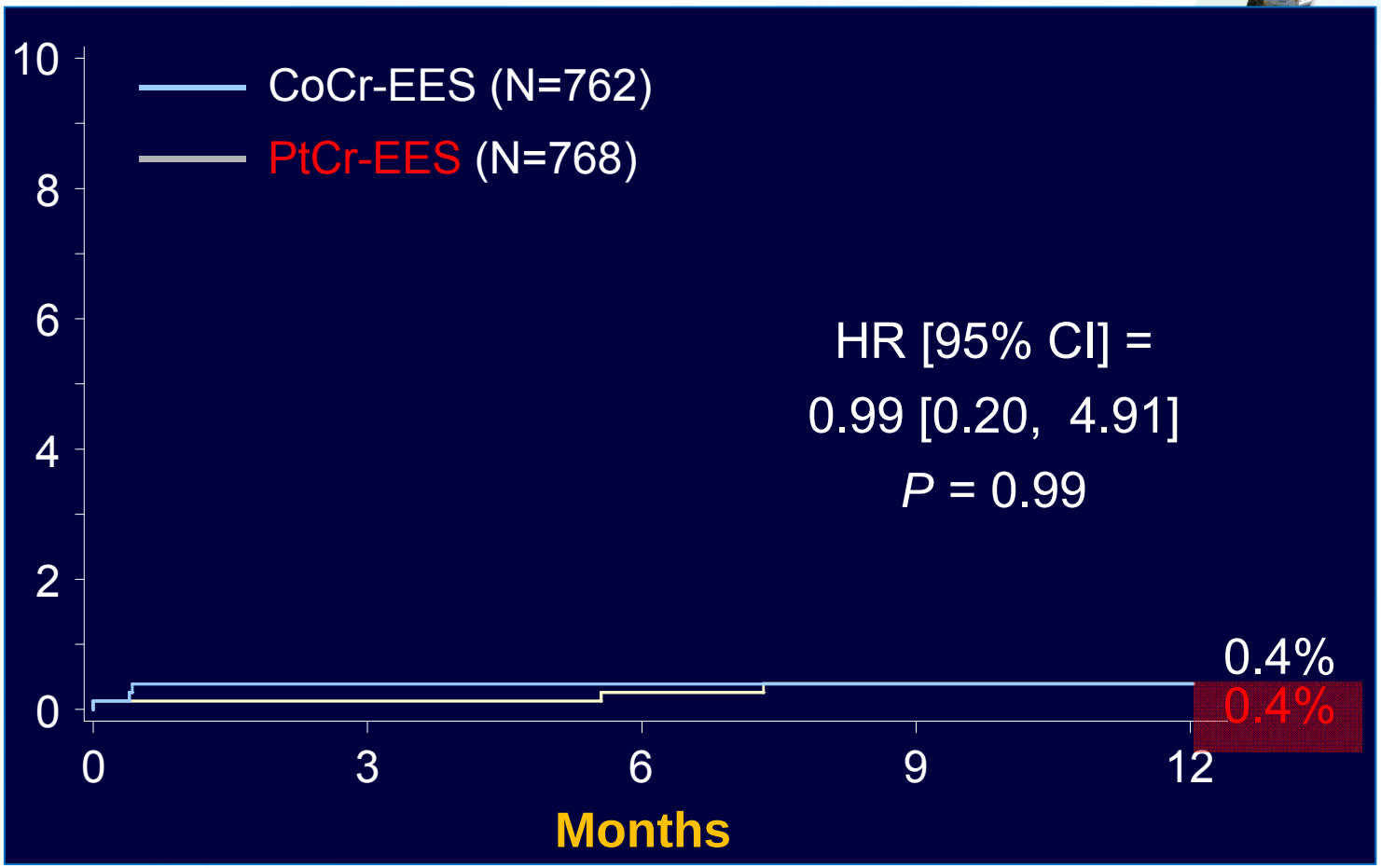
Presented at ACC 2011

PLATINUM Study

Platinum Chromium Element

Stent Thrombosis – ARC Def/Prob

12 Months – Intent-to-Treat



No. at risk					
CoCr-EES	762	755	752	745	728
PtCr-EES	768	761	758	752	741

Presented at ACC 2011

* All were definite ST

Conclusions

- A novel PtCr-EES has been developed, which has been shown to be **noninferior** to the predicate CoCr-EES for TLF, with non-significant differences in measures of safety and efficacy demonstrated through 12-month follow-up after PCI

PERSEUS Clinical Program

TAXUS Element stent

- Incorporates a platinum chromium metal alloy and thin strut design is:
  - Comparable in efficacy to the TAXUS Express stent in workhorse lesions
  - Superior in efficacy to the bare metal Express stent in small caliber vessels
- No clinical safety concerns regarding the novel platinum chromium alloy or Element stent design are evident

Categories of Latest DES

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* Drug-coated balloons

DES with Biodegradable Polymer

I. New Metallic DES with durable polymers
II. DES with biodegradable polymers
III. Non-polymeric DES
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Stent (Manufacturer)	Drug (Dosage)	Drug Release (%), Time (days)	Stent Platform	Strut/Max Coating Thickness, μm	Polymer Type (Duration of Biodegradation, Months)	Study (No. of Patients)	In-Stent Late Loss, mm (vs. Control)	Re (v
Supralimus (Sahajanand Medical)	Sirolimus (125 μg/19 mm)	50%, 9–11	SS	80/4–5	PLLA PLGA, PLC, PVP (7)	FIM (n = 100)	0.09	
Excel stent (JW Medical System)	Sirolimus (195–376 μg)	NA	SS	119/15	PLA (6–9)	Registry (n = 2,077)	0.21	
NEVO (Cordis)	Sirolimus (166 μg/17 mm)	80%, 30	CoCr	99	Reservoirs of PLGA (3)	RCT (Nevo n =202 vs. PES n = 192)	0.13 vs. 0.36†	
BioMatrix (Biosensors)	Biolimus A9 (15.6 μg/mm)	45%, 30	SS	112/10‡	Abluminal PLA (6–9)	RCT (BES n = 857 vs. SES n = 850)	0.13 vs. 0.19	20.
NOBORI (Terumo)	Biolimus A9 (15.6 μg/mm)	45%, 30	SS	112/10‡	Abluminal PLA (6–9)	RCT (BES n = 153 vs. PES n = 90)	0.11 vs. 0.32*	
Axxess (Devax Inc)	olimus A9 (22 μg/mm)	45%, 30	Nitinol	152/15‡	Abluminal PLA (6–9)	Registry (n = 302)	0.29 MB 0.29 SB	
XTENT (Xtent)	Biolimus A9 (15.6 μg/mm)	45%, 30	CoCr	NA	Abluminal PLA (6–9)	Registry (n = 100)	0.22	
SYNERGY (Boston Scientific)	Everolimus (LD 56 μg/20 mm) (SD 113 μg/20 mm)	50%, 60	PtCr	71/3 (LD) 4 (SD)	PLGA Rollcoat Abluminal (3)	RCT (SD vs. LD vs. PROMUS Element n = 291)	NA	
Combo (OrbusNeich)	EPC + sirolimus (5 μg/mm)	NA	SS	NA	Abluminal	NA	NA	
Elixir Myolimus (Elixir Medical)	Myolimus (3 μg/mm)	90%, 90	CoCr	80/<3	Abluminal PLA (6–9)	FIM (n = 15)	0.15	
Infinnium (Sahajanand)	Paclitaxel (122 μg/19 mm)	50%, 9–11	SS	80/4–5	PLLA PLGA, PLC PVP (7)	RCT (Infinn n = 111 vs. BMS n = 57)	0.54 vs. 0.90†	8
JACTAX Liberté (Boston Scientific)	Paclitaxel (9.2 μg/16 mm)	100%, 60	SS	97/<1‡	JAC polymer Abluminal (4)	FIM (n = 103)	0.33	

Garg S, Serruys PW. *JACC 2010;56(10 Suppl):S43-78.*

Biolimus-A9™ Eluting Stent

Biodegradable Polymer

I. New Metallic DES with durable polymers
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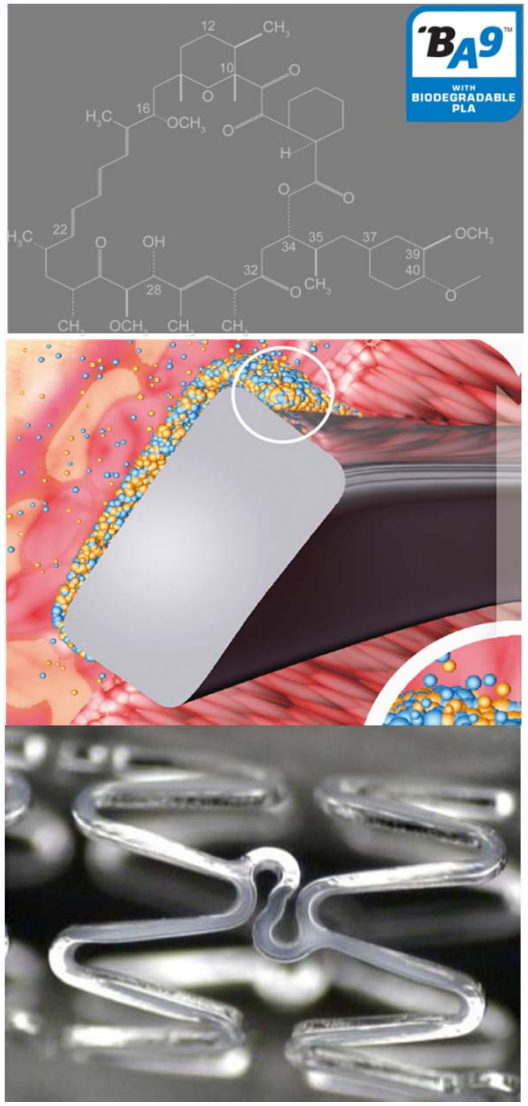
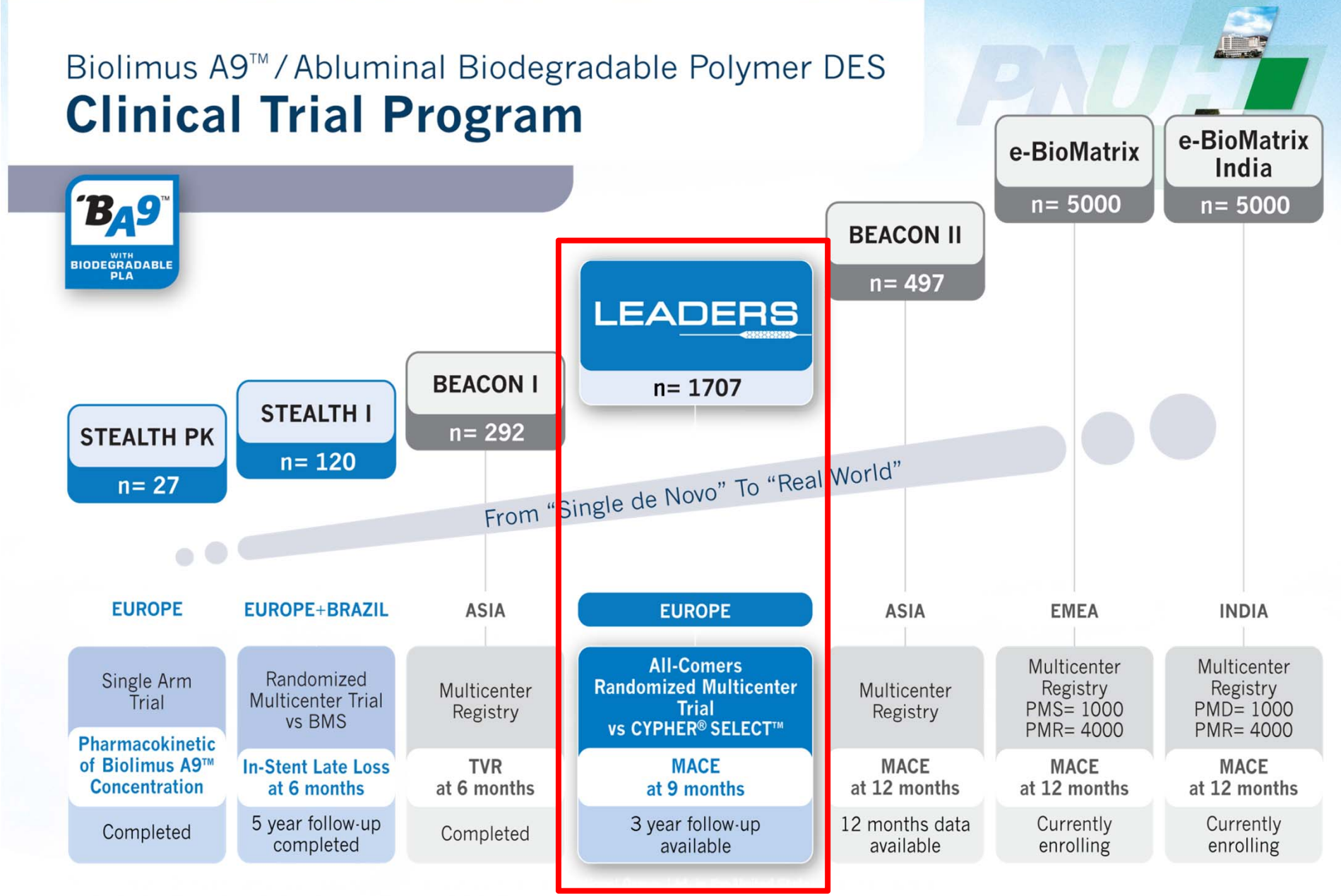
III. Non-polymeric DES
IV. Stents with novel coatings
V. Biodegradable stents
* Self-expanding stents
Dedicated bifurcation stents
Drug-eluting balloons



- Biolimus is a semi-synthetic sirolimus analogue with **10x higher lipophilicity** and similar potency as sirolimus.
- Biolimus is immersed at a concentration of 15.6 μg/mm into a biodegradable polymer, polylactic acid, and applied solely to **the abluminal stent surface** by a fully automated process.
- Biolimus is co-released with polylactic acid and completely desolves into carbon dioxide and water after a **6-9 months period**.
- The stainless steel stent platform has a strut thickness of 120 μm with a quadrature link design.

Biodegradable Polymer

Biolimus A9™ / Abluminal Biodegradable Polymer DES
Clinical Trial Program



Biodegradable Polymer

LEADERS: Trial Design

Stable and ACS Patients Undergoing PCI

Assessor-blind
1:1 Randomisation

N=1700 Patients

Biolimus Stent
BioMatrix Flex N=850

Sirolimus Stent
Cypher Select N=850

1:3 Randomisation

Clinical F/U
N=640

Angio F/U
N=210

Clinical F/U
N=640

Angio F/U
N=210

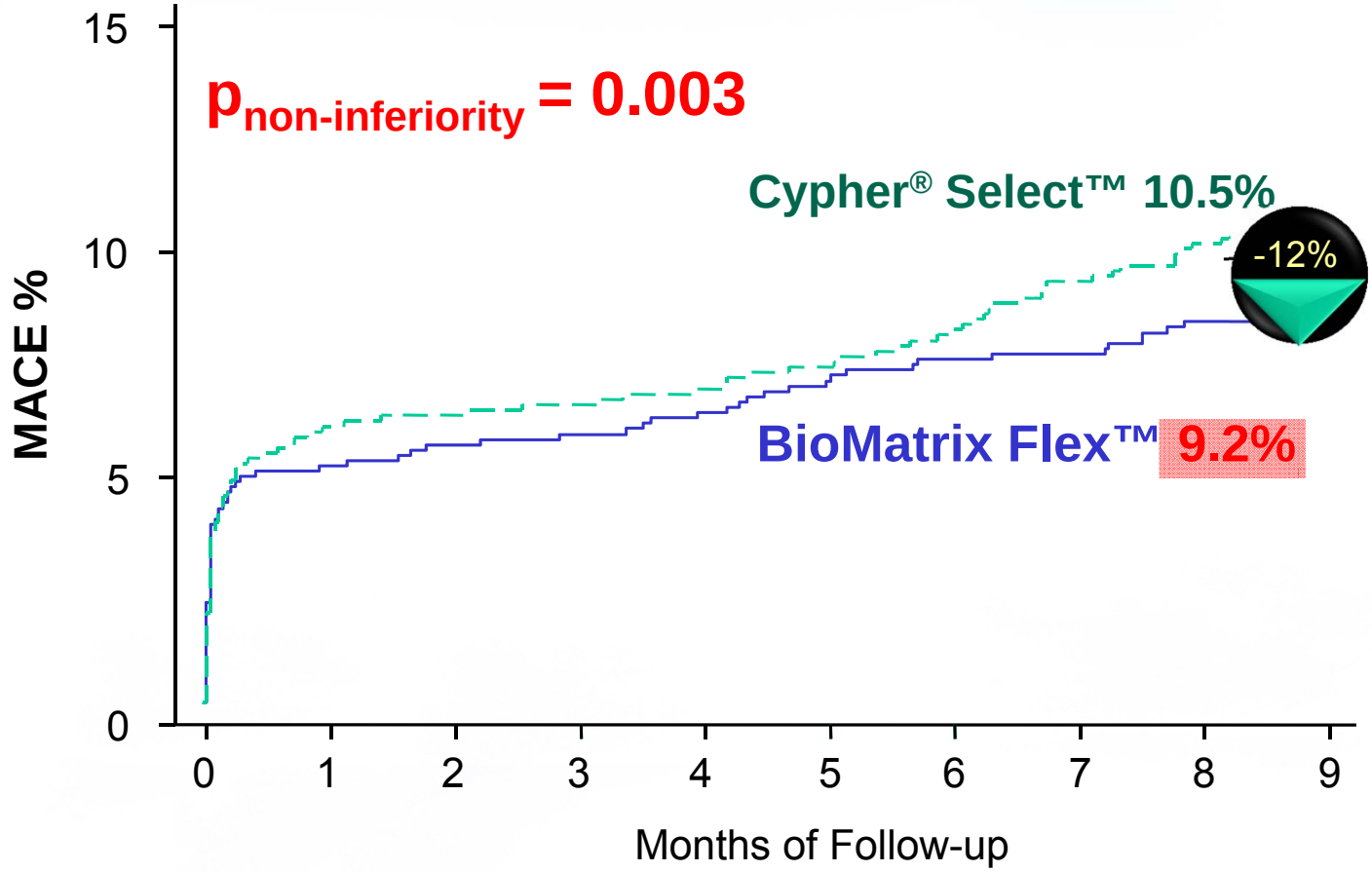
1º endpoint:	**CV death, MI, clinically-indicated TVR**
2º endpoints:	**Death, CV death, MI, TLR, TVR**
	Stent Thrombosis according to ARC
Angiographic study:	**In-stent % diameter stenosis**
	Late loss, binary restenosis

Biodegradable Polymer

LEADERS Trial

Primary Endpoint

MACE (Cardiac Death, MI and TVR) @ 9 Months



BioMatrix Flex™ reached its primary endpoint

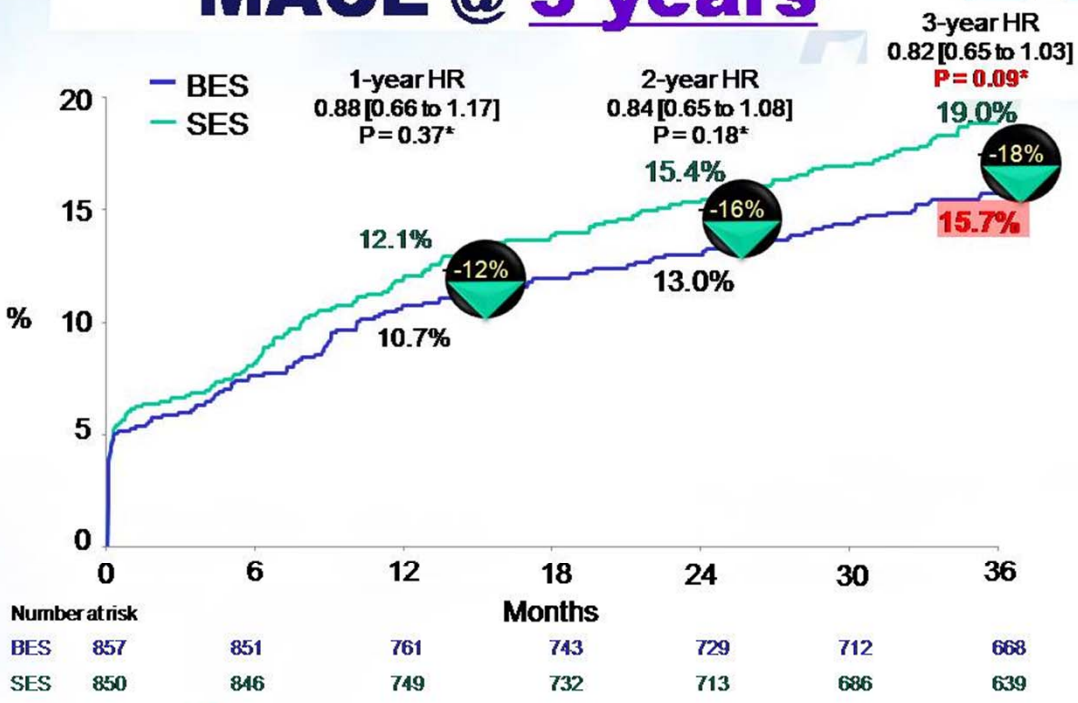
Windecker S. et al., The **Lancet 2008**; 372 No. 9644: 1163-1173

Biodegradable Polymer

LEADERS Trial

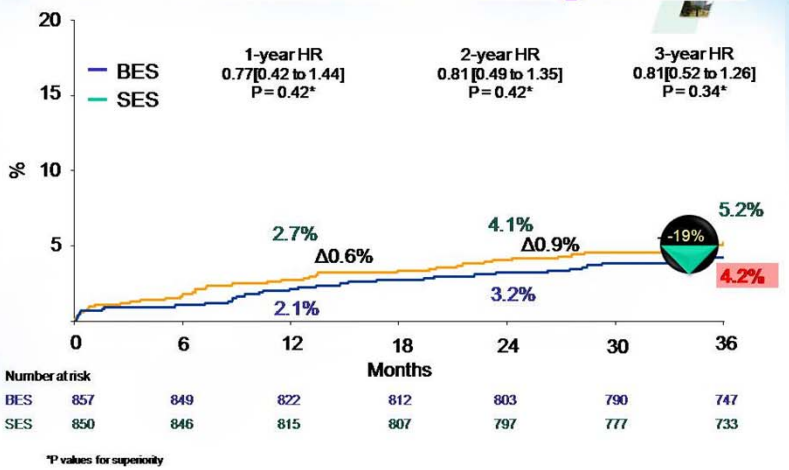
@ 3 years

MACE @ 3 years



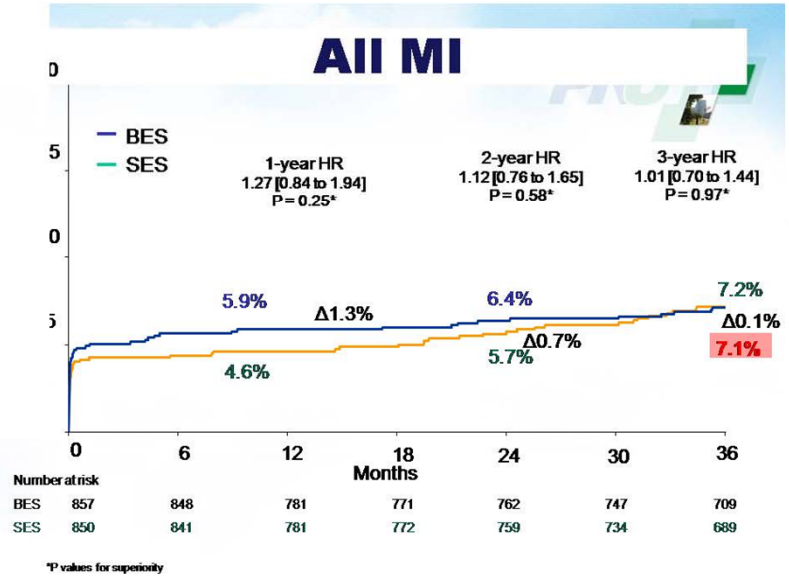
*P values for superiority
MACE = Cardiac Death, MI, or Clinically-Indicated TVR

Cardiac Death @ 3 years



*P values for superiority

All MI

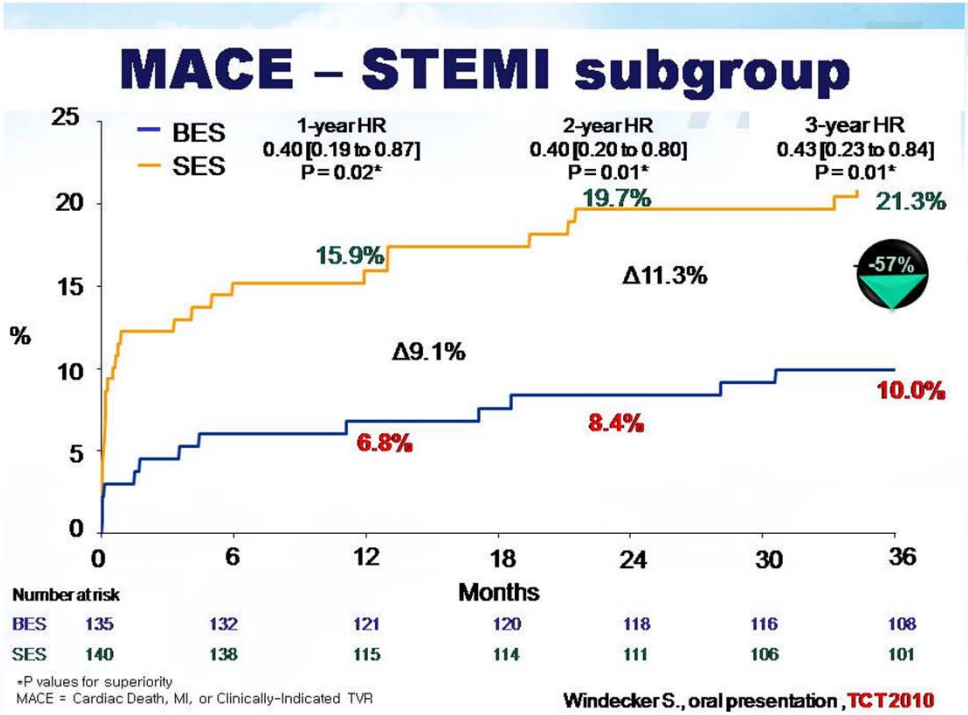


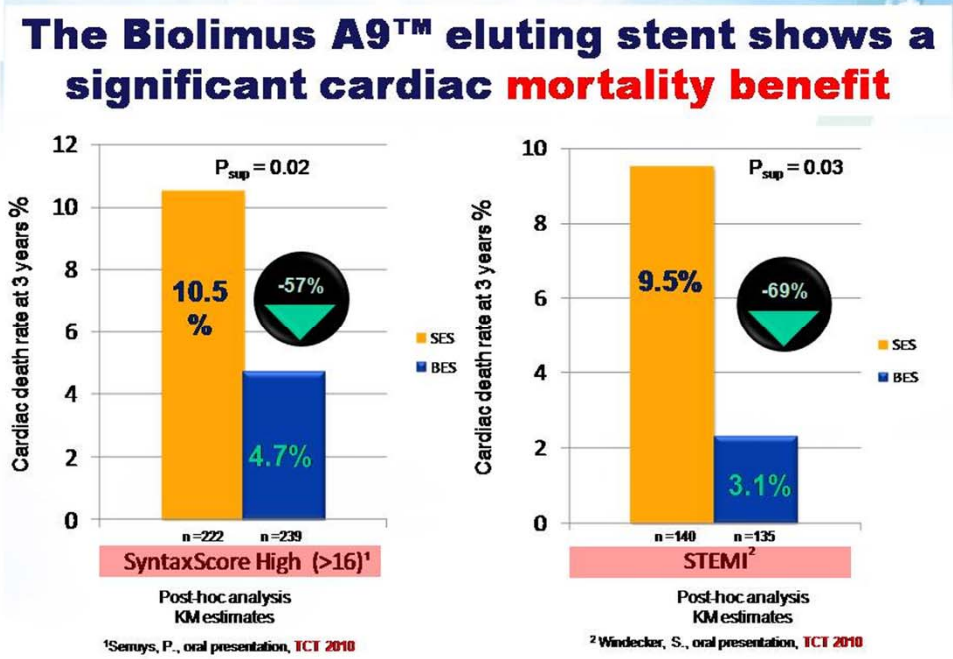
*P values for superiority

Serruys, P. W., oral presentation ,TCT 2010

LEADERS Trial

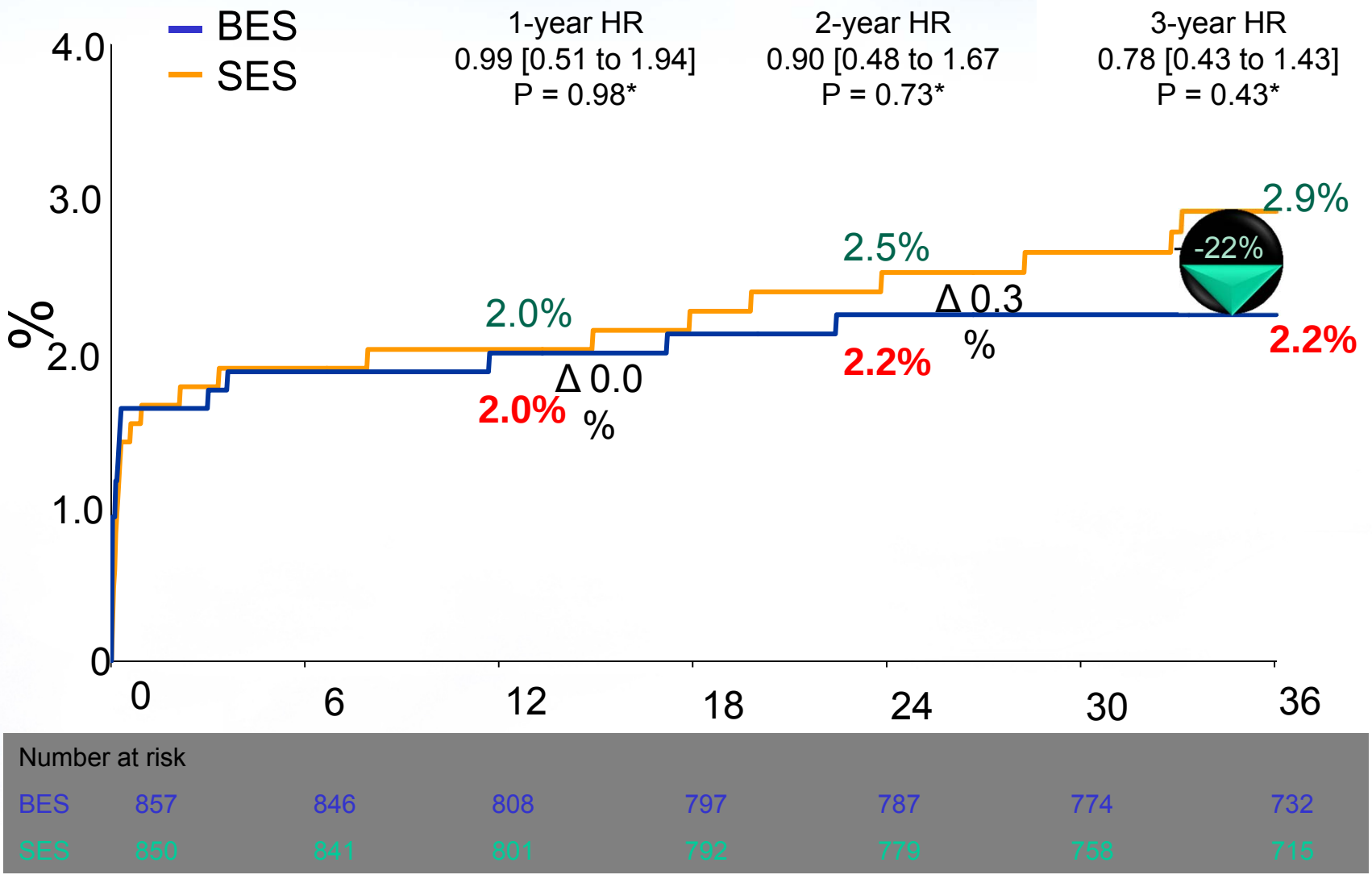
Biodegradable Polymer





Serruys, P. W., oral presentation ,TCT 2010

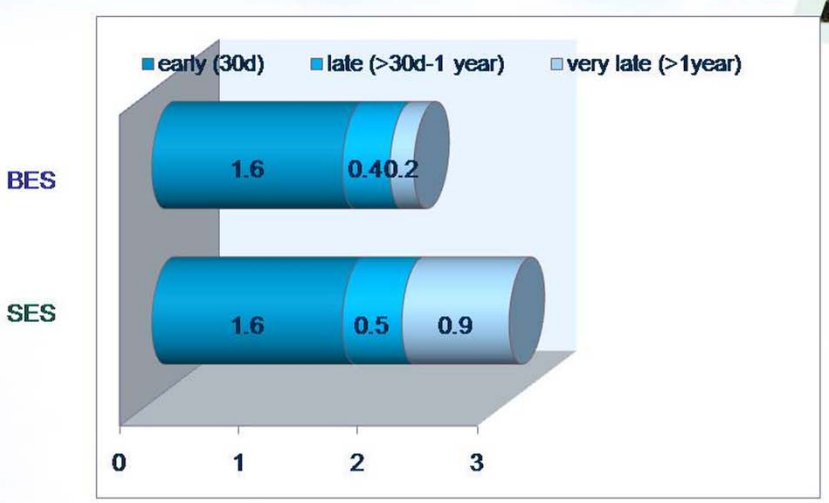
Definite ST through 3 years



*P values for superiority

Serruys, P. W., oral presentation, **TCT 2010**

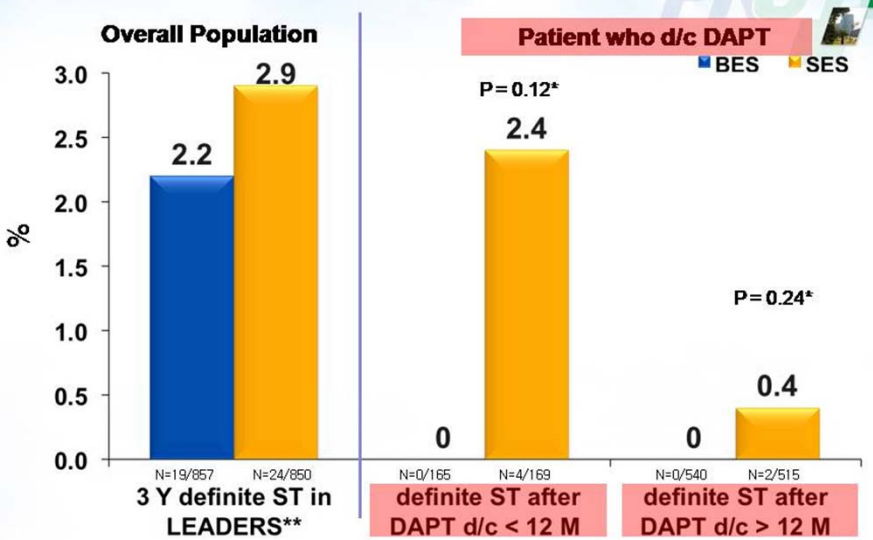
Definite Stent Thrombosis



Definite Stent Thrombosis %
According to ARC Definition

Serruys, P. W., oral presentation, TCT2010

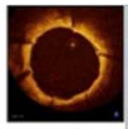
Effect of DAPT Discontinuation



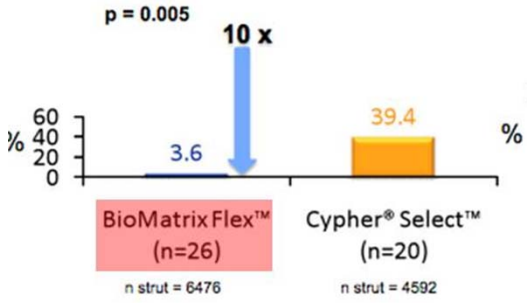
*P values for superiority (Fisher Exact Test)
** KM estimates

Serruys, P. W., oral presentation, TCT2010

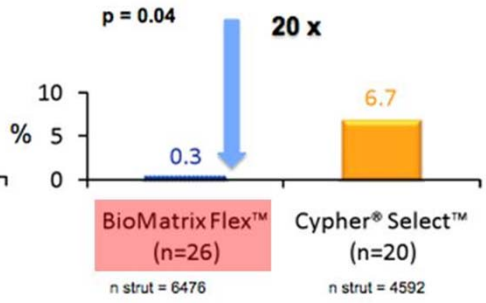
Superior Strut Coverage and Stent Apposition



Lesions with at least 5% uncovered struts



Lesions with at least 5% malapposed struts



The BioMatrix Flex™ stent with an abluminal biodegradable polymer achieved a 10 x better strut coverage and a 20 x better stent apposition vs. the Cypher® Select™ stent with a symmetric durable polymer at 9 months

Biodegradable Polymer

LEADERS Trial

Conclusions (I)

Overall population

- Non-inferiority of BES vs SES in an all-comers population was sustained up to 3 years

- In the overall LEADERS population there were similar outcomes for BES and SES with respect to MACE, Cardiac Death, MI and clinically-indicated TVR

- The Kaplan-Meier curves for MACE continue to diverge showing lower event rates for BES

Biodegradable Polymer

LEADERS Trial
Conclusions (II)

Subgroup analysis

- Biolimus eluting stent appears to offer an **advantage** in treating patients with **complex CAD**
  - Bifurcations
  - Multi-vessel disease
  - STEMI
  - High SYNTAX score

Very Late Stent Thrombosis

- Although this was an all-comers study, definite very late stent thrombosis events were **rare** (BES 0.2% vs SES 0.9% P_{Sup}= 0.43)
- There were no VLST events in BES patients between 2 and 3 year clinical FU
- No VLST events in patients where a BES was implanted in native coronary arteries

Nobori DES

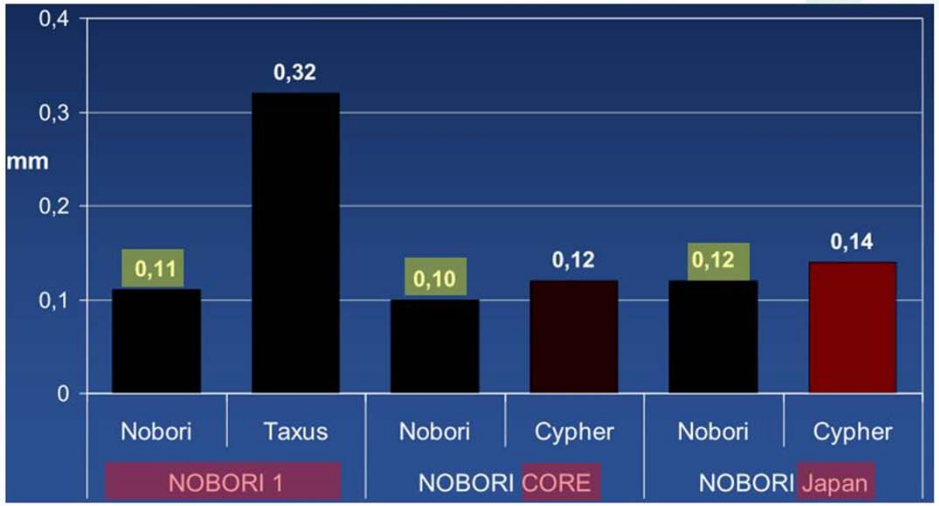
Biodegradable Polymer

Extensive Clinical Program (>20,000 pts)

		Status	
Foundation	NOBORI PK	Single arm – FU 4Y	N=20
	NOBORI 1 Phase 1	Randomized-Taxus – FU 4Y	N=120
	NOBORI 1 Phase 2	Ranomized -Taxus – FU 3Y	N=243
	NOBORI CORE	Comparative Cypher – FU 3Y	N=107
	NOBORI Japan	Randomized Cypher – FU 12M	N=323
Expansion All comers	NOBORI 2	Single Arm FU 6 M	N=3074
	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
	e-NOBORI	Enrolling	N=8000
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 DES Efficacy

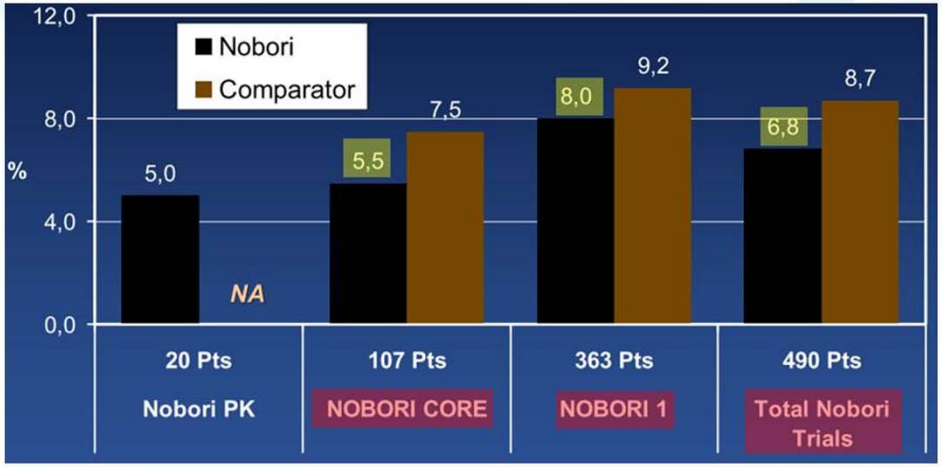
Late loss in pivotal trials



Angiographic FU @9 mo except NOBORI JAPAN @ 8 mo

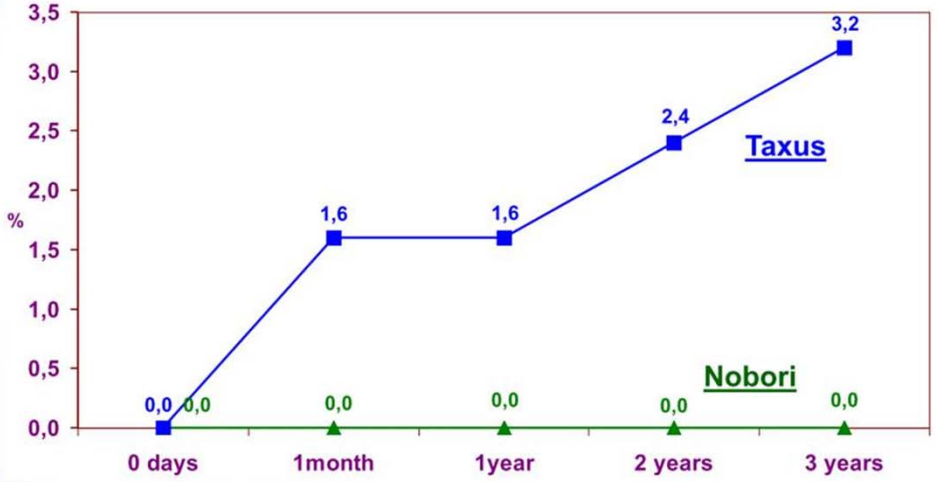
Biodegradable Polymer

MACE rate in NOBORI Trials @ 3 years



MACE = Cardiac Death, MI, Clinically driven TVR

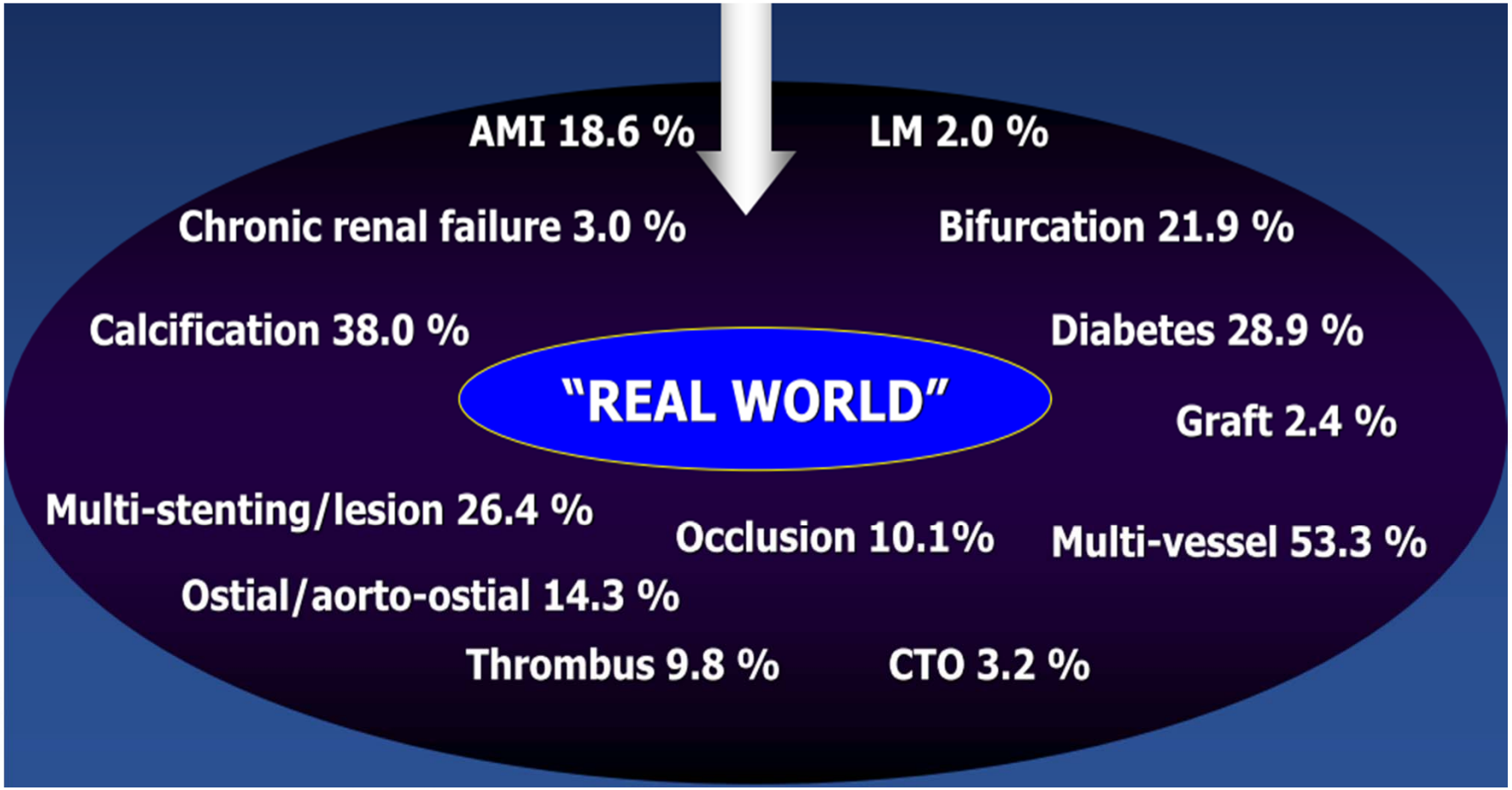
Long-Term ST in NOBORI 1



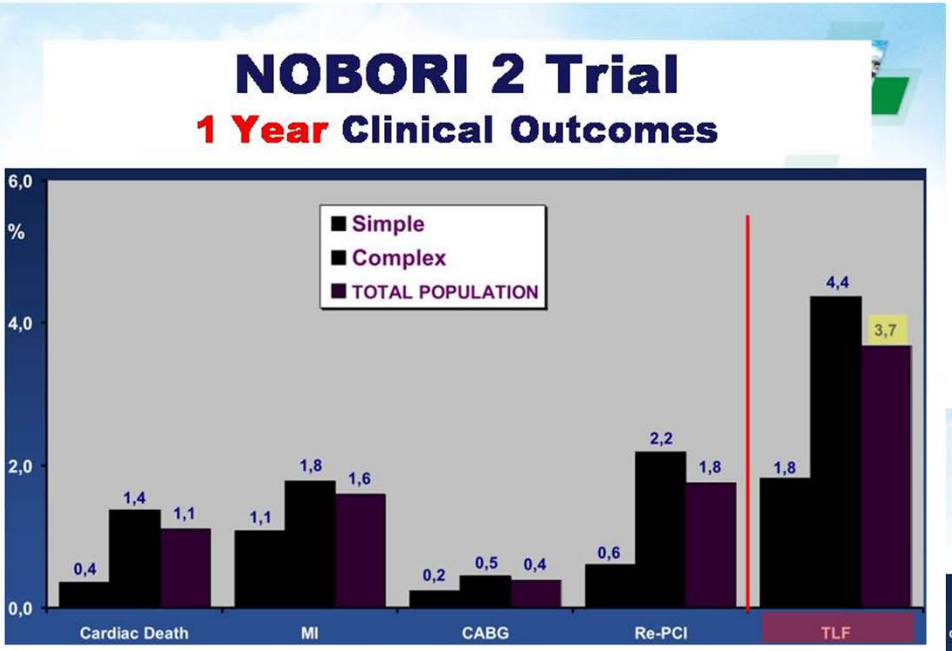
Biodegradable Polymer

NOBORI 2 Trial

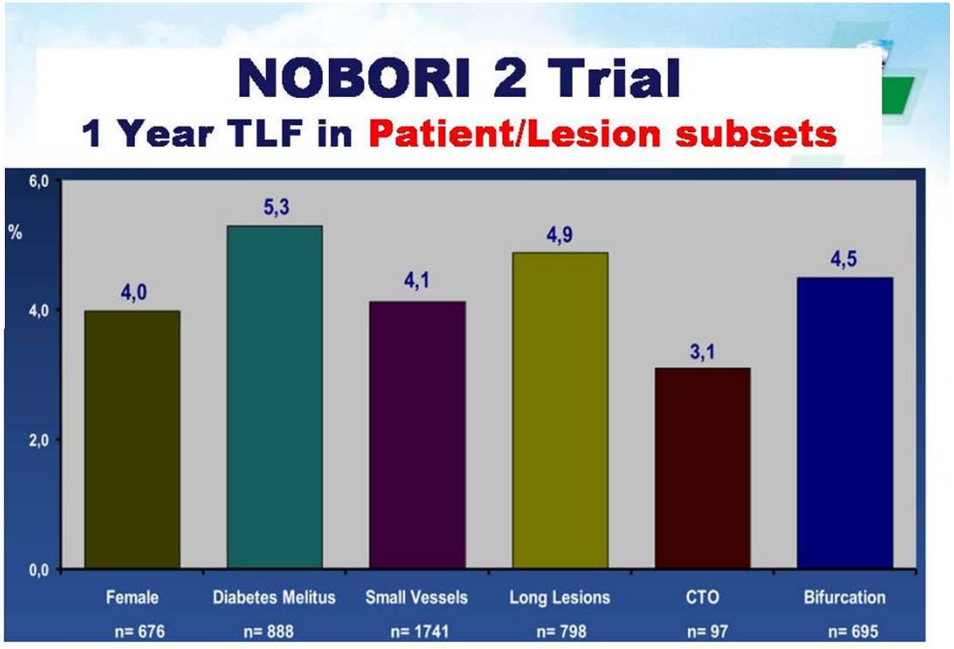
Complex lesions/patients



NOBORI 2 Trial



Primary Endpoint: **Target Lesion Failure** (Cardiac Death, target vessel related MI and TLR)



TLF = Target Lesion Failure (Cardiac death, MI Target vessel related, TLR)

DES with Biodegradable Polymer

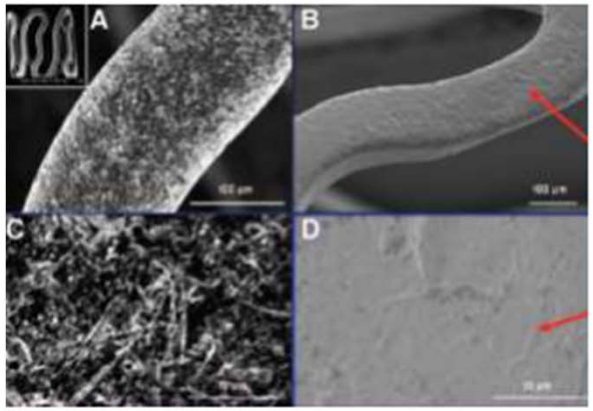
- Safety and efficacy of biodegradable polymer based limus releasing DES is at least as good as first generation durable polymer based DES
- Longer term follow-up in larger patient populations required to determine a potentially lower risk of very late stent thrombosis
- The phenomenon of late catch-up appears similar for durable and biodegradable polymer based DES

Categories of Latest DES

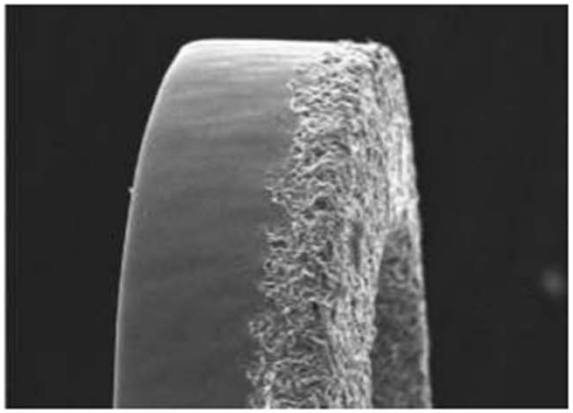
I. New Metallic DES with durable polymers
II. DES with biodegradable polymers
III. Non-polymeric DES
IV. Stents with novel coatings
V. Biodegradable stents
* Drug-coated balloons

Polymer-Free DES Platforms

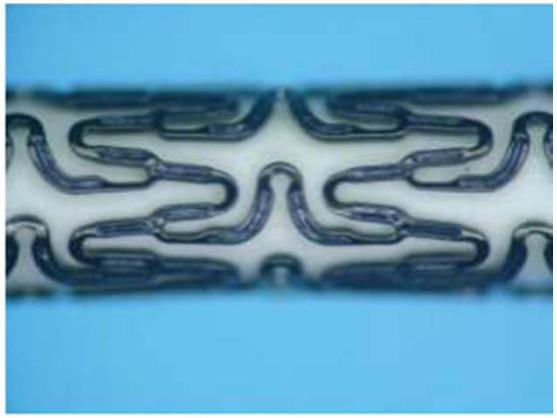
YUKON
Various Drugs



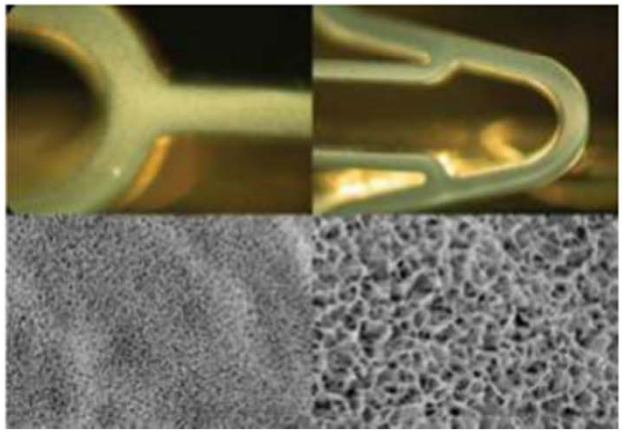
BioFreedom
Biolimus A9



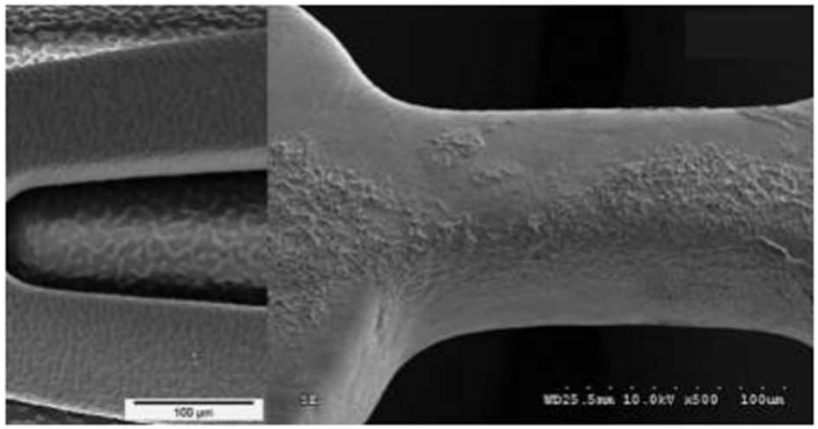
Optima
Tacrolimus



VESTAsync
Sirolimus

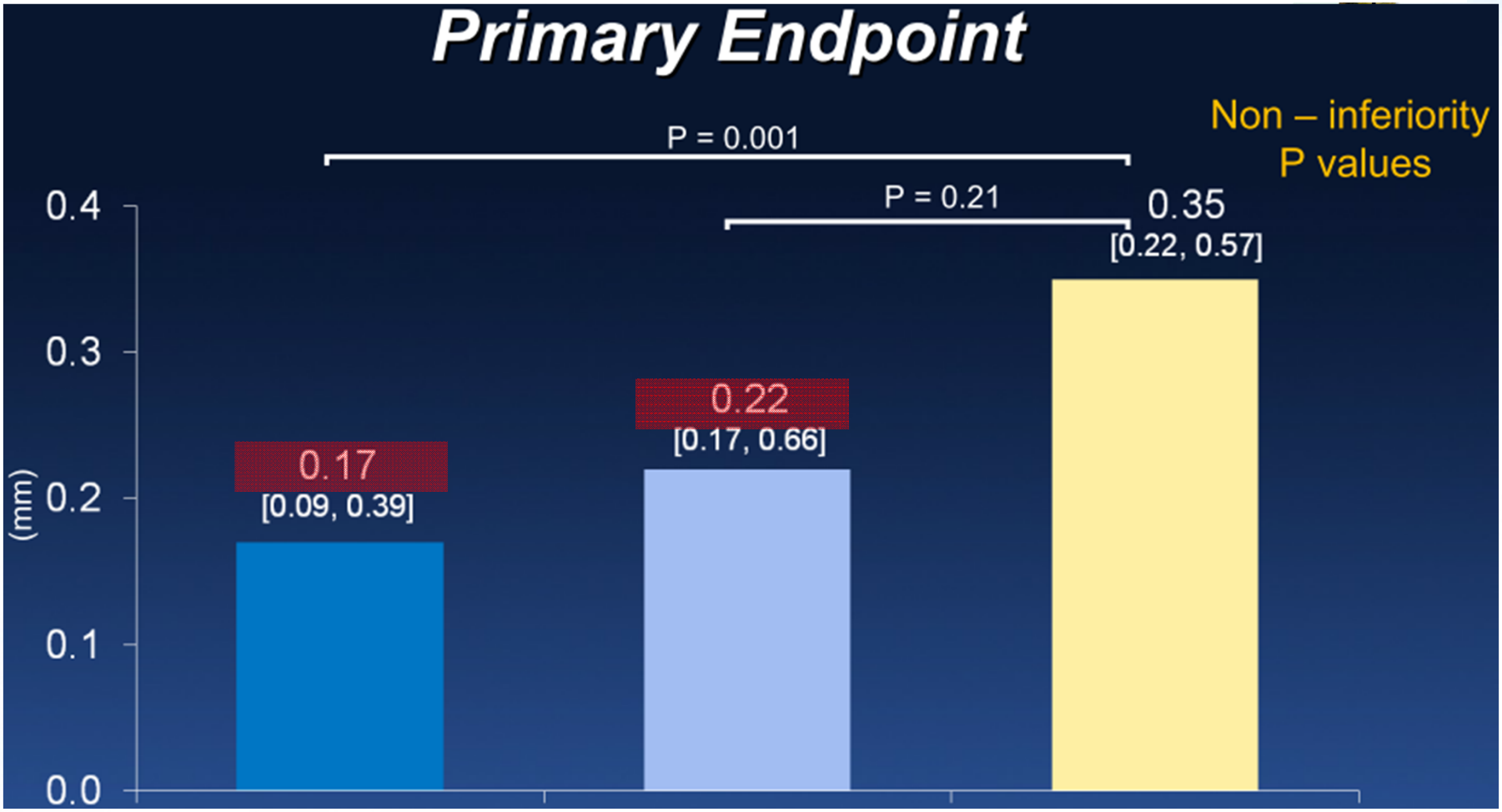


Amazon Pax
Paclitaxel



BioFreedom - FIM Study

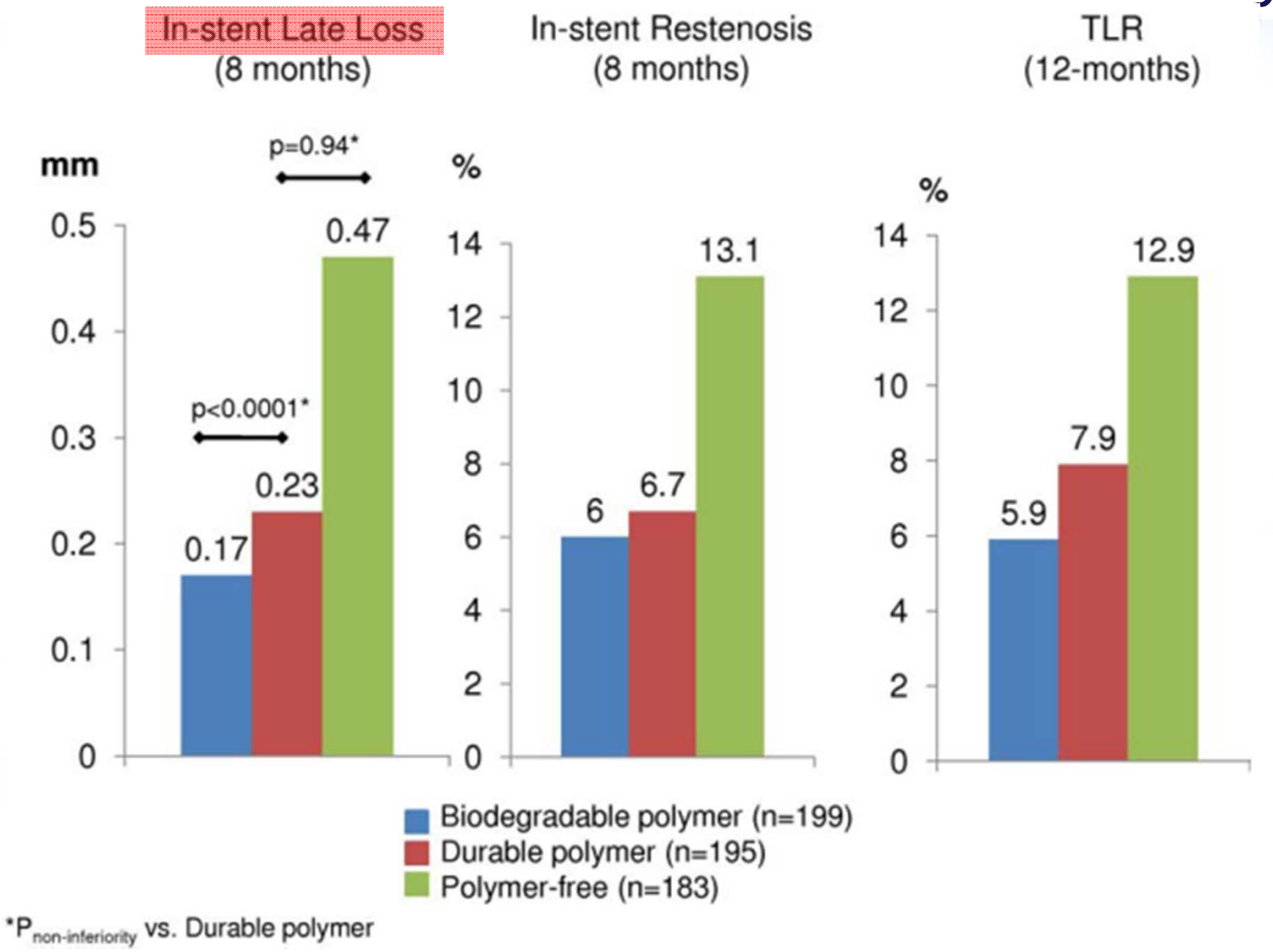
12 mo QCA In-Stent Late Lumen Loss



All values are presented as median [IQR]

Durable polymer, biodegradable polymer, and polymer-free rapamycin-eluting stents

Results from the ISAR-TEST-3 study



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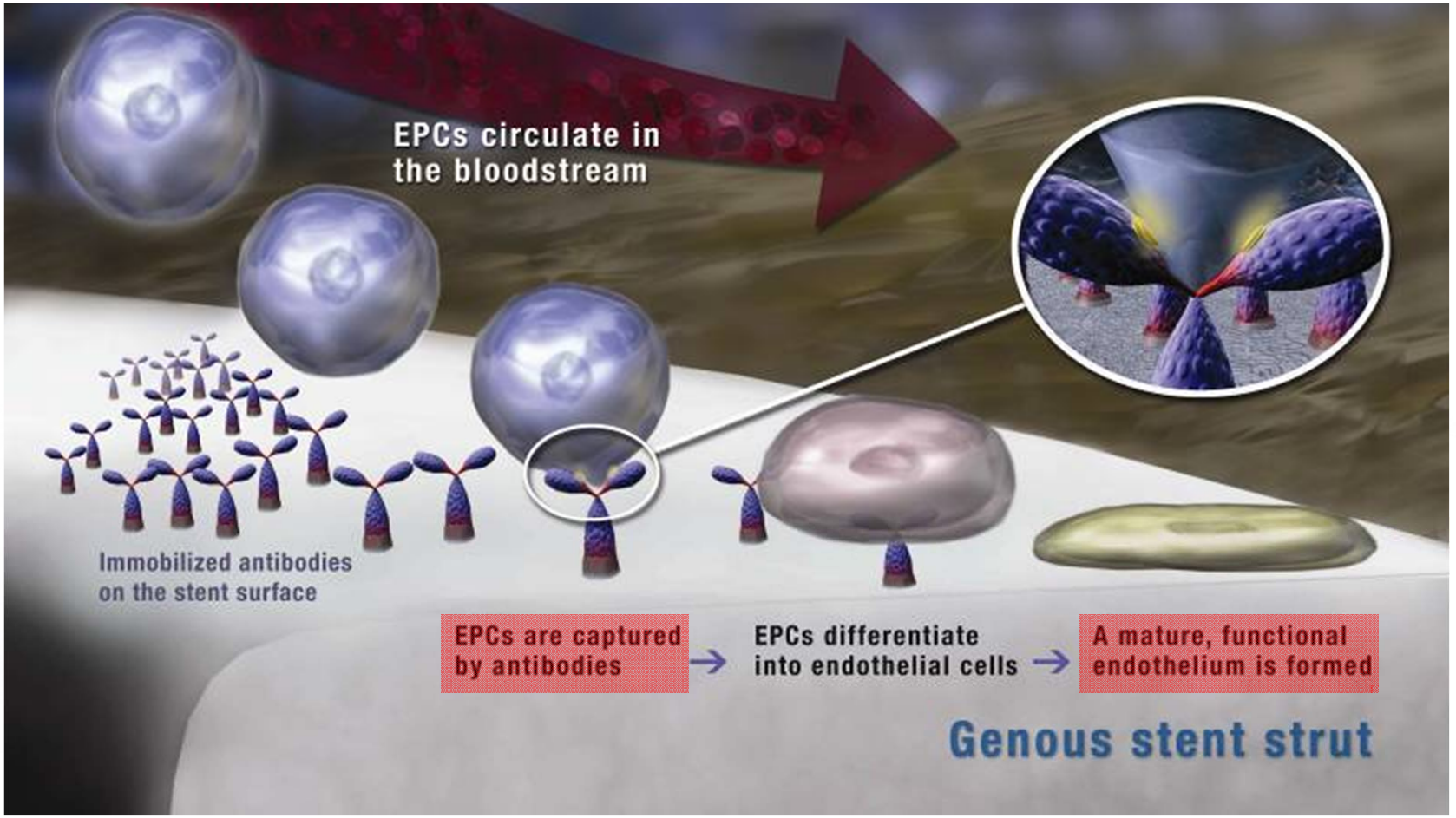
* Drug-coated balloons

Genous stent

EPC Capture Technology

Genous Technology:

Anti-CD34 Ab surface to promote healing through rapid stent endothelialization.



e-HEALING registry

Clinical Events @ 12 mo

	30 days	6 months	12 months
Cardiac Death	**0.6 %**	**1.1 %**	**1.6 %**
MI	**1.1 %**	**1.5 %**	**1.7 %**
Q-wave	0.2 %	0.2 %	0.3 %
Non Q-wave	1.0 %	1.3 %	1.4 %
TLR (Clinically Driven)	**0.2 %**	**2.7 %**	**4.4 %**
PCI	0.2 %	2.4 %	4.0 %
CABG	0.0 %	0.3 %	0.4 %
Primary outcome	**1.9 %**	**5.3 %**	**7.7 %**

Acute stent thrombosis	**0.2 %**
Sub-acute stent thrombosis	**0.5 %**
Late stent thrombosis	**0.3 %**

All events adjudicated by CEC
Worst MACE per patient = cardiac death, MI, CABG, and clinically driven TLR

e-HEALING compared to the DES groups of LEADERS

	Genous (e-HEALING)	Cypher (LEADERS)	BioMatrix (LEADERS)
Inclusion criteria	all comers	all comers	all comers
Number of patients	4996	850	857
Duration of follow-up	12 months	9 months	9 months
Cardiac death	1.6 %	2.5 %	1.6 %
MI	1.7 %	4.6 %	5.7 %
TLR Clinically Driven	4.4 %	4.9 %	4.3 %
MACE	7.7 % [1]	10.5 % [2]	9.2 % [2]
Stent thrombosis	1.2 % [3]	2.2 % [3]	2.7 % [3]
Recommended DAPT	4 weeks	12 months	12 months

All events adjudicated by CEC
1 Worst MACE per patient = cardiac death, MI, CABG, and clinically driven TLR
2 MACE = Cardiac Death, MI, TVR
3 ARC definite + probable

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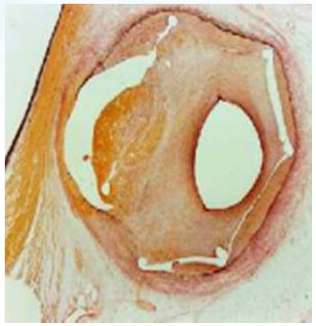
* Drug-coated balloons

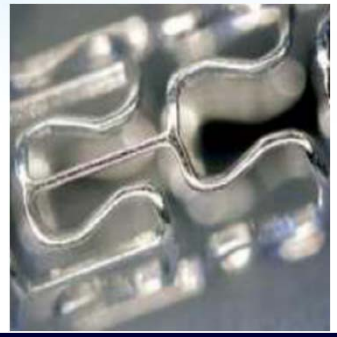
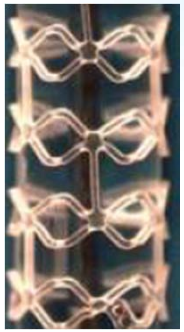
Biodegradable Stent

- PLLA stents
  - IGAKI-TAMAI stent
    - ✓ FIM
  - BVS (Abbott)
  - REVA Bioabsorbable stent

- Bioabsorbable Mg Alloy stent

Fully Biodegradable Stent Platforms



Van der Giessen, *Circulation* — **1996**

Animal studies
polymeric scaffolds revealing excessive inflammatory reactions

Tamai *Circulation* — **2000**

Igaki Tamai
First fully biodegradable non drug eluting scaffold
N=15

Erbel *Lancet* — **2007**

AMS-1
first bioabsorbable metallic non drug-eluting scaffold
N=64

Ormiston *Lancet* — **2008**

Bioresorbable vascular scaffold
first bioabsorbable drug eluting scaffold
N=31

Jabara *EuroPCR 2009* — **2009**

IDEAL BDS
Polyanhidride ester and salicylic acid, drug-eluting scaffold
N=11

Abizaid *TCT 2009* — **2009**

REVA
Polycarbonate stent, radiopaque, non drug-eluting scaffold
N=31

The ABSORB Family of Trials

ABSORB		ABSORB EXTEND
4 year F/U	1 year F/U	Enrolling
Cohort A	Cohort B	
Safety and Performance	Safety and Performance after assessing safety at 180 days in the Cohort A patients	Continuation of assessment of Safety and Performance
International N=30 4 sites	International N=101 12 sites	N=1,000 100 sites
Single *de novo* lesion	Up to two *de novo* lesions	Up to two *de novo* lesions, longer lesions, overlapping scaffolds

The ABSORB Trials are sponsored and funded by Abbott Vascular, Santa Clara, California

Bernard Chevalier, oral presentation, ACC 2011

ABSORB A – 4 Year Clinical Results

Hierarchical	6 Months 30 Patients	12 Months 29 Patients*	3 Years 29 Patients*	4 Years 29 Patients*
Ischemia Driven MACE, %(n)	3.3% (1)*	3.4% (1)*	3.4% (1)*	3.4% (1)*
Cardiac Death, %	0.0%	0.0%	0.0%	0.0%
MI, %(n)				
Q-Wave MI	0.0%	0.0%	0.0%	0.0%
Non Q-Wave MI	3.3% (1)**	3.4% (1)**	3.4% (1)**	3.4% (1)**
Ischemia Driven TLR , %				
by PCI	0.0%	0.0%	0.0%	0.0%
by CABG	0.0%	0.0%	0.0%	0.0%

No new MACE events between 6 months and 4 years

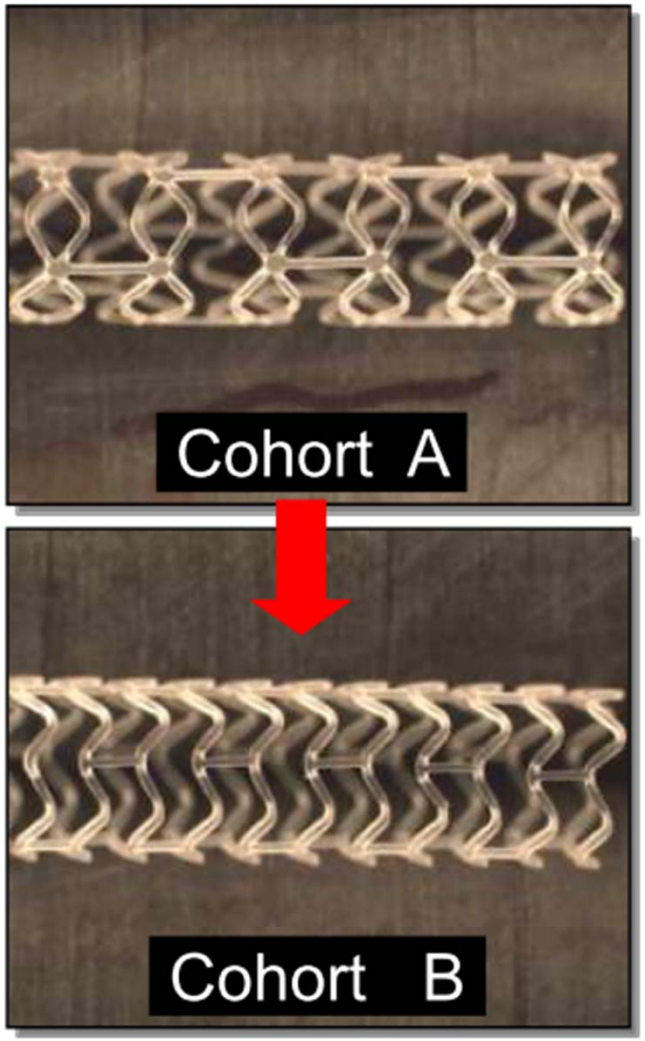
No scaffold thrombosis up to 4 years (All patients off clopidogrel)

*One patient withdrew consent after 6 months but the vital status of the patients and absence of cardiac event is known through the referring physician.

**This patient also underwent a TLR, not qualified as ID-TLR (DS = 42%) followed by post-procedural troponin qualified as non-Q MI and died from his Hodgkin's disease at 888 days post-procedure.

Ormiston et al. 2008, Serruys et al. 2009

ABSORB Cohort B Trial



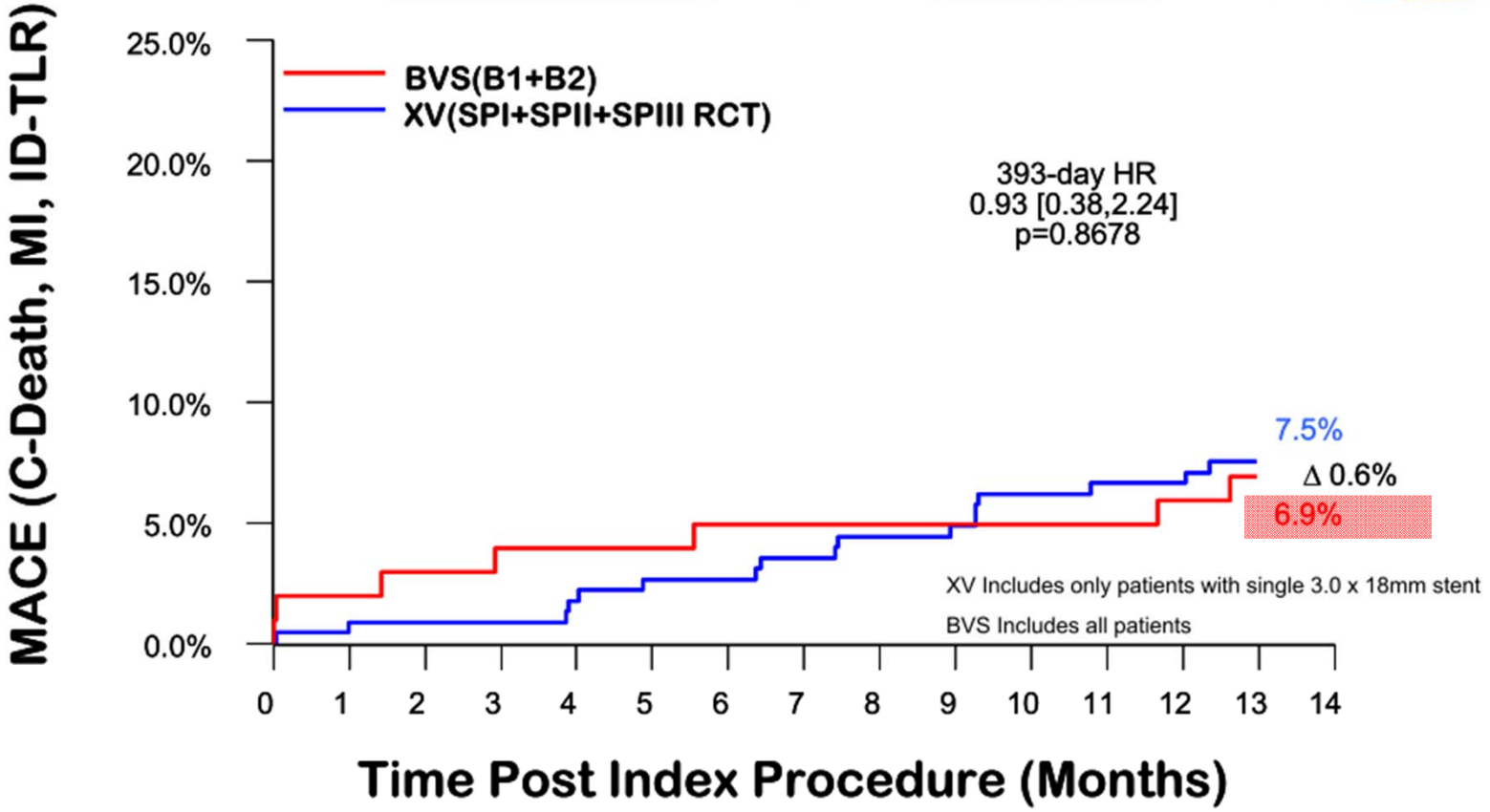
Evaluation of the ABSORB Bioresorbable Everolimus-Eluting Vascular Scaffold in the Treatment of Patients with de novo Native Coronary Artery Lesions

1-Year Clinical Results

Bernard Chevalier, oral presentation, **ACC 2011**

ABSORB B KM estimate of MACE

BVS vs Spirit I+II+III (EES)



Patients at risk	0 days	37 days	194 days	284 days	365 days	393 days
BVS(B1+B2)	101	99	96	96	95	94
XV(SPI+SPII+SPIII RCT)	227	224	219	211	209	208

Bernard Chevalier, oral presentation, **ACC 2011**

ABSORB B

Clinical Results – Intent to treat

Non-Hierarchical	30 Days N = 101	6 Months N = 101	9 Months N = 101	12 Months N = 101
Cardiac Death %	0	0	0	0
Myocardial Infarction % (n)	2.0 (2)	3.0 (3)	3.0 (3)	3.0 (3)
Q-wave MI	0	0	0	0
Non Q-wave MI	2.0 (2)	3.0 (3)	3.0 (3)	3.0 (3)
Ischemia driven TLR % (n)	0	2.0 (2)	2.0 (2)	4.0 (4)
CABG	0	0	0	0
PCI	0	2.0 (2)	2.0 (2)	4.0 (4)
Hierarchical MACE % (n)	2.0 (2)	5.0 (5)	5.0 (5)	6.9 (7)
Hierarchical TVF % (n)	2.0 (2)	5.0 (5)	5.0 (5)	6.9 (7)

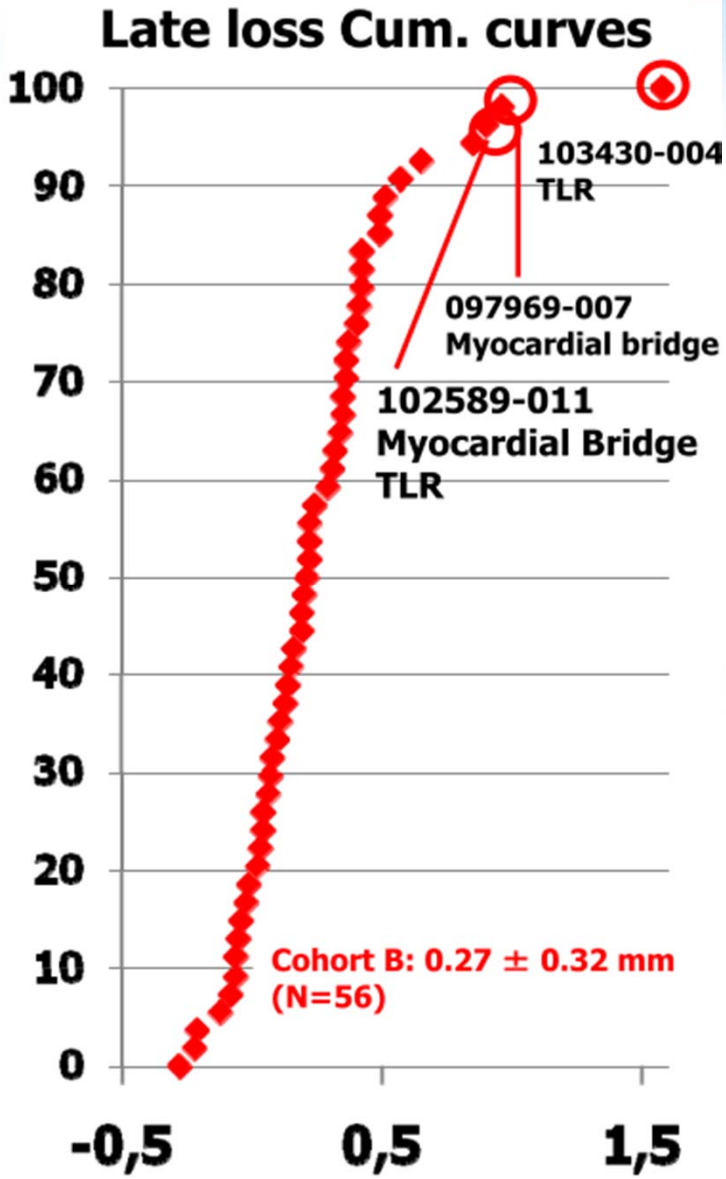
No scaffold thrombosis by ARC or Protocol

MACE: Cardiac death, MI, ischemia-driven TLR
TVF: Cardiac death, MI, ischemia-driven TLR, ischemia-driven TVR

Bernard Chevalier, oral presentation, **ACC 2011**

ABSORB B – QCA results @12 mo

N=56	Proximal	In-scaffold	Distal
Minimal Luminal Diameter			
Post procedure	2.43	2.27	2.18
At 12 months	2.30	2.00	2.10
P value	0.003	<0.001	0.047
Late Loss, mm	0.12	0.27	0.07
Diameter Stenosis, %			
Post procedure	13	15	15
At 12 months	12	21	13
P value	0.75	<0.001	0.10
Binary restenosis	0%	3.57%	0%



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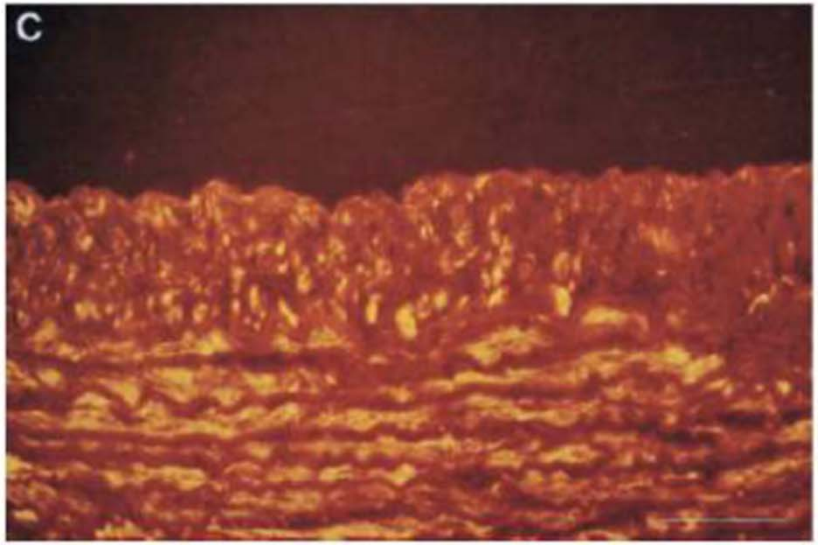
* Drug-coated balloons

Drug-Coated Balloon Catheters

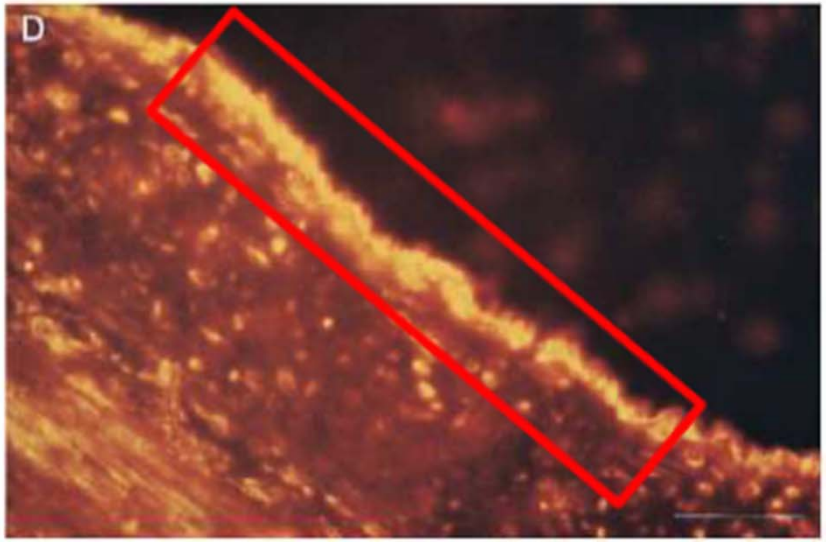
Mechanism of action

A lipophilic drug applied on a carrier is passively transferred to the intima of the coronary artery by balloon expansion. Variable tissue retention rates determine local inhibition of neointimal hyperplasia.

Immunofluorescence micrographs after staining with a monoclonal anti-tubulin AB



Control animal seven days after BD showing heterogeneous staining within the neointima



Histologic section seven days after local paclitaxel delivery showing an intensely stained “fluorescence band” at the luminal cell lining

Herdeg et al, JACC 2000

Drug-Coated Balloon Catheters

Drug

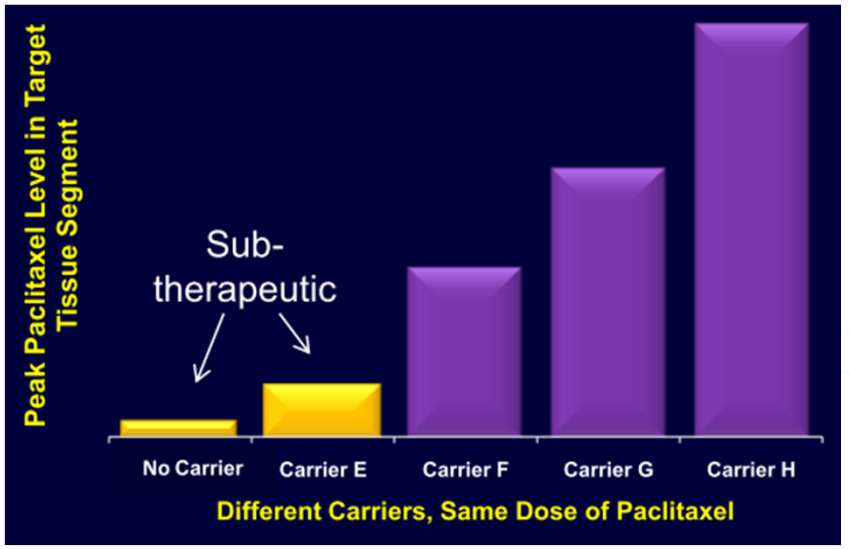
Paclitaxel is lipophilic, had a high absorption rate (10-15%), and is transferred quickly to the endoluminal surface

- other drugs (i.e. limus) also being tested

Carrier

Governs total drug load, coating durability and uniformity, vessel uptake and downstream drug dose

- i.e. lopromide



Platforms

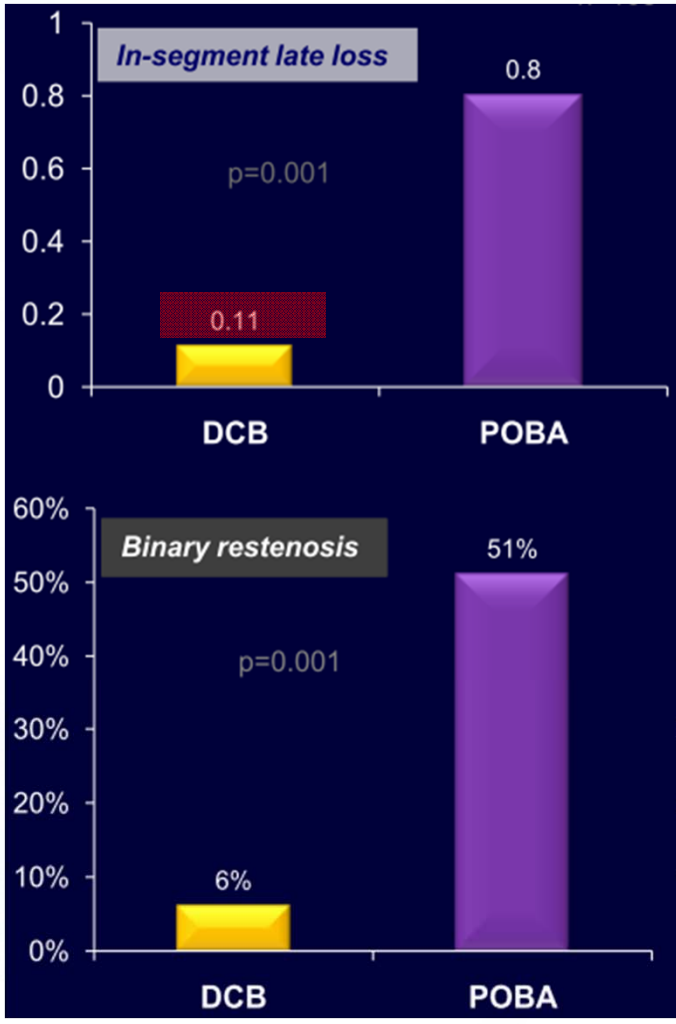
Dior (Eurocor)
Moxy (Lutonix, Inc.)
Paccocath (Bayer Schering)
SeQuent Please (B. Braun)

Gray WA et al. Circulation 2010;121:2672-2680

Drug-Coated Balloon Catheters

Paccocath ISR I%II @ 6 mo

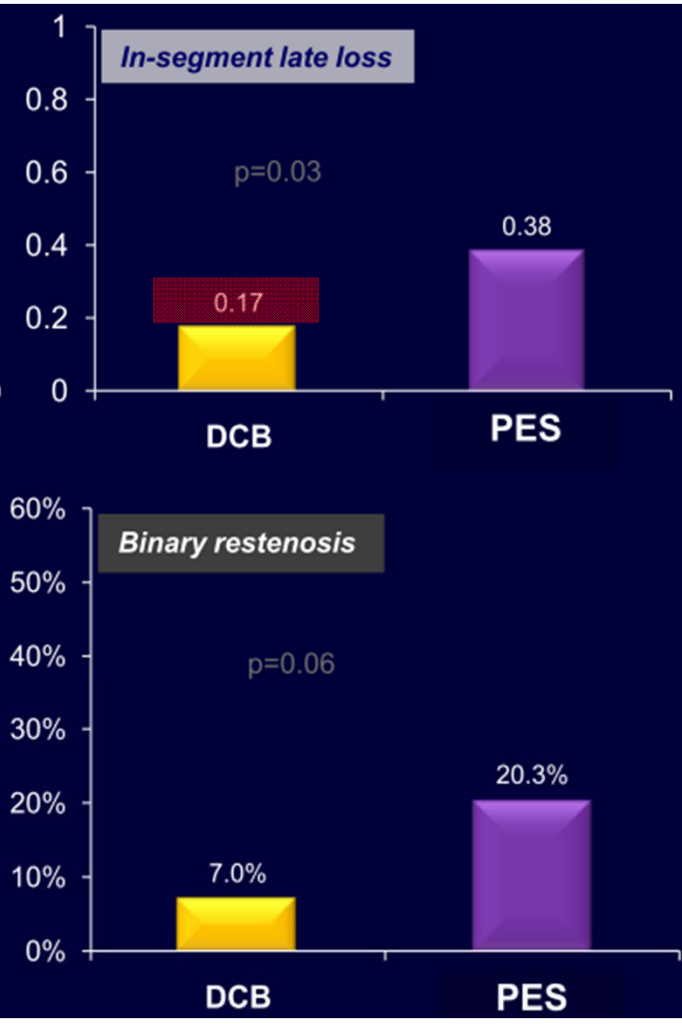
N=108



Scheller B et al. Clin Res Cardiol 2008

PEPCAD II @ 6 mo

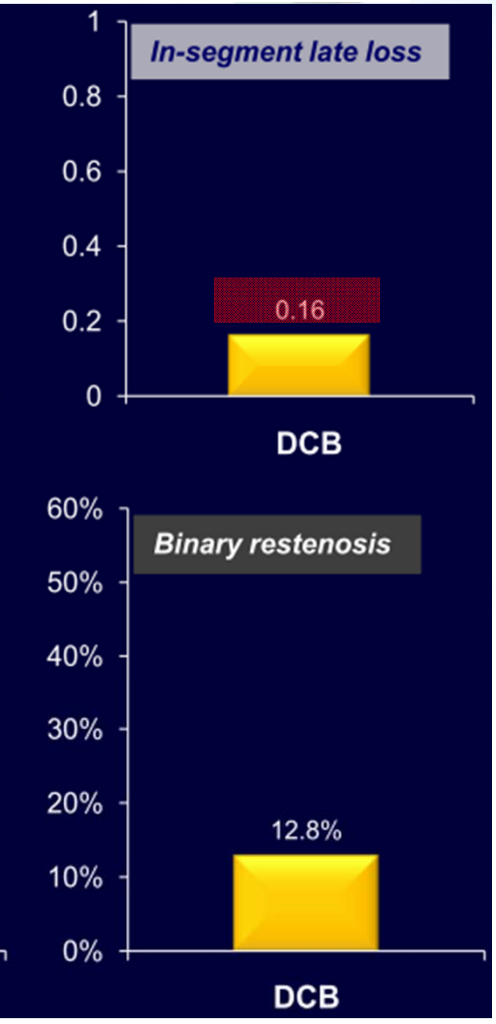
N=131



Unverdorven et al, Circulation 2009

PERVIDEO I @ 6mo

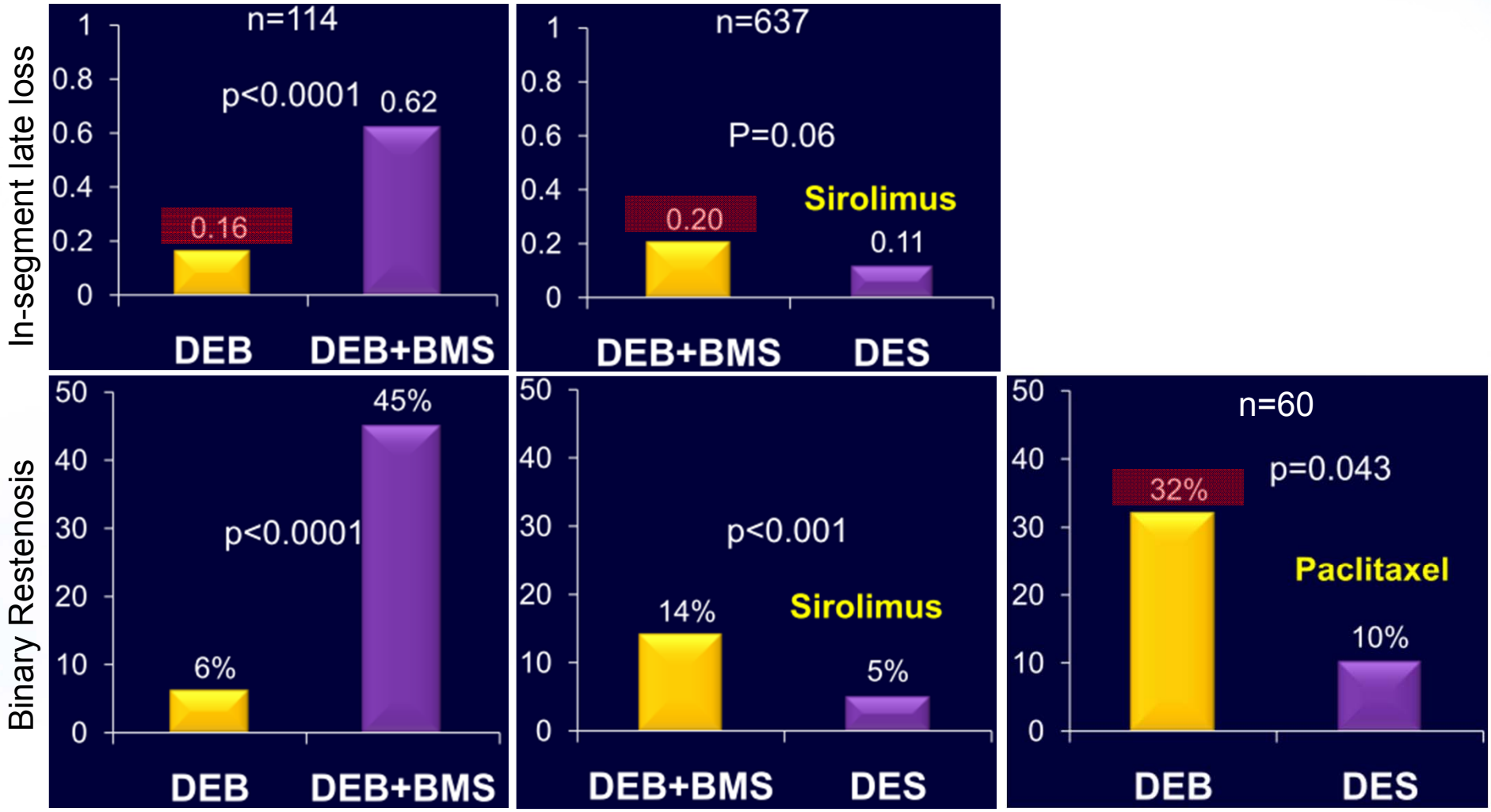
N=41



Mauri L, TCT 2010

Drug-Coated Balloon for Native, De-Novo Coronary Artery Disease

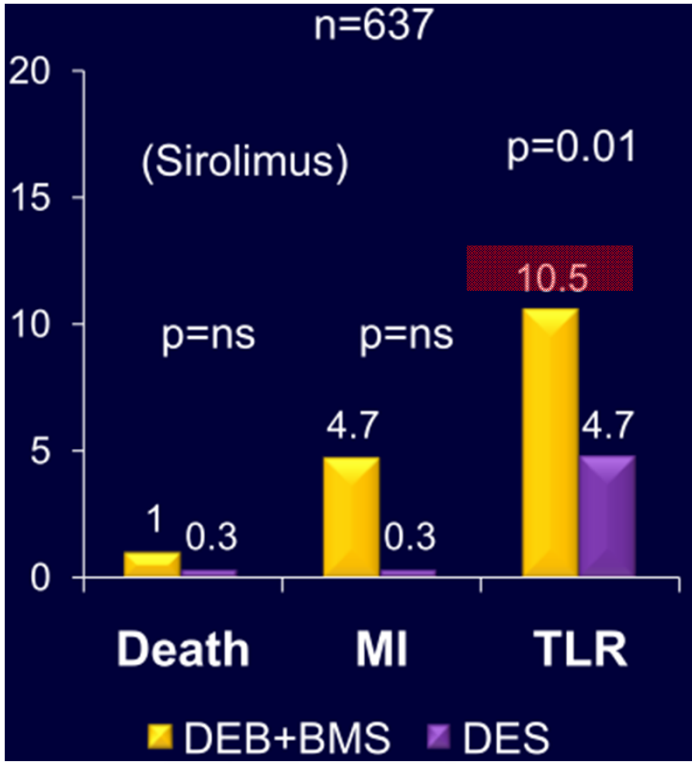
PEPCAD I - SVD | **PEPCAD III** | **PICCOLETO - SVD**



Drug-Coated Balloon for Native, De-Novo Coronary Artery Disease

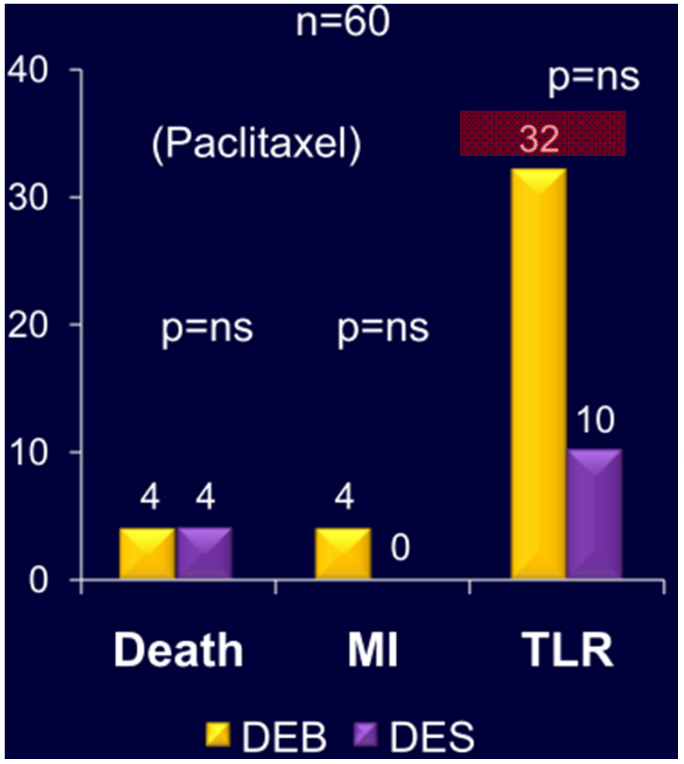
Clinical follow-up at 9 months

PEPCAD III



Hamm et al. AHA 2009

PICOOLETO - SVD

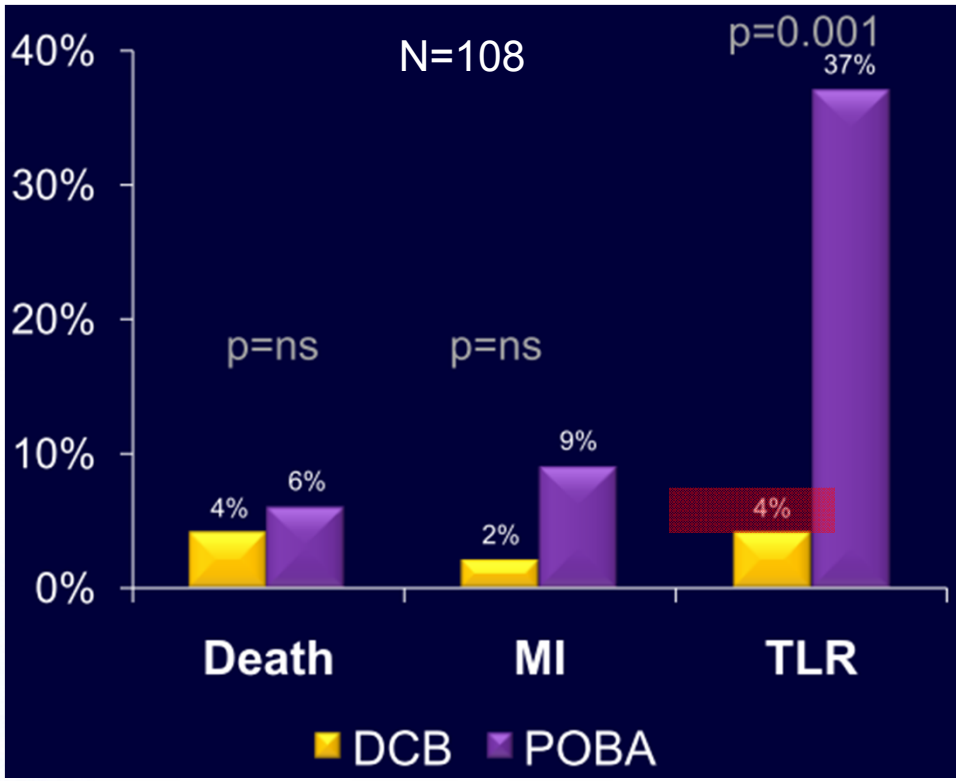


Cortese et al. Heart 2010

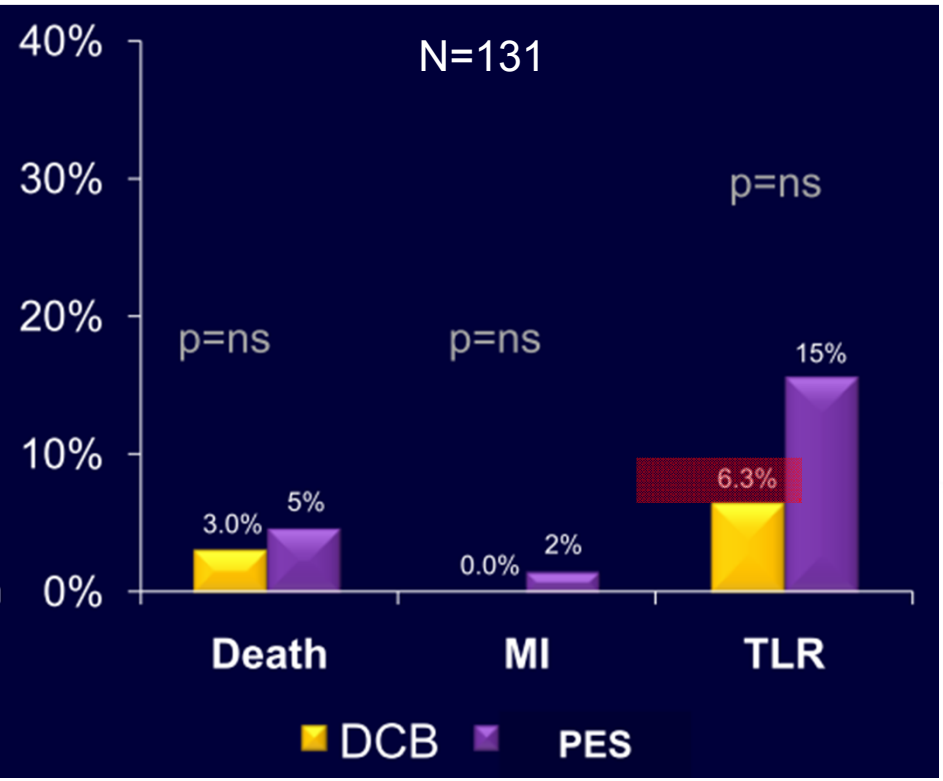
Drug-Coated Balloon for ISR

Clinical follow-up at 12 months

Paccocath ISR I&II



PEPCAD II



Summary of Latest Generation DES

- Newer generation durable polymer DES have improved safety and efficacy compared with early generation DES
  - Current gold standard (**Resolute, Xience V, Promus Element, ,…)**
- The majority of future generation DES are based on biodegradable polymer drug release with similar safety and efficacy as durable polymer DES
  - Appealing concept
- Polymer-free DES may even further decrease polymer related adverse events, but potentially at the cost of reduced efficacy
- Fully biodegradable DES platforms will lead to a paradigm shift in the treatment of CAD
  - Safety and efficacy comparable to current DES
  - Restoration of normal arterial vasculature
- Stents with novel coatings: Genous stent
- Drug-coating balloons are an attractive alternative to DES in the treatment of in-stent restenosis but not for de novo CAD