Recent Updates from the Cypher Trials

Alexandre Abizaid, MD, PhD

Inst. Dante Pazzanese, Sao Paulo, Brazil

Columbia University, New York, USA

Angioplasty Summit 2005

Seoul, Korea

Updates from the Cypher Trials:

- Diabetes Meta-Analysis
- ISAR Diabetes
- ARTS II
- SIRIUS 3-year FU
- FIM 4-year FU

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CYPHER Trials DM Patients

Studies	DM Patients		Gender (M%)		Age (yrs)		IDDM pts	
	Cypher	Control	Cypher	Control	Cypher	Control	Cypher	Control
SIRIUS	131	148	64%	59%	63.4	62.1	38	44
E-SIRIUS	33	48	64%	60%	62.7	62.7	7	11
C-SIRIUS	12	12	50%	83%	64.9	58.8	1	2
DIRECT	70	-	73%	-	61.9	-	16	-
SVELTE	27	-	74%	-	63.4	-	2	-
RAVEL	19	25	68%	80%	63.6	63.0	5	5
Integrated	292	233	67%	63%	63.0	62.2	69	62

Abizaid et al ACC 2005

CYPHER Trials – DM Patient Demographics

	Sirolimus (%) (n=292)	Control (%) (n=233)
Male	66.8	62.7
Mean age (years)	63.0	62.2
Prior MI	28.4	38.4
Prior PCI	30.5	22.7
IDDM	23.6	26.6
Hyperlipidemia	76.3	70.1
Hypertension	74.6	78.9
Current Smoker	16.6	19.4

CYPHER Trials –Procedural Characteristics in DM pts

	Sirolimus (n=292)	Control (n=233)
Post-procedure hospital length of stay (days)	1.33 ± 1.08 (0,13)	1.48 ± 1.76 (0,25)
IIb/IIIa inhibitor use during procedure (%)	47.6%	44.6%

CYPHER Trials – DM pts QCA In-Stent

		Sirolimus (N_{BL}= 289) ($N_{F/U}$= 211)	Control (N_{BL}= 231) ($N_{F/U}$= 158)	P-value
Ref Diameter (mm)		2.65	2.65	0.9557
MLD (mm)	pre	0.95	0.90	0.1263
	post	2.53	2.52	0.8582
	8Mon fu	2.28	1.34	<0.0001
% DS	pre	64.3	66.0	0.1023
	post	6.7	7.0	0.7016
	8Mon fu	14.2	49.7	<0.0001
Late Loss (mm)		0.26	1.19	<0.0001
Acute Gain (mm)		1.58	1.62	0.2829
Restenosis (%)		5.7	50.6	<0.0001

RAVEL QCA F/U is excluded from the 8-Month QCA results

CYPHER Trials – DM pts QCA In-Segment

		Sirolimus (N_{BL}= 289) ($N_{F/U}$= 211)	Control (N_{BL}= 231) ($N_{F/U}$= 158)	P-value
Ref Diameter (mm)		2.65	2.65	0.9557
MLD (mm)	pre	0.95	0.90	0.1263
	post	2.24	2.24	0.9026
	8Mon fu	1.95	1.29	<0.0001
% DS	pre	64.3	66.0	0.1023
	post	17.4	17.5	0.9382
	8Mon fu	27.0	51.9	<0.0001
Late Loss (mm)		0.32	0.96	<0.0001
Acute Gain (mm)		1.29	1.33	0.2730
Restenosis (%)		11.8	52.5	<0.0001

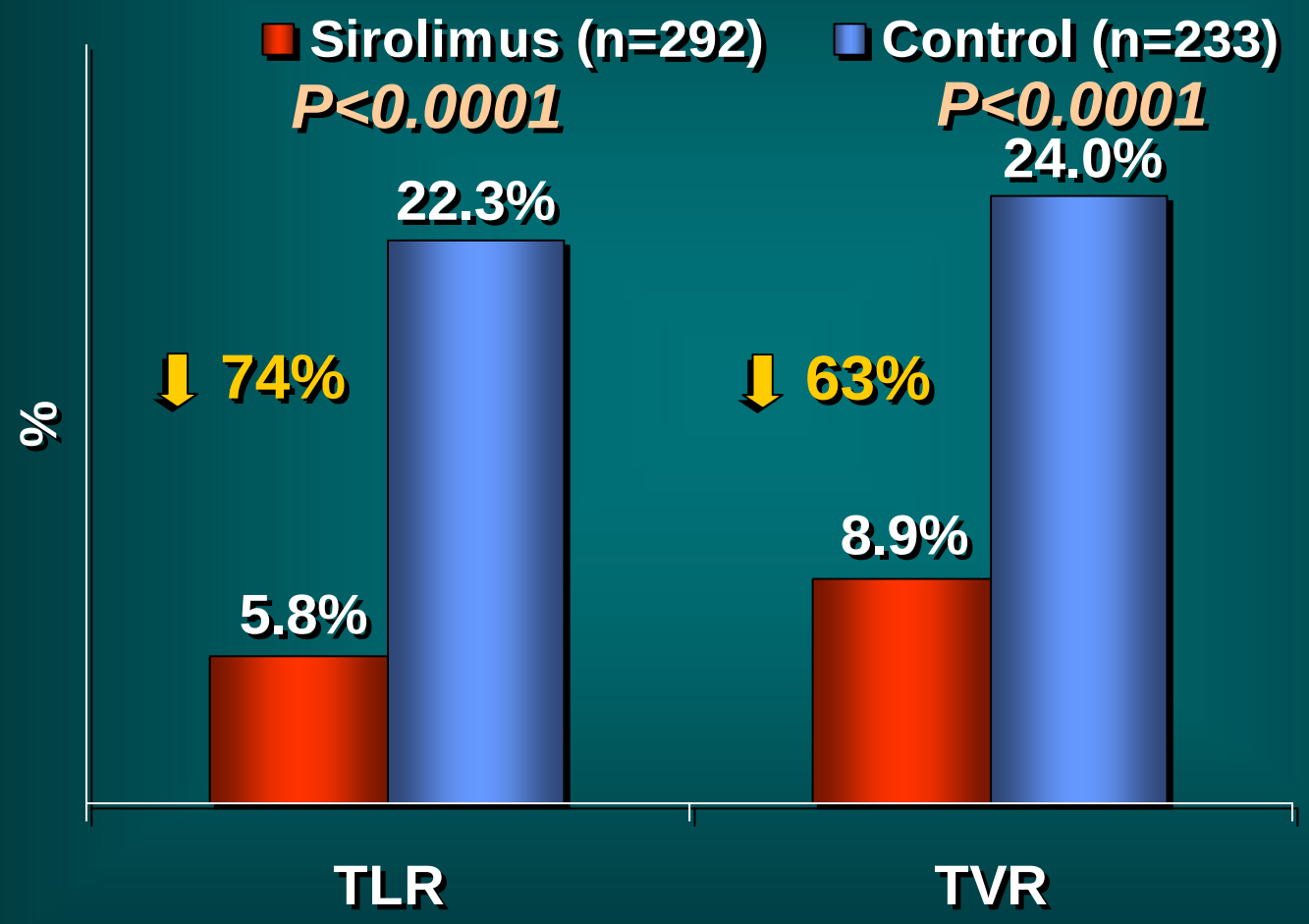
RAVEL QCA F/U is excluded from the 8-Month QCA results

CYPHER Trials - Stent Thrombosis in DM pts

	Sirolimus (%) (n=292)	Control (%) (n=233)
Acute (≤ 24 hours)	0	0
Subacute (1-30 days)	0.3% (1)	0
Late (31-270 days)	0.3% (1)	0.4% (1)
Total	*0.6% (2)*	*0.4% (1)*

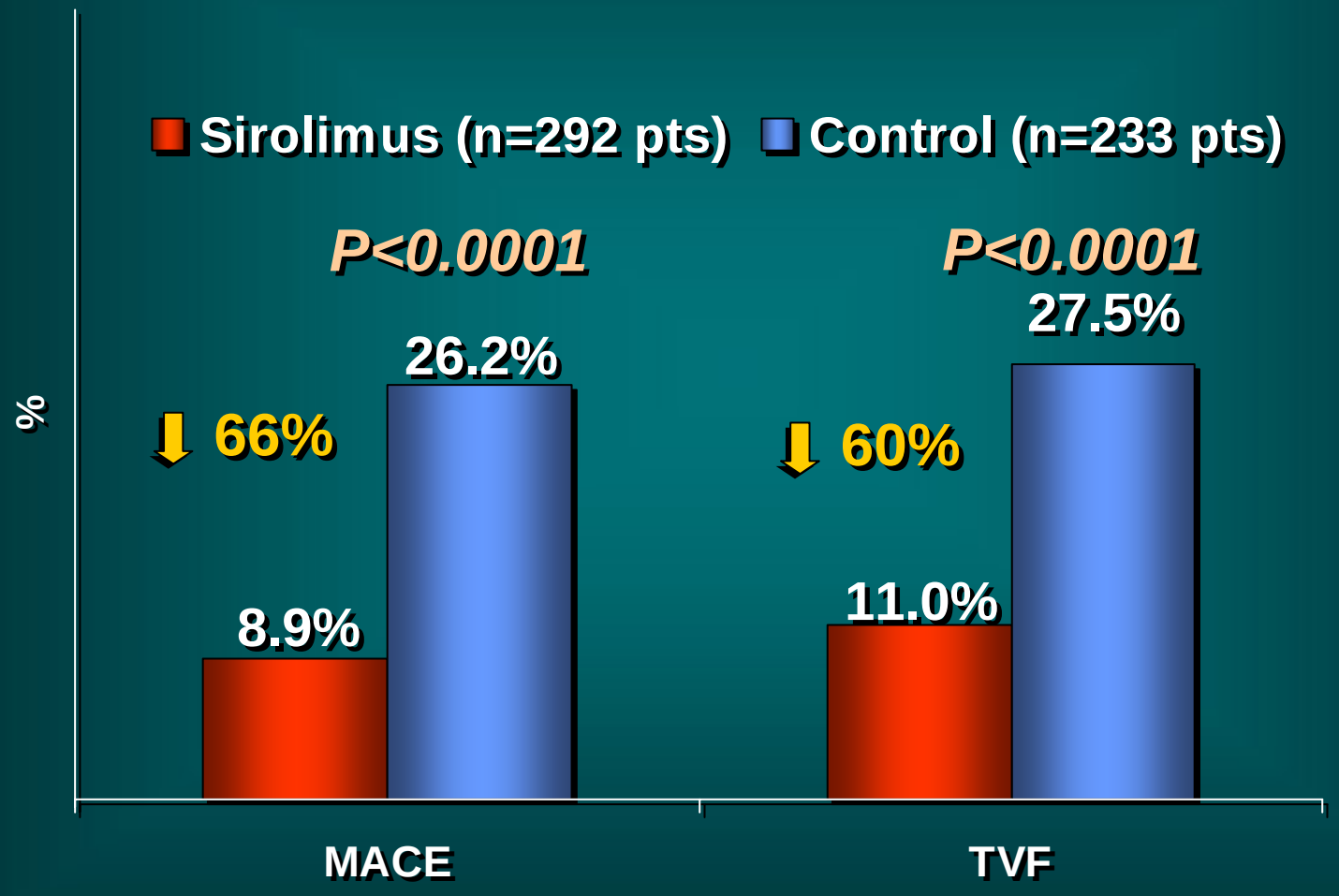
CYPHER Trials - Clinical Events in DM pts

All Events (to 9 months)

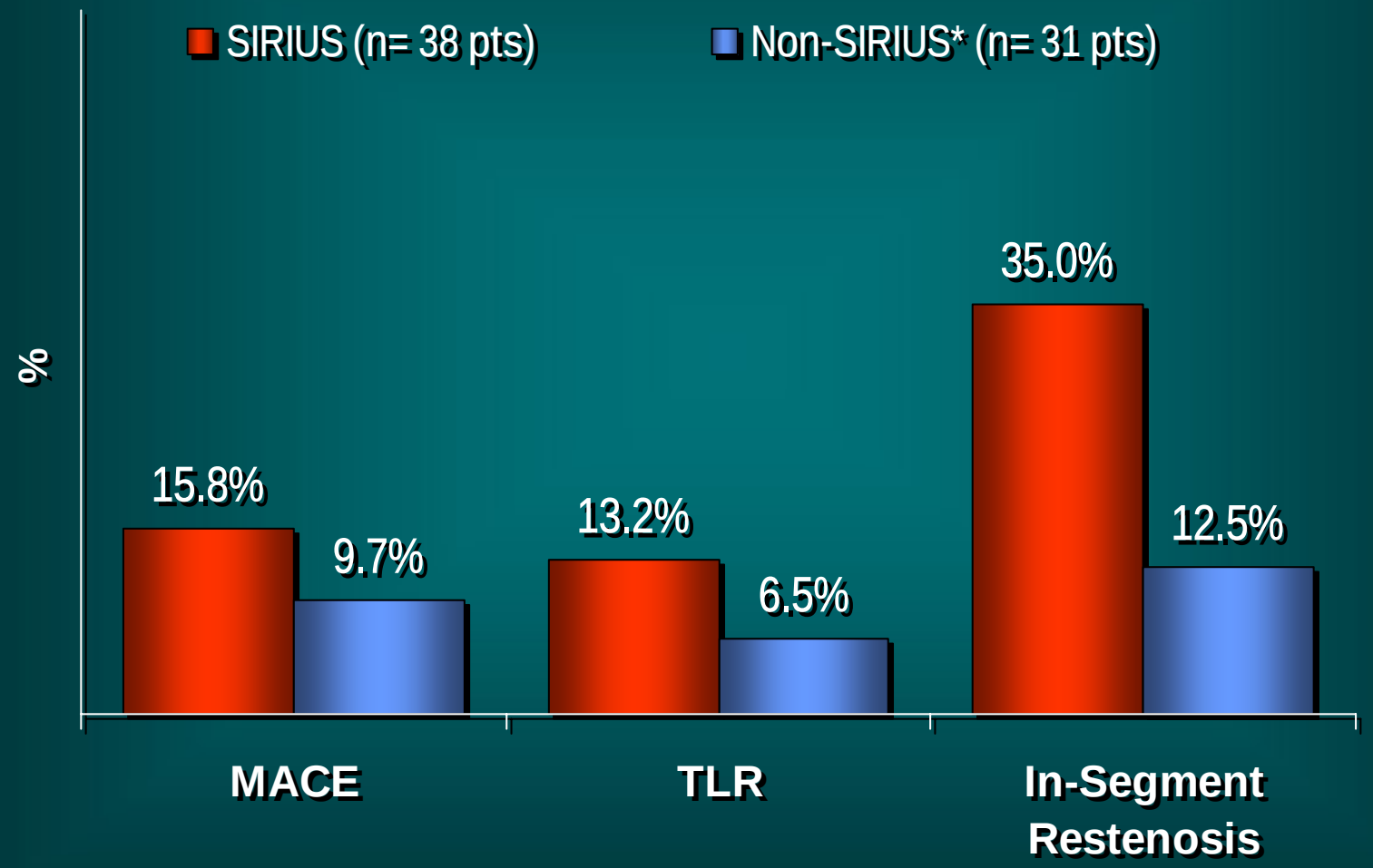


CYPHER Trials - Clinical Events in DM Pts

All Events (to 9 months)



CYPHER Trials - Clinical Events in IDDM pts
All Events (to 9 months)



RAVEL QCA F/U is excluded from the 8-month QCA F/U analysis

** Non-SIRIUS Studies include RAVEL, E-SIRIUS, C-SIRIUS, DIRECT, SVELTE*

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Study Protocol

Patients with Diabetes Mellitus (n = 250)

CYPHER (n = 125)

TAXUS (n = 125)

1° EP: Late lumen loss at 6 months (in-segment analysis)

2° EP: Angiographic restenosis at 6 months ≥ 50% diameter stenosis (in-segment analysis).

Target lesion revascularization at 6 months.

Kastrati et al ACC 2005

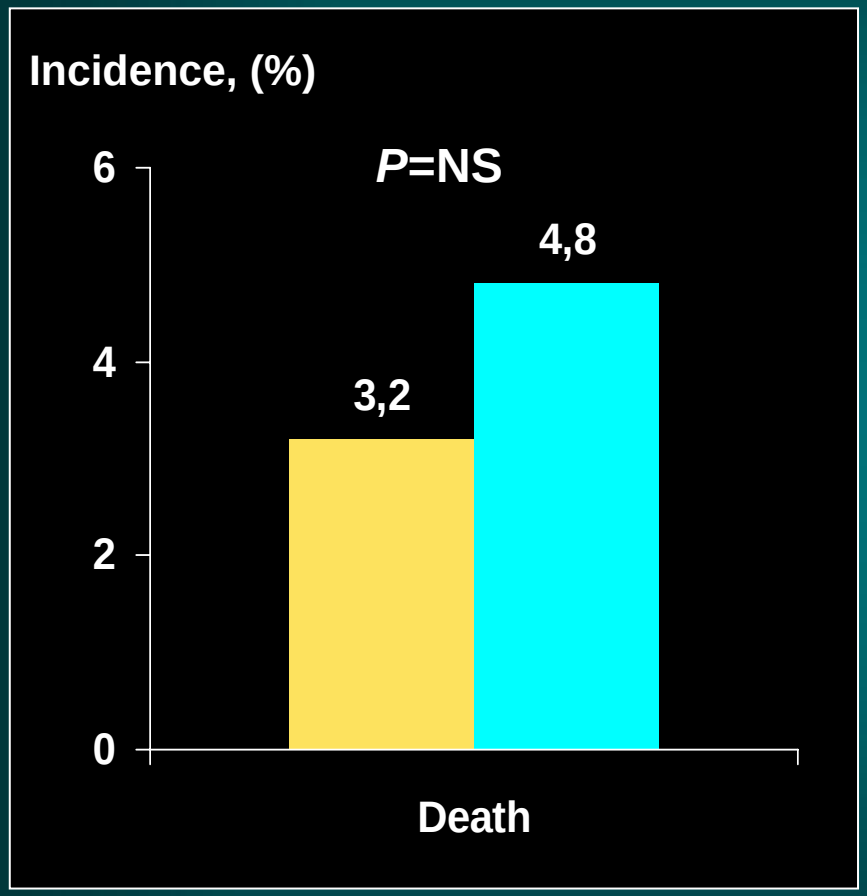
Clinical Characteristics I

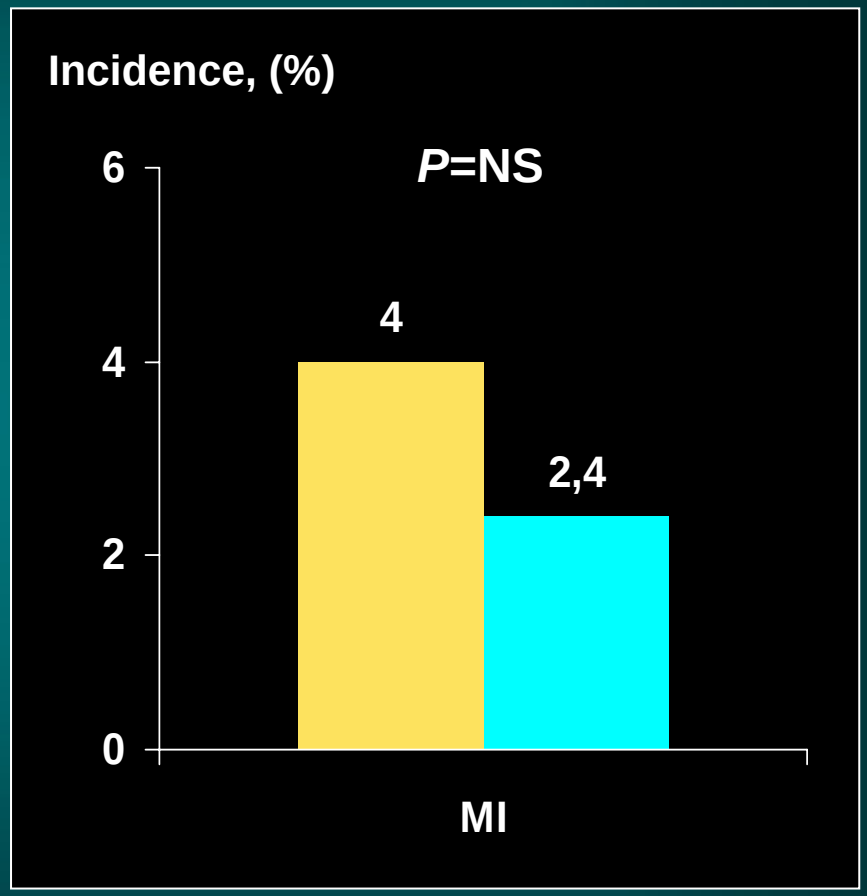
	CYPHER (n = 125)	TAXUS (n = 125)	*P*
Age, years	67.7±10.2	68.3±9.6	.63
Women, (%)	26	29	.57
Treatment of diabetes			.36
No drugs (%)	19	19	
Oral hypoglycem, (%)	44	52	
Insulin (%)	37	29	
Hemoglobin A1c, %	7.3±1.1	7.4 ±1.6	.69

Angiographic Characteristics II

	CYPHER (n- 125)	TAXUS (n=125)	*P*
Lesion length	13.8±7.6	12.4±7.7	.16
Vessel size, mm	2.70±0.50	2.75±0.56	.46
MLD, mm	1.03±0.37	1.12±0.40	.09
DS, (%)	61.1±13.1	59.4±11.9	.27

Clinical Outcome at 9 Months

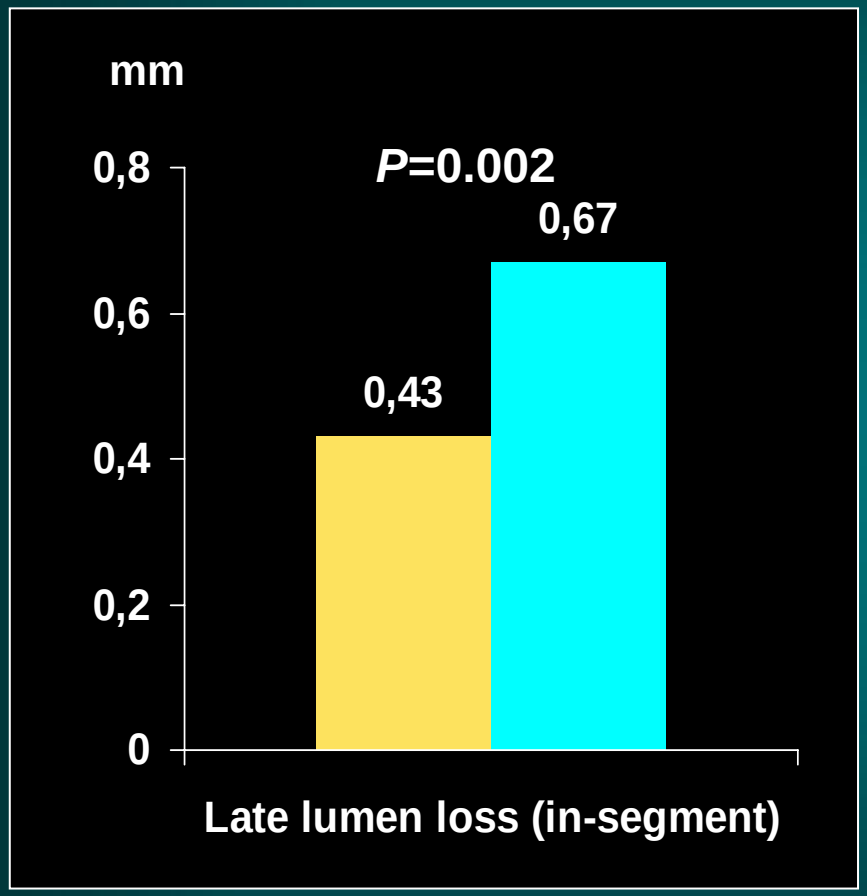


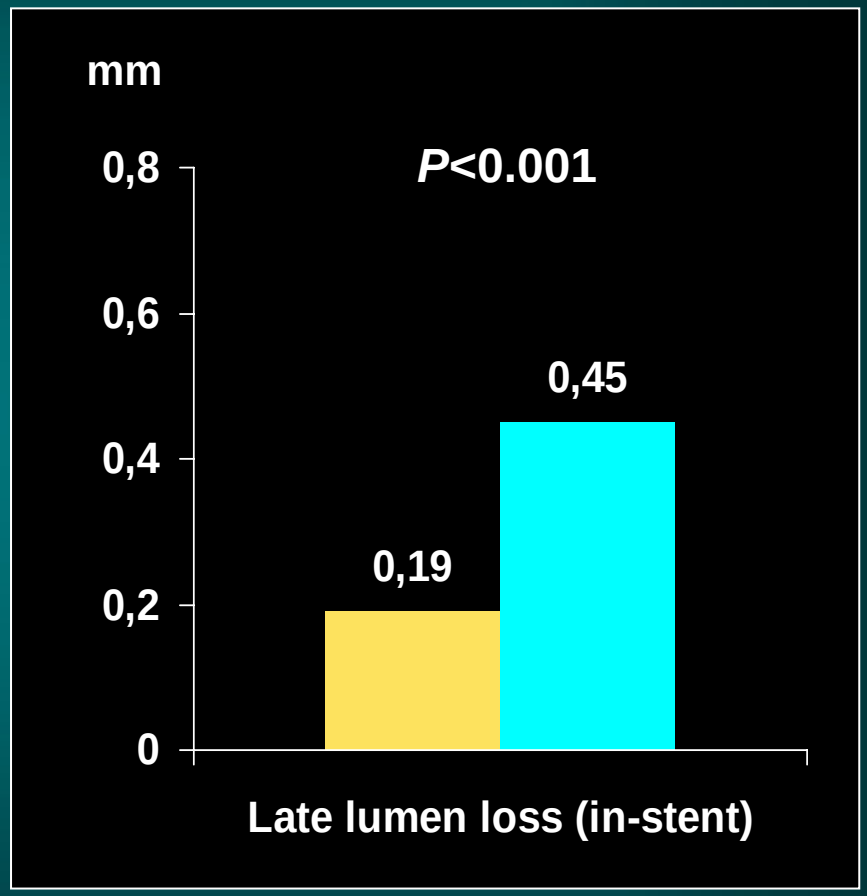


CYPHER

TAXUS

Late Lumen Loss

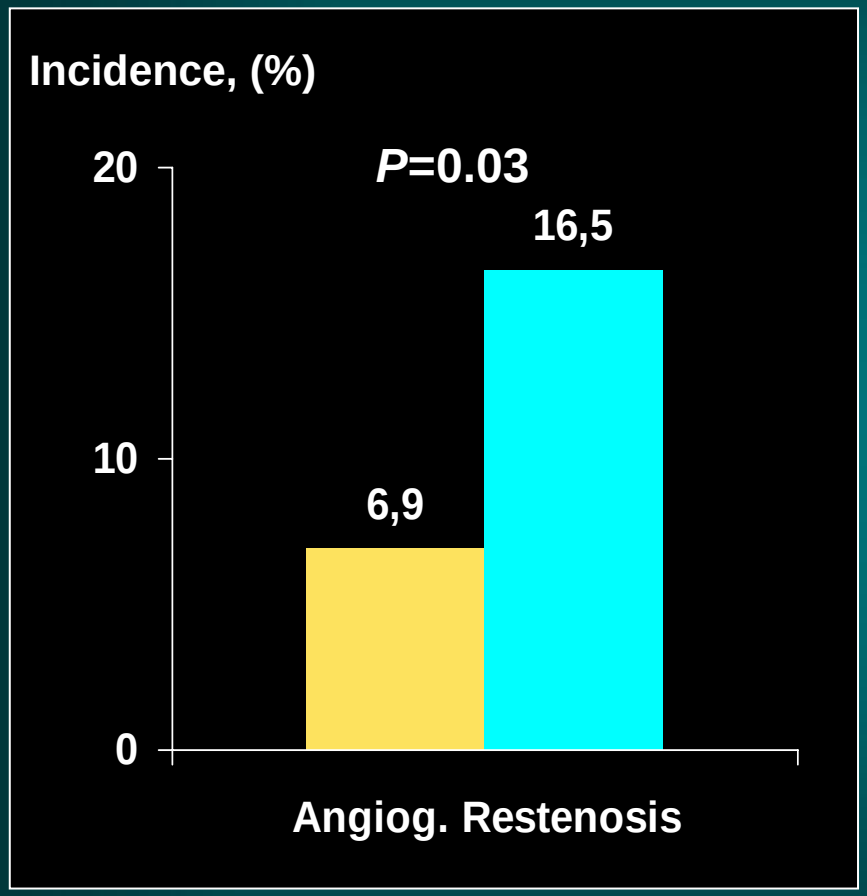


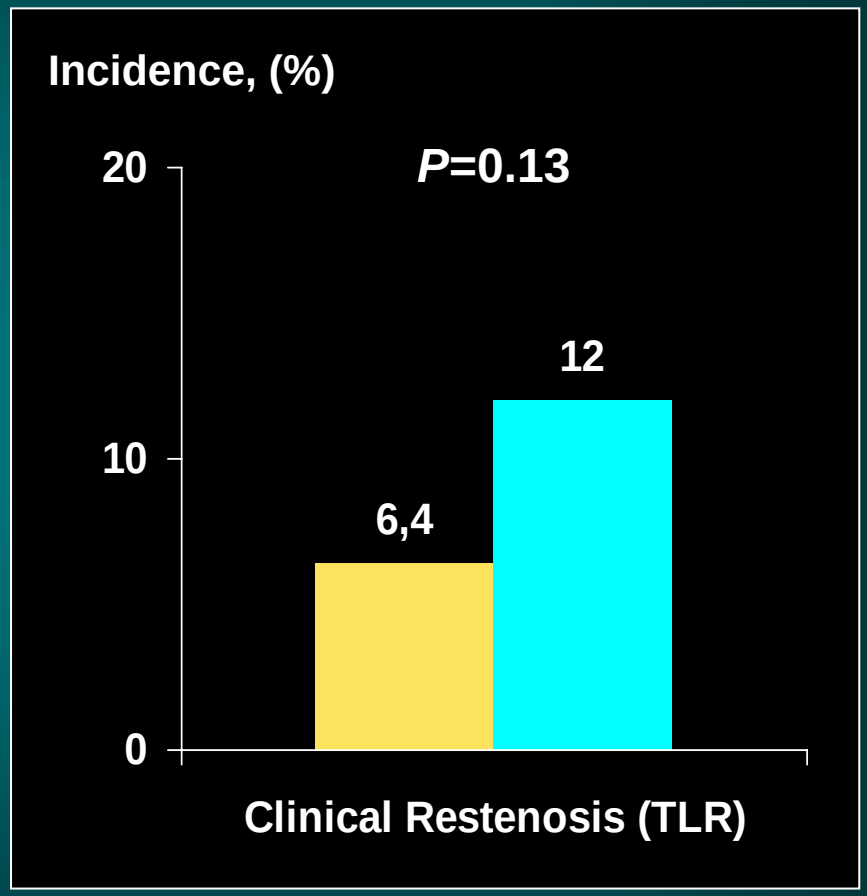


CYPHER

TAXUS

Restenosis





CYPHER

TAXUS

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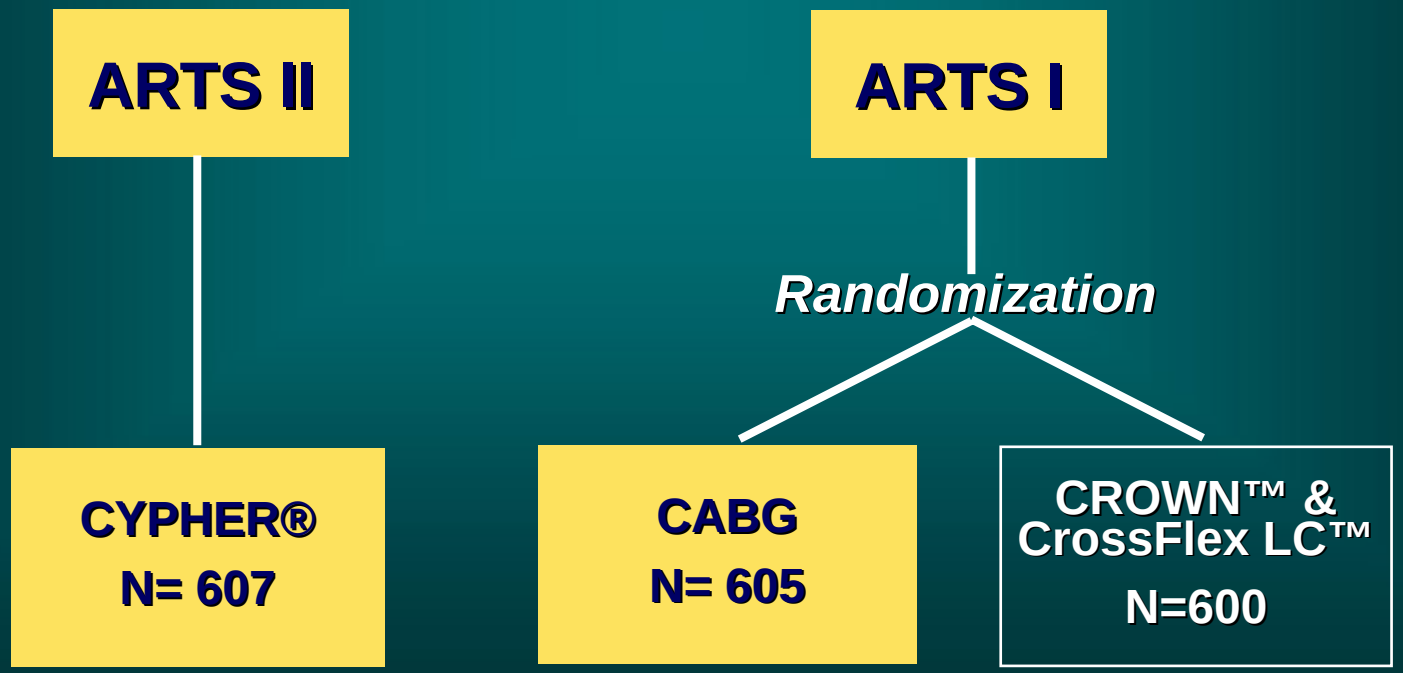
ARTS II: Study Design

- Single arm, multicenter trial
- 607 patients in 45 centers from 19 countries
- Main goal of the ARTS II trial is to demonstrate non-inferiority in clinical effectiveness and cost-effectiveness with the CYPHER® stent compared to the previous results of the ARTS I trial



Serruys P., et al., ACC 2005 (Sunday March 6th); Oral Presentation.

ARTS II: Baseline Demographics

	ARTS II N=607	ARTS I (CABG) N=605	ARTS I (PCI) N=600
Male (%)	77	76	77
Age (years)	**63** ↗	61	61
Body mass index (kg/m^2)	28	27	27
Previous MI (Q-wave)	**34 (18)** ↘	42 (24)	44 (26)
Diabetes (IDDM)	**26 (5)** ↗	16 (3)	19 (4)
Hypertension	**67** ↗	45	45
Hypercholesterolemia	**74** ↗	58	58
Family history	36	42	39
Current smokers	**19** ↘	26	28
Ejection fraction	60	60	61
Unstable angina	37	35	37

Figures in Orange indicate statistical difference (95% CI) between ARTS II and ARTS I groups

ARTS II: Lesion Characteristics

% of patients	ARTS II N=607 pts N=2160 les.	ARTS I (CABG) N=605 pts N=1638 les.	ARTS I (PCI) N=600 pts N=1606 les.
2-VD	46	66	69
3-VD	**54** ↗	30	27
% of lesions			
LAD location	42	41	39
LCx location	29	29	29
RCA location	29	30	31
Discrete (<10mm)	61	68	66
Tubular (10-20mm)	27	25	27
Diffuse (>20mm)	**12** ↗	7	7
Type C lesion	**14** ↗	8	8
Side branch involvement	34	32	35

ARTS II:Procedural Characteristics

	ARTS II N=607 pts N=2160 les.	ARTS I (CABG) N=605 pts N=1638 les.	ARTS I (PCI) N=600 pts N=1606 les.
Lesions, #	3.6 ↗	2.8	2.8
Stented les. / anast. seg., #	3.2 ↗	2.6	2.5
Stents, #	3.7 ↗	-	2.8
Direct stenting, %	35 ↗	-	3
Max. inflation pressure, atm	16.4 ↗	-	14.6
Total stent length, mm	73 ↗	-	48
(range)	12-253	-	8-165
Gp IIb/IIIa inhibitor use, %	33 ↗	-	-
Use of arterial conduit, %	-	93	-
Duration of procedure, mins	85 ↘	193	99
Hospital stay, days	3.4	9.6	3.9

ARTS II: MACCE up to 1 year *

MACCE	ARTS II N=607	ARTS I (CABG) N=602	ARTS I (PCI) N=600
Death	1.0%	2.7%	2.7%
CVA	0.8%	1.8%	1.8%
MI	1.2%	3.5%	5.0%
(re) CABG	2.0%	0.7%	4.7%
(re) PCI	5.4%	3.0%	12.3%
Any MACCE	10.4%	11.6%	26.5%

* Complete follow-up in 97%

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SIRIUS - Study Design

n = 1058 patients

***De Novo* Coronary Lesions**

Diameter: 2.5-3.5 mm
Length: 15-30 mm

Control
Bx VELOCITY™
n = 525

Sirolimus-eluting
Bx VELOCITY™
n = 533

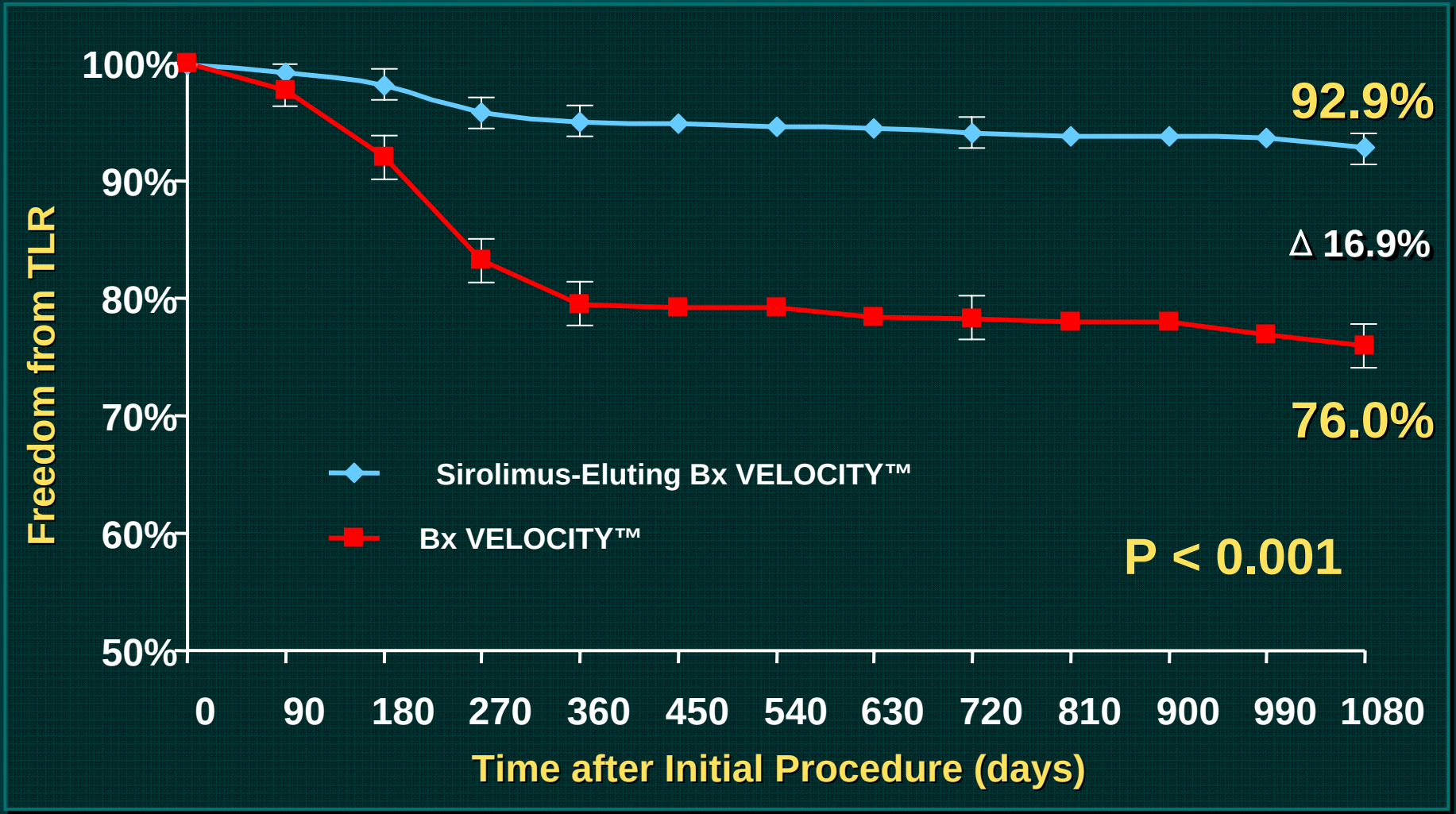
Primary Endpoint: **target vessel failure (TVF) = cardiac death, MI or TVR (FU at 9 mos)**

Angiographic Substudy: **first 850 pts (FU at 8 mos)**

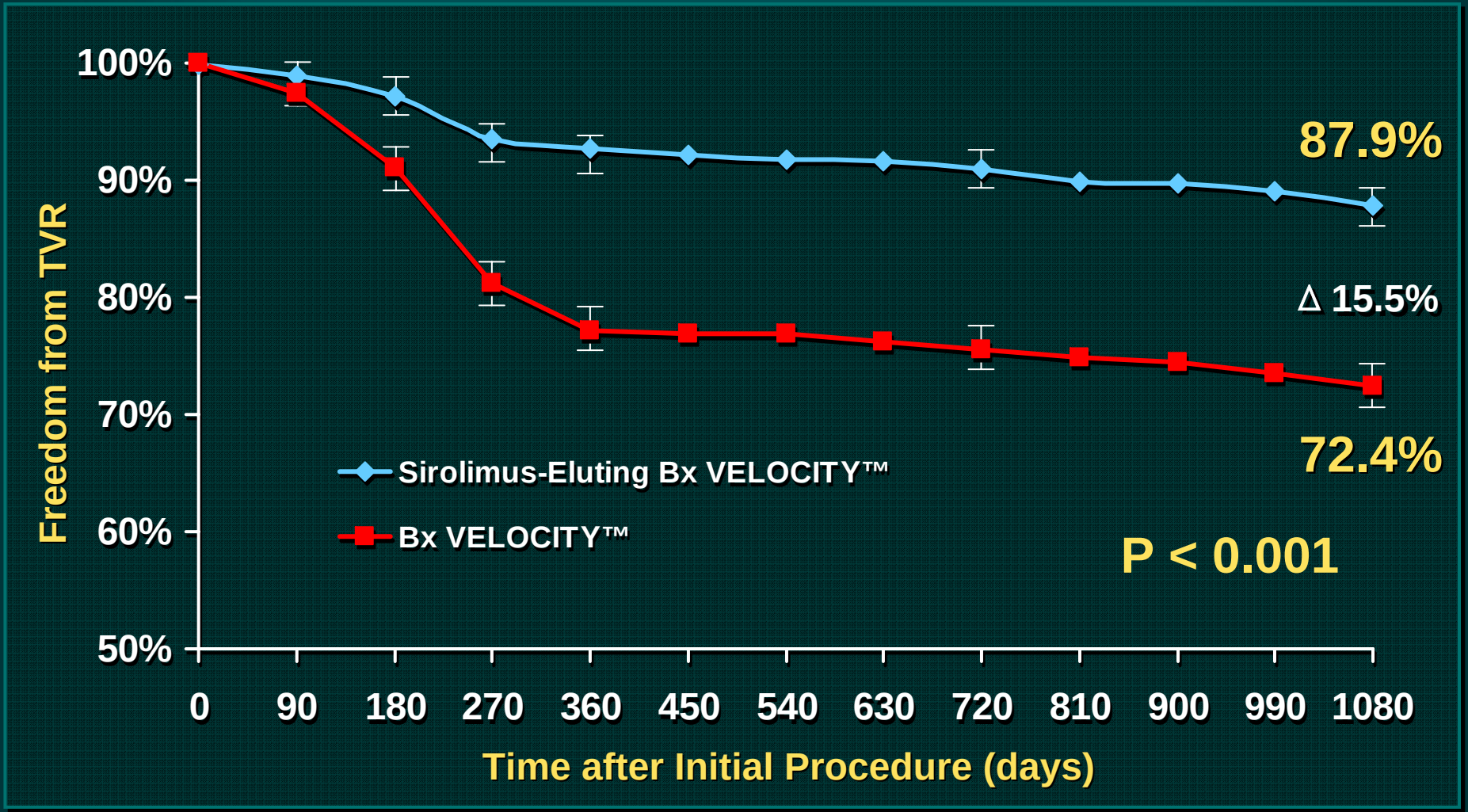
IVUS Substudy: **250 pts at selected sites (FU at 8 mos)**

Leon et al ACC 2005

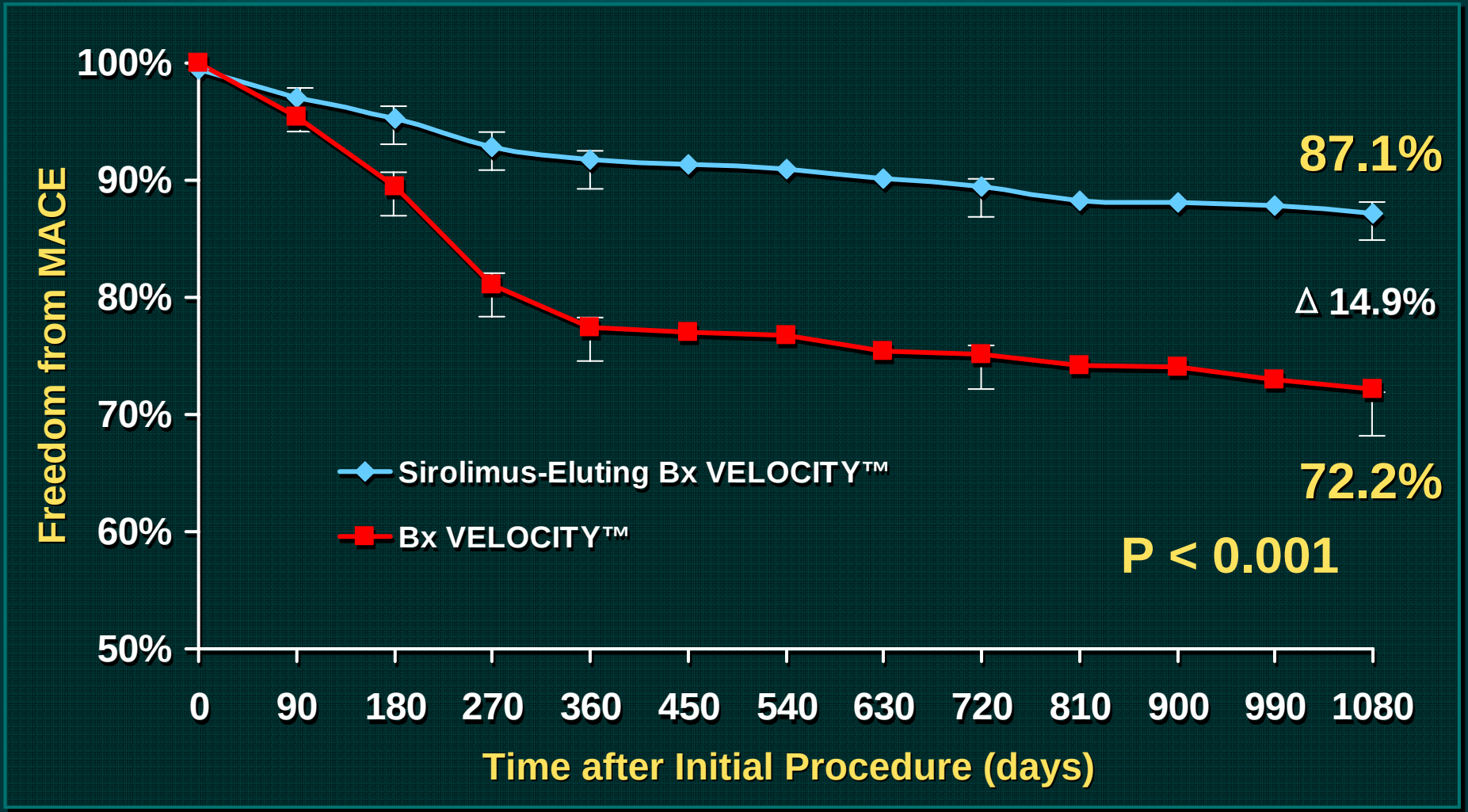
SIRIUS - Survival Free from TLR
(up to 3 yrs)



SIRIUS - Survival Free from TVR
(up to 3 yrs)



SIRIUS - Survival Free from MACE
(up to 3 yrs)



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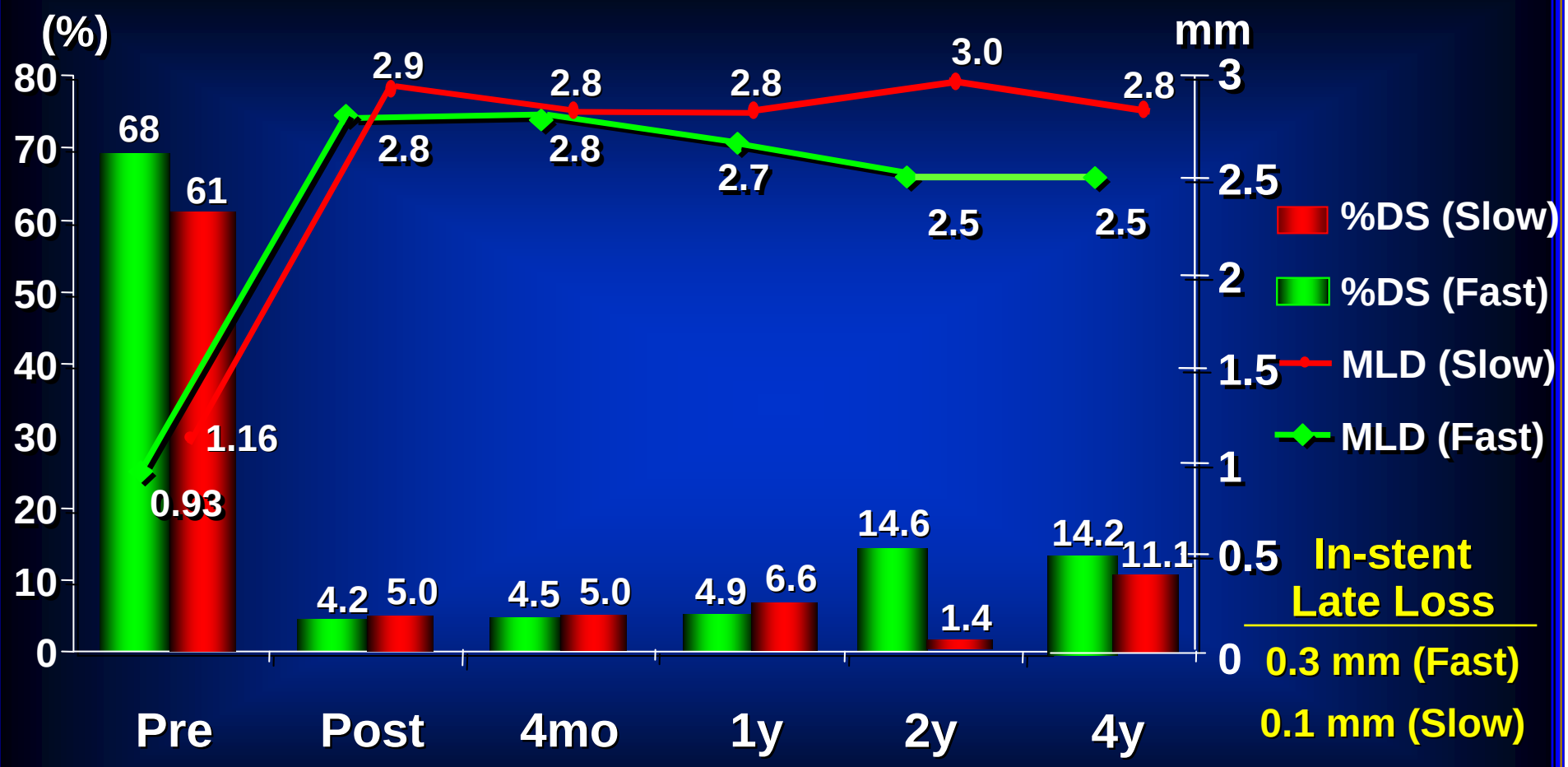
FIM: Changes in % DS and MLD In-stent

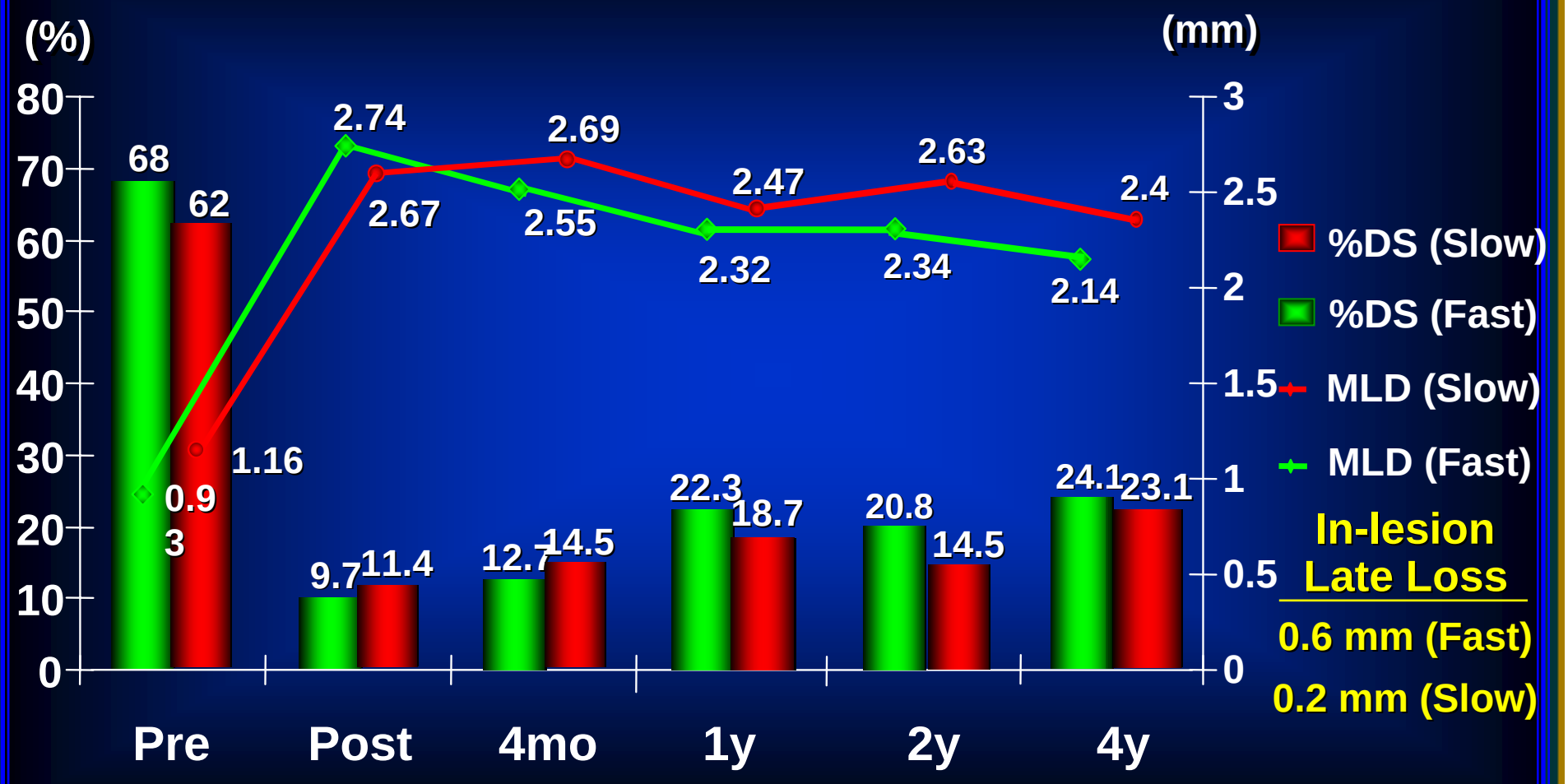
Dante Pazzanese



Sousa et al. Circulation in press

FIM: Changes in % DS and MLD In-lesion

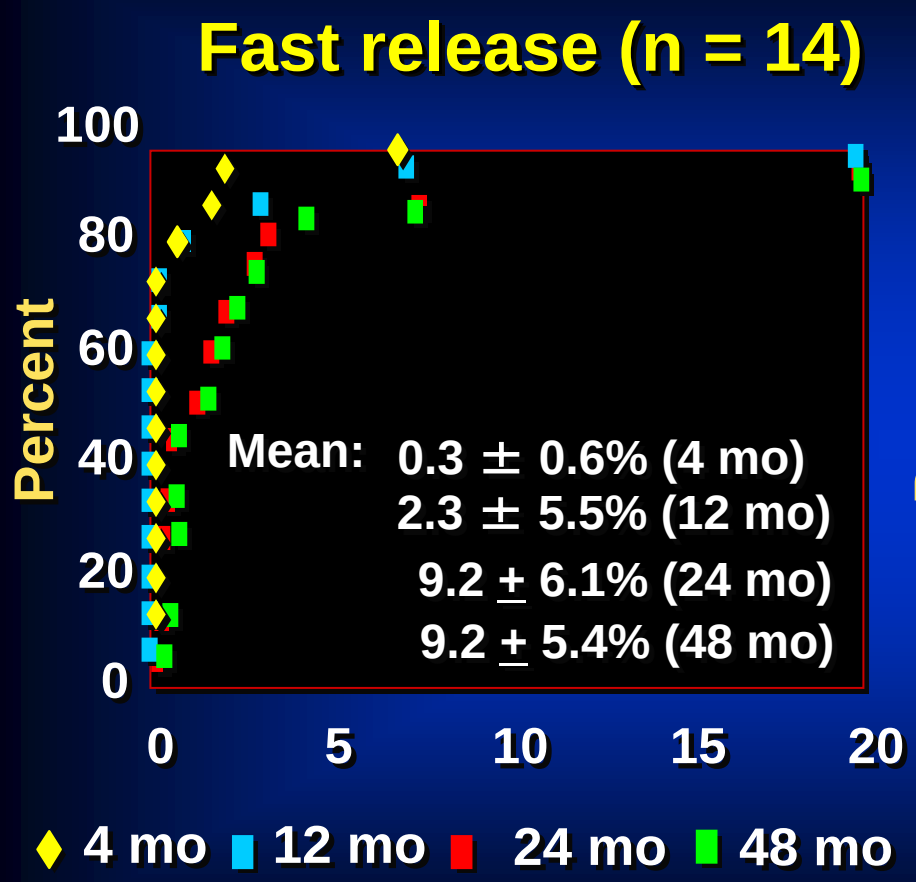
Dante Pazzanese

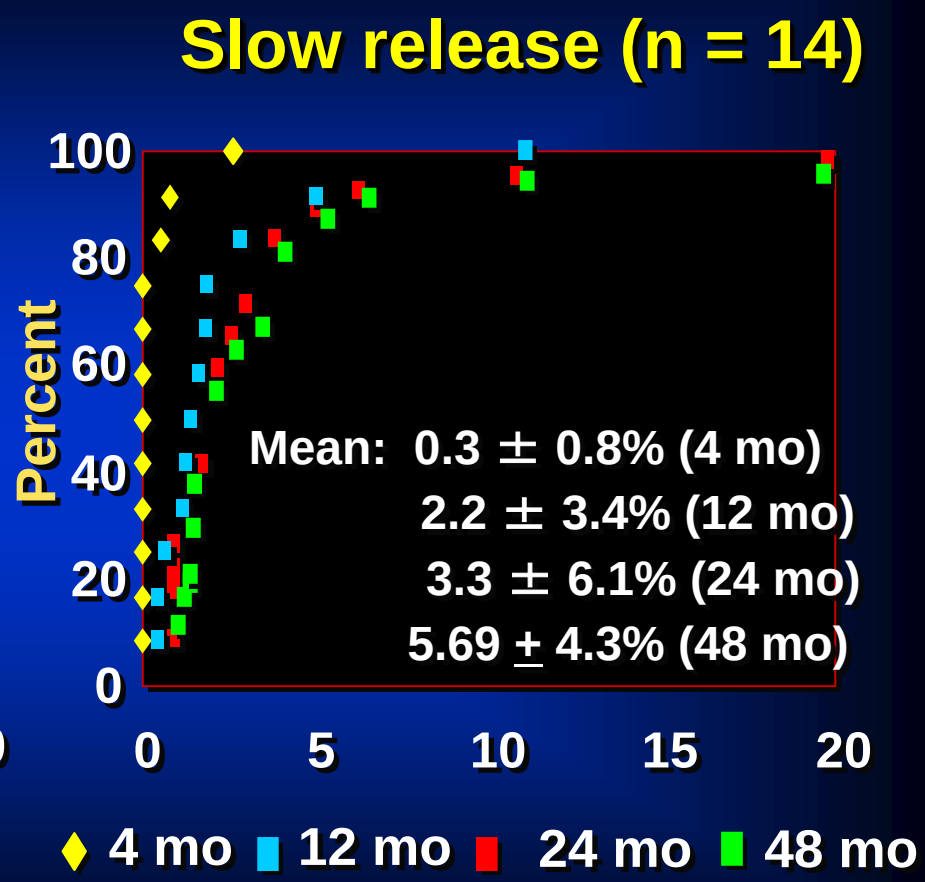


QCA : J. Popma

Neointimal Hyperplasia (% Obstruction)

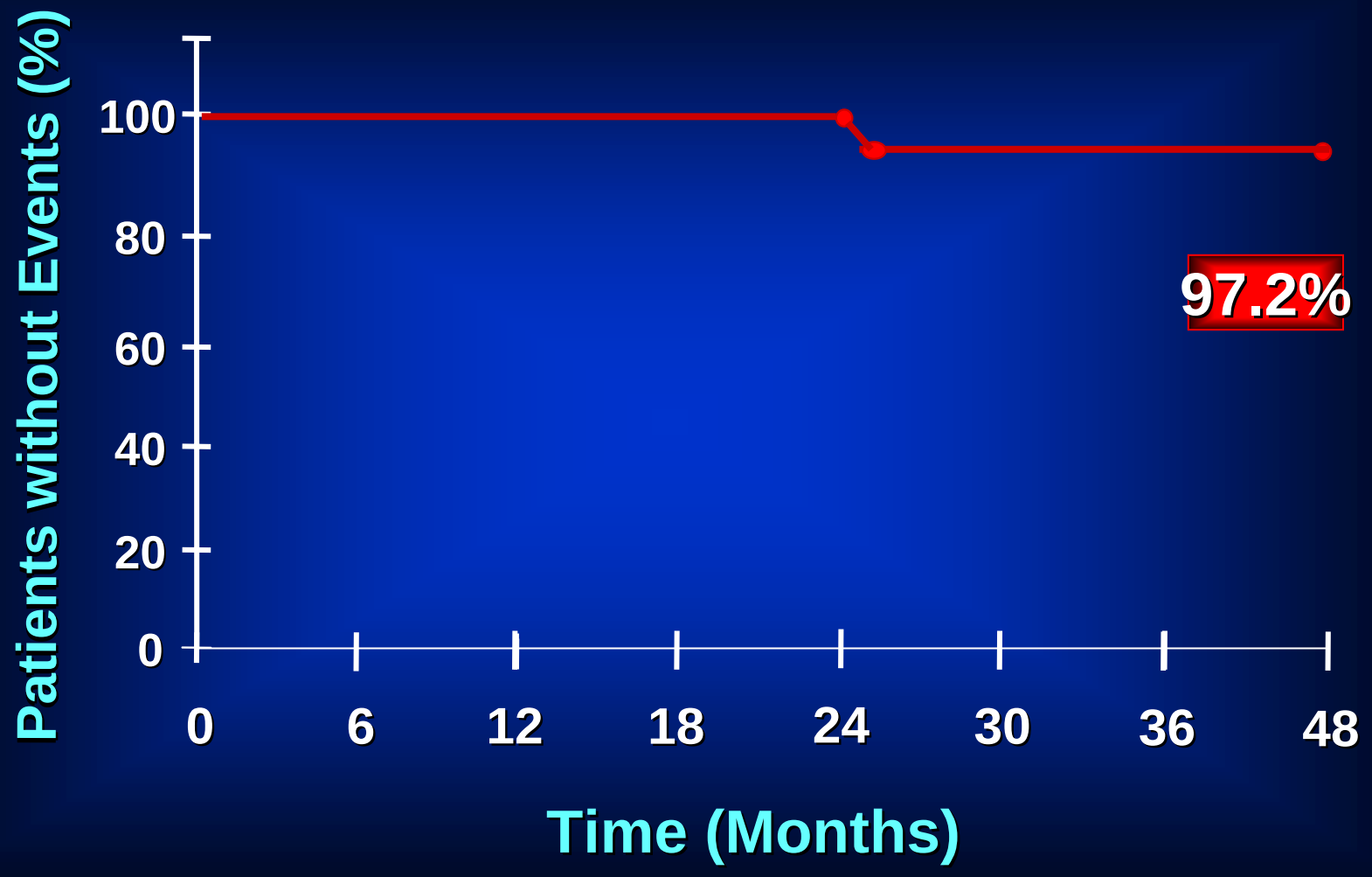
Cumulative Distribution Curves





FIM Trial Event Free Survival: TLR

Dante Pazzanese



FIM Trial: 4-Year Event Free Survival

Dante Pazzanese