

PAINT trial

***P*ercutaneous *I*ntervention with biodegradable-polymer based paclitaxel-eluting, sirolimus-eluting, or bare stents for the treatment of de novo coronary lesions**

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Heart Institute – InCor

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euroPCR 2008 - Late breaking trials
Tuesday 13th May, 2008
15:30 to 18:30, Room 1

Potential conflicts of interest

Pedro A. Lemos MD PhD

I have the following potential conflicts of interest to report:

Consulting: BSC, Scitech

Employment in industry

Stockholder of a healthcare company

Owner of a healthcare company

Lecture fee: Biotronik, BSC, CMS, Cordis

I do not have any potential conflict of interest



Key facts

- I. Current scientific evidences for paclitaxel- and sirolimus-eluting stents are mostly derived from only two stent formulations.
- II. DES are complex biodevices that do not follow a “class effect”: other DES with the same drugs should be, ideally, tested in the context of clinical trials
- III. Any difference between the drugs paclitaxel and sirolimus can not only be tested when the stents are similar in all other components



PAINT trial

Rationale

I. Main hypothesis:

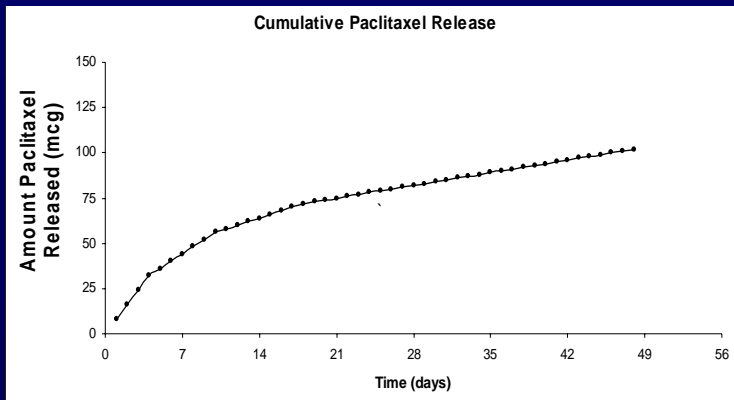
- 2 novel formulations of DES with paclitaxel or sirolimus, eluted in biodegradable polymers, are effective in reducing neointimal proliferation, in comparison to bare stents

II. The study design allows the evaluation of 2 DES that only differ on the type of drug

- Both DES use the same metal platform
- Both DES have the same polymeric coating



Infinnium™ Paclitaxel-Eluting Stent & Supralimus™ Sirolimus-Eluting Stent



- Slow drug release profile
 - 50% release within 9 days
 - 100% within 48 days
- Drug released from the porous surface by diffusion
- Polymers breaks into CO₂ & H₂O.
- No residual polymer after 7 m.

Total drug content (µg)

	19-mm	23-mm	29-mm
Infinnium	122	147	185
Supralimus	125	151	191

Drug dose (µg)

Infinnium 2.5-3.5 x 19 mm	122
Taxus 2.5-3.0 x 20 mm	135
Supralimus 2.5-3.5 x 19 mm	125
Cypher 2.5-3.0 x 18 mm	153



Study Design

280 patients treated with coronary stenting for:

- De novo coronary lesion in a native vessel
- Vessel size 2.5-3.5 mm
- Single stent per lesion up to 29-mm stent length

Randomization (1:2:2)

Matrix BMS
(n=59 pts)

Infinnium PES
(n=113 pts)

Supralimus SES
(n=108 pts)

9-month angiographic follow-up (n=265; 95%)

9-month IVUS
sub-study

60-month clinical follow-up

← Clopidogrel for 1 year



Main Exclusion Criteria

- Q wave MI < 48 hours or recent (Q wave or non Q) MI with still elevated cardiac markers
- Ejection fraction < 30%
- Serum creatinine > 2.0 mg/dl (177 μ mol/l)
- PCI < 6 months in any segment of the target vessel
- Previous PCI (at any time) <5mm from target lesion
- Angiographic thrombus
- Occluded target vessel
- Ostial location
- Bifurcation with SD >2.5mm or that may need stent
- Severe calcification
- Severe tortuosity



Study Objectives

Primary

- To compare the in-stent luminal loss of the 2 DES (Infinium or Supralimus) with the control BMS
 - Sample size: 82% power
 - Difference in LL of at least 0.25 mm
 - Multiple comparison testing at a 0.05 significance level
 - Attrition rate of 15%
 - Intention-to-treat

Main Secondary

- To compare the incidence of adverse cardiac events up to 5 years
- To compare the 9-month binary restenosis
- To compare the cost-effectiv. profile up to 5 years
- To compare the 9-month IVUS NIH obstruction



Study Coordination

Steering Committee

- Pedro A. Lemos , Princ. Investigator
- Expedito E. Ribeiro
- Bruno M. Machado
- Maurício de Rezende Barbosa
- César R. Medeiros
- Itamar Ribeiro Oliveira
- Eulógio E. Martinez
- Valter C. Lima
- J. Airton Arruda
- Fábio S. de Brito Jr.
- Paulo R. A. Caramori

Data Safety and Adjudication Committee

- Antonio Carlos Carvalho, President
- Luciano Drager
- Carlos Augusto Campos

Contract Research Organization

Fundação Zerbini, São Paulo,
Brazil

Database management

Coreware, São Paulo,
Brazil

Angiographic core lab

Cardialysis BV, Rotterdam,
The Netherlands

Partial Corporate Sponsoring

Sahajanand MT, Surat, India
CMS Medical, Goiânia, Brazil



Multicenter in Brazil

Enrollment by Center

Pedro A. Lemos InCor	105 pts
Bruno Moulin HUCAM	39 pts
Marco Perin Hosp. Sta Marcelina	32 pts
Ludmilla de Oliveira Natal Hospital Center	23 pts
Valter C. Lima UNIFESP	18 pts
Antonio A. G. Lima HU Walter Cantidio	15 pts
J. Airton de Arruda Intercath Meridional	19 pts
Paulo R. A. Caramori PUCRS	14 pts
Cesar R. Medeiros Rede D'Or de Hospitais	9 pts
Mauricio R. Barbosa Biocor	4 pts
Fabio S. Brito Jr. Hospital São Camilo	2 pts

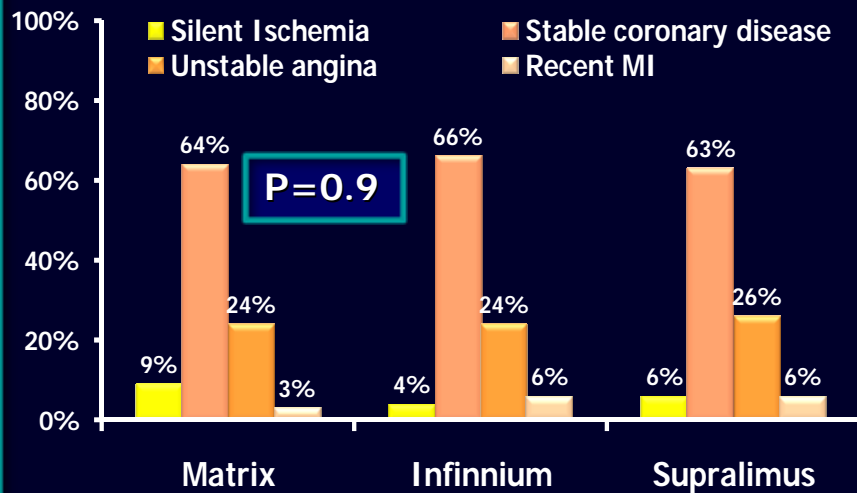


Baseline Characteristics

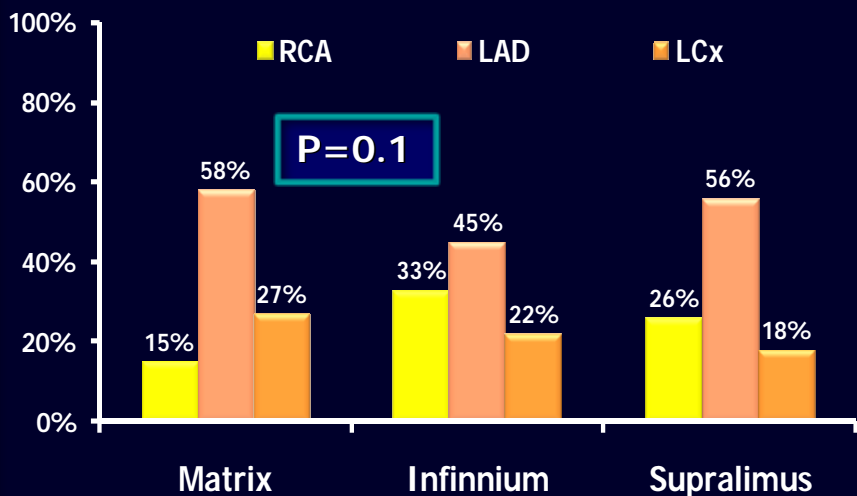
	Matrix <i>(n=59 pts)</i>	Infinnium <i>(n=113 pts)</i>	Supralimus <i>(n=108 pts)</i>	P
Age, y	59±9	60±10	60±11	0.6
Male	66	61	67	0.7
Hypertension	86	84	89	0.6
Diabetes	25	28	34	0.4
Previous MI	38	28	33	0.5
Previous PCI	19	16	15	0.8
Previous CABG	3	10	6	0.2
Multivessel disease	42	37	36	0.7



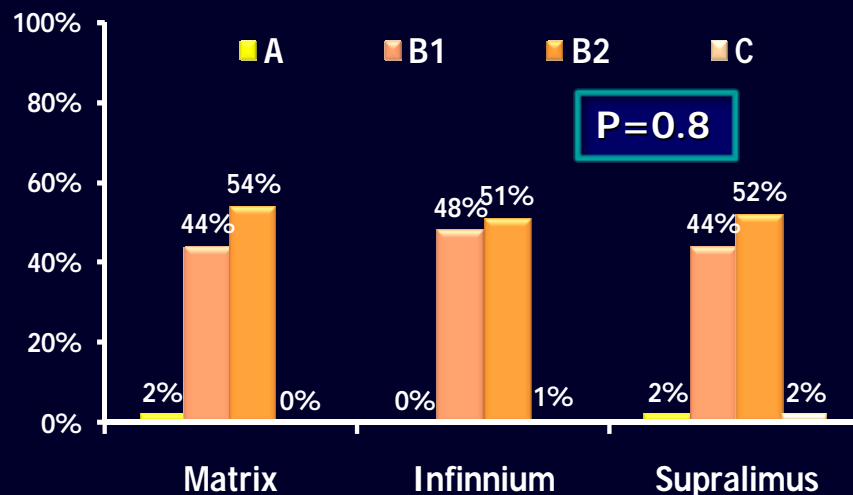
Clinical Presentation



Treated Vessel



Lesion Type





Procedure Characteristics and Acute QCA

	Matrix <i>(n=59 pts)</i>	Infinnium <i>(n=113 pts)</i>	Supralimus <i>(n=108 pts)</i>	P
St. diameter, mm	3.1±0.4	3.1±0.4	3.1±0.3	0.8
St. length, mm	21.6±3.7	21.9±4.0	21.5±3.5	0.6
Ref. diameter, mm	2.70±0.52	2.71±0.50	2.72±0.47	0.9
Lesion length, mm	12.4±5.0	12.7±5.5	12.2±5.1	0.7
In-stent MLD post, mm	2.43±0.37	2.46±0.40	2.47±0.36	0.8
In-segment MLD post, mm	2.12±0.42	2.14±0.45	2.15±0.45	1.0



9-month QCA findings

	Matrix (n=55 pts)	Infinnium (n=103pts)	Supralimus (n=96 pts)	P-value DES vs. BMS
<u>In-stent</u>				
9-m MLD, mm*	1.53±0.61	↓ 1.92±0.54	↓ 2.15±0.51	<0.01
9-m late loss, mm*	0.90±0.45	↓ 0.54±0.45	↓ 0.32±0.44	<0.01
9-m binary rest.	25.5	↓ 8.7	↓ 4.2	<0.01
<u>In-segment</u>				
9-m MLD, mm*	1.47±0.59	↓ 1.81±0.49	↓ 1.99±0.48	<0.01
9-m late loss, mm*	0.65±0.50	↓ 0.33±0.42	↓ 0.16±0.42	<0.01
9-m binary rest.	25.5	↓ 8.7	↓ 4.2	<0.01

*p<0.05 for Infinnium vs. Supralimus

Matched results: analysis only includes patients with both post-procedure and follow-up QCA

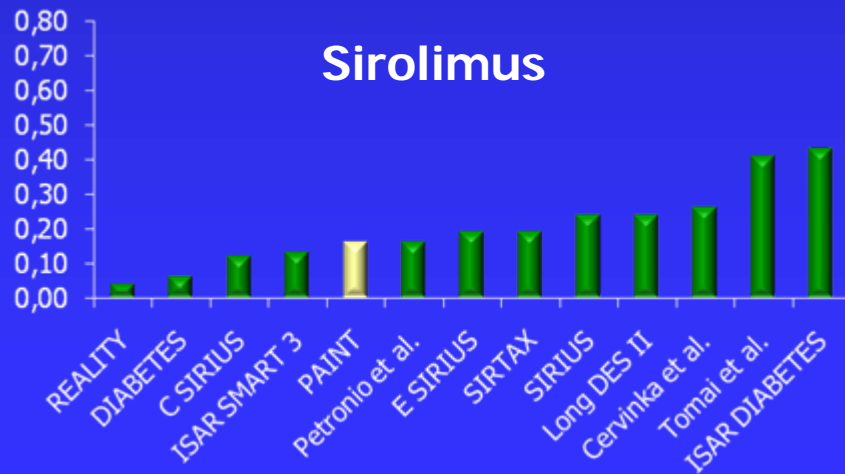
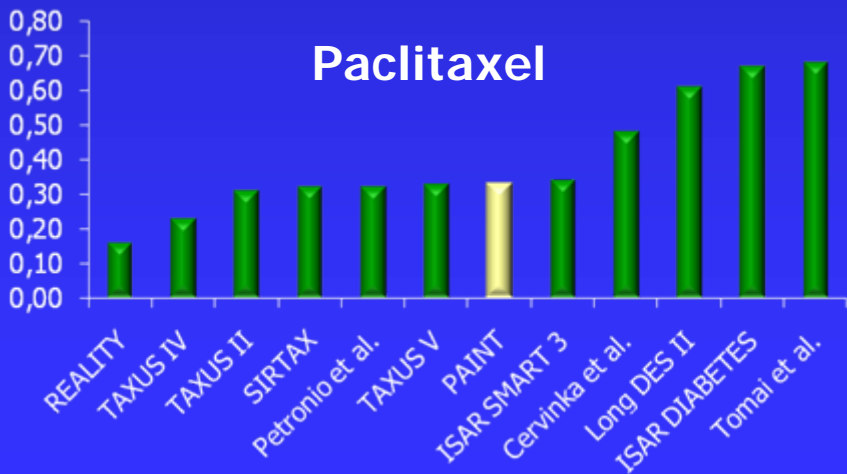


Late QCA Across Clinical Trials

In-segment binary restenosis



In-segment late loss

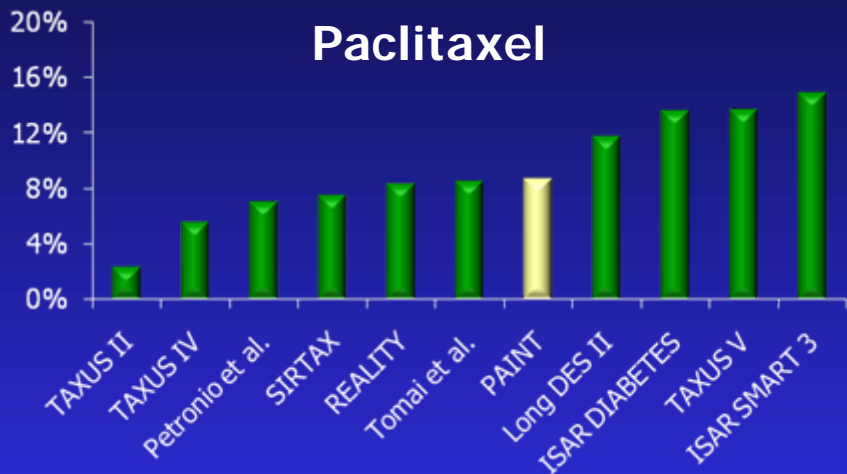




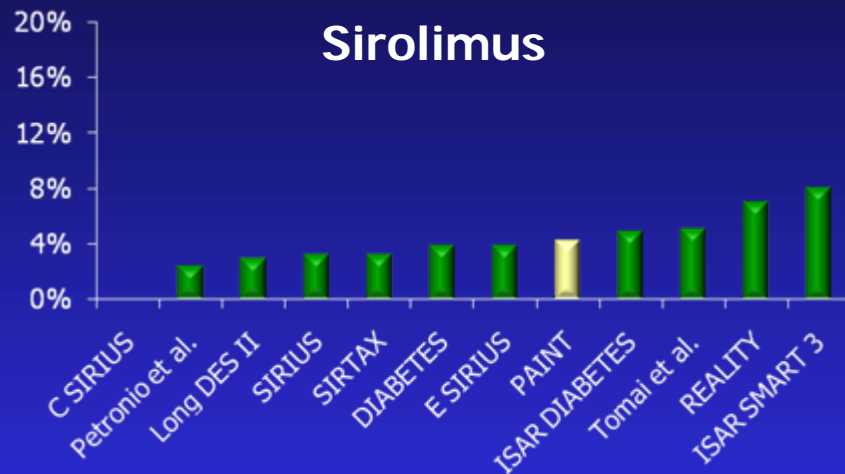
Restenosis Across Clinical Trials

In-stent Binary Restenosis

Paclitaxel

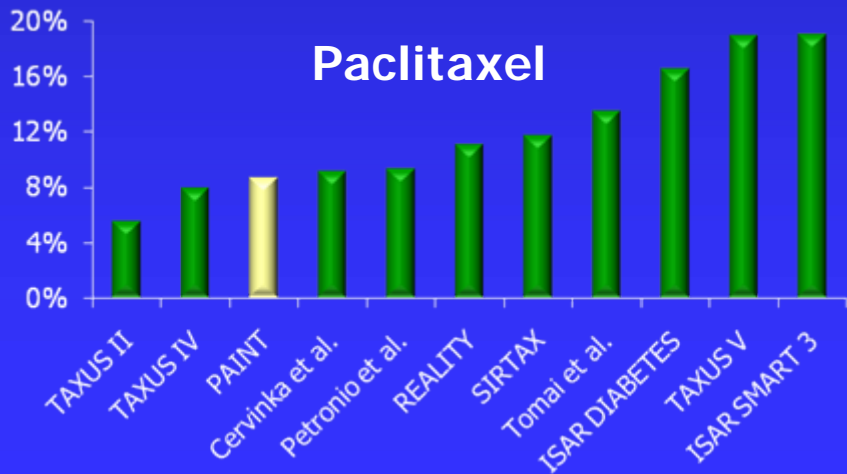


Sirolimus

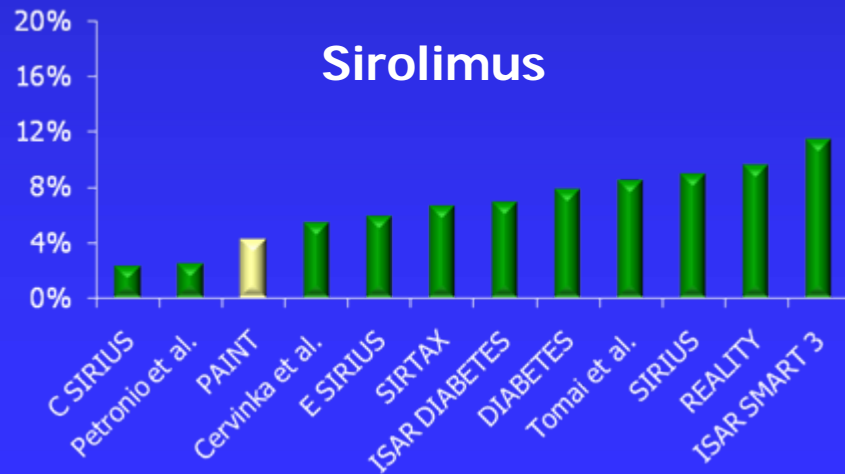


In-segment Binary Restenosis

Paclitaxel

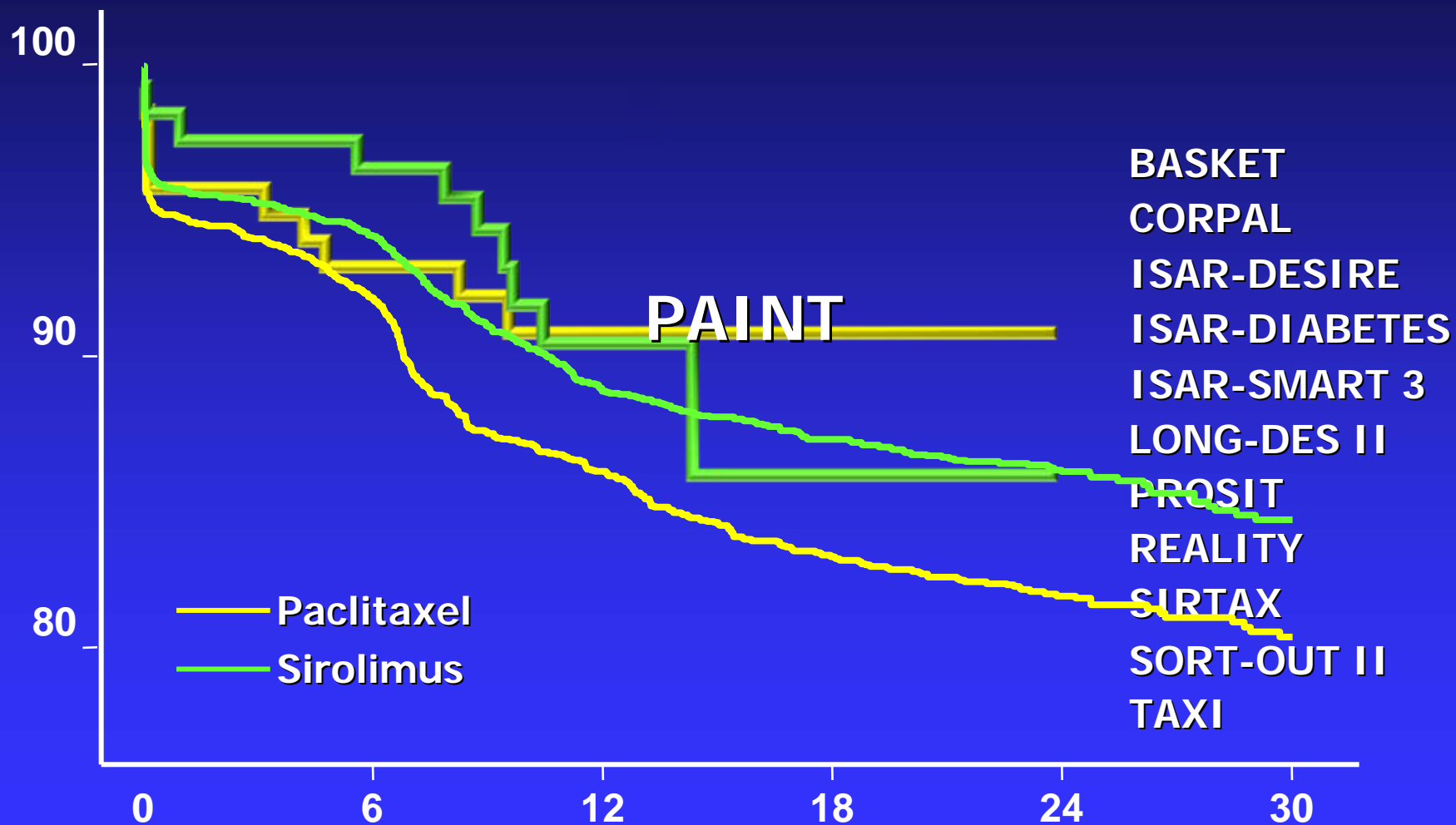


Sirolimus





MACE Across Head-to-Head Sirolimus vs. Paclitaxel Trials





10-Month Clinical Outcomes

	Matrix <i>(n=59 pts)</i>	Infinnium <i>(n=113 pts)</i>	Supralimus <i>(n=108 pts)</i>	P
Cardiac Death	0	0	1.0	0.5
Myocardial infarction	6.8	5.4	6.1	0.9
Target lesion revasc.	12.7	4.5	4.6	<0.01
Target vessel revasc.	12.7	4.5	5.6	<0.01
Any event	16.1	9.4	8.4	0.07
Any ARC thrombosis	1.7	1.8	1.8	1.0
Definite	1.7	0.9	0.9	0.9
Late Definite/probable	0	0.9	0.9	0.8

ARC=Academic Research Consortium

Kaplan-Meier estimates; p values by log-rank test



Conclusions I

Compared to bare stents, implantation of Infinnium paclitaxel- and Supralimus sirolimus-eluting stents resulted in:

- **Significantly lower angiographic lumen late loss and binary restenosis at 9 months**
- **No case of edge restenosis (in any group)**
- **The reduction in neointimal proliferation of both DESs led to a significant reduction in the need for subsequent revascularization**
- **Similar rates of death, myocardial infarction, and stent thrombosis at 10-month follow-up**



Conclusions II

The head-to-head comparison between Infinnium and Supralimus, which use the same platform and polymeric coating, permitted to explore the isolate effect of the drugs sirolimus and paclitaxel:

- **The sirolimus stent was associated with a significantly larger NIH inhibition than paclitaxel**
- **However, the angiographic superiority of the sirolimus-stent was not translated into better clinical outcomes:**
 - **both sirolimus and paclitaxel stents were associated with a ~5% TLR rate and a MACE rate ~9% at 10 months**