



***Preliminary One-Year Outcome
After Sirolimus-eluting Stent Implantation
The j-Cypher Registry Update***

Takeshi Kimura MD. Kyoto University Hospital

Takeshi Morimoto MD. Kyoto University Hospital

Kazuaki Mitsudou MD. Kurashiki Central Hospital

on behalf of the j-Cypher Registry Investigators

Key Concepts of the j-Cypher Registry



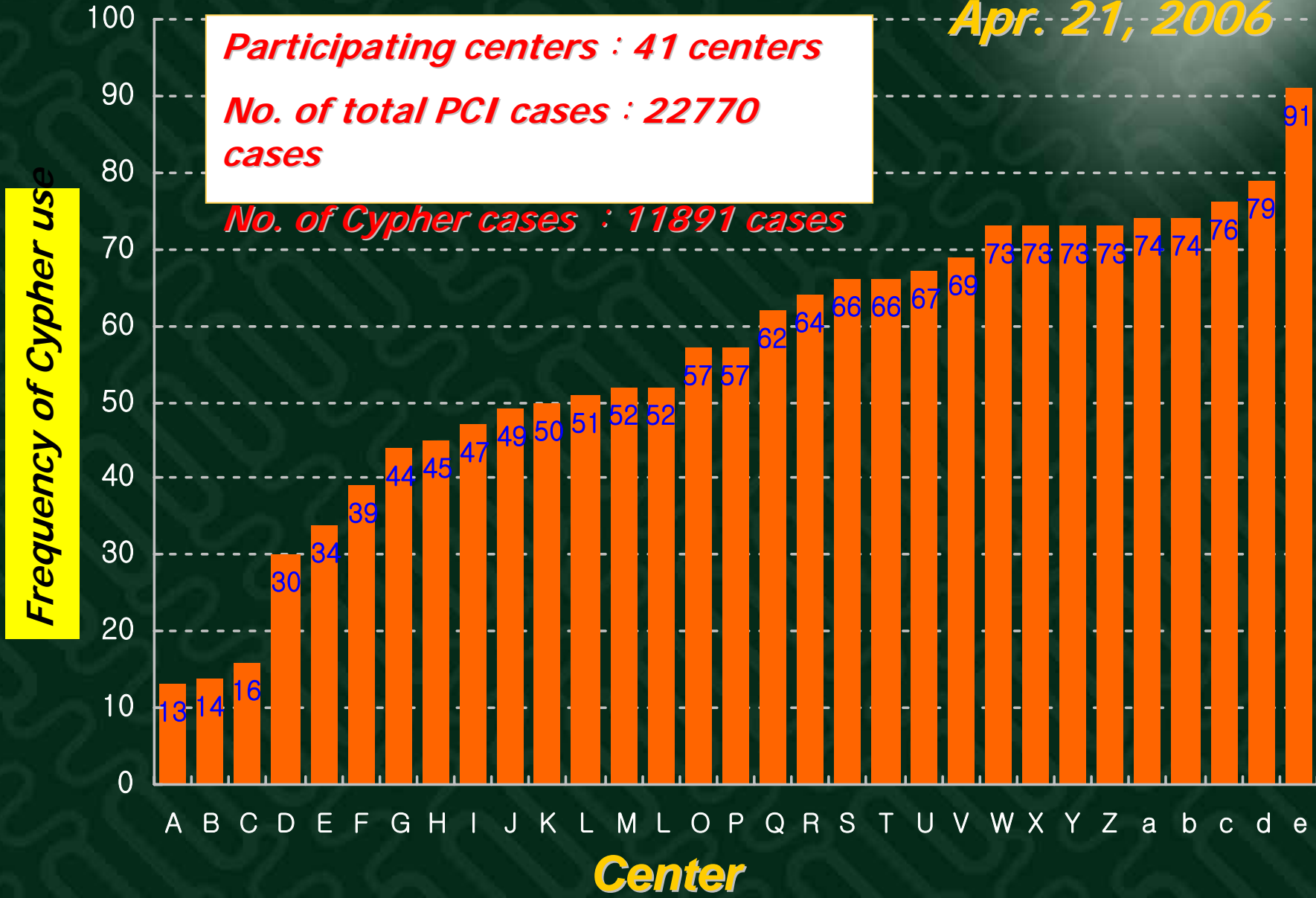
- 1. Physician-directed registry of consecutive patients undergoing SES implantaion (both on and off-label indication)***
- 2. Data management independent of the company***
- 3. Invitation of high volume centers to encompass a large number of high risk patients***
- 4. Data monitoring and auditing to assure quality of the data***
- 5. On-site data input via internet***
- 6. Collaborative work with co-medical stuff in each participating center***

Penetration of the Cypher™ Stent

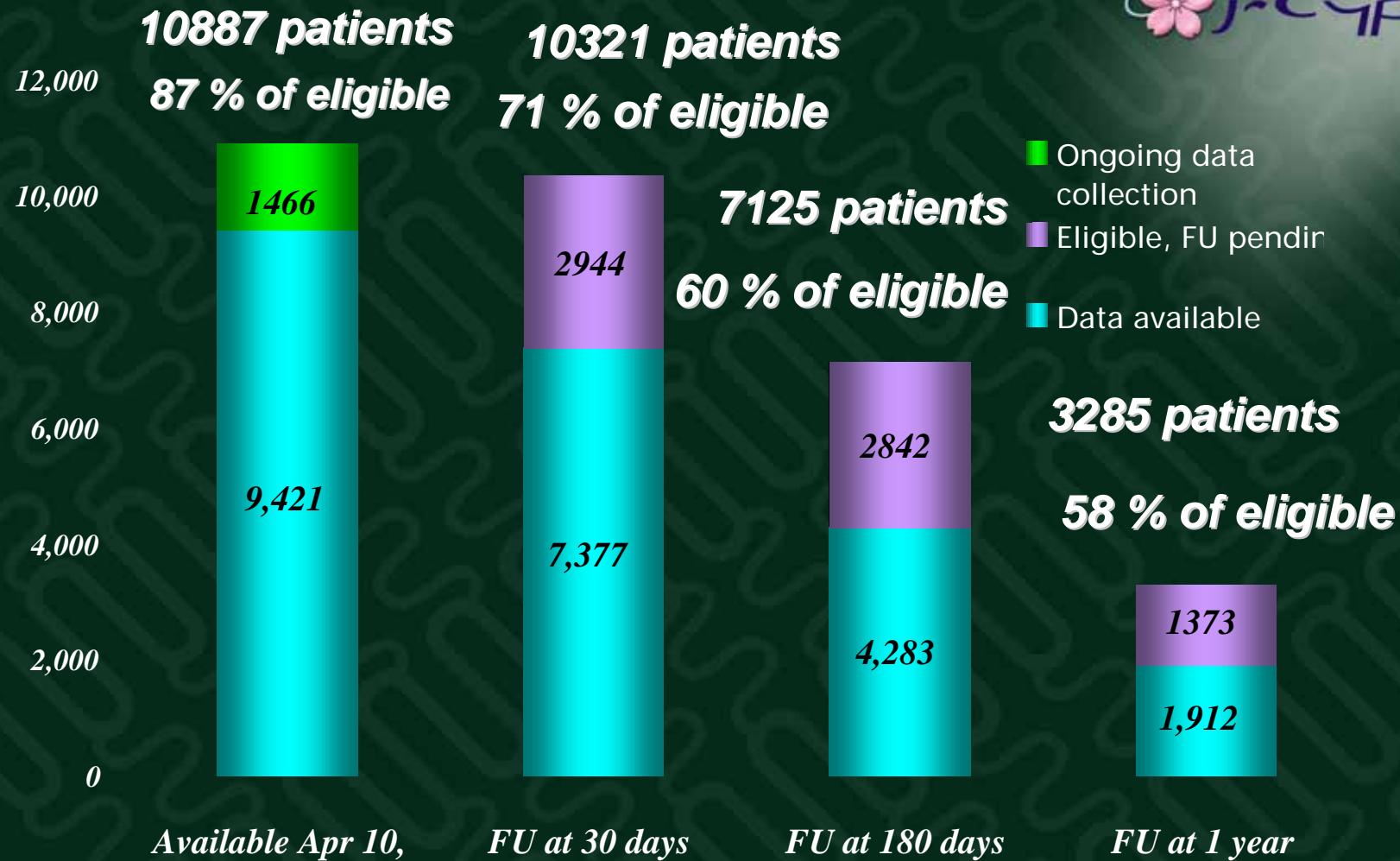


Apr. 21, 2006

Participating centers : 41 centers
No. of total PCI cases : 22770 cases
No. of Cypher cases : 11891 cases



Patient Enrollment and Data Collection



2006
Monitoring safety and efficacy of SES in the midst of expanding indication of PCI is the primary objective of the j-Cypher registry !

Strength of the j-Cypher Registry



- 1. The large sample size of the registry makes it possible to evaluate clinically important low-frequency events such as stent thrombosis and/or mortality.***
- 2. Consecutive enrollment of patients and the large sample size could reveal real world scenario in high risk subgroups such as those patients undergoing LMCA stenting and / or full-metal jacket multivessel stenting.***
- 3. Prospective data input on technical details of PCI such as related to bifurcation stenting and on compliance to anti-platelet therapy could provide unique and clinically useful information.***

Baseline Characteristics



	<i>j-CYPHER</i>	<i>e-CYPHER</i>	<i>P Value</i>
	<i>N=9421</i>	<i>N=15157</i>	
<i>Age</i>	<i>68 ± 10</i>	<i>62 ± 11</i>	<i>0.0001</i>
<i>> 80 y.o.</i>	<i>12 %</i>	<i>4 %</i>	<i>0.0001</i>
<i>Male</i>	<i>76 %</i>	<i>78 %</i>	<i>0.0005</i>
<i>Diagnosis</i>			<i>0.0001</i>
<i>Stable Angina</i>	<i>55 %</i>	<i>42 %</i>	
<i>UAP / NSTEMI</i>	<i>14 %</i>	<i>33 %</i>	
<i>STEMI</i>	<i>7 %</i>	<i>13 %</i>	
<i>Silent Ischemia / OMI</i>	<i>19 %</i>	<i>10 %</i>	
<i>Coronary Stenosis</i>	<i>5 %</i>	<i>3 %</i>	

Baseline Characteristics



	<i>j-CYPHER</i>	<i>e-CYPHER</i>	<i>P Value</i>
	<i>N=9421</i>	<i>N=15157</i>	
<i>Prior MI</i>	<i>29 %</i>	<i>30 %</i>	<i>0.11</i>
<i>Prior PCI</i>	<i>55 %</i>	<i>29 %</i>	<i>0.0001</i>
<i>Prior CABG</i>	<i>7 %</i>	<i>11 %</i>	<i>0.0001</i>
<i>Multi-vessel Disease</i>	<i>52 %</i>	<i>57 %</i>	<i>0.0001</i>
<i>Diabetes</i>	<i>43 %</i>	<i>29 %</i>	<i>0.0001</i>
<i>On Insulin</i>	<i>10 %</i>	<i>10 %</i>	<i>1.0</i>
<i>Hemodialysis</i>	<i>5 %</i>	<i>N.A.</i>	
<i>Hx of Heart Failure</i>	<i>13 %</i>	<i>N.A.</i>	
<i>PVD</i>	<i>11%</i>	<i>7 %</i>	<i>0.0001</i>
<i>Hx of Stroke</i>	<i>9 %</i>	<i>3 %</i>	<i>0.0001</i>

Procedural Characteristics



j - CYPHER ***e - CYPHER*** ***P Value***
N=9421 ***N=15157***

<i>Staged PCI</i>	<i>10%</i>	<i>N.A.</i>	
<i>Treated exclusively</i>			
<i>by CYPHER</i>	<i>92 %</i>	<i>98 %</i>	<i>0.0001</i>
<i>N of lesions / pt</i>	<i>1.4 ± 0.8</i>	<i>1.2 ± 0.5</i>	<i>0.0001</i>
<i>N of stents / lesion</i>	<i>1.3 ± 0.6</i>	<i>1.2 ± 0.4</i>	<i>0.0001</i>
<i>N of stents / pt</i>	<i>1.8 ± 1.1</i>	<i>1.4 ± 0.7</i>	<i>0.0001</i>

Procedural Characteristics



j - CYPHER ***e - CYPHER*** ***P Value***
N=13296 ***N=18295***

<i>Stent length / lesion (mm)</i>	<i>28.7 ± 15.4</i>	<i>N.A.</i>	
<i>Stent length / pt (mm)</i>	<i>39.9 ± 26.3</i>	<i>27.3 ± 16.1</i>	<i>0.0001</i>
<i>Direct stenting (%)</i>	<i>24</i>	<i>34</i>	<i>0.0001</i>
<i>Pressure at deployment (atm)</i>	<i>17.7 ± 4.5</i>	<i>14.3 ± 2.8</i>	<i>0.0001</i>
<i>Post-dilation (%)</i>	<i>41</i>	<i>21</i>	<i>0.0001</i>

Adverse Lesion Characteristics



	<i>j - CYPHER</i>	<i>e - CYPHER</i>	<i>P Value</i>
	<i>N=13296</i>	<i>N=18295</i>	
<i>STEMI culprit lesion</i>	<i>676 lesions (5 %)</i>	<i>N.A.</i>	
<i>Unprotected LMCA</i>	<i>383 lesions (3 %)</i>	<i>1 %</i>	<i>0.0001</i>
<i>In-stent restenosis</i>	<i>1913 lesions (14 %)</i>	<i>10 %</i>	<i>0.0001</i>
<i>Ostial lesion</i>	<i>1170 lesions (9 %)</i>	<i>8 %</i>	<i>0.003</i>
<i>CTO</i>	<i>1216 lesions (9 %)</i>	<i>2 %</i>	<i>0.0001</i>
<i>Vessel size < 2.5mm</i>	<i>4129 lesions (31 %)</i>	<i>8 %</i>	<i>0.0001</i>
<i>Lesion length > 30mm</i>	<i>1797 lesions (14 %)</i>	<i>5%</i>	<i>0.0001</i>
<i>Heavily calcified lesion</i>	<i>1159 lesions (9 %)</i>	<i>N.A.</i>	
<i>Bifurcation</i>	<i>2507 lesions (19 %)</i>	<i>9 %</i>	<i>0.0001</i>

Stent Thrombosis



Definition

Acute / Subacute (Within 1 month)

- *Angiographic documentation of stent occlusion*
- *MI and / or sudden cardiac death without proven patency of the stent*

2

Late (Beyond 1 month)

- *Angiographic documentation of stent occlusion with MI and / or sudden cardiac death*

%

1

0.39

*(95% C.I.
0.28-0.54)*



30 days

N=7377

0.19



31-180 days

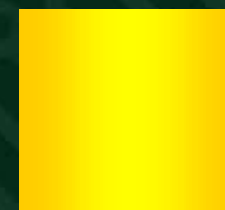
N=4283

0

181 - 365 days

N=1912

0.58



Cumulative

Stent Thrombosis



within 365 days 37 cases (0.58%)

Angiographically confirmed 29 cases

Possible (SCD) 8 cases

including BMS thrombosis in 2 patients

Death 13 cases

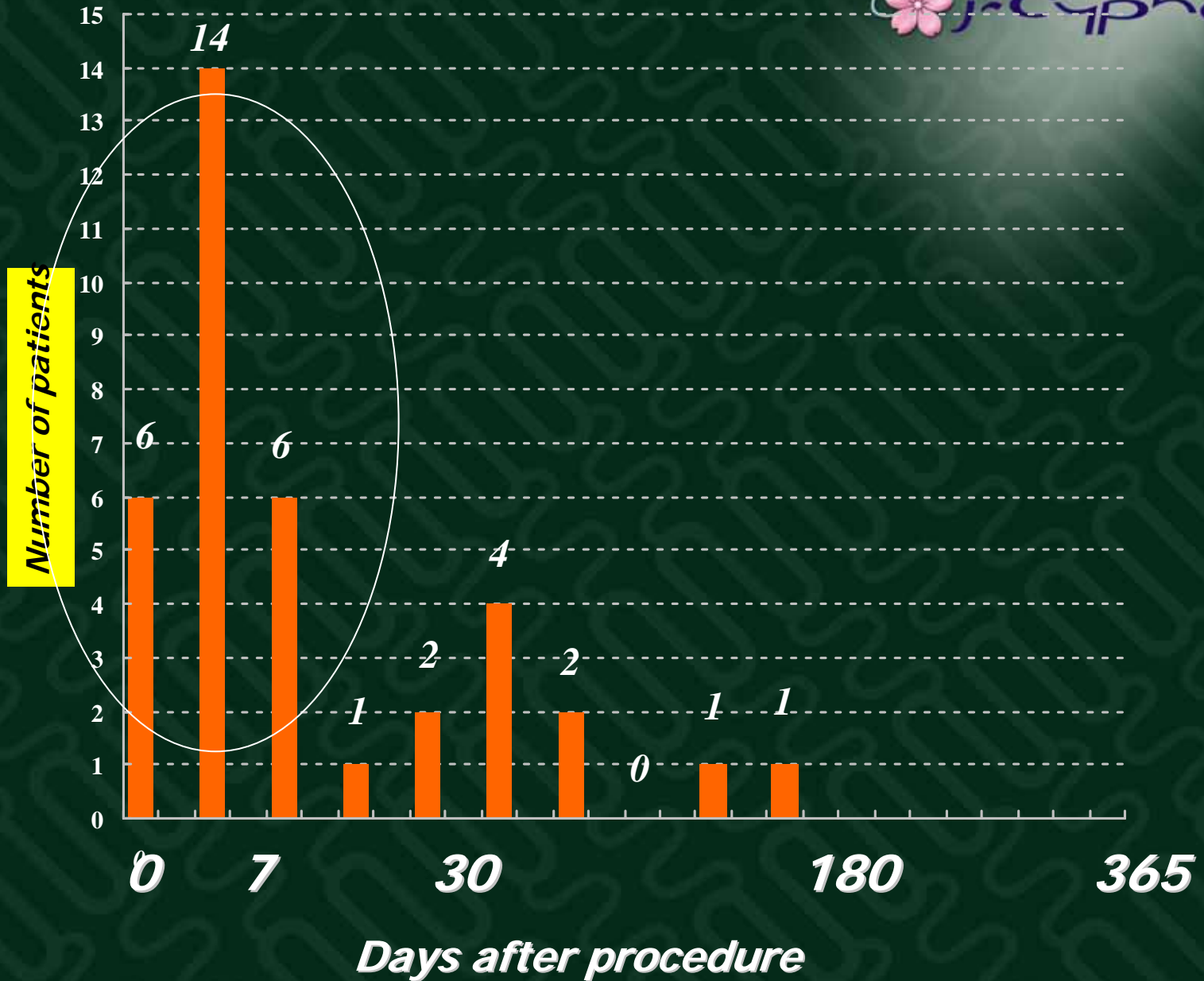
Q-MI 8 cases

Non Q-MI 9 cases

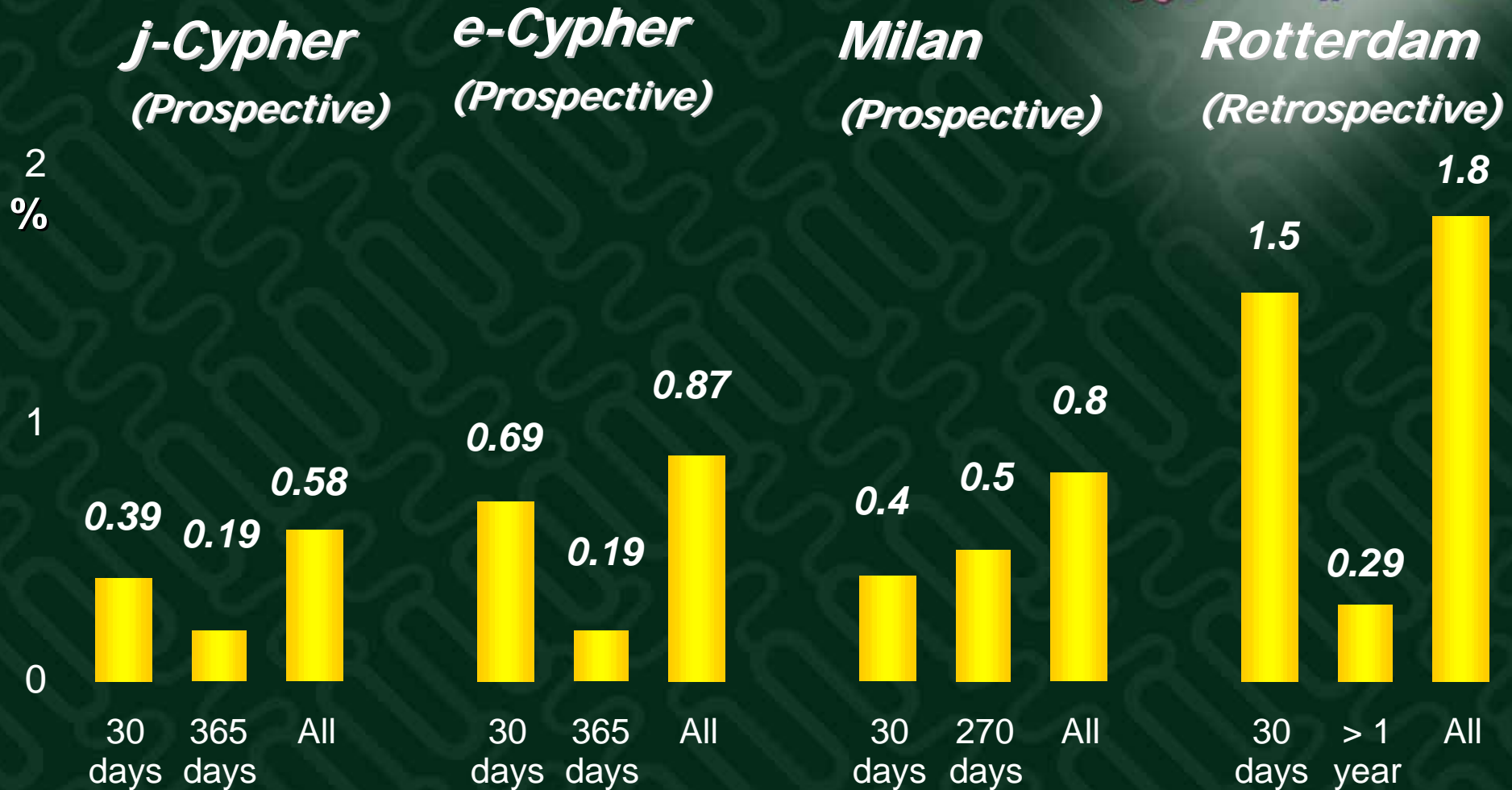
UAP 5 case

Asymptomatic 2 cases

Timing of Stent Thrombosis



Cypher Stent Thrombosis



7377 pts (30 days)
4283 pts (180days)
1912 pts (365days)

13060 pts

1062 pts

1017pts

*Iakovou I, et al.
 JAMA, 2005/*

*Ong ATL, et al.
 JACC, 2005.*

Predictors of Stent Thrombosis



Univariate analysis

Stent thrombosis in 37 lesions (0.58%)

Ostial Cx	(+) N= 118	3.4 %	p = 0.0001
	(-) N=7259	0.45 %	
Two stents for bifurcation	(+) N=383	2.4 %	p = 0.0001
	(-) N=6994	0.4 %	
Emergency procedure	(+) N=777	1.4 %	p=0.0002
	(-) N=6547	0.4 %	
Bifurcation	(+) N= 1871	0.86 %	p = 0.01
	(-) N=5506	0.38 %	
Unprotected LMCA	(+) N=293	1.4 %	p=0.03
	(-) N=7084	0.47 %	

Predictors of Stent Thrombosis

Univariate analysis



Stent thrombosis in 37 lesions (0.58%)

Creatinine ≥ 1.2 mg/dl (+) N= 1441 0.9 % p = 0.01
(-) N=5910 0.39 %

Diabetes (+) N=3203 0.72 % p = 0.02
(-) N=4174 0.34 %

STEMI (+) N= 523 0.96 % p = 0.13
(-) N=6854 0.47 %

Pretreatment with Ticlopidine (+) N= 5576 0.41 % p = 0.06
(-) N=1799 0.78 %

Ef < 40% (+) N=728 0.82 % p=0.22
(-) N=5786 0.48 %

Predictors of Stent Thrombosis at 30 Days



Multivariate analysis

**SAT 37 patients (0.58%)
in 7377 patients**

Factors	O.R.	95%C.I.	P Value
Two-stents for bifurcation	1.97	(1.17 - 3.38)	0.01
Emergency procedure	1.87	(1.16 - 2.88)	0.01
Ostial Cx	2.2	(1.17 - 3.63)	0.02
Diabetes	1.45	(1.04 - 2.08)	0.03

Stent Thrombosis

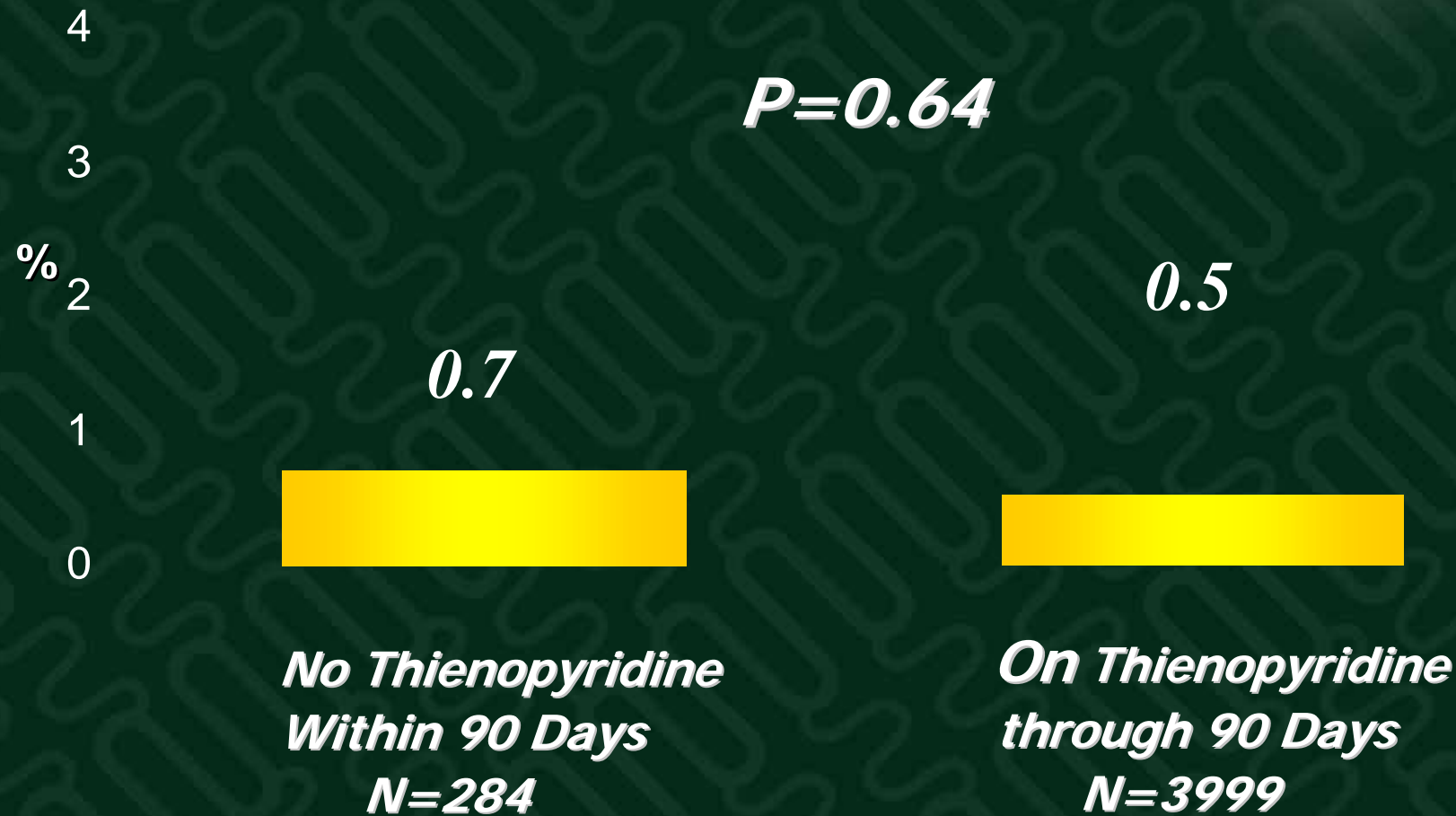
within 365 days 37 cases (0.58%)



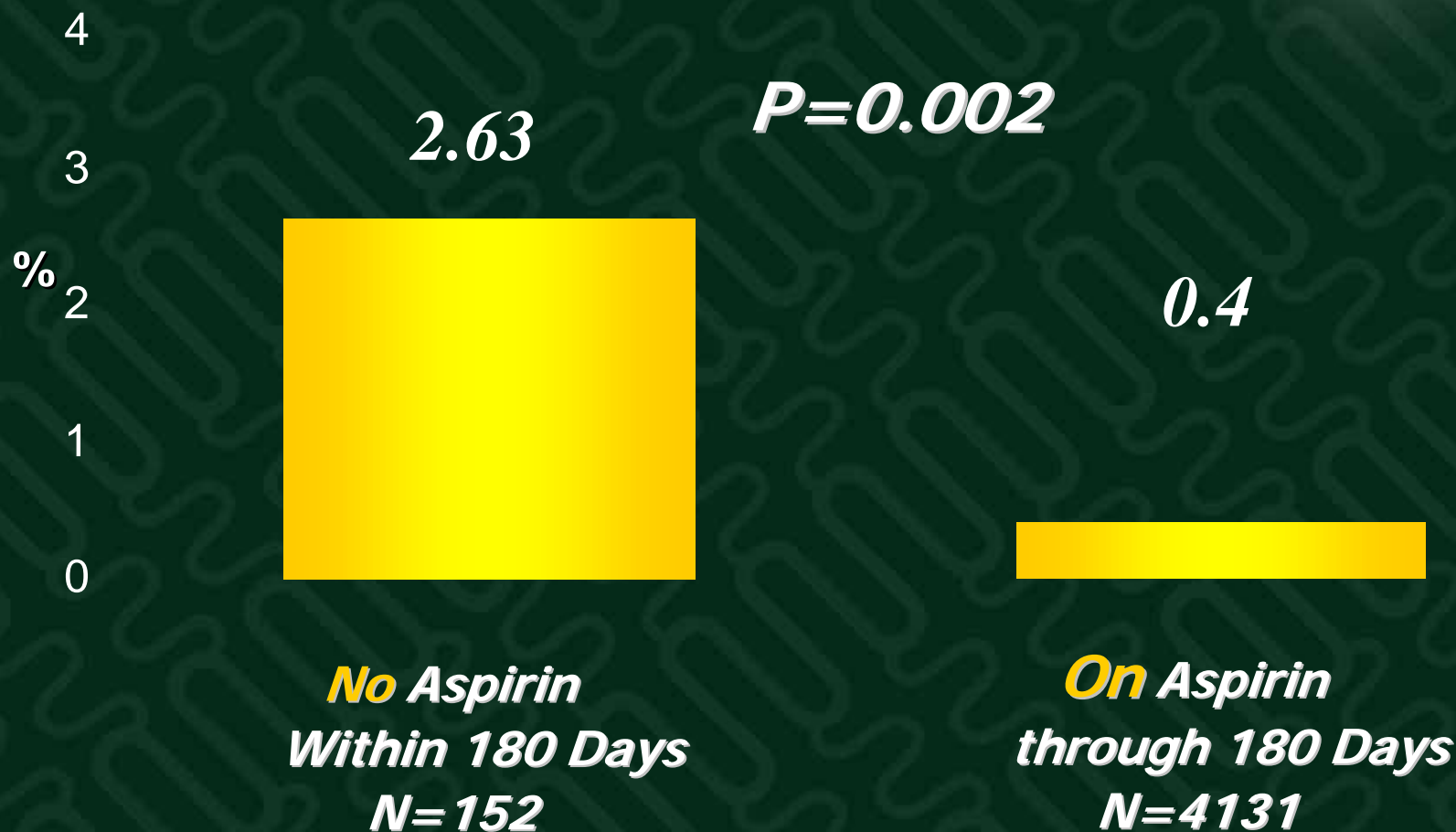
Anti-platelet Tx at time of stent thrombosis

- Withdrawal of both aspirin and thienopyridine 2 Cases***
- Thienopyridine monotherapy 2 Cases***
- On dual anti-platelet therapy 33 Cases***

Stent Thrombosis and Premature Withdrawal of Anti-platelet Tx Among Patients Who Completed 6 Months FU



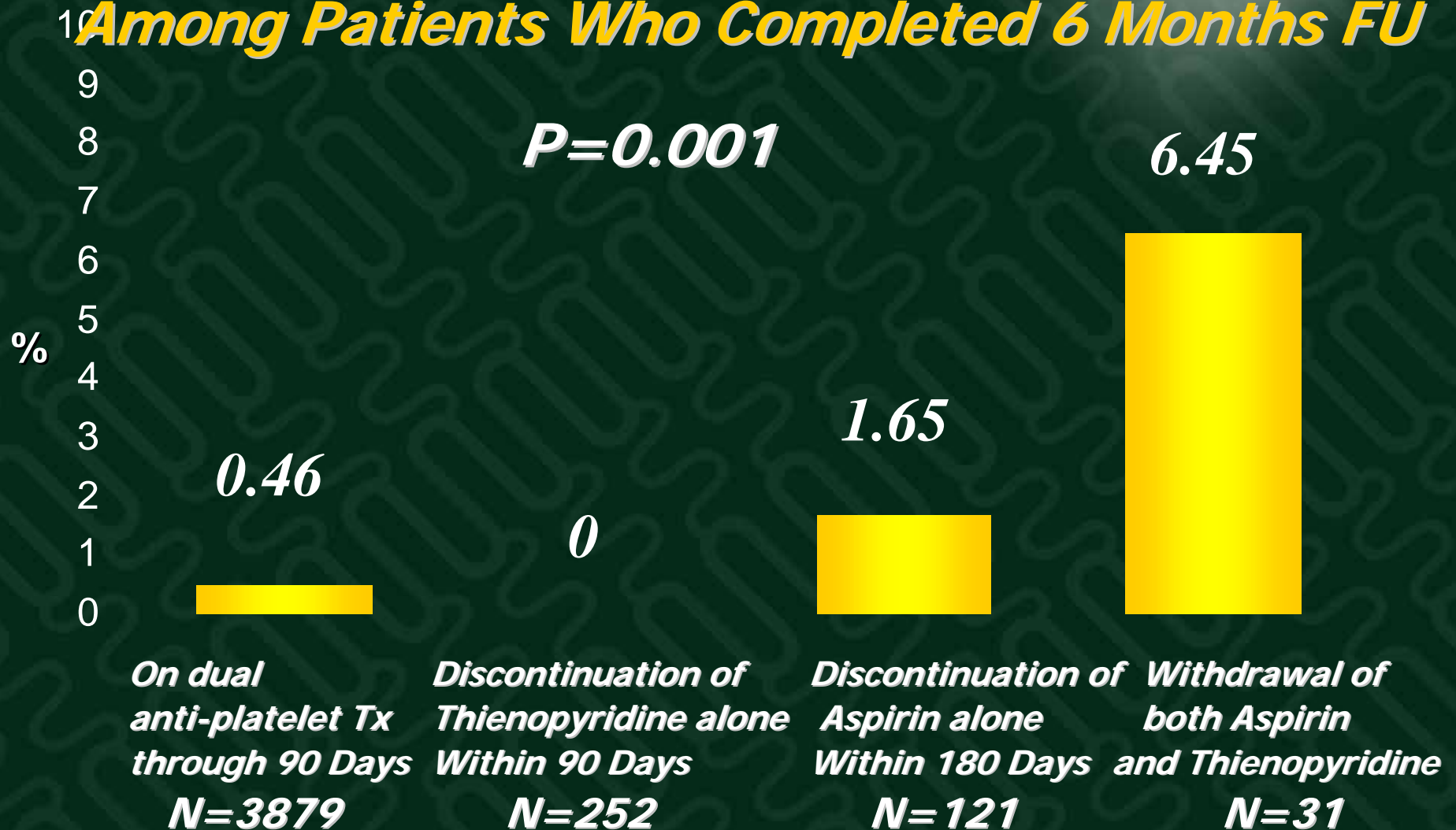
Stent Thrombosis and Premature Withdrawal of Anti-platelet Tx Among Patients Who Completed 6 Months FU



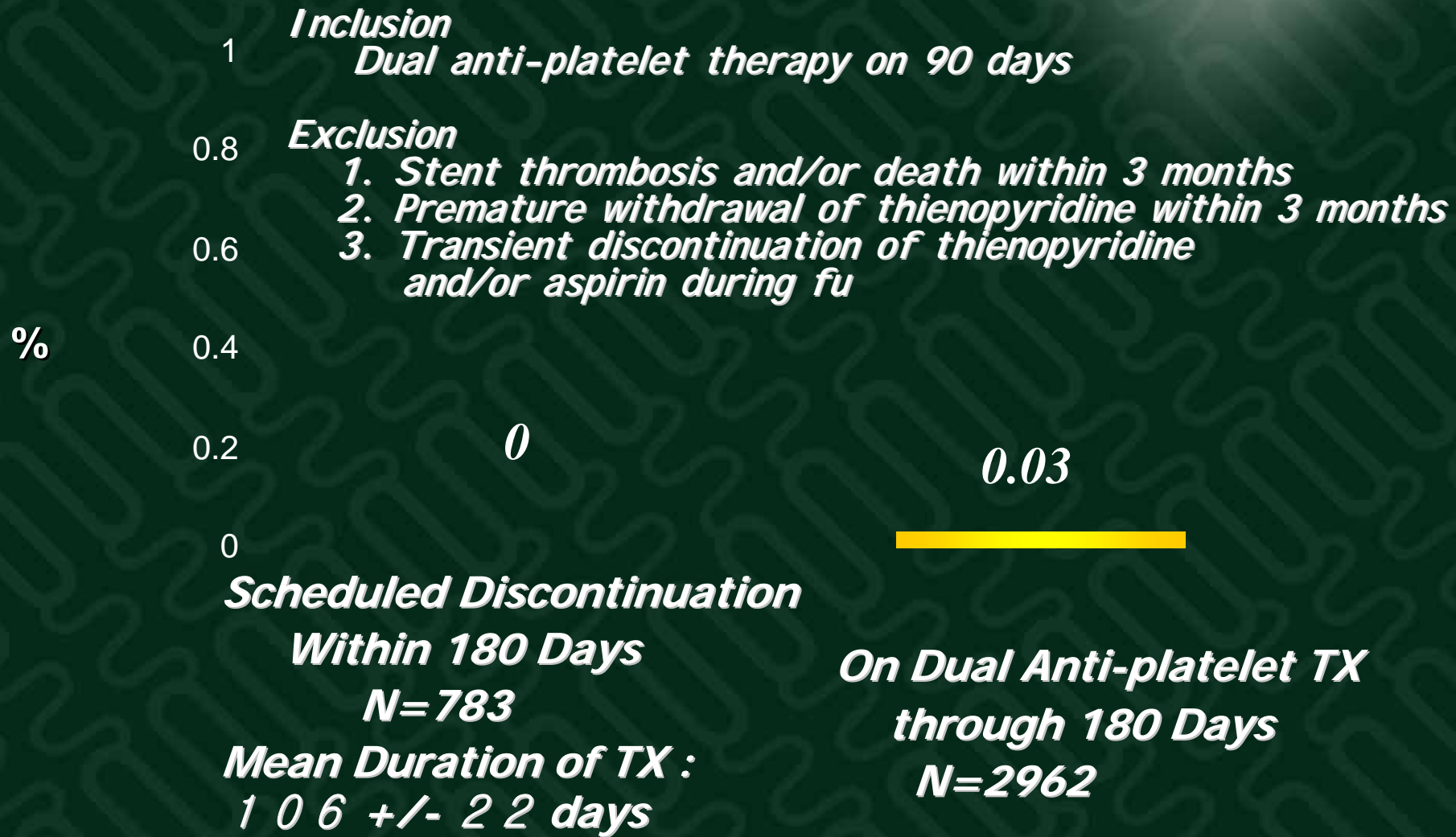
Stent Thrombosis and

Premature Withdrawal of Anti-platelet Tx

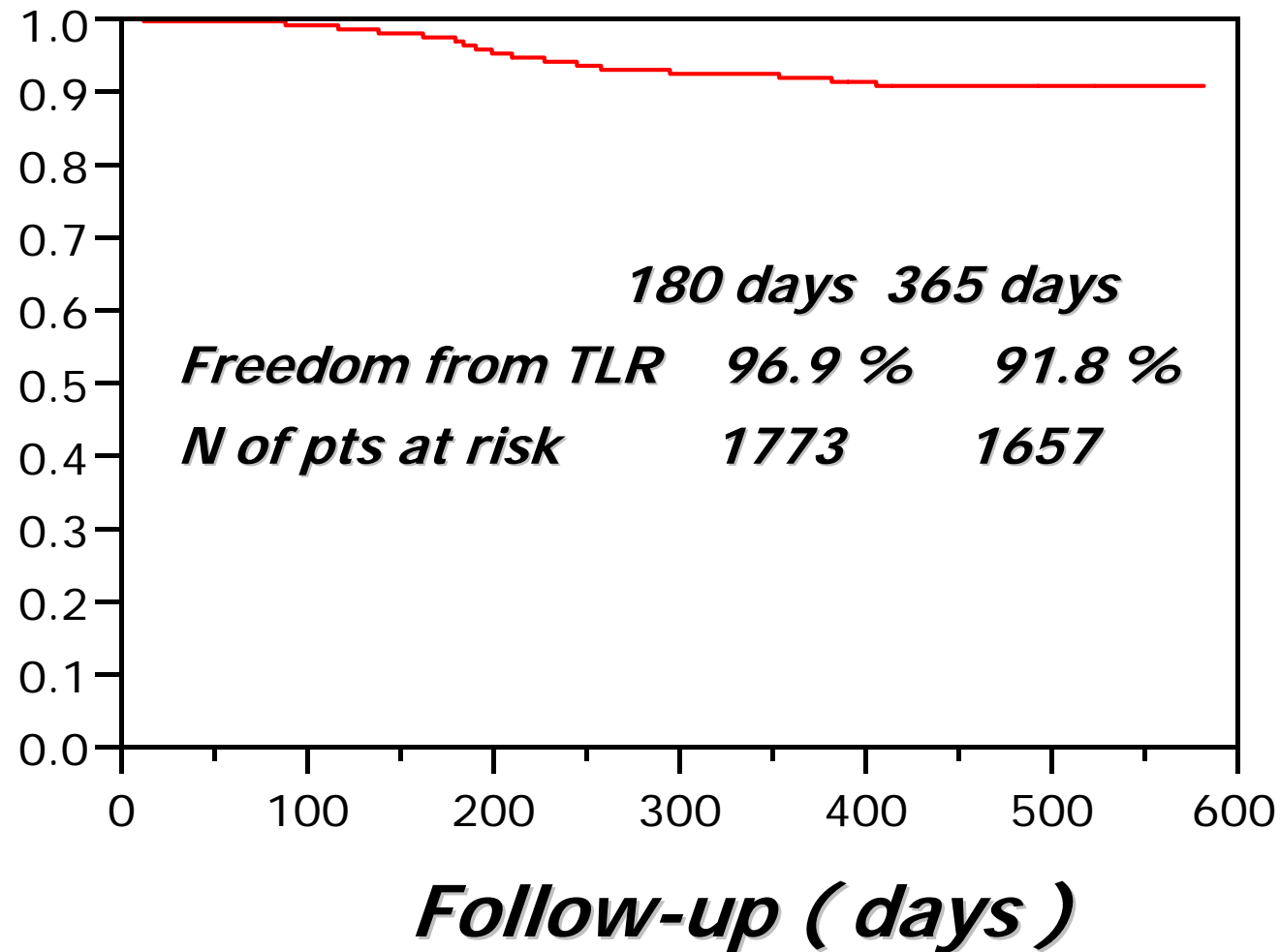
Among Patients Who Completed 6 Months FU



Duration of Thienopyridine Administration and Stent Thrombosis During 91- 180 Days Among Patients Who Completed 6 Months FU



Freedom from TLR



Predictors of TLR at 365 Days



Univariate analysis

**TLR in 142 lesions (6.4%)
out of 2222 lesions with Cypher™ placement**

Hemodialysis	(+) N= 95	23.2 %	p = 0.0001
	(-) N=2127	5.6 %	
Diabetes	(+) N=1046	8.7 %	p=0.0001
	(-) N=1181	4.5 %	
Stent Restenosis	(+) N=442	14.2 %	p = 0.0001
	(-) N=1785	5.0 %	
CTO	(+) N= 177	11.9 %	p = 0.0023
	(-) N= 2050	6.0 %	

Predictors of TLR at 365 Days

Univariate analysis



**TLR in 142 lesions (6.4%)
out of 2222 lesions with Cypher™ placement**

Calcification	Heavy	N= 113	14.2 %	p=0.02
	Mild / Mod	N= 1209	6.4 %	

Lesion location	RCA	N= 692	9.0 %	p = 0.001
	LAD	N=936	5.2 %	
	CX	N=496	4.2 %	
	LMCA	N=72	5.6 %	

Ostial RCA	Yes	N= 74	23.0 %	p = 0.001
	Non-ostial RCA	N= 618	7.3 %	
	Non-RCA	N= 1535	5.3 %	

Predictors of TLR at 365 Days

Univariate analysis



**TLR in 142 lesions (6.4%)
out of 2222 lesions with Cypher™ placement**

Lesion length	< 20 mm	N= 1522	4.9 %	p = 0.001
	20 -30 mm	N= 434	8.5 %	
	> 30 mm	N= 268	12.3 %	
Vessel size	≥ 2.5 mm	N= 1580	6.1 %	p=0.23
	< 2.5 mm	N= 732	8.1 %	
MLD post	≥ 2.5 mm	N= 1493	5.7 %	p=0.033
	< 2.5 mm	N= 732	8.1 %	

Predictors of TLR at 365 Days

Univariate analysis



**TLR in 142 lesions (6.4%)
out of 2222 lesions with Cypher™
placement**

Number of stents	1	N= 1707	4.8 %	p = 0.0001
	2	N= 426	10.1 %	
	3	N= 78	14.1 %	
	≥ 4	N= 16	50.0 %	

Length of stents	≤ 33 mm	N= 1724	5.0 %	p= 0.0001
	33 - 66 mm	N= 441	9.5 %	
	> 66 mm	N= 60	26.7 %	

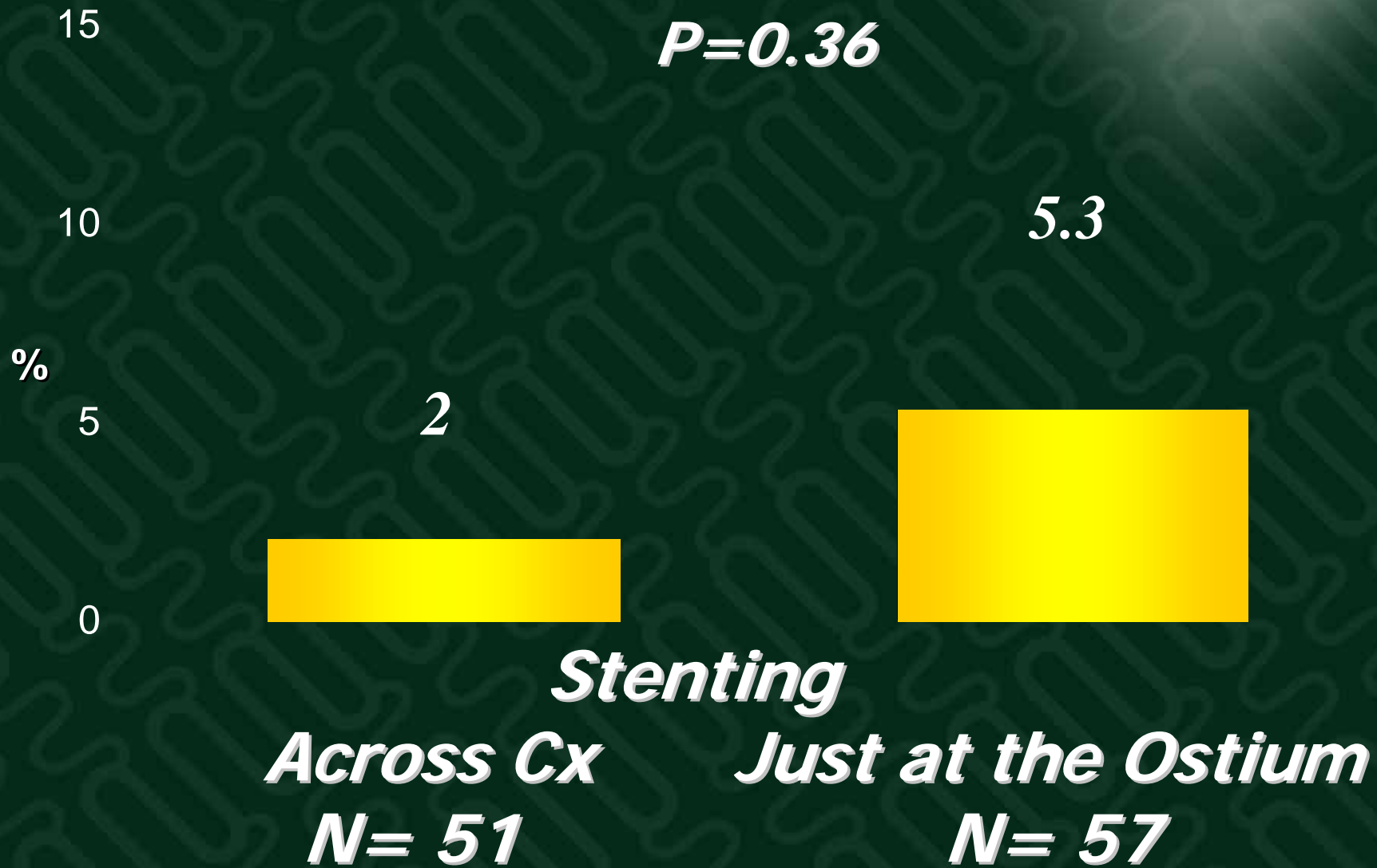
Predictors of TLR at 365 Days
Including Lesions Treated by BMS



Multivariate analysis **TLR 142 lesions (6.4%)**
in 2222 lesions

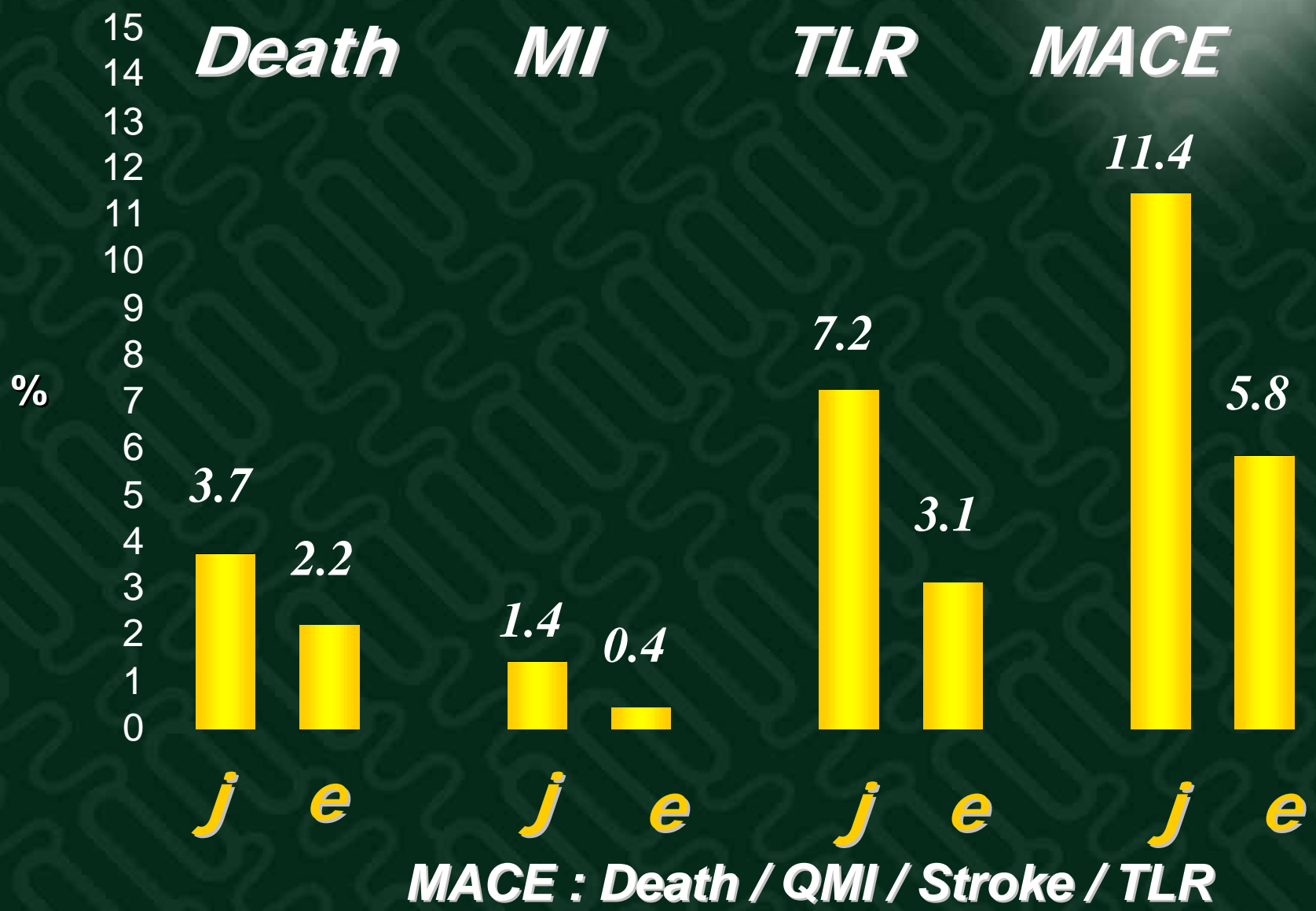
Factors	O.R.	95%C.I.	P Value
Dialysis	2.02	(1.57 - 2.56)	0.0001
In-stent restenosis	1.65	(1.38 - 1.96)	0.0001
Total stent length	1.01	(1.01 - 1.02)	0.0001
Diabetes	1.3	(1.1 - 1.55)	0.0022
RCA	1.3	(1.09 - 1.56)	0.0042
MLD-post	0.63	(0.46 - 0.87)	0.0005
Heavy calcification	1.43	(1.04 - 1.93)	0.03

Target Lesion Revascularization Rate in Ostial LAD Lesion



Clinical Outcome at 365 days

J-Cypher vs e-Cypher Registries



Summary



Preliminary One-year Result from the j-Cypher Registry suggests

- 1. SES implantation under Ticlopidine anti-platelet regimen seemed not to be associated with exaggerated incidence of stent thrombosis as compared with those reported in previous RCTs and registries.***
- 2. Use of SES in high risk patients is quite prevalent in the real world clinical practice in Japan, which so far seemed to be associated with low rate of repeated revascularization and acceptable rate of major adverse cardiac events.***

Summary



Preliminary One-year Result from the j-Cypher Registry suggests

- 3. The j-Cypher registry encompasses a large number of patients with high risk characteristics and could be a very powerful clinical tool to evaluate adequacy of expanding indication of PCI using SES in terms of long-term survival.***
- 4. Complete data collection with longer follow-up is mandatory to confirm safety and efficacy of SES in the real world clinical practice in Japan.***