



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

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on behalf of the j-Cypher Registry Investigators

Disclosure



Takeshi Kimura

Grant

Cordis Cardiology Japan

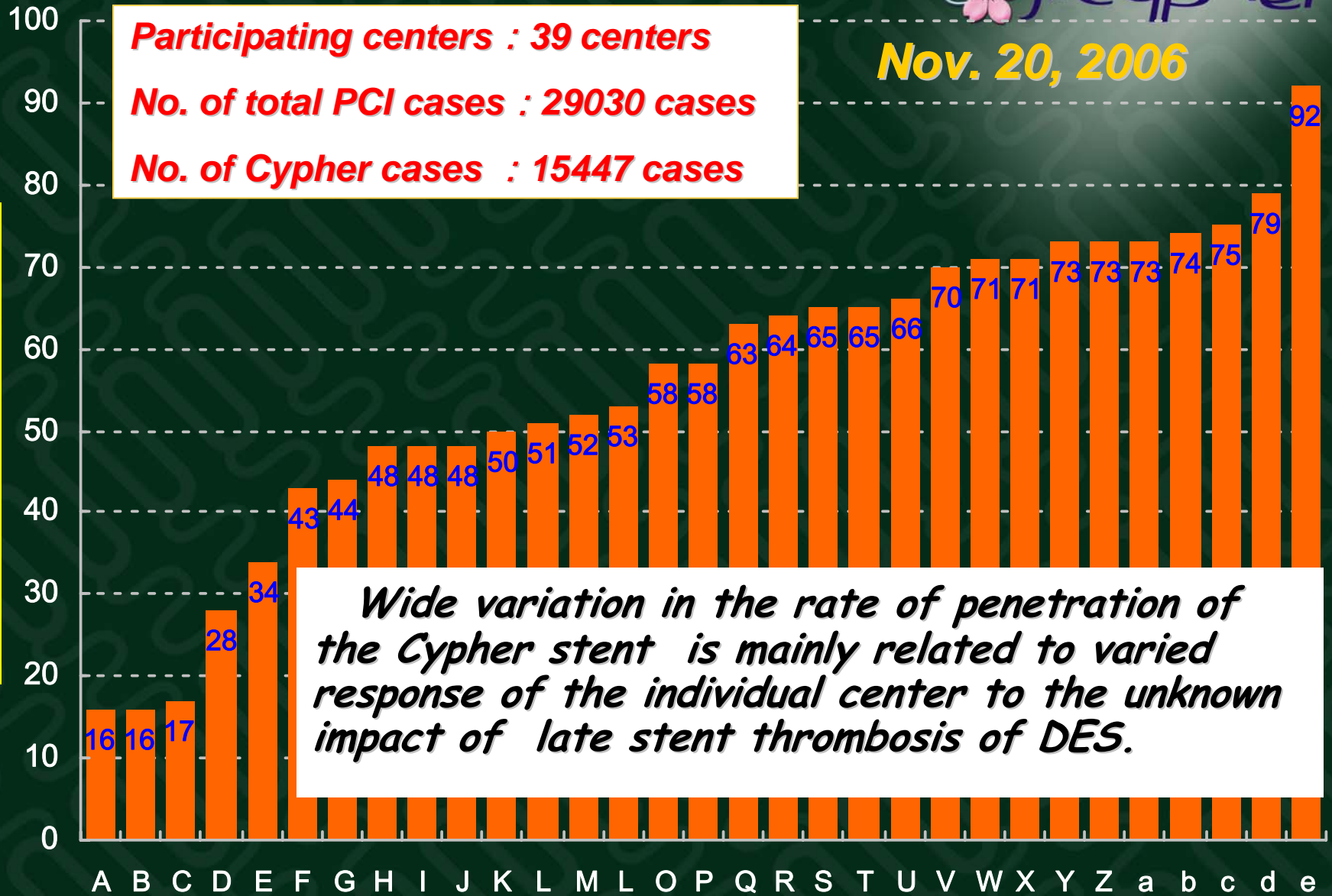
Penetration of the Cypher™ Stent



Nov. 20, 2006

Participating centers : 39 centers
 No. of total PCI cases : 29030 cases
 No. of Cypher cases : 15447 cases

Frequency of Cypher use



Wide variation in the rate of penetration of the Cypher stent is mainly related to varied response of the individual center to the unknown impact of late stent thrombosis of DES.

Center

Study Patients for the Current Analysis



Total N of Pts Enrolled 15455 pts

Exclusion

*1724 pts with repeated registration
for the j-Cypher Registry*

First registration for j-Cypher 13731 pts

Eligible for 1-year follow-up 5860 pts

*745 pts from 9 centers
with follow-up < 60%
(pre-specified by protocol)*

Study Patients 5115 pts

Complete 1-year follow-up 4417 pts (86%)

Baseline Characteristics



	j-CYPHER	e-CYPHER	P Value
	N=5115	N=15157	
Age	68 ± 10	62 ± 11	0.0001
> 80 y.o.	12 %	4 %	0.0001
Male	75 %	78 %	0.0005
Clinical presentation			0.0001
Stable Angina	54 %	42 %	
UAP / NSTEMI	14 %	33 %	
STEMI	7 %	13 %	
Silent Ischemia / OMI	19 %	10 %	
Coronary Stenosis	5 %	3 %	
Off-label Use	80%	N.A.	

Urban P, et al. Circulation. 2006;113:1434-1441.

Baseline Characteristics



	j-CYPHER	e-CYPHER	P Value
	N=5115	N=15157	
Prior MI	29 %	30 %	0.11
Prior PCI	53 %	29 %	0.0001
Prior CABG	8 %	11 %	0.0001
Multi-vessel Disease	55 %	57 %	0.0001
Diabetes	44 %	29 %	0.0001
On Insulin	10 %	10 %	1.0
CKD (CCr < 60)	51 %	N.A.	
Hemodialysis	6 %	N.A.	
Hx of Heart Failure	13 %	N.A.	
PVD	12%	7 %	0.0001
Hx of Stroke	9 %	3 %	0.0001

Procedural Characteristics



	j - CYPHER N= 7690	e - CYPHER N=18295	P Value
Stent length / lesion (mm)	29.0 ± 15.5	N.A.	
Stent length / pt (mm)	41.2 ± 27.4	27.3 ± 16.1	0.0001
Direct stenting	24 %	34 %	0.0001
IVUS use	41 %	N.A.	
Pressure at deployment (atm)	17.6 ± 5.2	14.3 ± 2.8	0.0001
Post-dilation	41 %	21 %	0.0001

Current Anti-thrombotic Therapy



Adjunctive to Cypher Stent Placement in Japan

Intra-procedure

Unfractionated Heparin 5000 - 10000 U

Pre- and post-procedure

Aspirin 81 - 200 mg indefinitely

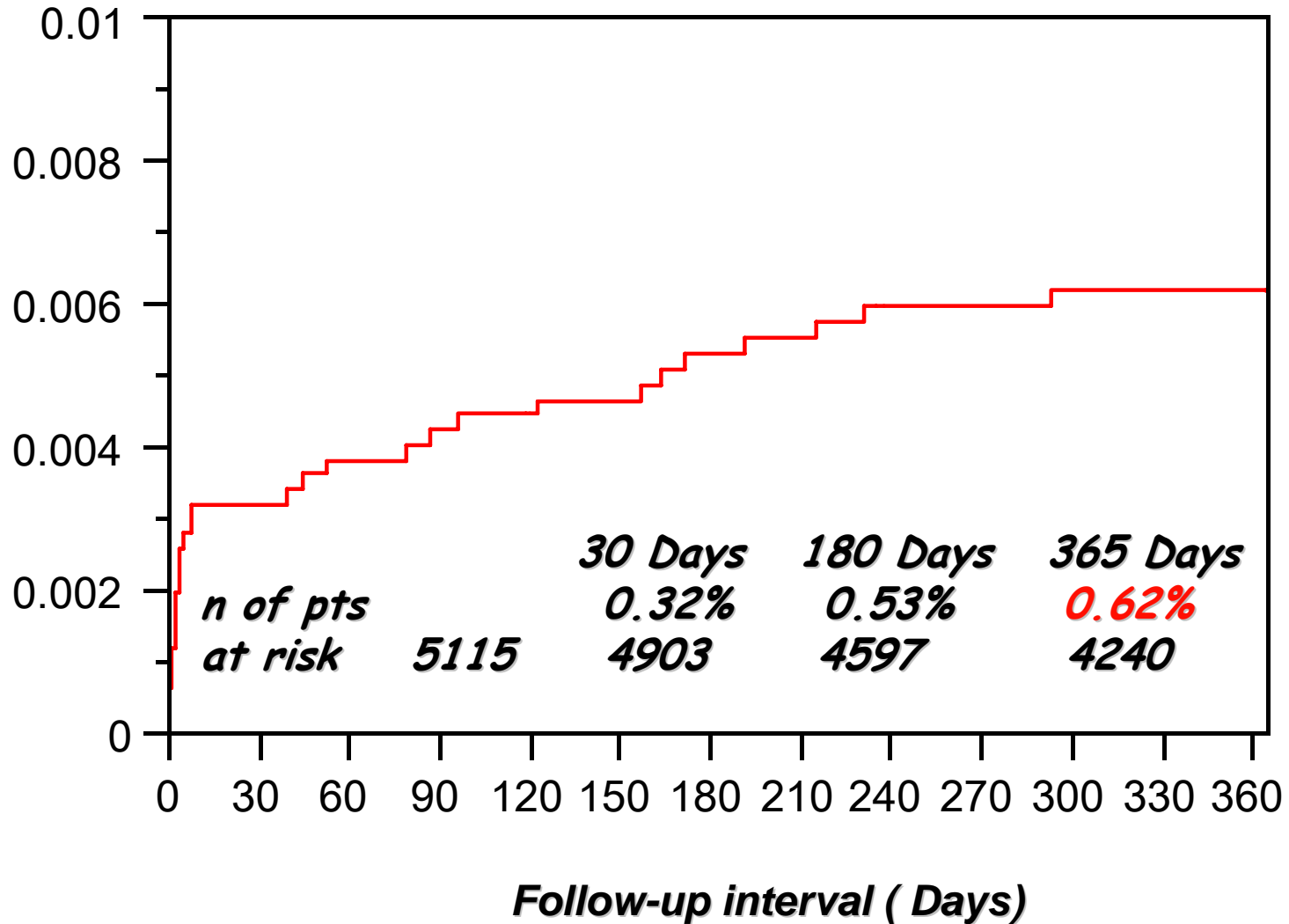
Ticlopidine 200 mg / day at least 3 months

More contemporary anti-thrombotic agents such as clopidogrel, GP(IIb/IIIa) antagonists, and bivalirudin are not available.

Stent Thrombosis in j-Cypher



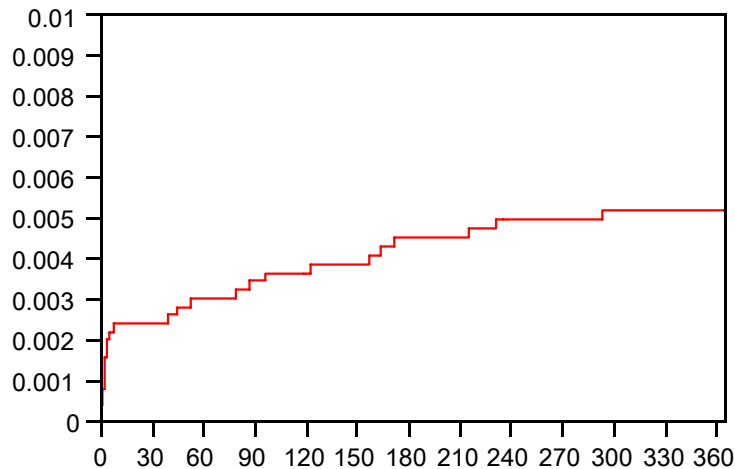
ARC Definite / Probable



Stent Thrombosis in j-Cypher

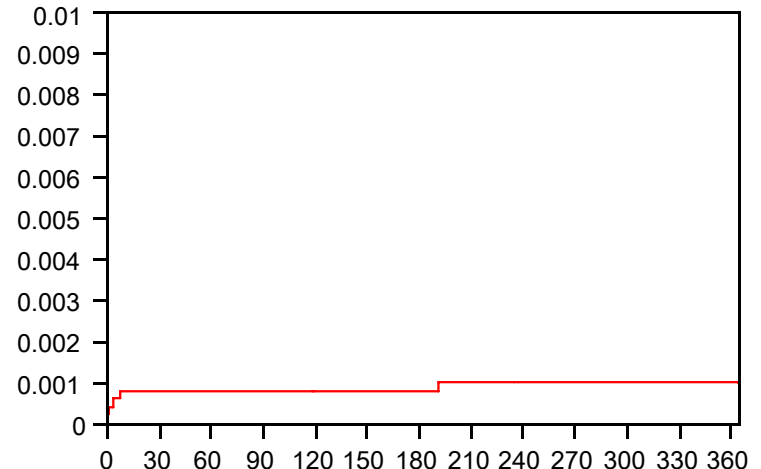


ARC Definite



Follow-up interval (Days)

ARC Probable



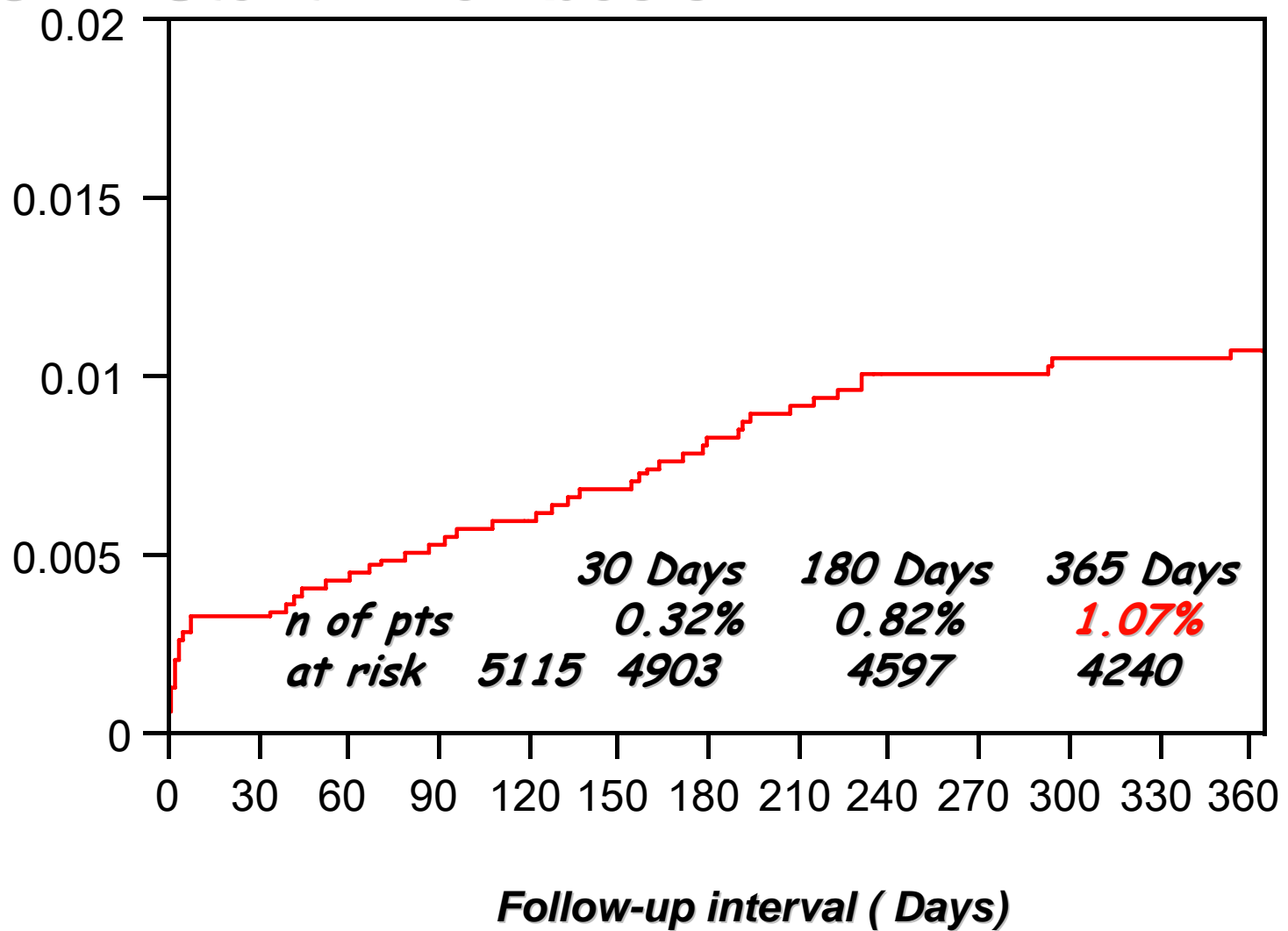
Follow-up interval (Days)

	30 Days	180 Days	365 Days
ARC Definite	0.24%	0.45%	0.52%
ARC Probable	0.08%	0.08%	0.1%
n of pts at risk	5115	4597	4240

Stent Thrombosis in j-Cypher



ARC All Stent Thrombosis

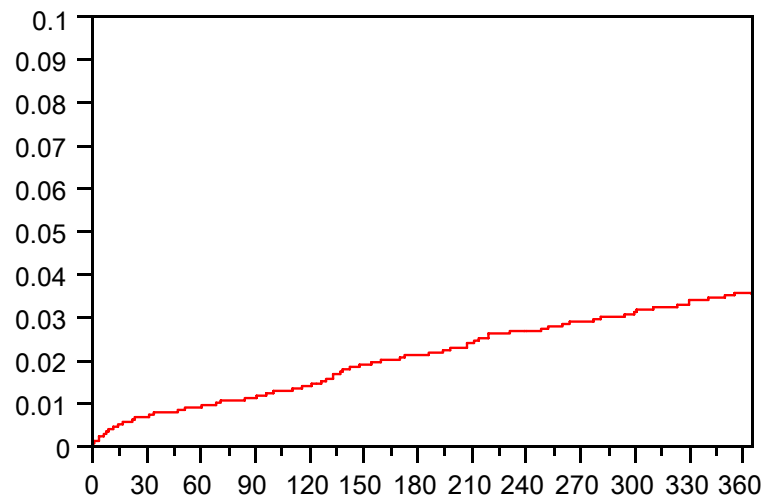


One-Year Mortality in j-Cypher

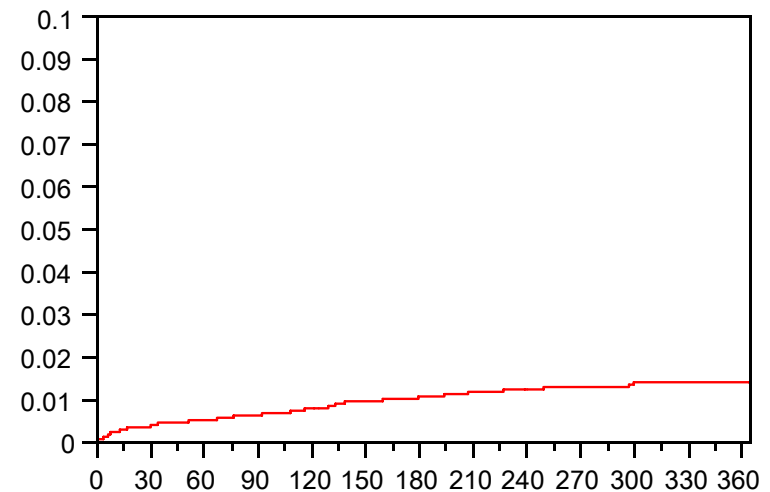


All-cause mortality

Cardiac mortality



Follow-up interval (Days)



Follow-up interval (Days)

All-cause mortality
Cardiac mortality

<i>30 Days</i>	<i>180 Days</i>	<i>365 Days</i>
<i>0.66%</i>	<i>2.12%</i>	<i>3.57%</i>
<i>0.36%</i>	<i>1.03%</i>	<i>1.41%</i>

n of pts at risk

5115

4916

4615

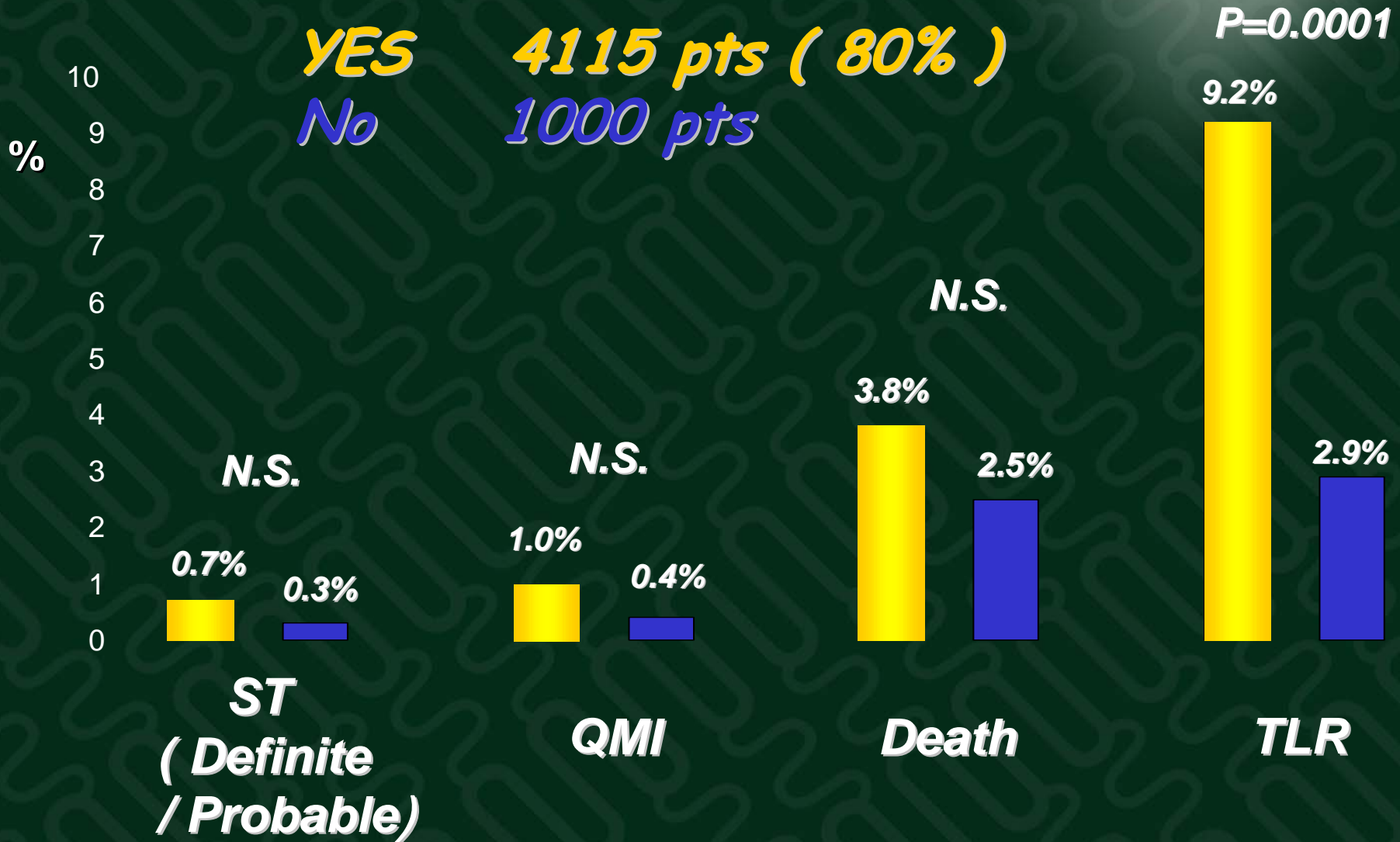
4250

One-year Event Rate in Selected Subgroups



Off-label Use

YES 4115 pts (80%)
No 1000 pts



Predictors of Stent Thrombosis Through 1 Year (ARC Definite / Probable)



**Stent thrombosis in 30 patients
among 5115 patients**

Univariate analysis

Variables	Present		Absent		P Value
	N	Incidence	N	Incidence	
Two stent for bifurcation	282	3.05%	4833	0.48%	0.0001
Ostial CX	72	2.93%	5043	0.59%	0.03
Emergency	558	1.96%	4544	0.46%	0.002
Hemodialysis	285	1.52%	4830	0.57%	0.001
LVEF \leq 40%	506	1.49%	3896	0.51%	0.03
\geq 2 vessels treated	1000	1.33%	3848	0.41%	0.003
\geq 3 stents used	1125	1.33%	3970	0.4%	0.01
Bifurcation	1284	1.17%	3831	0.44%	0.02
Multivessel CAD	2309	1.05%	2806	0.27%	0.001

Predictors of Stent Thrombosis Through 1 Year (ARC Definite / Probable)



**Stent thrombosis in 30 patients
among 5115 patients**

Univariate analysis

Variables	Present		Absent		P Value
	N	Incidence	N	Incidence	
CTO	597	1.29%	4518	0.53%	0.09
Concomitant use of BMS	512	1.28%	4584	0.55%	0.12
STEMI	369	1.2%	4736	0.58%	0.24
Unprotected LMCA	193	1.17%	4922	0.6%	0.5
Ostial LAD	277	1.17%	4838	0.59%	0.34
Ostial RCA	196	1.07%	4919	0.6%	0.12
Diabetes (Insulin)	504	1.05%	4611	0.57%	0.3

Predictors of Stent Thrombosis Through 1 Year (ARC Definite / Probable)



**Stent thrombosis in 30 patients
among 5115 patients**

Univariate analysis

Variables	Present		Absent		P Value
	N	Incidence	N	Incidence	
Lesion length \geq 30mm	971	0.98%	4144	0.53%	0.22
Diabetes	2247	0.85%	2868	0.44%	0.12
Vessel size < 2.5mm	1836	0.81%	3279	0.51%	0.25
CKD (CCr < 60 / Non-HD)	2306	0.74%	2524	0.41%	0.1
Off-label use	4115	0.69%	1000	0.32%	0.28
IVUS use	2316	0.64%	2799	0.60%	0.62
Male gender	3818	0.63%	1295	0.59%	0.58
Age \geq 75	1506	0.57%	3609	0.64%	0.55
In-stent restenosis	1018	0.51%	4097	0.65%	0.89

Predictors of Stent Thrombosis Through 1 Year (ARC Definite / Probable)



Multivariate analysis

**ST 30 patients (0.62%)
in 5015 patients**

Factors	O.R.	95%C.I.	P Value
Two-stent approach for bifurcation	2.05	(1.22 - 3.3)	0.0085
Hemodialysis	2.04	(1.22 - 3.16)	0.009
Emergency procedure	1.73	(0.97 - 2.82)	0.06

Duration of Thienopyridine Administration and Stent Thrombosis Between 61- 365 Days



4417 pts who completed 1 year FU

Death within 2 months : 46 pts

Premature withdrawal of anti-platelet Tx within 2 months : 168 pts

Information on anti-platelet Tx not available: 49 pts

4155 pts with dual anti-platelet Tx. at 2 months

1728 pts with discontinuation of thienopyridine within 1 year

2427 pts with dual anti-platelet Tx. through 1 year

Mean Duration of Tx 145 +/- 73 days

Stent Thrombosis Between 61- 365 Days

0.23%

0.45%

p=0.23

Limitations When Comparing Clinical Outcome Between BMS and DES in the Real World



- 1. Heavy selection bias when using concurrent BMS group as the control group.*
- 2. Marked differences in baseline demographics and improvement in terms of technology, technique and concomitant medical management when using historical BMS control group.*

Despite those limitations, however, we should make some comparison in order to be sure that we are not doing harm to our patients by placing DES in the real world clinical practice !!

CREDO-KYOTO PCI / CABG Registry

(Coronary REvascularization Demonstrating Outcome Study in Kyoto)

***Multi-center (30 centers) registry of patients
undergoing first coronary revascularization
from 2000 - 2002 excluding acute MI***

Interim analysis in 9873 patients

<i>Isolated Coronary Revascularization</i>	<i>9389 pts</i>
<i>PCI</i>	<i>6876 pts</i>
<i>Stent Use</i>	<i>82%</i>
<i>Isolated CABG</i>	<i>2513 pts</i>
<i>IMA Use</i>	<i>94 %</i>
<i>CABG combined with other operation</i>	<i>484 pts</i>
<i>Mean Follow-up Interval of Survivors 1314 ± 452 Days</i>	
<i>Follow-up rate at</i>	
<i>1 year</i>	<i>97%</i>
<i>2 years</i>	<i>95%</i>
<i>3 years</i>	<i>73%</i>

Comparison Between BMS and SES Using Historical Control



CREDO-Kyoto Registry 9873 pts

j-Cypher Registry
Current Analysis 5115 pts

CABG
: **2997 pts**

PCI without stent
: **1249 pts**

PCI using BMS
5627 pts

**Prior
PCI / CABG**
: **2826 pts**

STEMI
: **306 pts**

PCI using SES
1983 pts

Comparison Between BMS and SES Using Historical Control

CREDO-Kyoto versus j-Cypher



Baseline characteristics

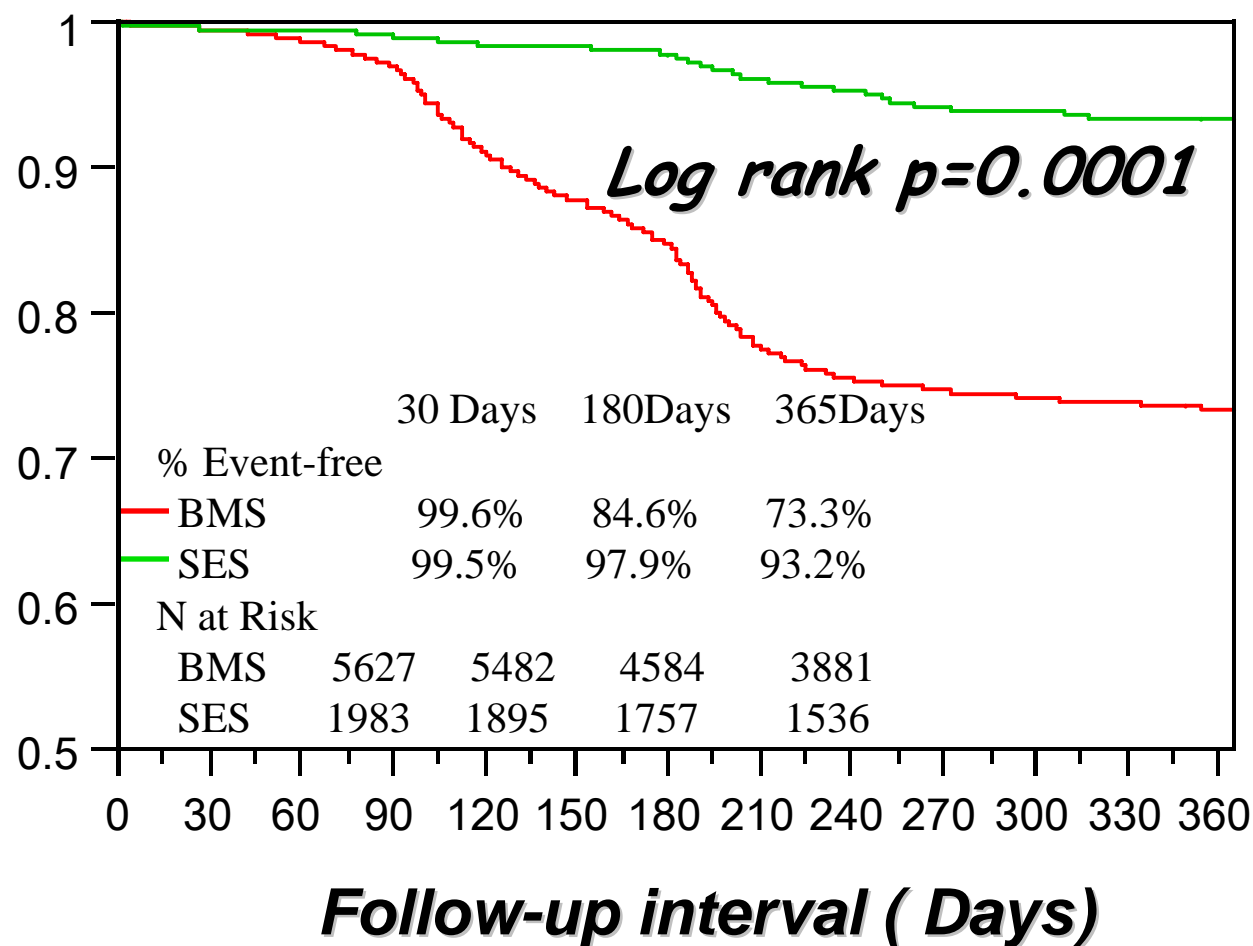
	CREDO	j-Cypher	p Value
N	5627	1983	
Age	67.5±10.1	68.2±10.4	0.0036
Male	71%	71%	0.65
Emergency	5.9%	7.3%	0.03
Heart failure	12%	12%	0.72
Diabetes	37%	42%	0.0001
Hemodialysis	3.2%	5.0%	0.0003
CCr < 60	39%	49%	0.0001
EF < 40%	6.5%	9.3%	0.0002
Target LMCA	2.0%	4.4%	0.0001
N of target vessels	1.31±0.56	1.33±0.58	0.33
Statin Tx at discharge	32%	44%	0.0001

Comparison Between BMS and SES Using Historical Control

CREDO-Kyoto versus j-Cypher



Target Lesion Revascularization

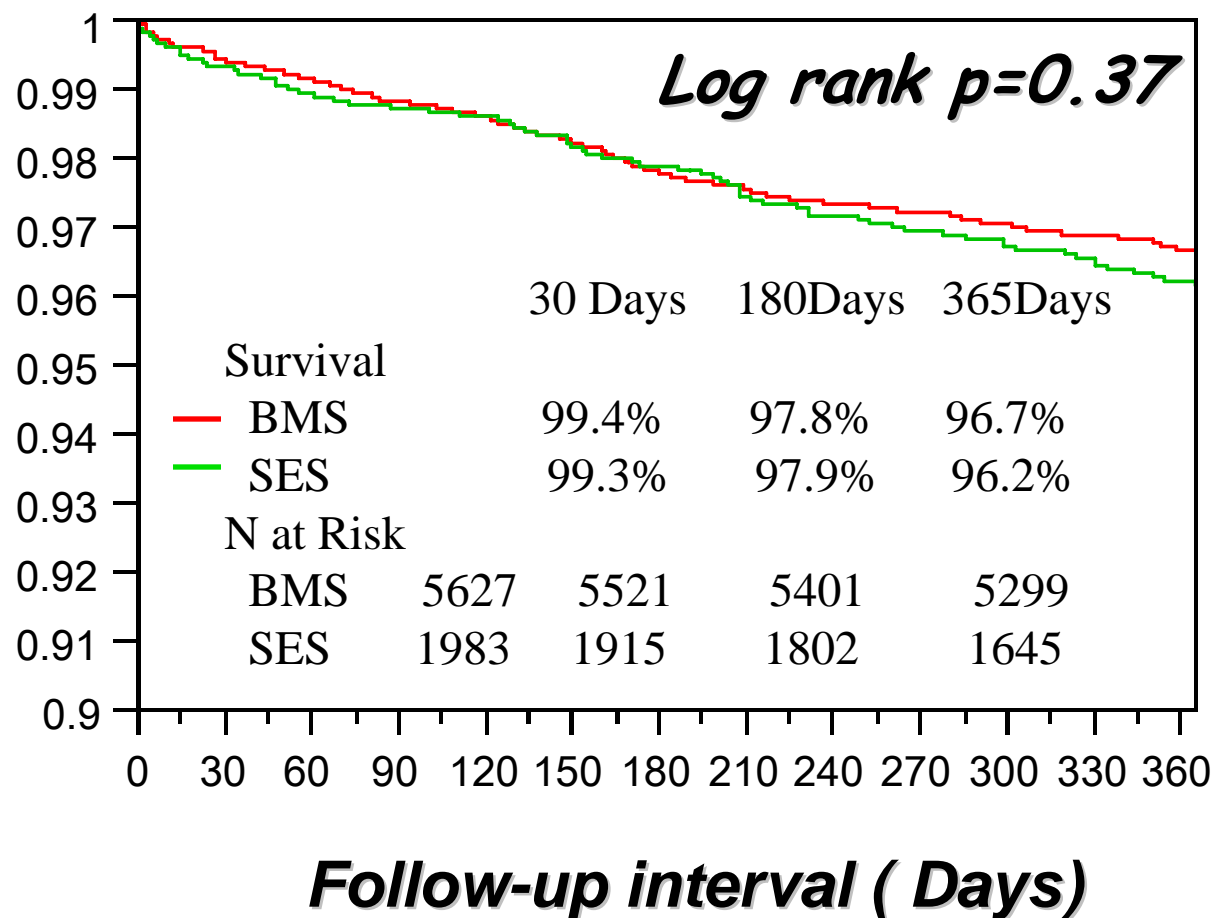


Comparison Between BMS and SES Using Historical Control

CREDO-Kyoto versus j-Cypher



All-cause Mortality

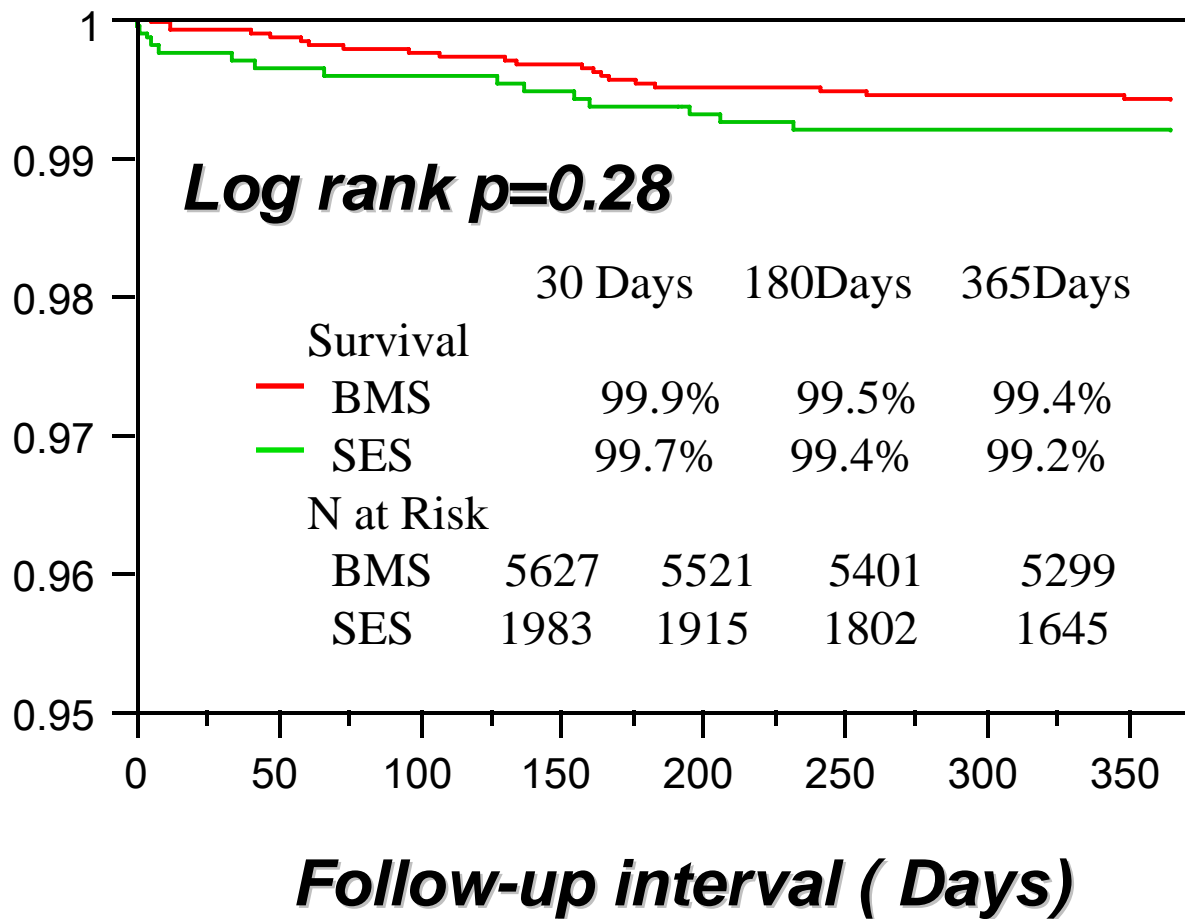


Comparison Between BMS and SES Using Historical Control

CREDO-Kyoto versus j-Cypher



Sudden Death

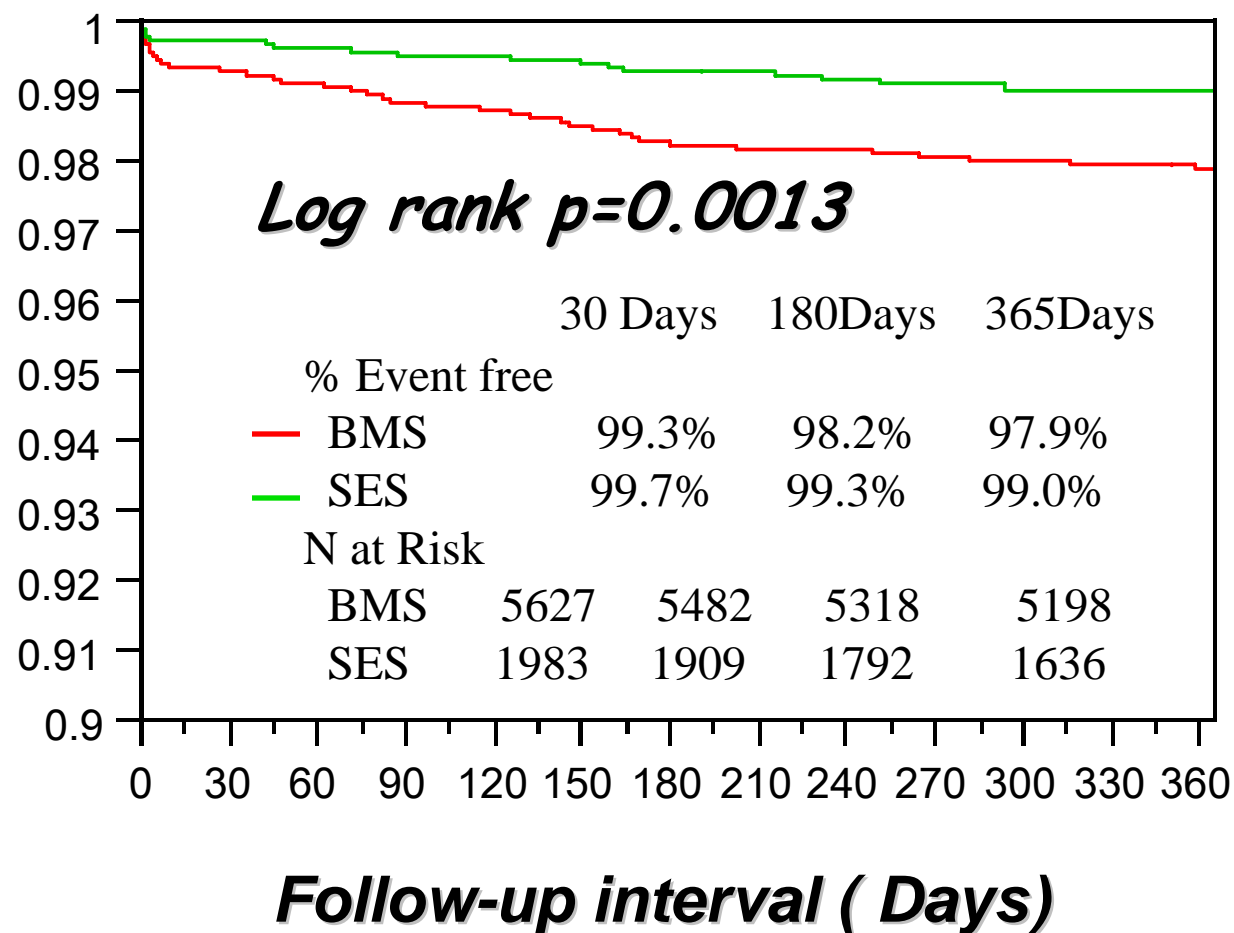


Comparison Between BMS and SES Using Historical Control

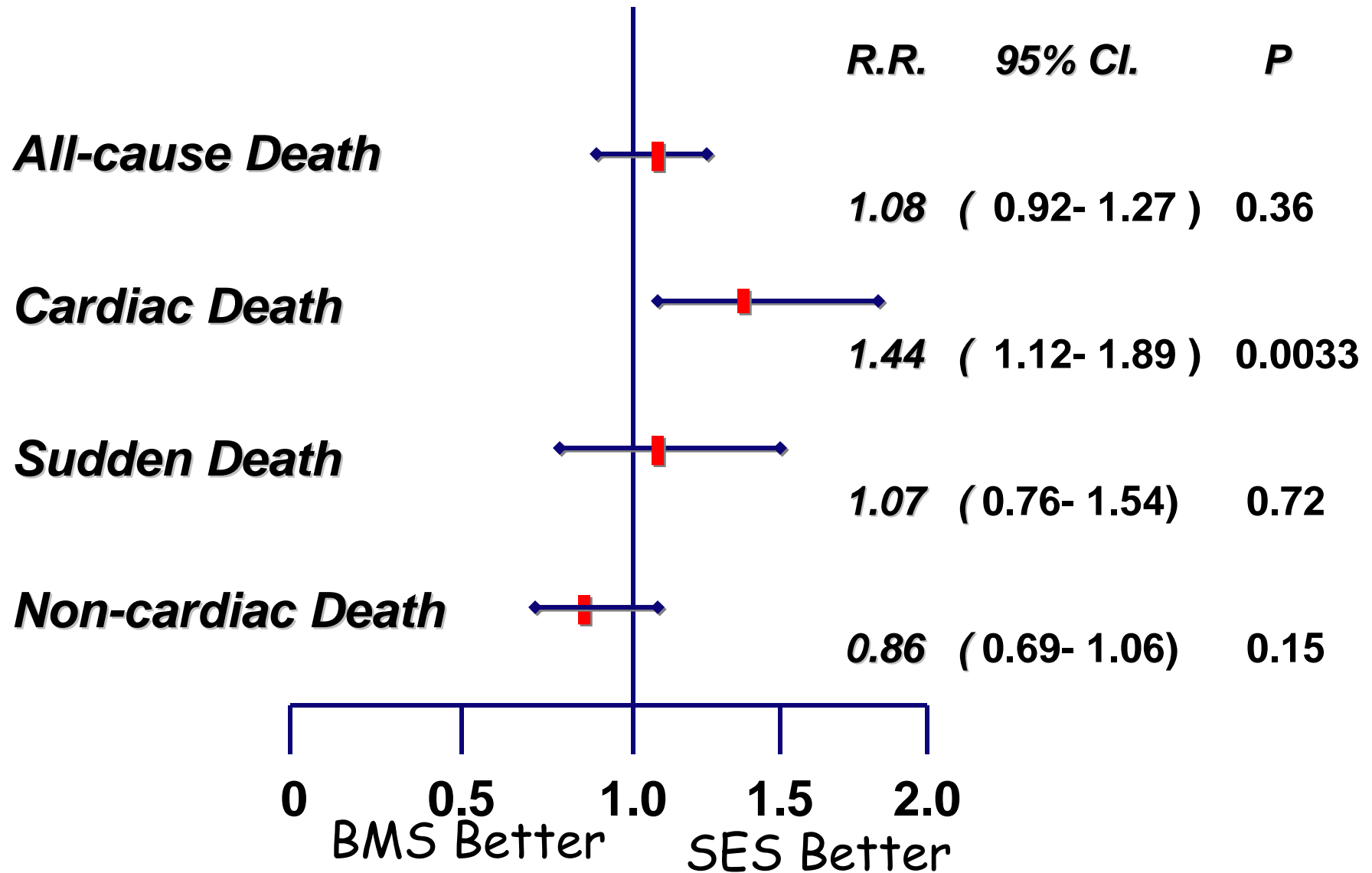
CREDO-Kyoto versus j-Cypher



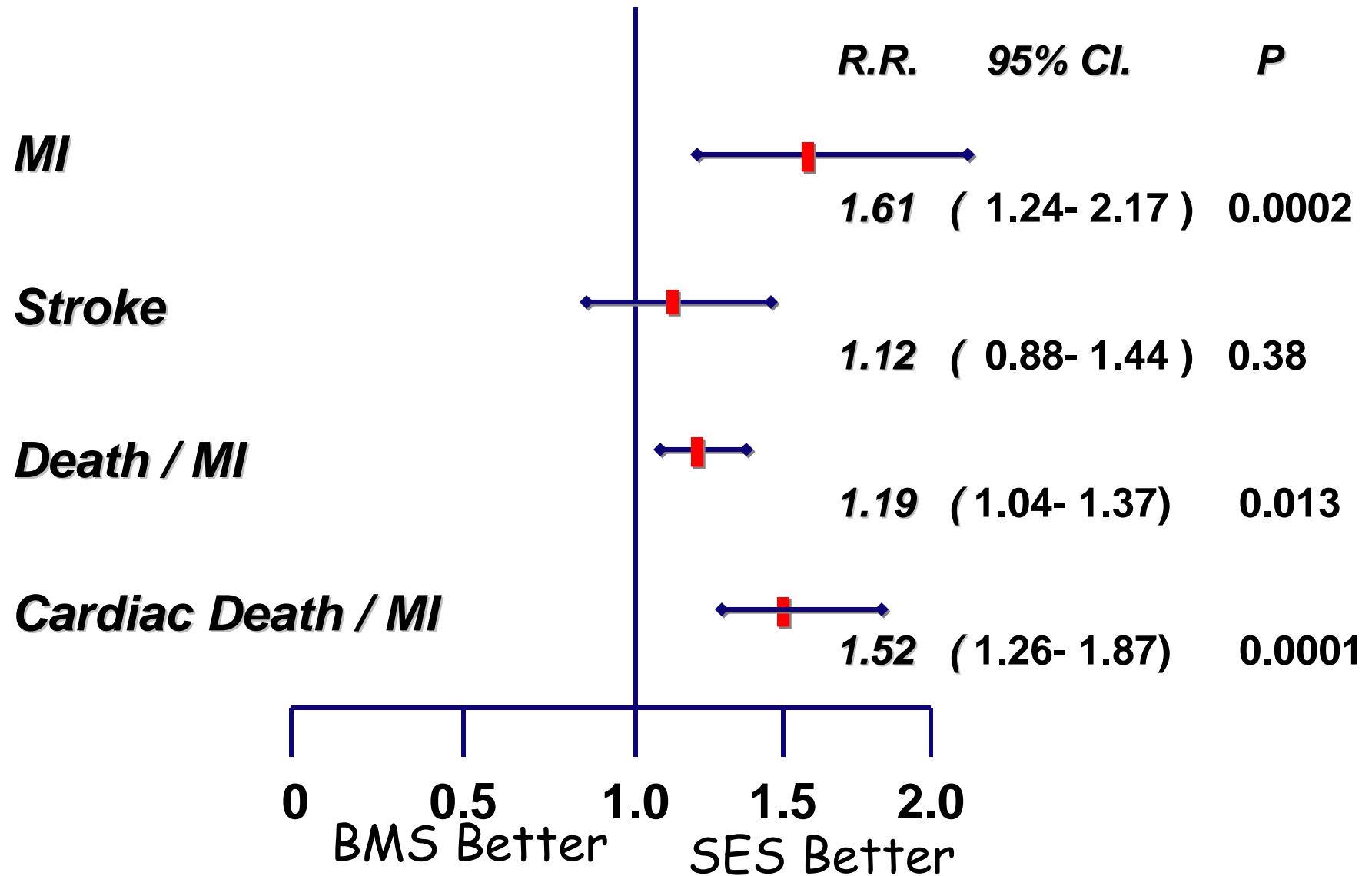
Myocardial Infarction



Adjusted Risk of Cardiovascular Events : BMS vs. SES



Adjusted Risk of Cardiovascular Events : BMS vs. SES



Summary



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

- 1. Stent thrombosis rate up to 1 year under Ticlopidine anti-platelet regimen in Japan seemed to be lower as compared with those reported from other registries in the real world, despite the fact that high risk patients such as diabetes and CKD were quite prevalent in the j-Cypher registry.*
- 2. Although we have data only up to 1 year, attenuation of the rate of stent thrombosis was seen between 6 months and 1 year.*
- 3. Two-stents approach for bifurcation and hemodialysis were identified to be independent predictors of stent thrombosis. Other more common factors such as diabetes, CKD not on HD, and multivessel stenting did not adversely affect stent thrombosis.*

Summary



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

- 4. Extended dual anti-platelet therapy up to 1 year as compared to discontinuation of thienopyridine within 1 year did not have favorable effect on stent thrombosis.*
- 5. Compared to a historical control of BMS, PCI using SES in the j-Cypher registry was associated with similar mortality, less myocardial infarction, and strikingly less TLR at 1 year, despite prevalence of more morbid patients such as diabetes, CKD, elderly, and left main stenting in the SES group.*