New Generation Drug-Eluting Stent in Korea

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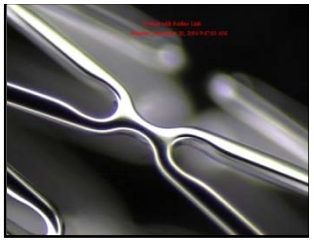
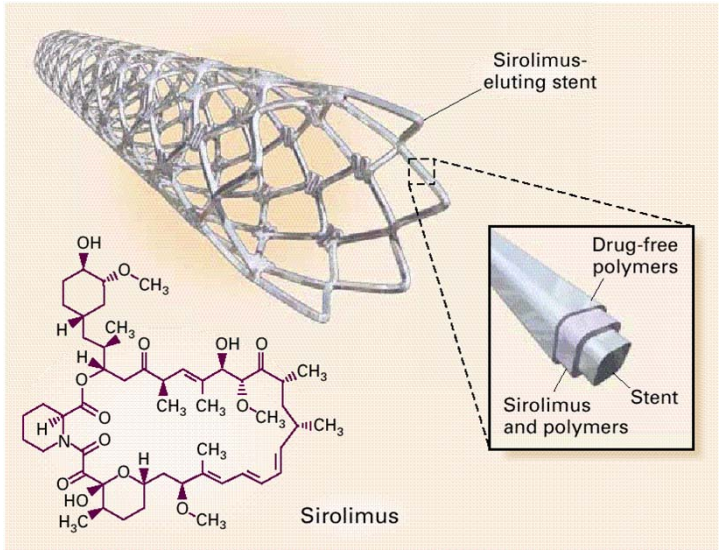
Purpose

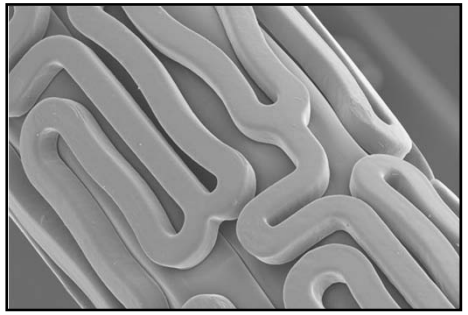
- To briefly introduce the outcomes of new generation drug-eluting stent (DES), as compared with the early generation DES, assessed in Korea.

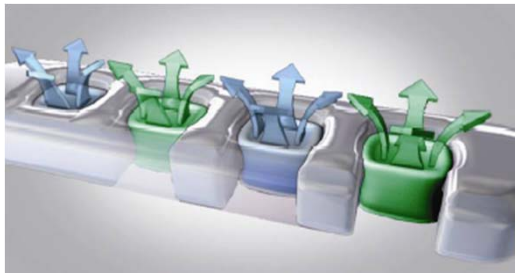
Drug-Eluting Stents



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







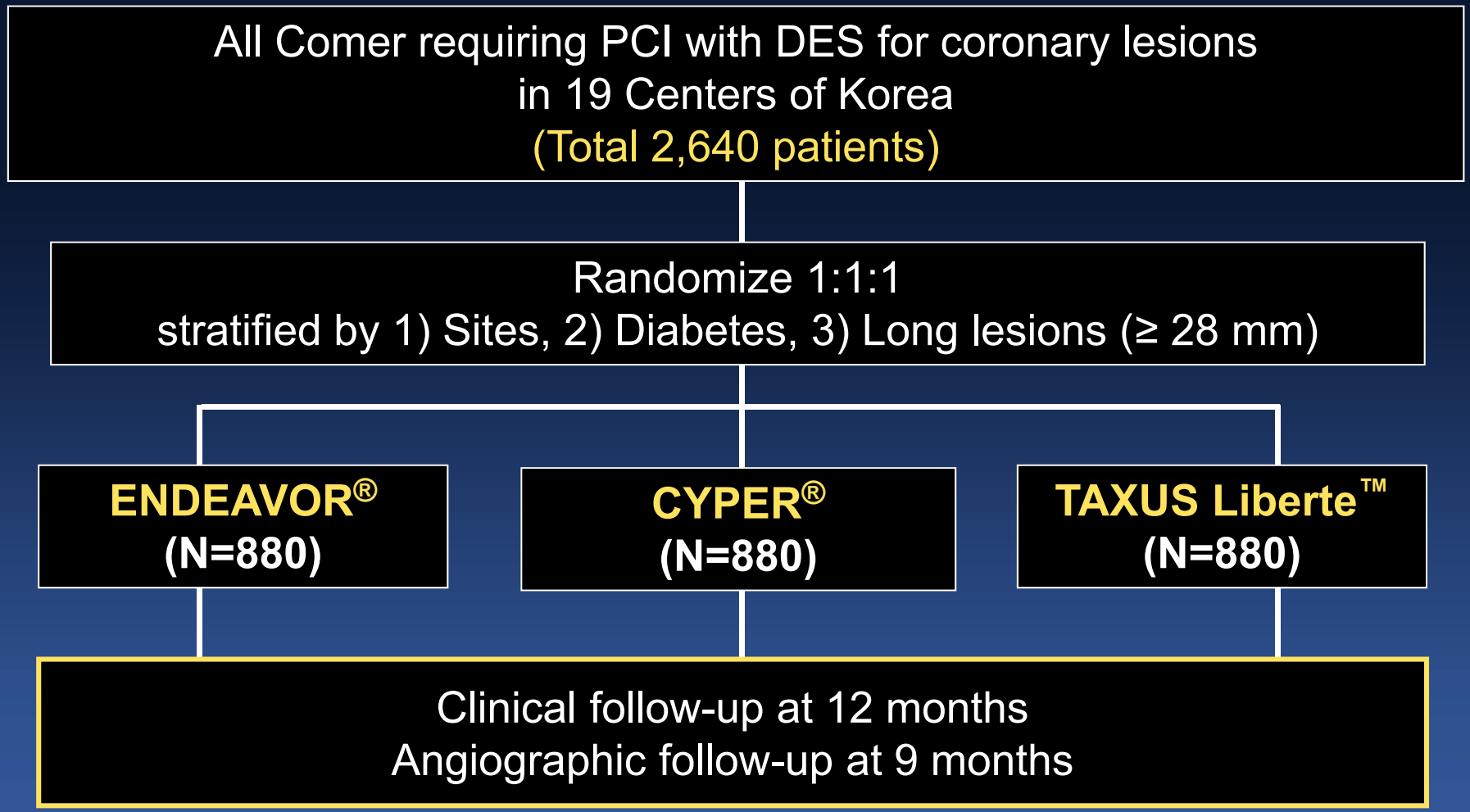
Clinical Research
Multicenter, Published or Presented

Major Studies Performed in Korea

- ZEST
- Long-DES III
- ESSENCE-DIABETES
- EXCELLENT
- IRIS-DES
- PRECOMBAT Series

Randomized Controlled Study

ZEST Trial

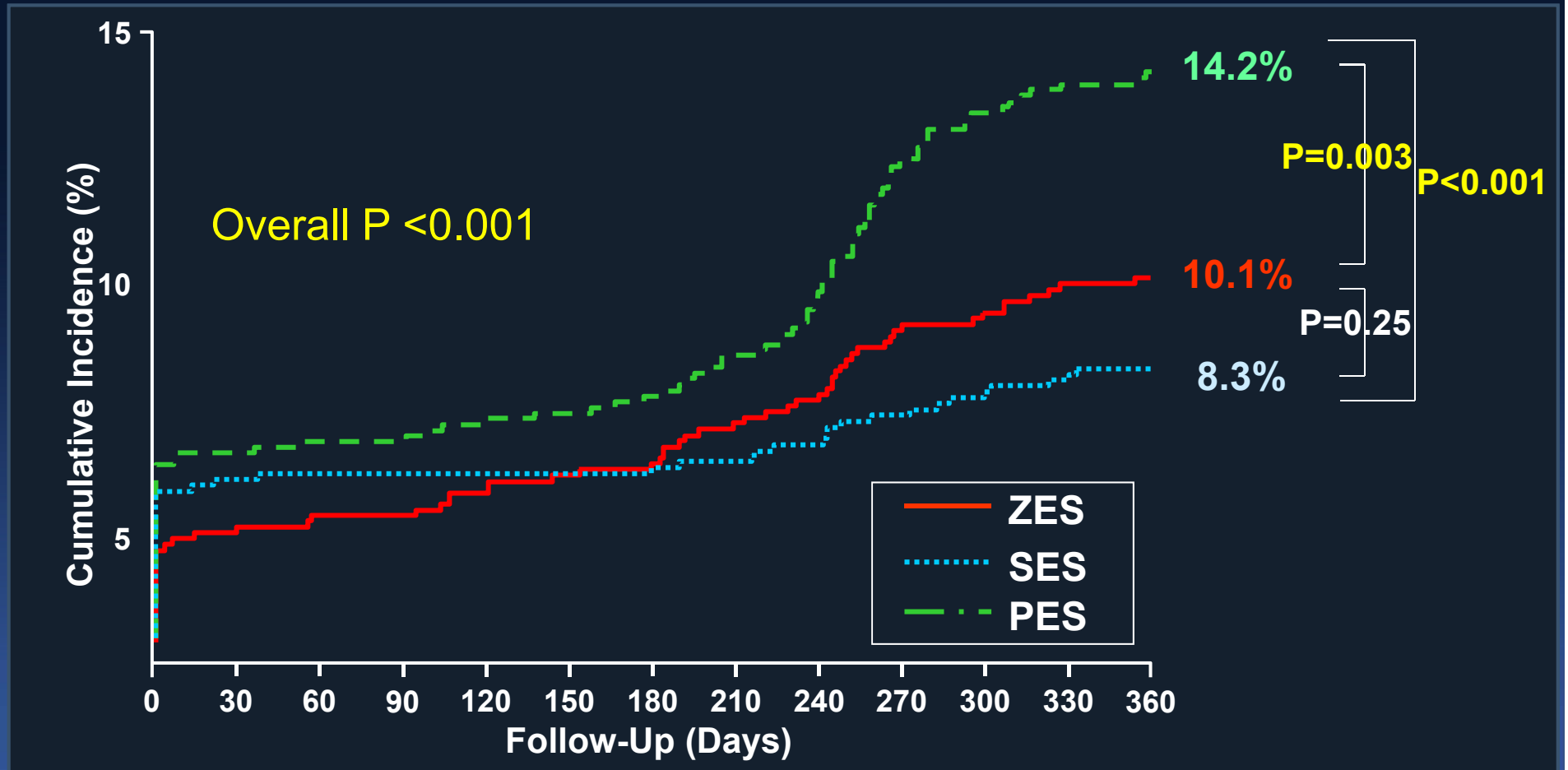


Park DW et al. J Am Coll Cardiol 2010;56:1187

ZEST

Primary End Point at 12 Month

Death, MI, Ischemia-driven TVR

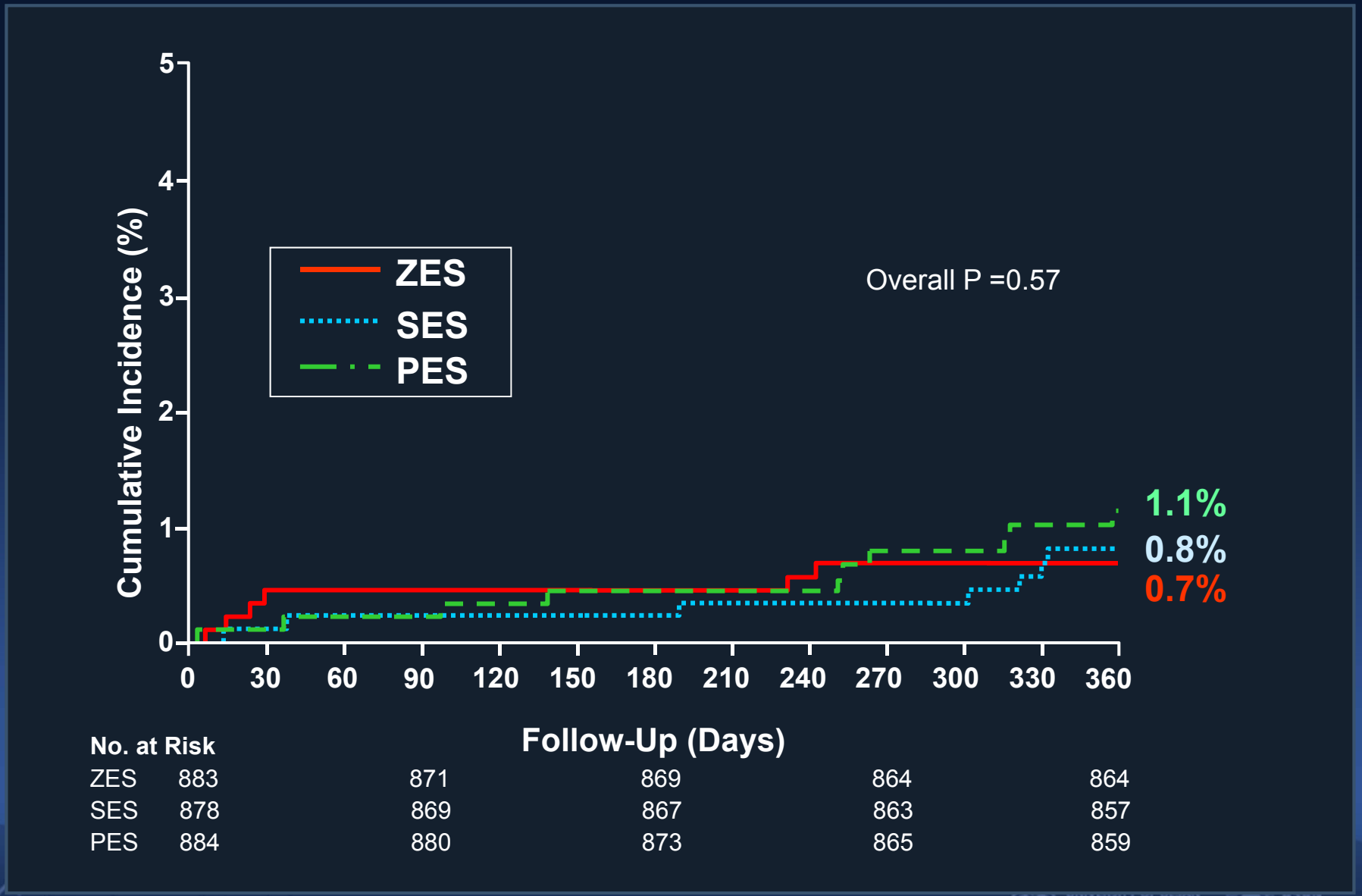


No. at Risk

ZES	883	827	816	790	782
SES	878	816	813	802	792
PES	884	821	808	763	745

ZEST

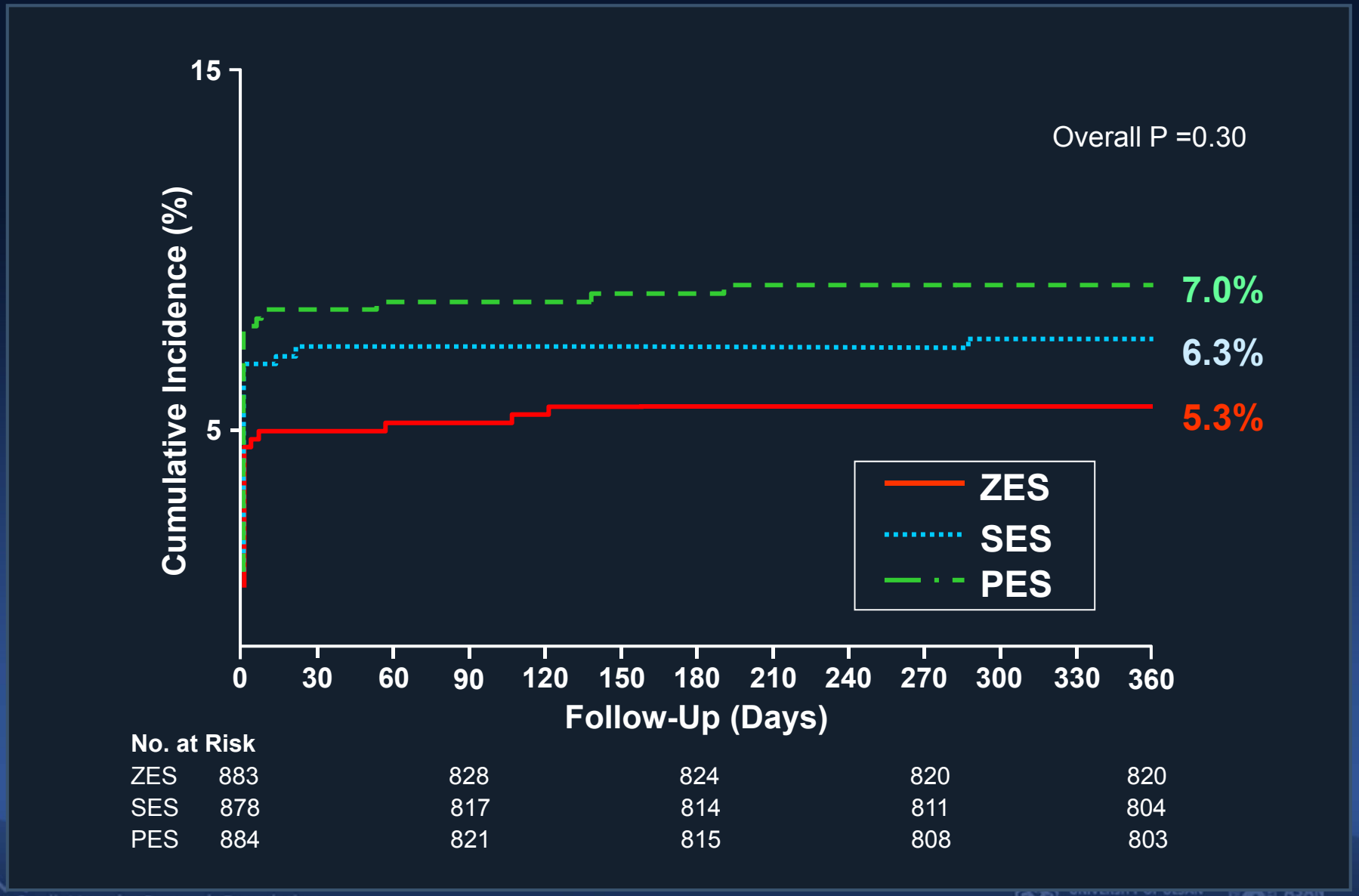
Death at 12 Month



No. at Risk					
ZES	883	871	869	864	864
SES	878	869	867	863	857
PES	884	880	873	865	859

ZEST

MI at 12 Month

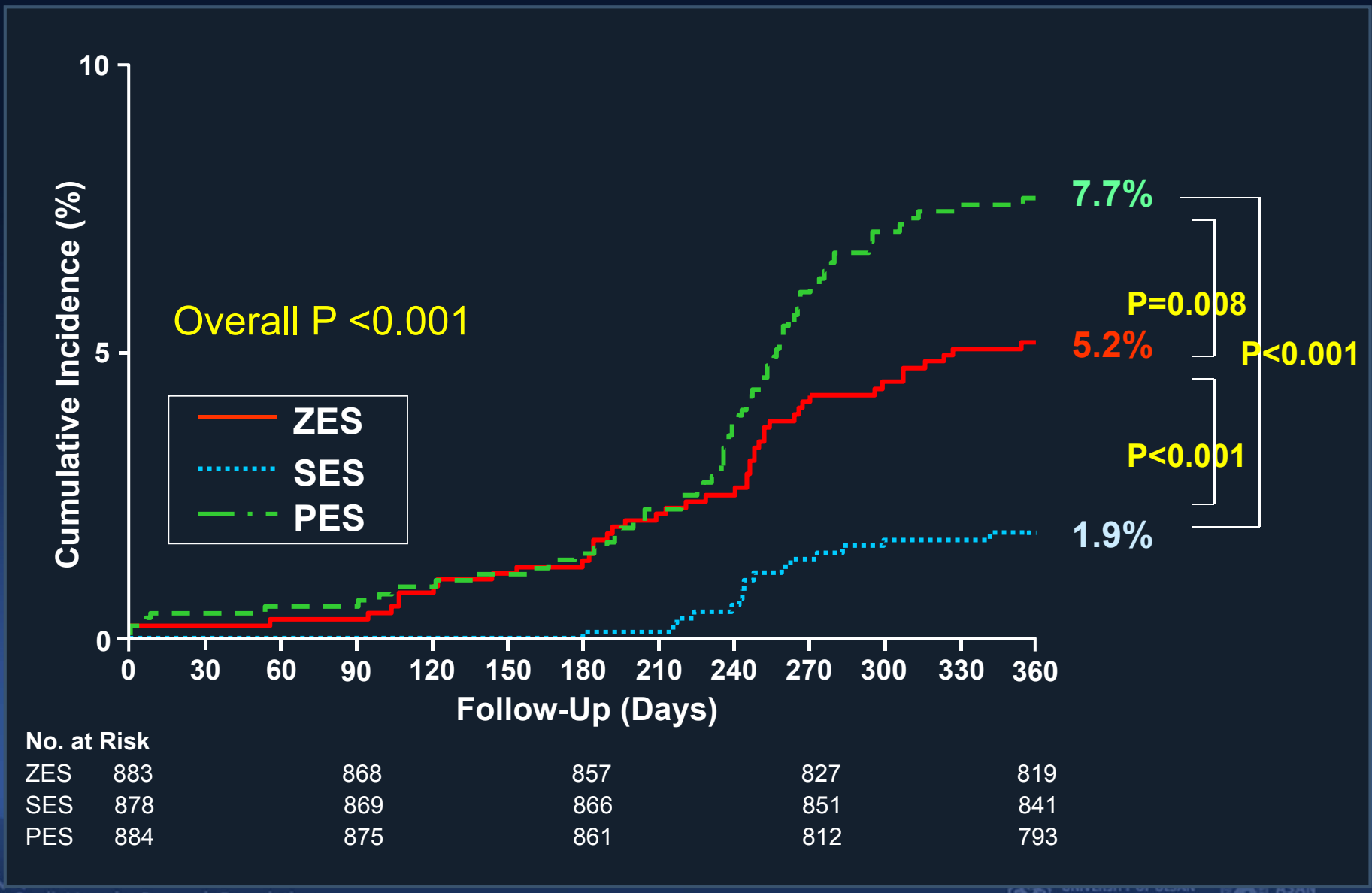


No. at Risk

ZES	883	828	824	820	820
SES	878	817	814	811	804
PES	884	821	815	808	803

ZEST

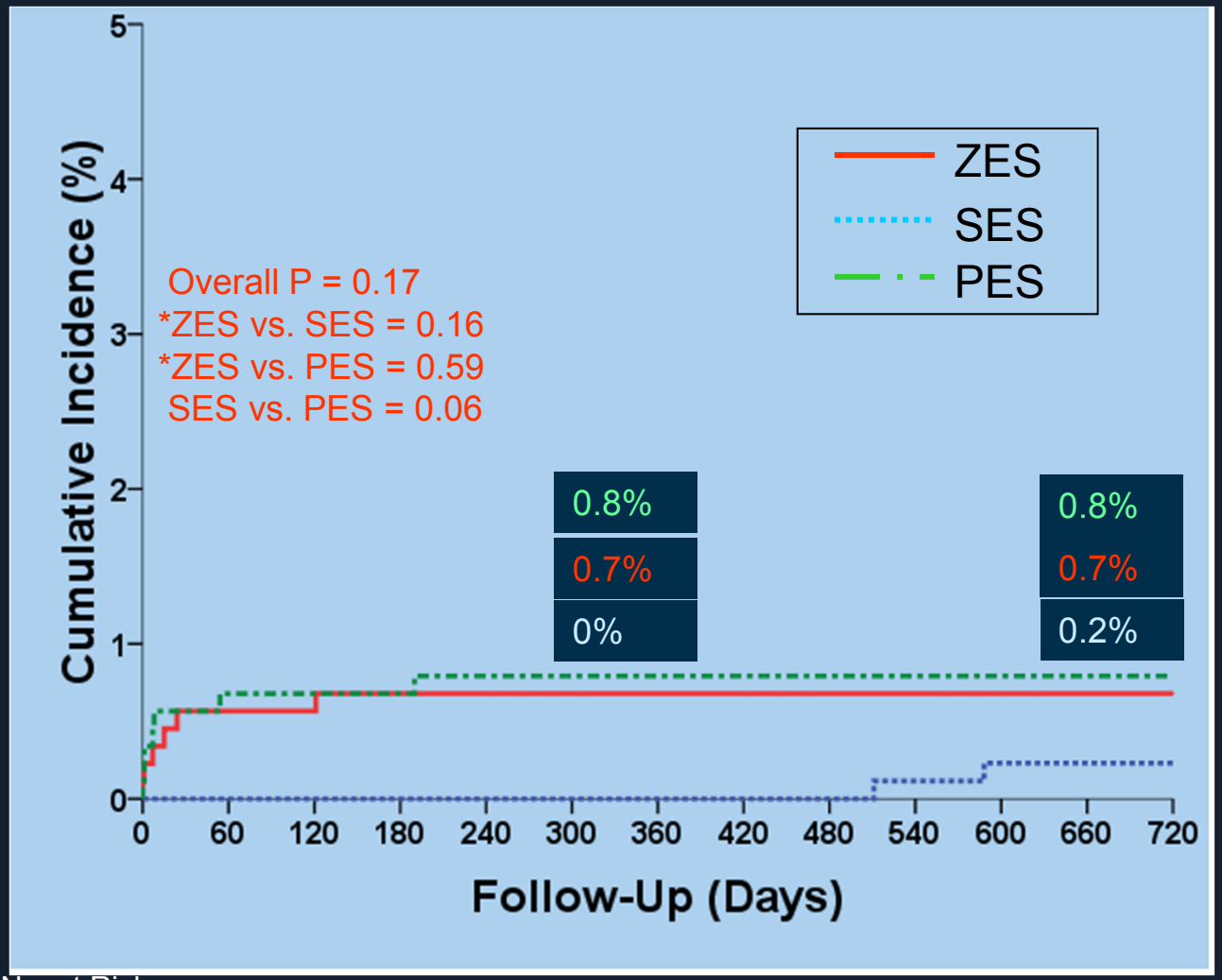
Ischemia-Driven TVR at 12 Month



No. at Risk					
ZES	883	868	857	827	819
SES	878	869	866	851	841
PES	884	875	861	812	793

ZEST

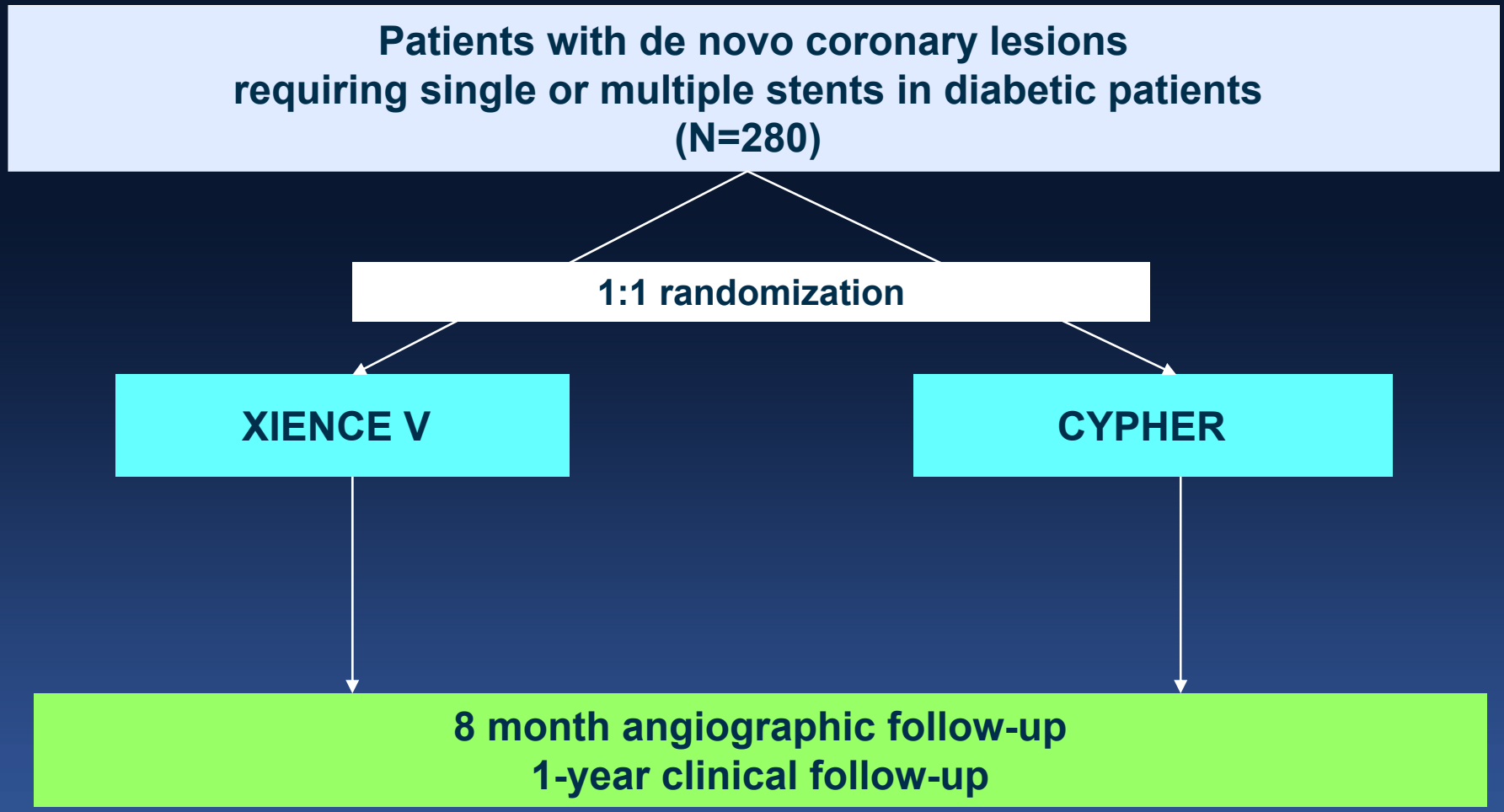
Definite or Probable ST at 24 Mo



No. at Risk

ZES	883	876	874	871	681
SES	878	895	870	869	673
PES	884	875	868	864	660

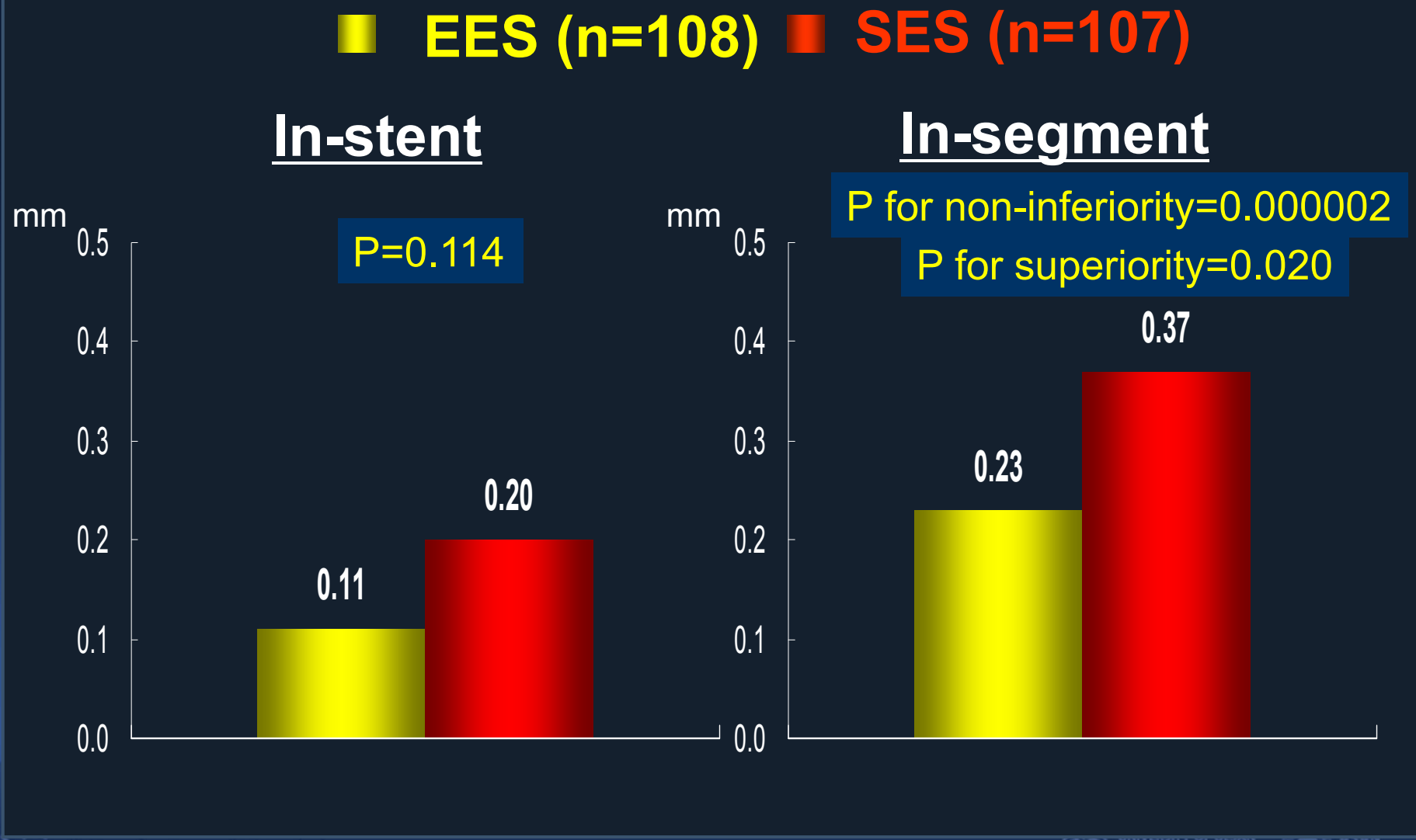
ESSENCE-DIABETES



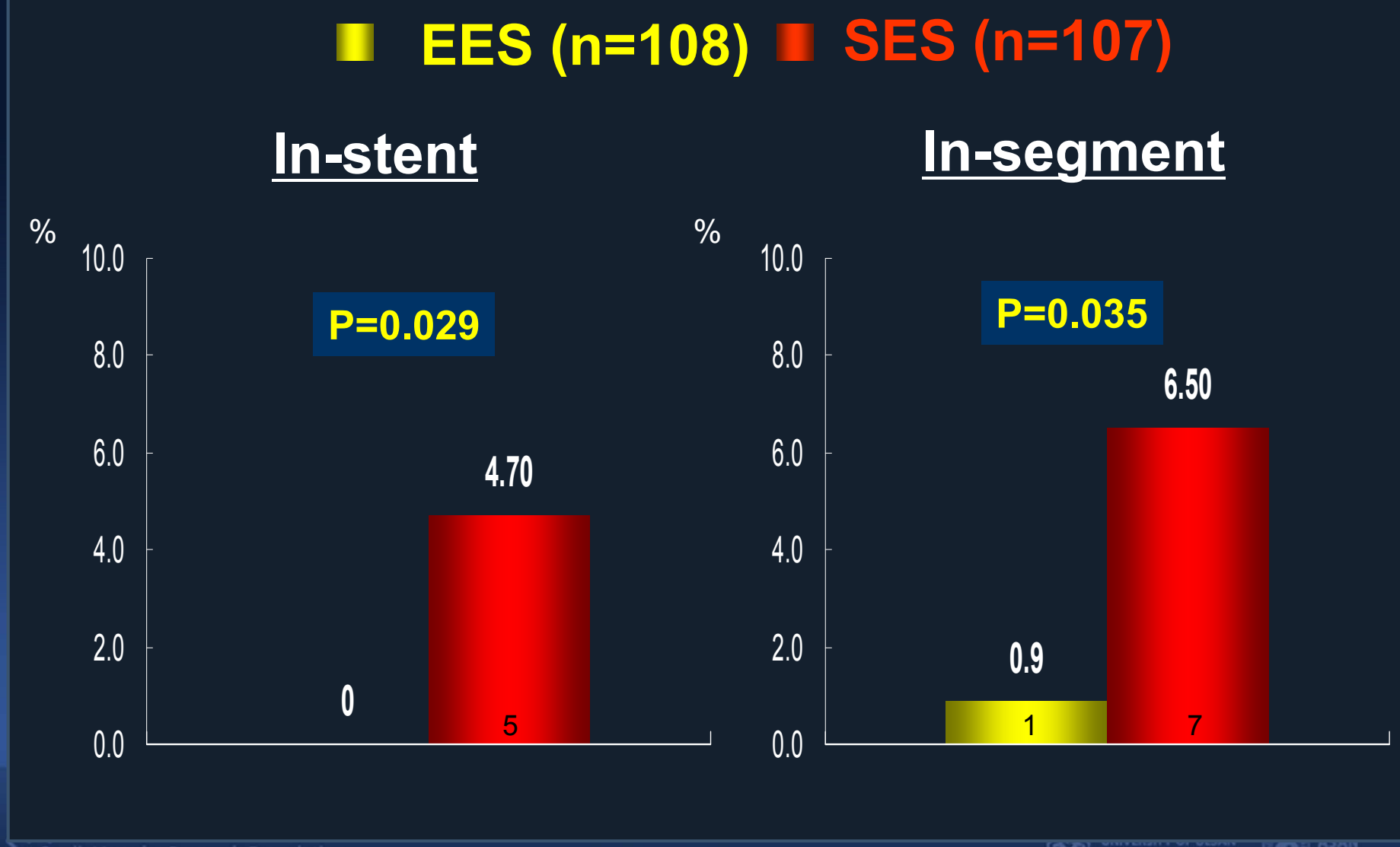
Primary end-point: Angiographic in-segment late loss at 8-month angiography
Secondary end-point: Clinical outcomes at 12 month follow-up
IVUS results at 8 month angiographic follow-up (selected center)

Primary End Point : Late loss

Using the definition of maximal regional late loss



Restenosis Rate



ESSENCE-DIABETES

Clinical Outcomes at 12-Month

	EES	SES	P
Patients	149	150	
Death	2 (1.3%)	5 (3.3%)	
Cardiac	1	2	0.448
Non-cardiac	1	3	
MI	0	2 (1.3%)	0.498
Stent thrombosis	1 (0.7%) *	1 (0.7%) *	
Acute	0	0	0.999
Subacute	1	1	
Late	0	0	
Ischemic driven TVR	1 (0.7%)	6 (4.0%)	0.121
Ischemic driven TLR	1 (0.7%)	4 (2.6%)	0.371
Death/MI/ischemic driven TVR	3 (2.0%)	10 (6.6%)	0.085
Death/MI/ischemic driven TLR	3 (2.0%)	8 (5.3%)	0.218

* Both patients died suddenly without angiographic follow-up within 1 month post-procedure and were adjudicated as probable stent thrombosis by the ARC definition

LONG-DES III

Patients requiring PCI with DES for long coronary lesions:
Lesion length ≥ 25mm **receiving single or multiple stents**
(*total stent length ≥ 28mm*)

Stratified randomization by Enrolling sites

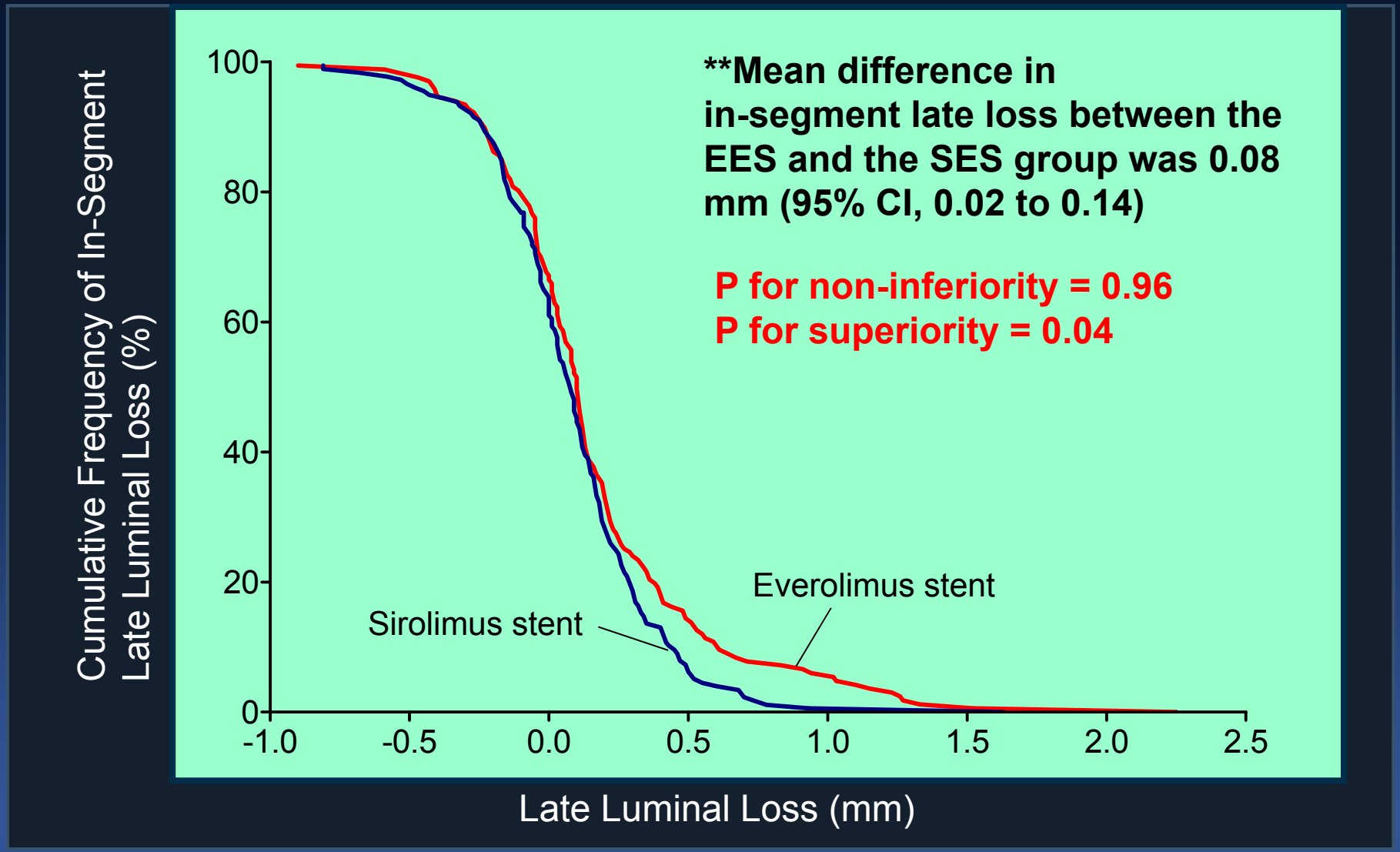
Xience V (n=225)

Cypher (n=225)

9 months Angiographic follow-up
12 months Clinical follow-up

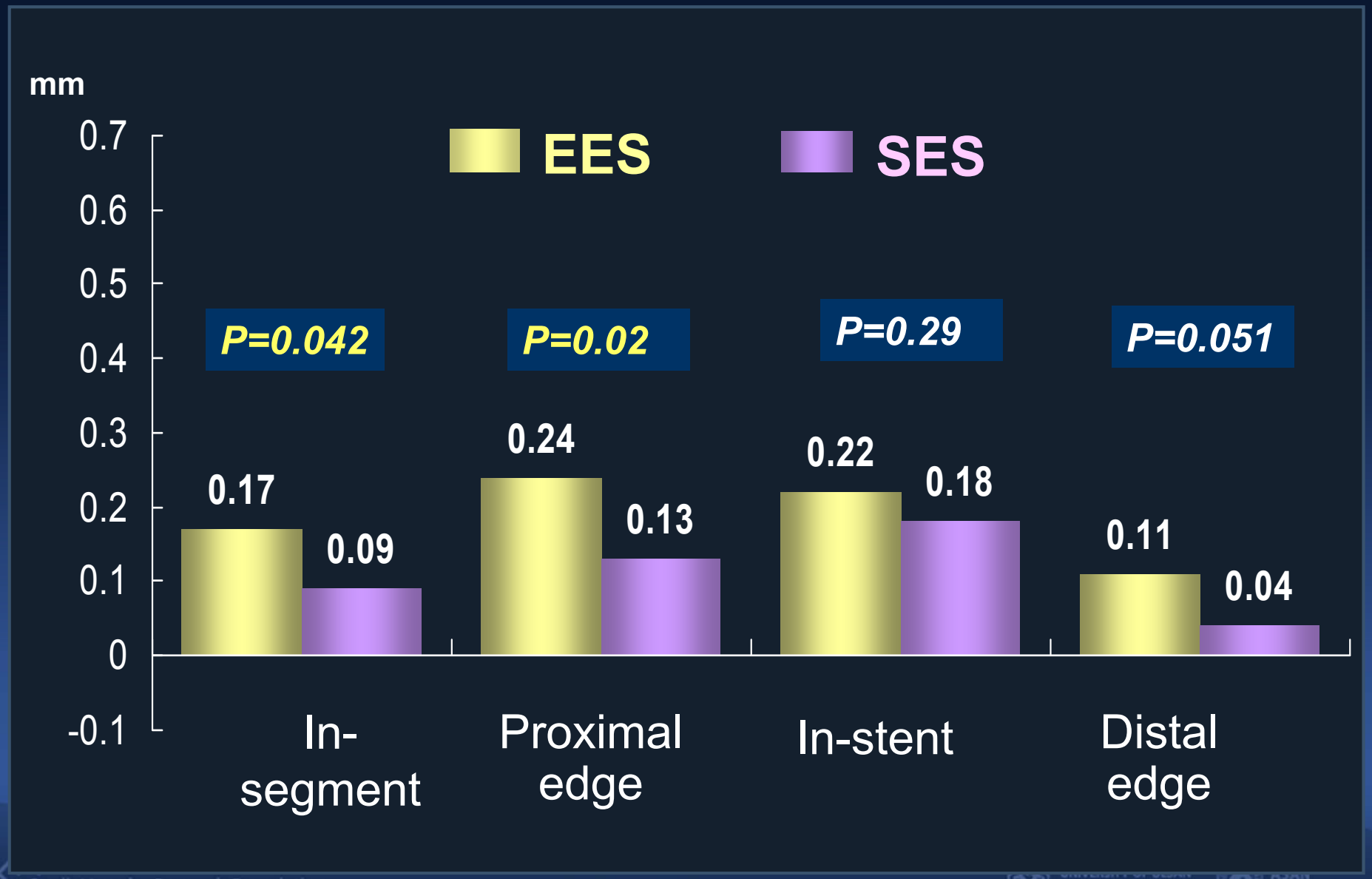
****Primary endpoint: In-segment late loss at 9 months angiographic follow-up**

Primary Endpoint: In-Segment Late Loss

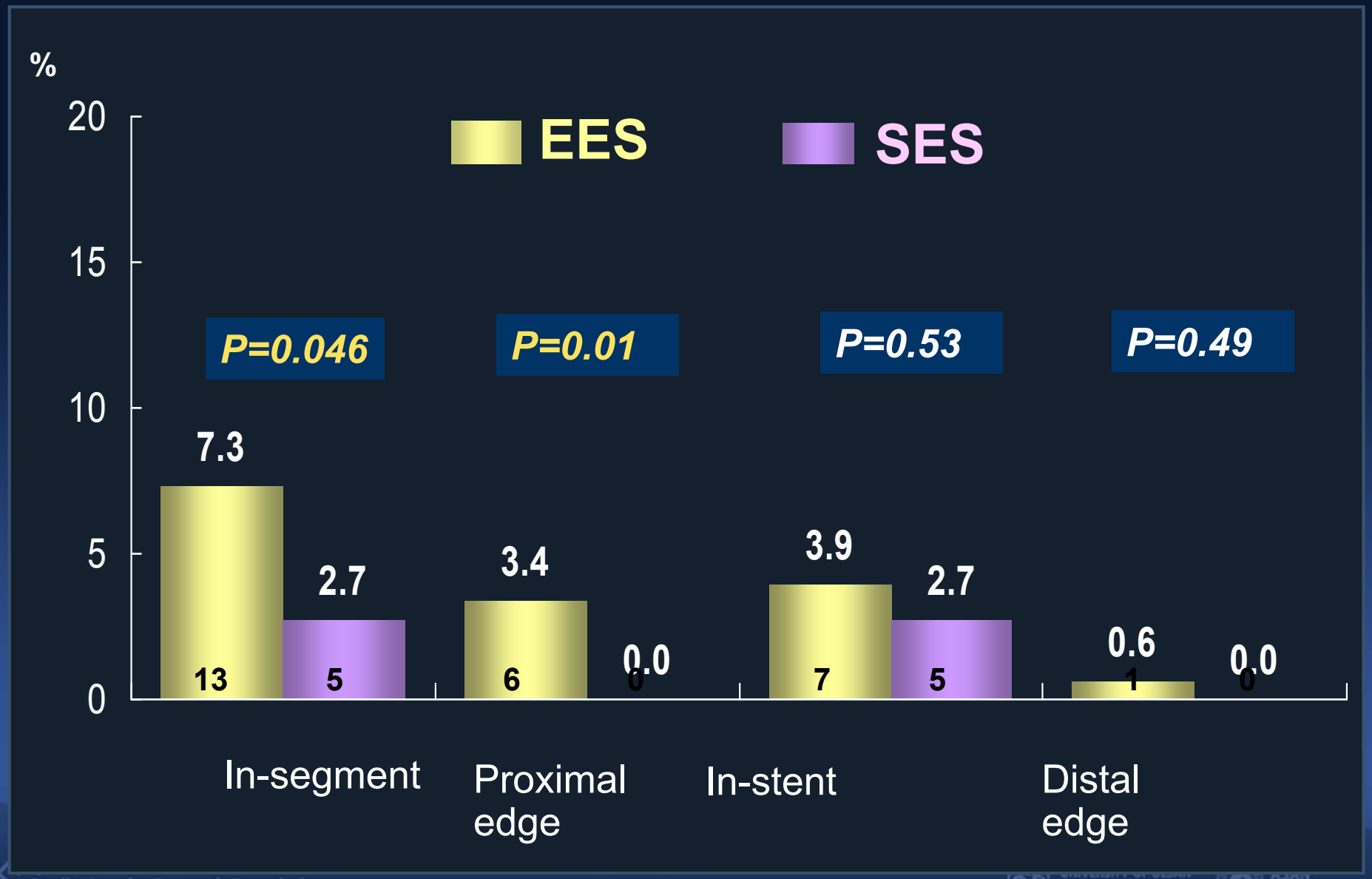


"Primary results failed to show the noninferiority of EES and instead demonstrated the statistical superiority of the SES"

Late Loss


mm
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
-0.1
EES
SES
P=0.042
P=0.02
P=0.29
P=0.051
0.17
0.09
0.24
0.13
0.22
0.18
0.11
0.04
In-segment
Proximal edge
In-stent
Distal edge

Binary Restenosis Rate

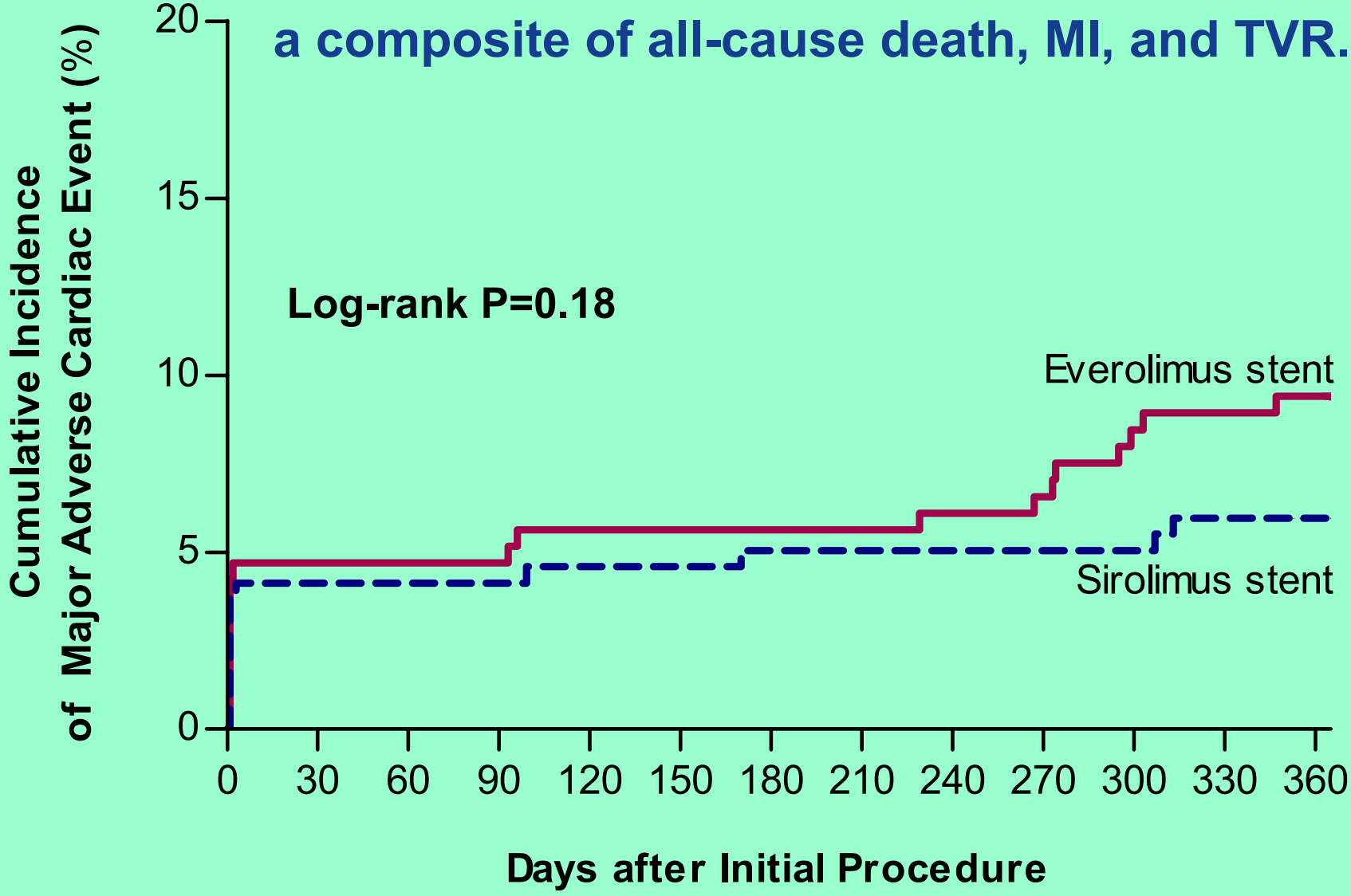


Clinical Outcomes at 12 Mo

Clinical outcomes	EES (224 Patients)	SES (226 Patients)	P Value
Death	1 (0.4)	0	0.50
Cardiac	0	0	NA
Noncardiac	1 (0.4)	0	0.50
Myocardial infarction	22 (9.8)	18 (8.0)	0.49
Q-wave	0	0	NA
Non-Q-wave	22 (9.8)	18 (8.0)	0.49
Death or myocardial infarction	23 (10.3)	18 (8.0)	0.40
Stent thrombosis, definite or probable	1 (0.4)	0	0.50
Target-lesion revascularization	7 (3.1)	5 (2.2)	0.55
Target-vessel revascularization	9 (4.0)	6 (2.7)	0.42
Major adverse cardiac events†	32 (14.3)	23 (10.2)	0.18
Target-lesion failure, defined post hoc‡	29 (12.9)	22 (9.7)	0.28

†Major adverse cardiac events were defined as a composite of all-cause death, MI, and TVR.
‡Target-lesion failure was a composite of death from cardiac causes, target-vessel MI, and TLR.

12 Months MACE:
a composite of all-cause death, MI, and TVR.

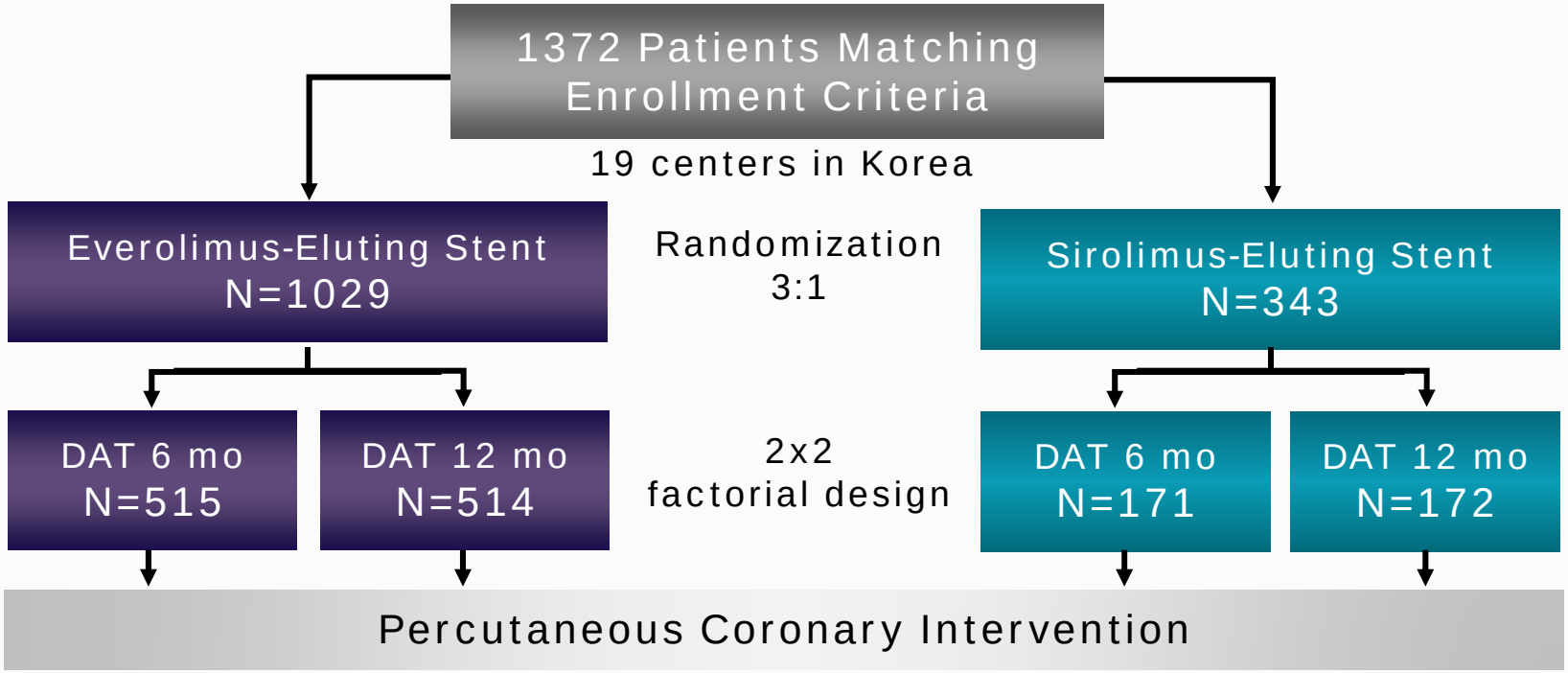


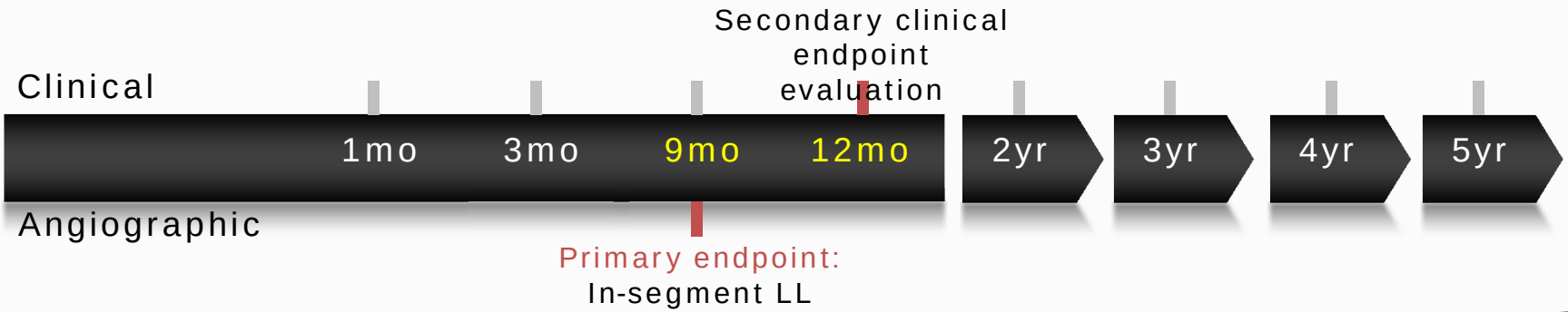
No. at Risk

Everolimus stent	224	203	201	199	190
Sirolimus stent	226	209	207	207	199

EXCELLENT

Prospective, open label, two-arm, randomized multi-center trial





Seoul National University Hospital Cardiovascular Center

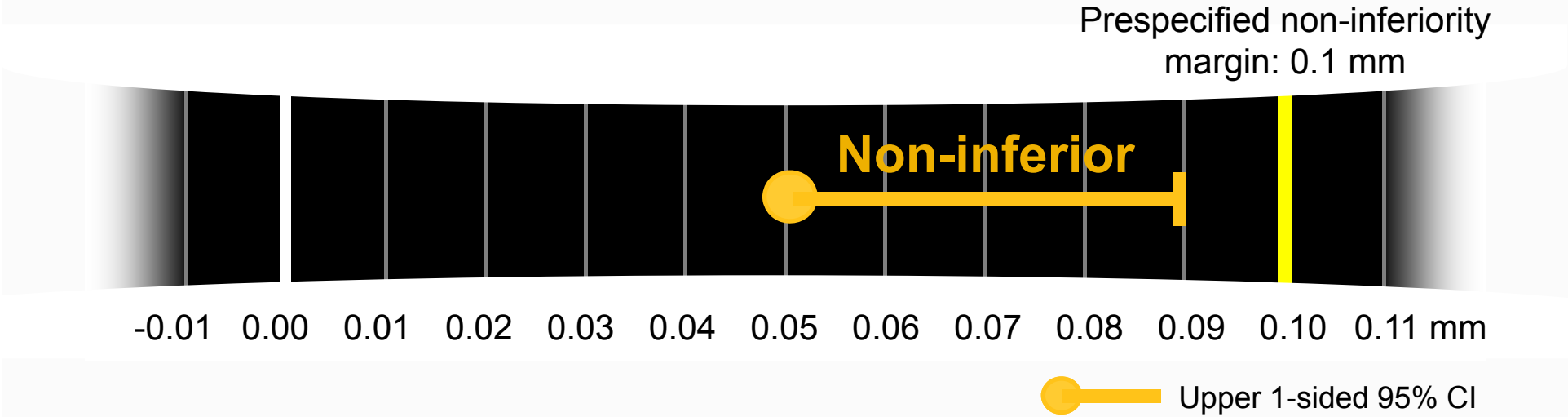
Am Heart J 2009 May;157:811-817
Kim HS ACC 2010, Kwon HC ACC 2011.

EXCELLENT-RCT

1˚ Endpoint

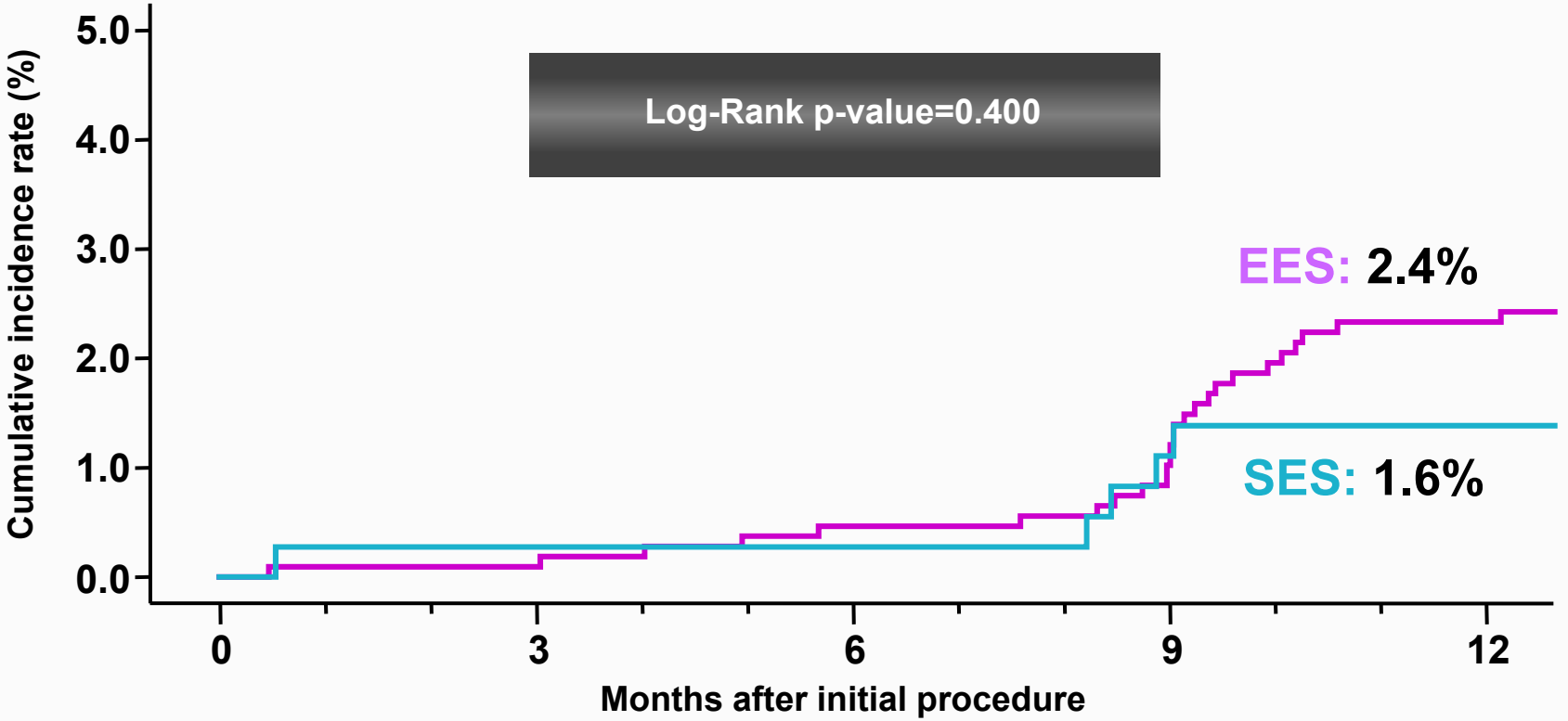
In-segment Late Loss

EES (N=935)	SES (N=266)	Mean ΔLL: 0.05 mm Upper 1-sided 95% CI: 0.09 mm	Non-inferiority p-value
0.10±0.36 mm	0.05±0.34 mm		0.017



2˚ Endpoint

Target Lesion Revascularization



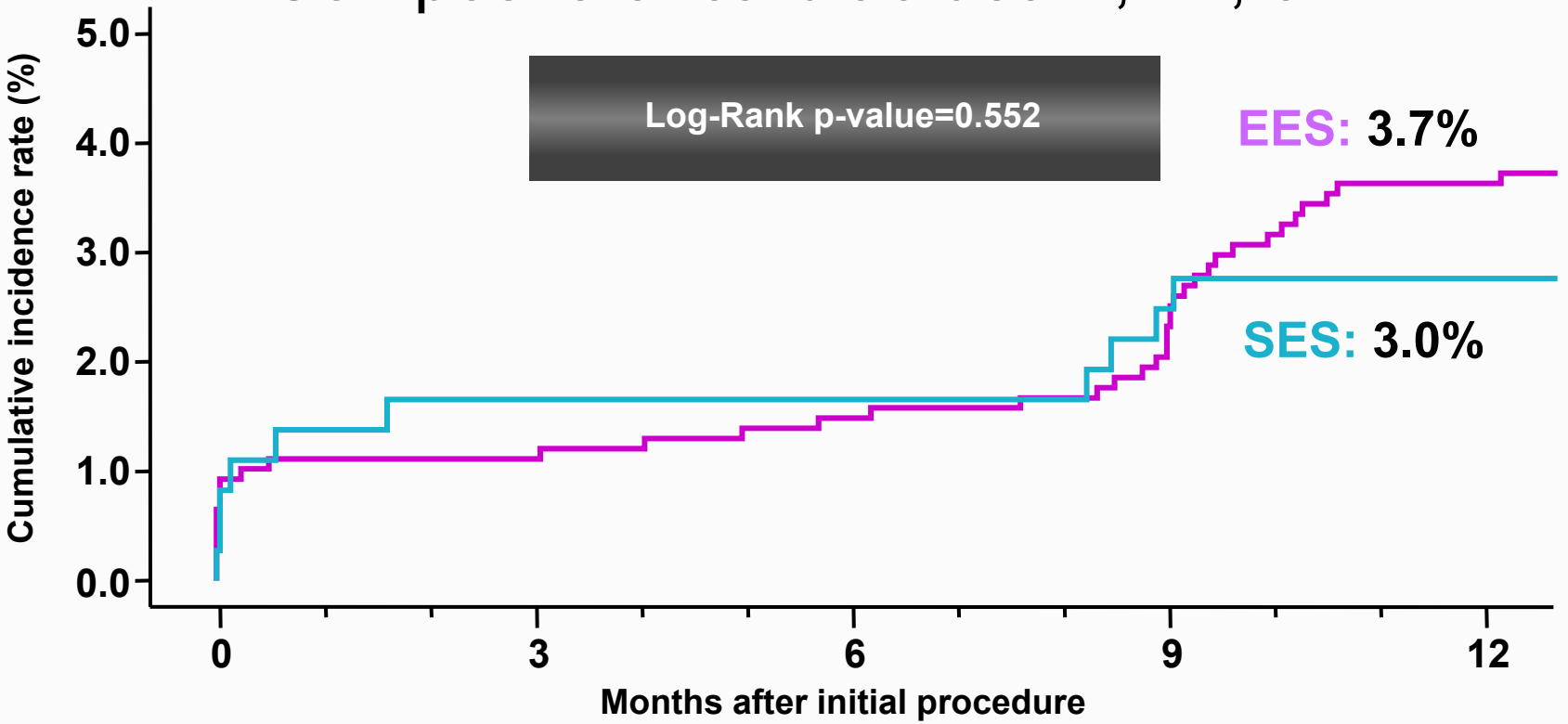
Patient Number at Risks

EES	1079	1056	1049	1042	1018
SES	364	348	346	343	340

2˚ Endpoint

Target Lesion Failure

: Composite of cardiac death, MI, or ID-TLR



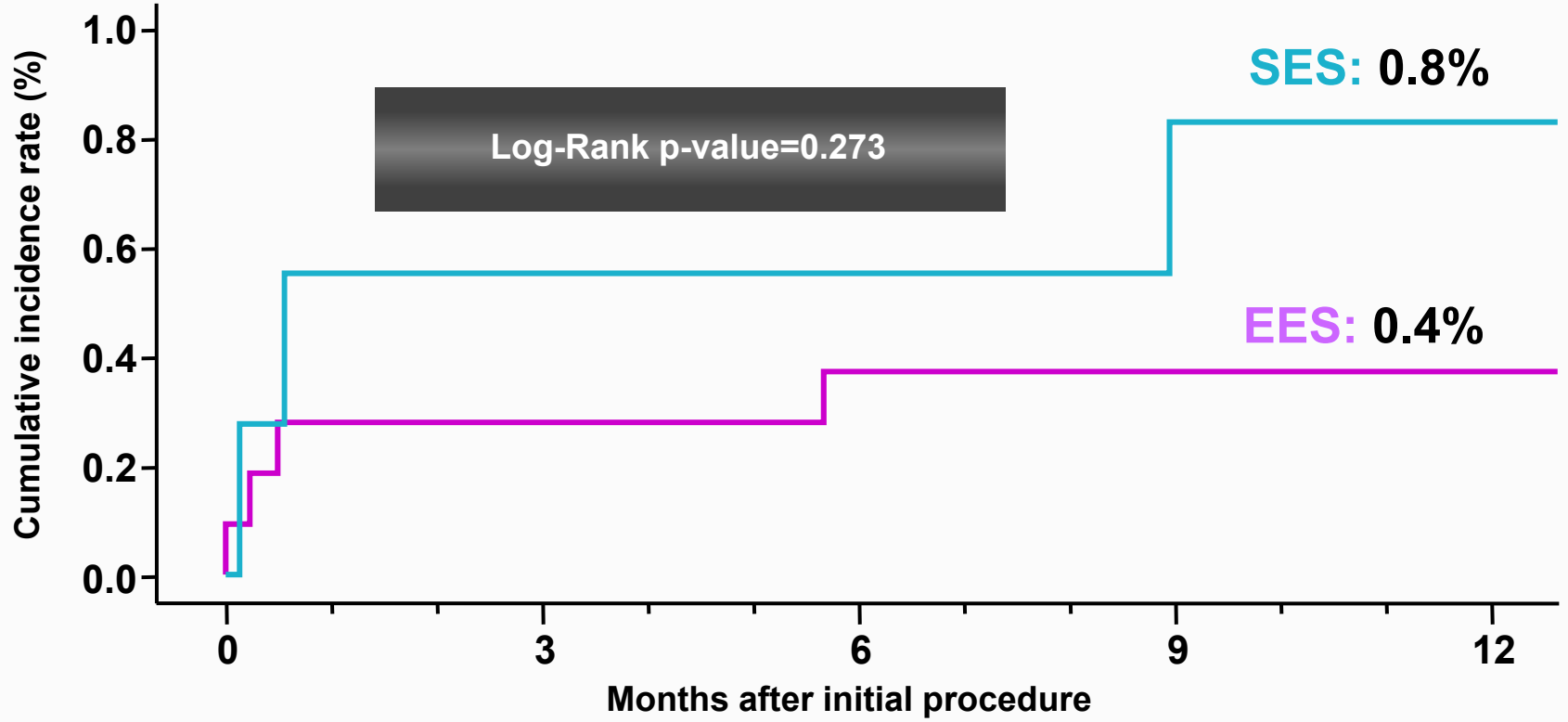
Patient Number at Risks

EES	1079	1046	1039	1032	1007
SES	364	345	343	340	337

2˚ Endpoint

Stent Thrombosis

: Definite/Probable ST by ARC definition

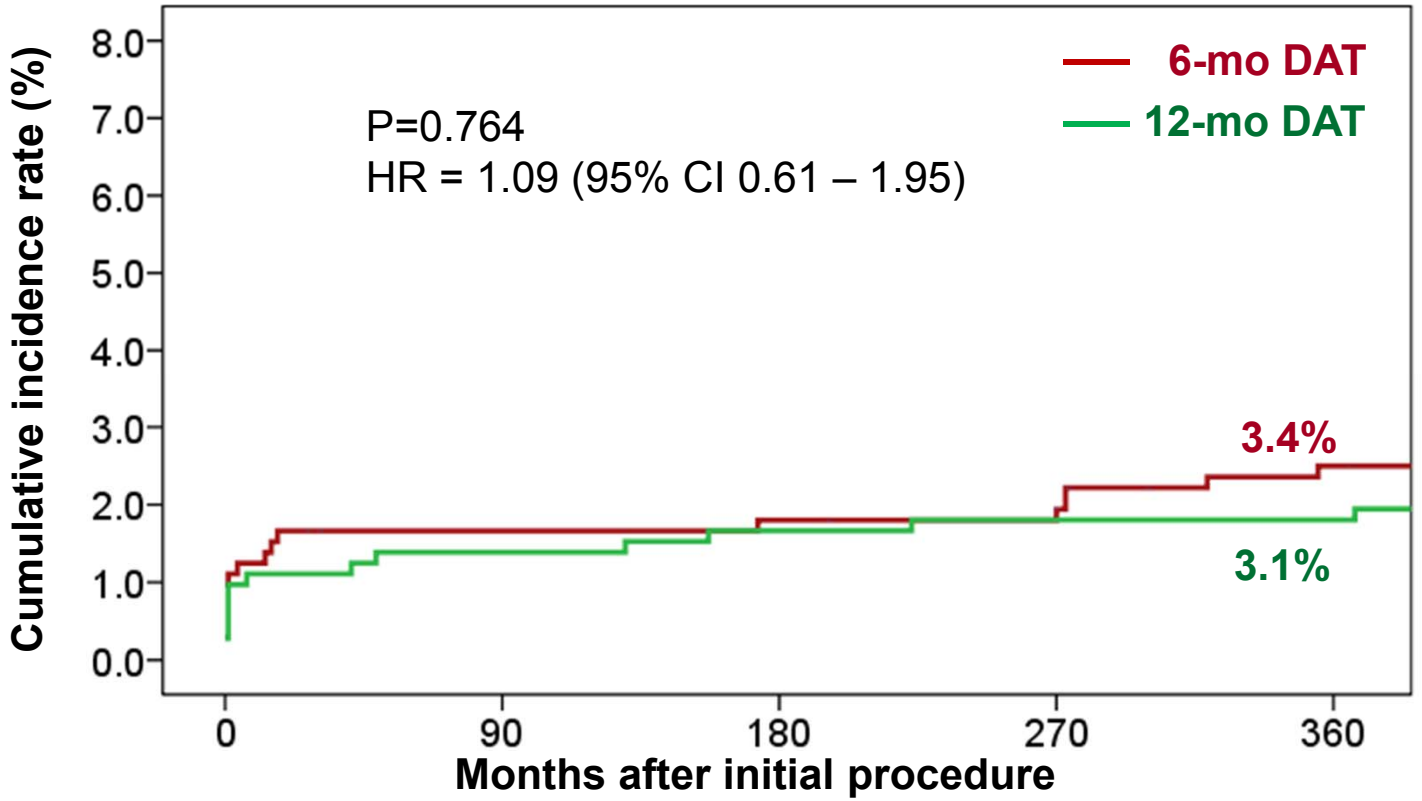


Patient Number at Risks

EES	1079	1055	1051	1048	1040
SES	364	347	345	344	342

Safety Endpoint

(Death, MI, stent thrombosis, CVA, or TIMI major bleeding)



Patient Number at Risks

6-month	722	708	707	706	698
12-month	721	710	706	704	699

Non-randomized Registry

Evaluation of Effectiveness and Safety of the First, Second, and New Drug-Eluting Stents in Routine Clinical Practice

IRIS-DES Registry

Consecutive PCI patients receiving New DES in 55 centers without a mixture of other DES

Prospective Enrollment

DESSIAN Registry	K-XIENCE Registry	IRIS-PRIME Registry	IRIS-NOBORI Registry	IRIS-BIOMATRIX Registry	IRIS-ELEMENT Registry	IRIS-GENOUS-STEMI Registry	IRIS-GENOUS-DM Registry
Patents with CYPHER (N=3,000)	Patents with XIENCE (N=3,000)	Patents with XIENCE PRIME (N=2,000)	Patents with NOBORI (N=1,000)	Patents with BIOMATRIX (N=1,000)	Patents with PROMUS ELEMENT (N=2,000)	STEMI with GENOUS (N=1,000)	DM Patents with GENOUS (N=300)

Clinical follow-up at 1-, 6-, and 12-months, and annually up to 5 years

*Primary end point: Composite of Death, MI, and TVR at 12-months

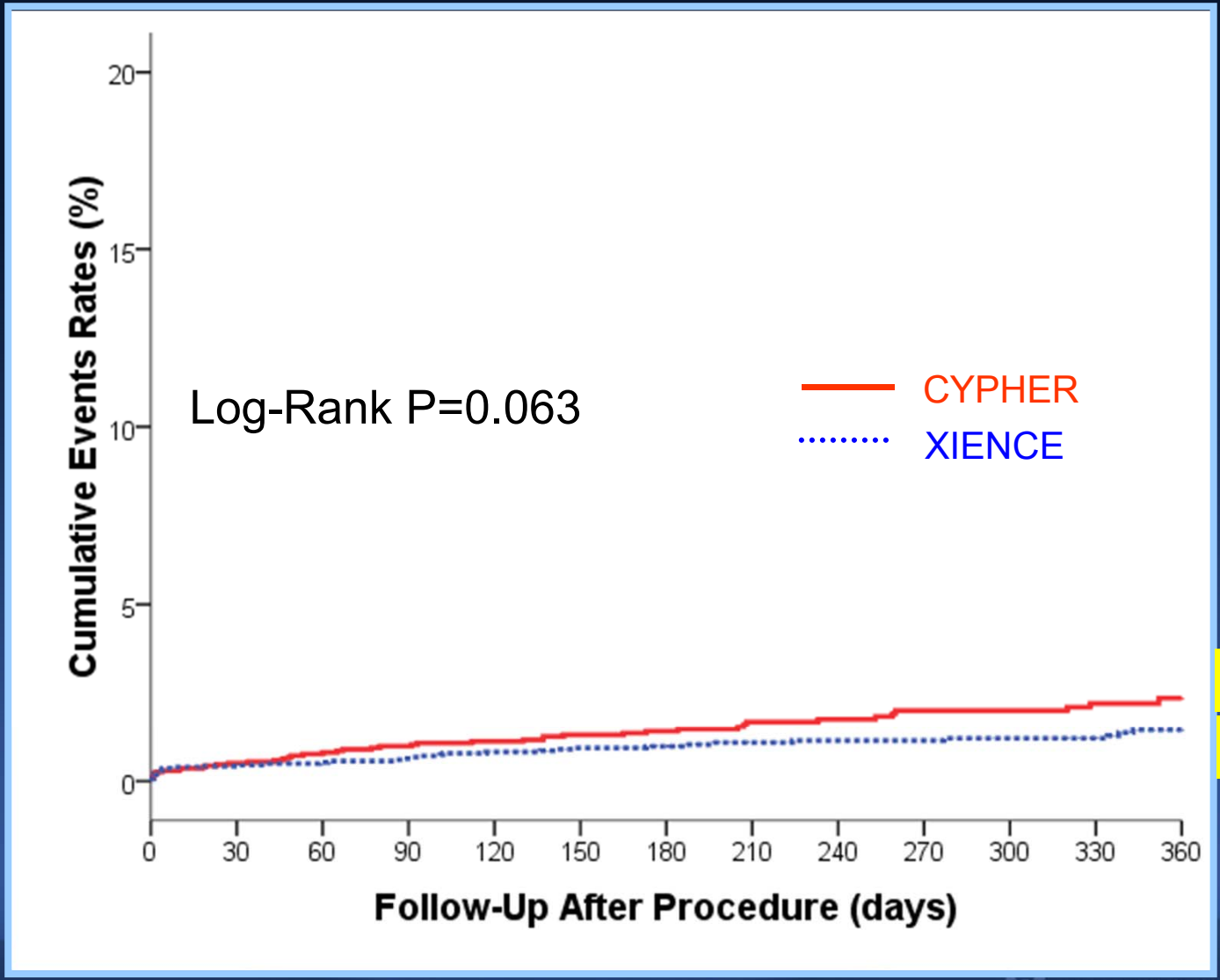
CardioVascular Research Foundation

Preliminary presented in ACC 2011

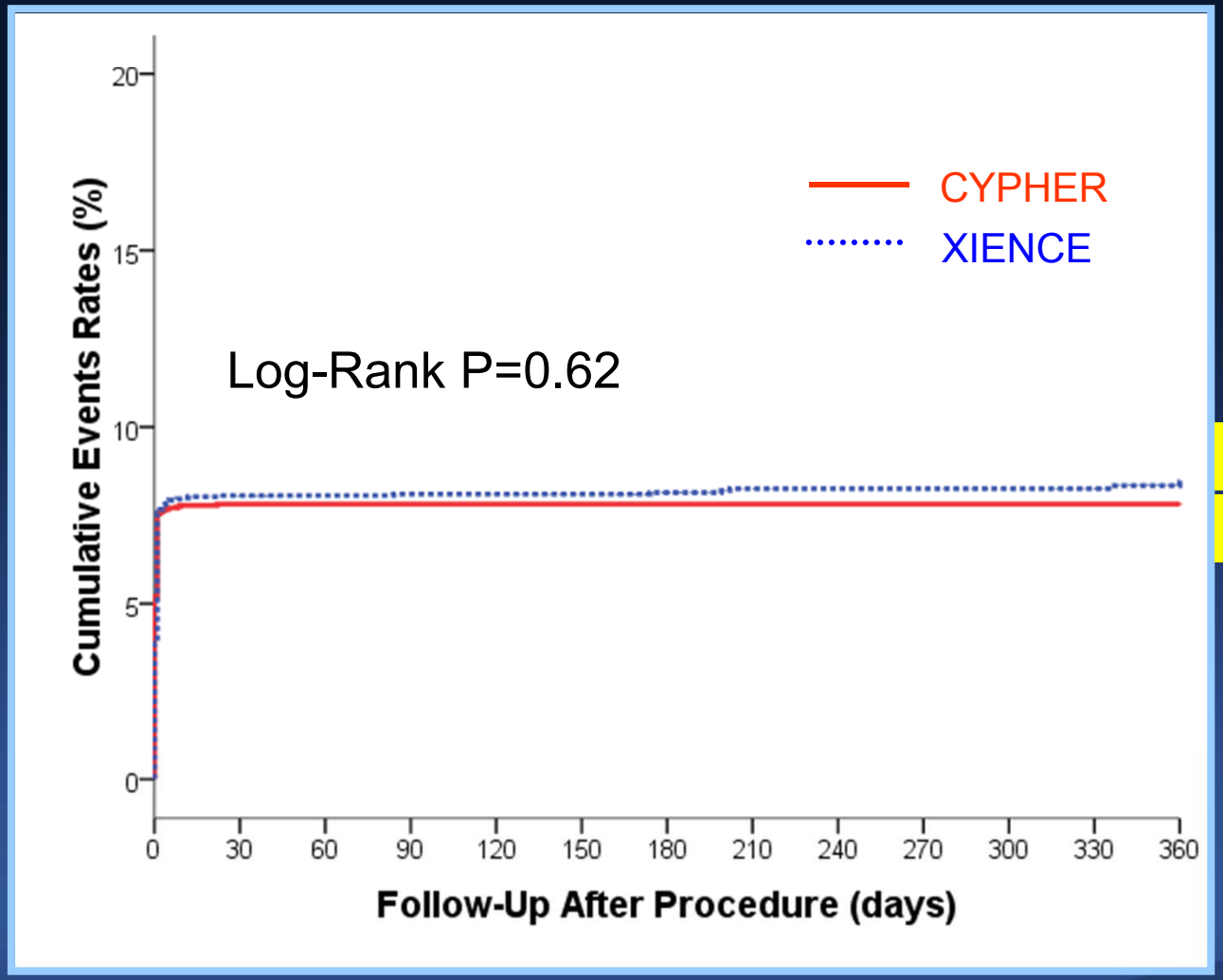
UNIVERSITY OF ULSAN COLLEGE MEDICINE

ASAN Medical Center

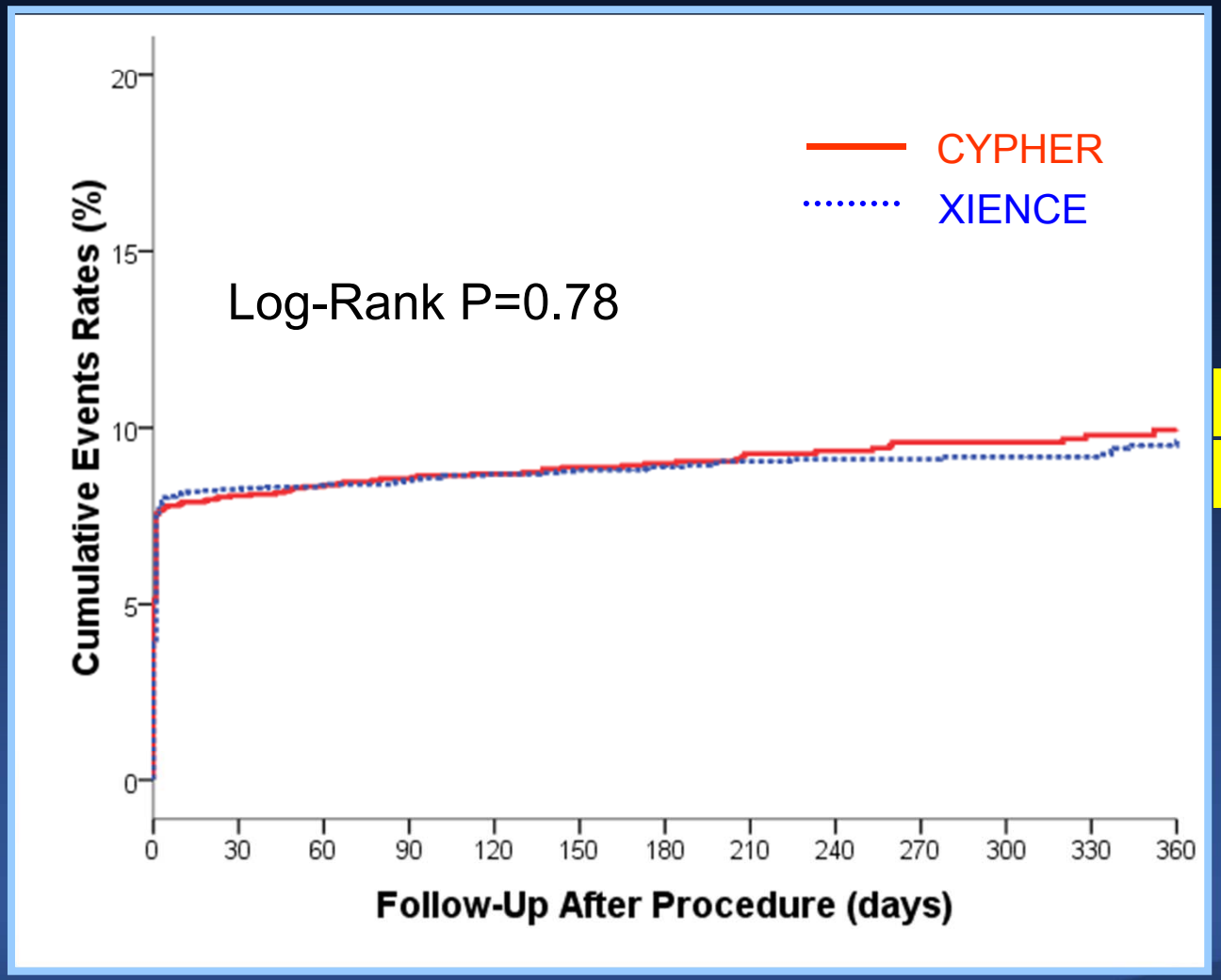
Unadjusted K-M Event Curves
All-cause mortality



Myocardial Infarction



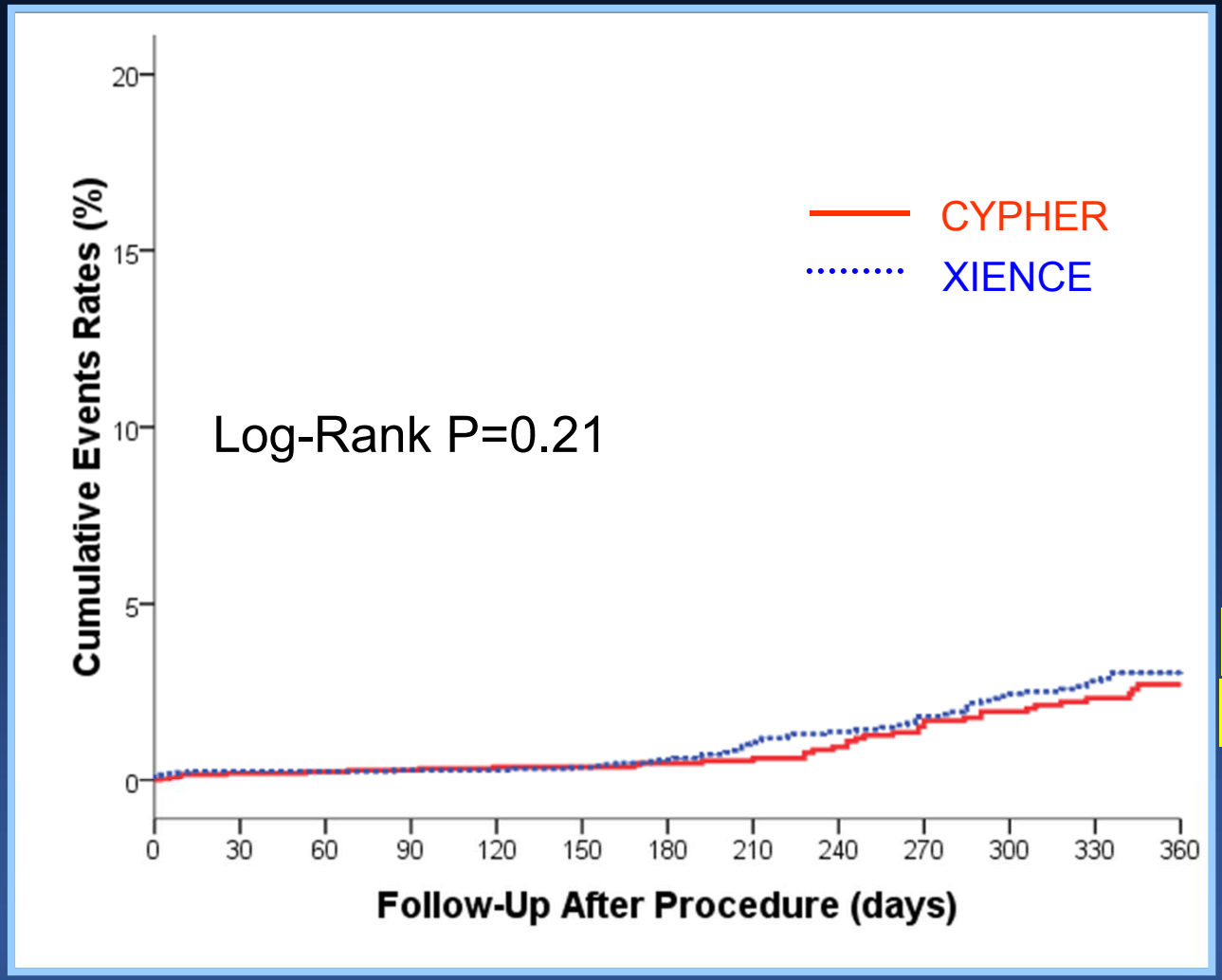
Death or Nonfatal MI



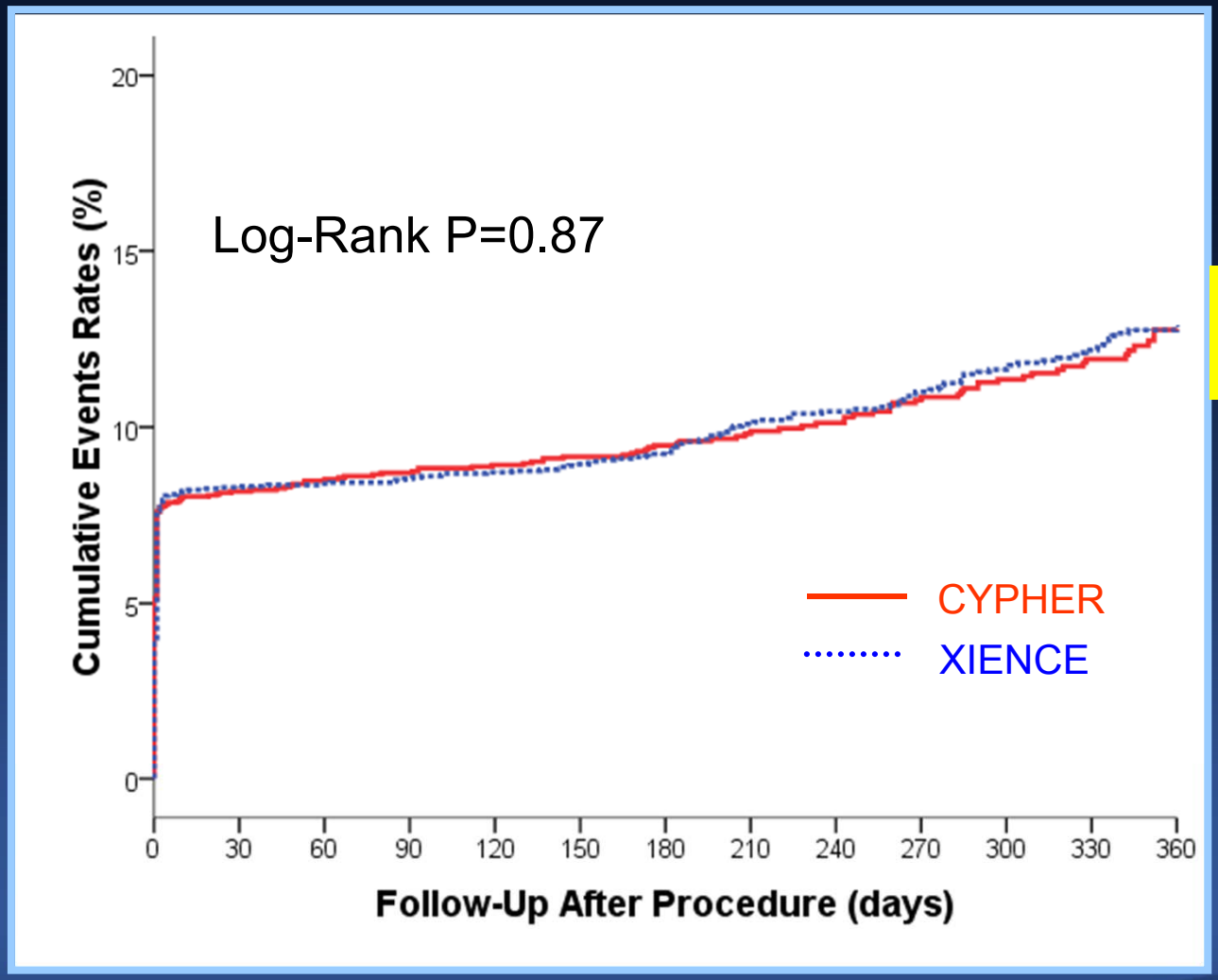
9.9%

9.6%

Target-Vessel Revascularization



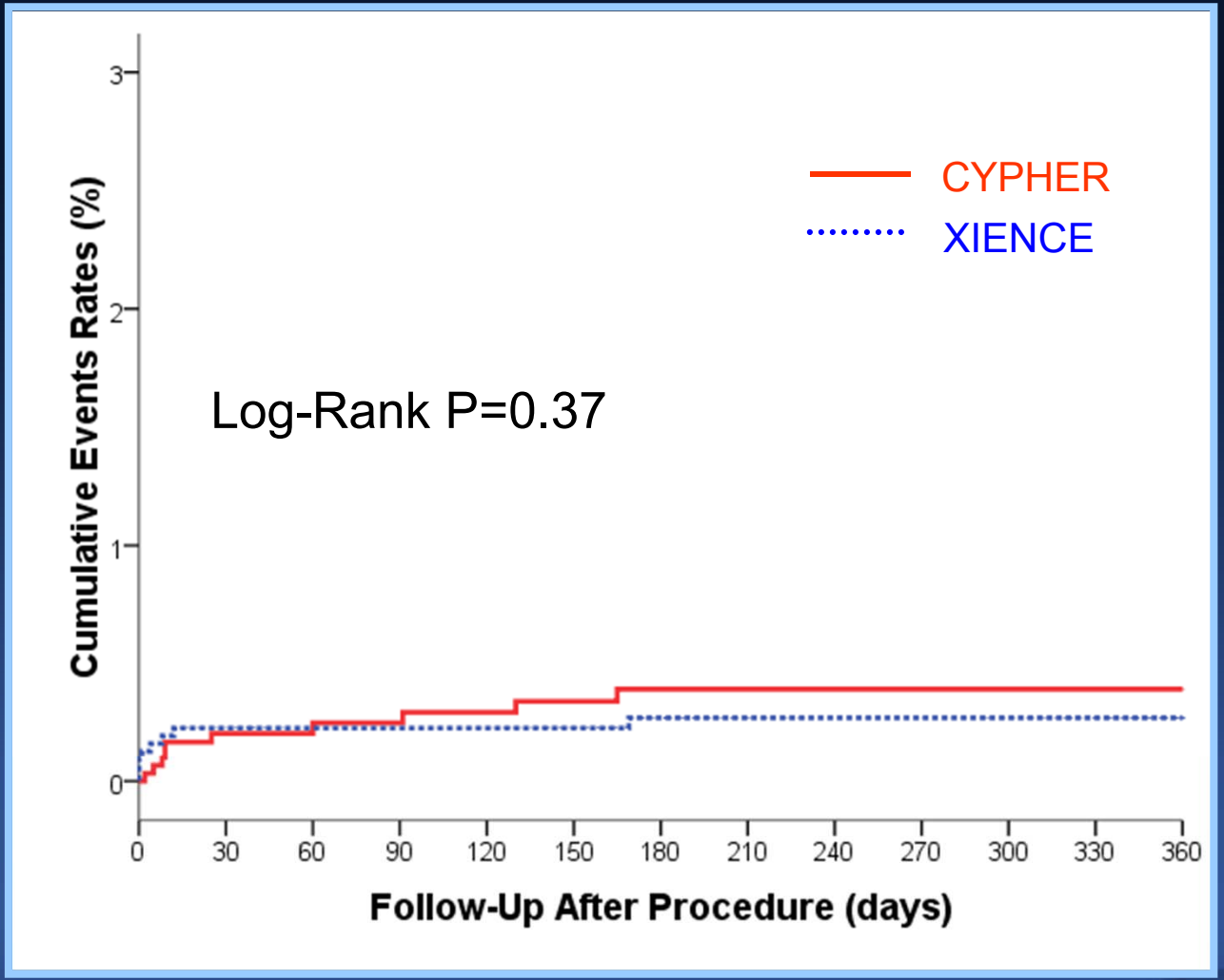
MACE (Death, MI, TVR)



12.9%

12.8%

ST (definite or probable)

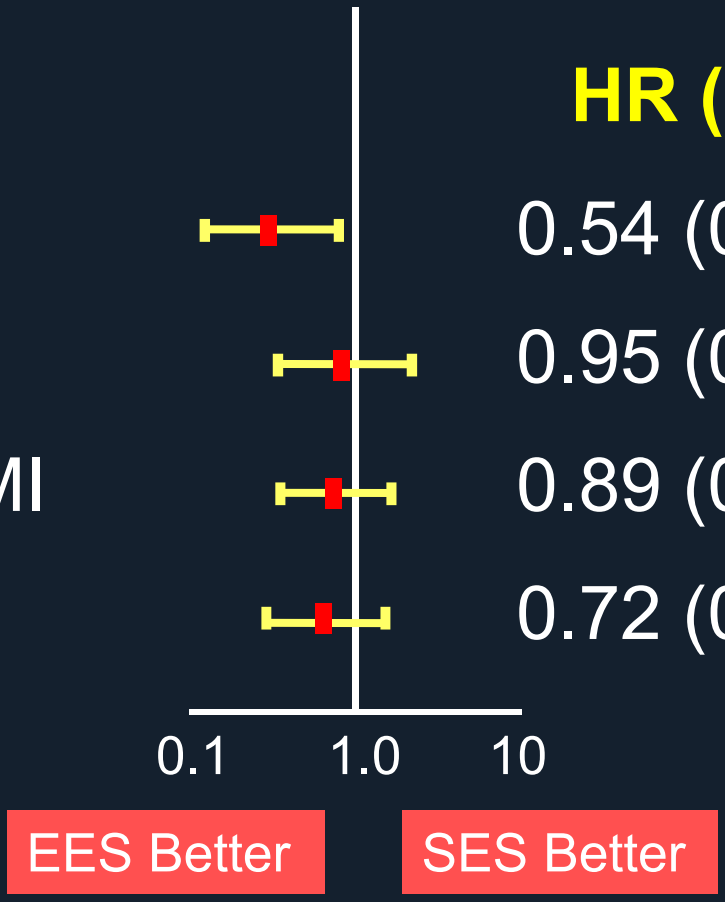


0.4%

0.3%

Adjusted Clinical Events for 1 Year

Outcomes	HR (95% CI)	P
Death	0.54 (0.31-0.92)	0.03
MI	0.95 (0.80-1.14)	0.61
Death or MI	0.89 (0.75-1.05)	0.17
ST *	0.72 (0.25-2.12)	0.55



*definite or probable stent thrombosis

Adjusted Clinical Events for 1 Year

Outcomes	HR (95% CI)	P
TLR	1.21 (0.80-1.84)	0.37
TVR	1.36 (0.94-1.96)	0.10
Stroke	0.80 (0.38-1.65)	0.54
MACE	0.81 (0.59-1.13)	0.22

*MACE = death, MI, TVR

PRECOMBAT Series

PRE-COMBAT
for unprotected left main disease
Up to 13 cardiac centers in Korea

Randomization of 600 (1:1)

- **PCI with Cypher N=300**
- **CABG N=300**

PRE-COMBAT-2
for unprotected left main disease

PRECOMBAT-Eligible Patients Treated with Xience V stent

Pts randomizable in the PRECOMBAT N=300

PRE-COMBAT-3
for unprotected left main disease

PRECOMBAT-Eligible Patients Treated with Promus Element stent

Pts randomizable in the PRECOMBAT N=300

Primary Endpoint (MACCE):

2-year death, MI, Stroke, and ischemic driven TVR

Comparison:

(1) Primary analysis : PRECOMBAT-Eligible Cohort with historical patients enrolled in PRECOMBAT randomization (either PCI or CABG)

(2) Secondary analysis : diverse comparisons with the patients in the PRECOMBAT-1 and -2 trial

Conclusion

- The safety and efficacy of the new generations DESs appears to be clinically equivalent to the early generation DESs in Korea.

- However, the difference of stent-related outcomes between the new and early generation DESs needs to be further investigated in complex patient subsets .