Angioplasty Summit – TCTAP 2012

Seoul, Korea 25th April 2012

Very Long-term Outcomes With Biolimus-Eluting Stents from an All-comers RCT: LEADERS 4 Year Data

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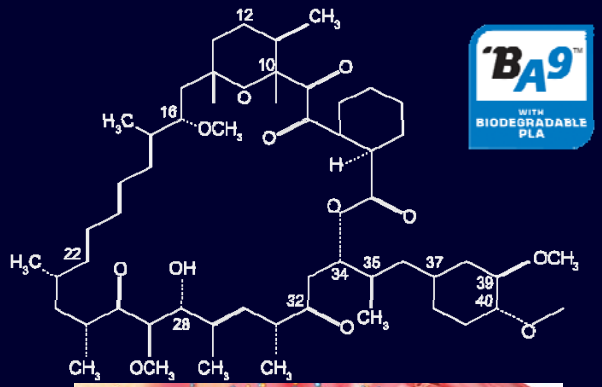
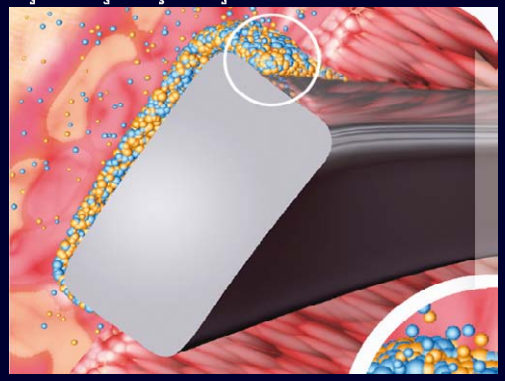
Biolimus-A9™ Eluting Stent



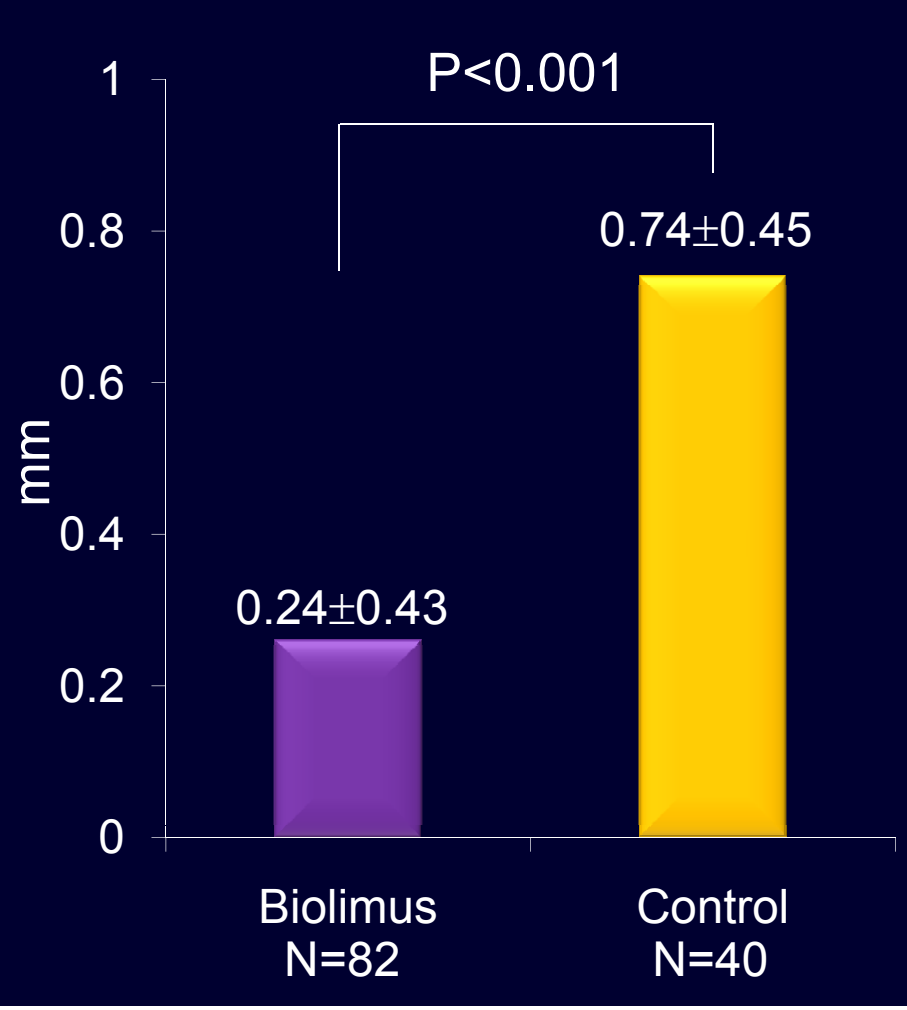


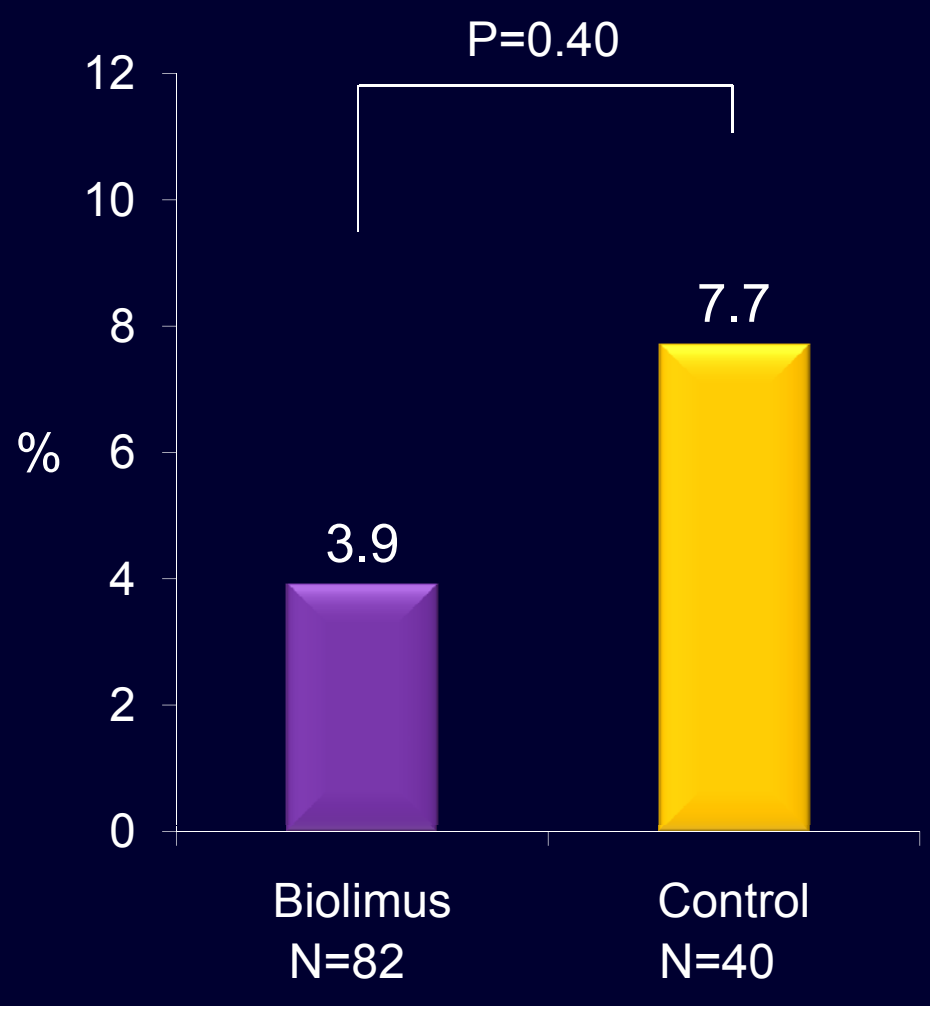
- Biolimus is a semi-synthetic sirolimus analogue with **10x higher lipophilicity** and similar potency as sirolimus.
- Biolimus is immersed at a concentration of 15.6 μg/mm into a biodegradable polymer, polylactic acid, and applied solely to **the abluminal stent surface** by a fully automated process.
- Biolimus is co-released with polylactic acid and completely desolves into carbon dioxide and water after a **6-9 months period**.
- The stainless steel stent platform has a strut thickness of 112 μm with a **quadrature link** design.

Biosensors-Biolimus A9 Stent – Angiographic Results

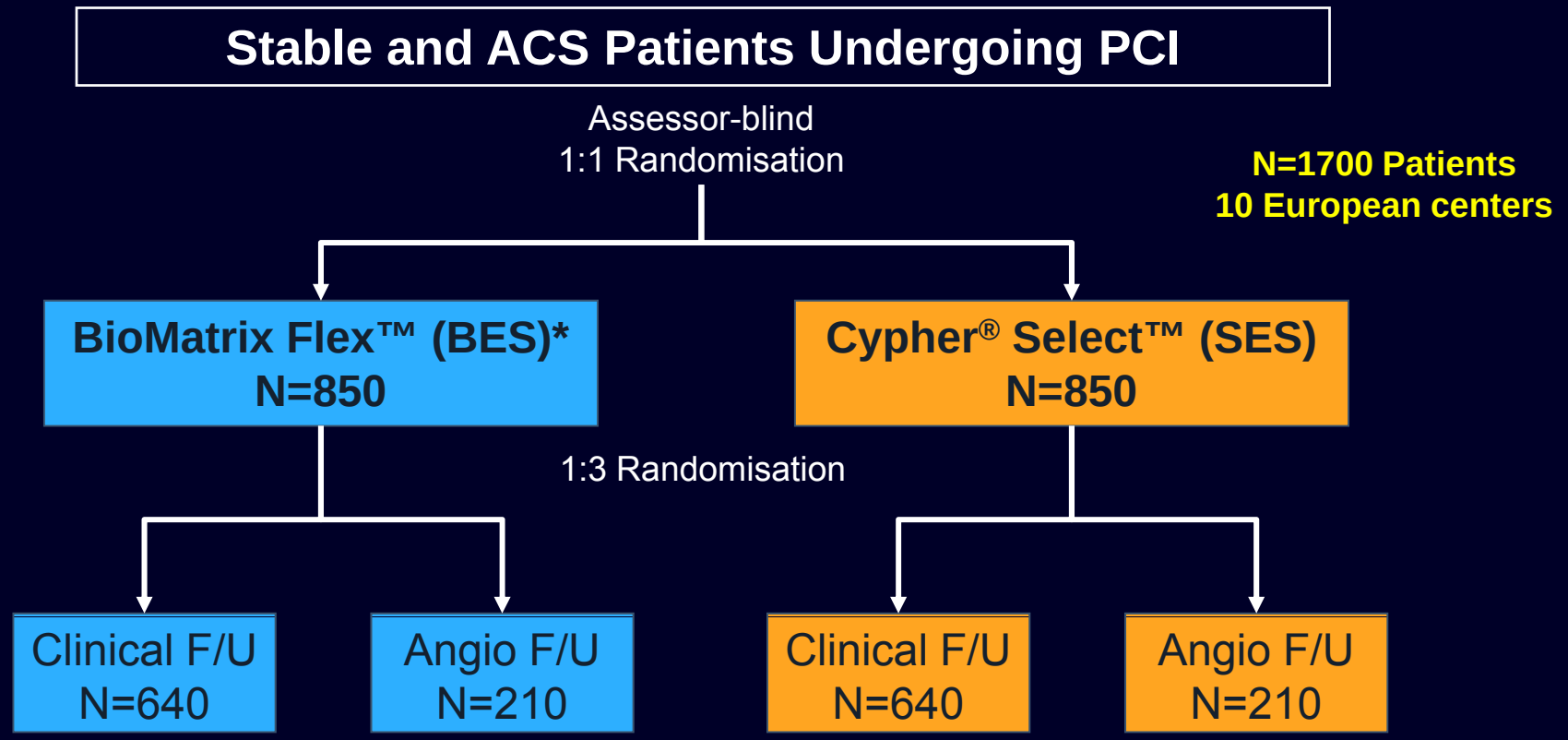
BioMatrix versus Bare Metal Stent: STEALTH

Costa M et al. Am J Cardiol 2006;98:443-6





LEADERS "All-Comers" Trial Design

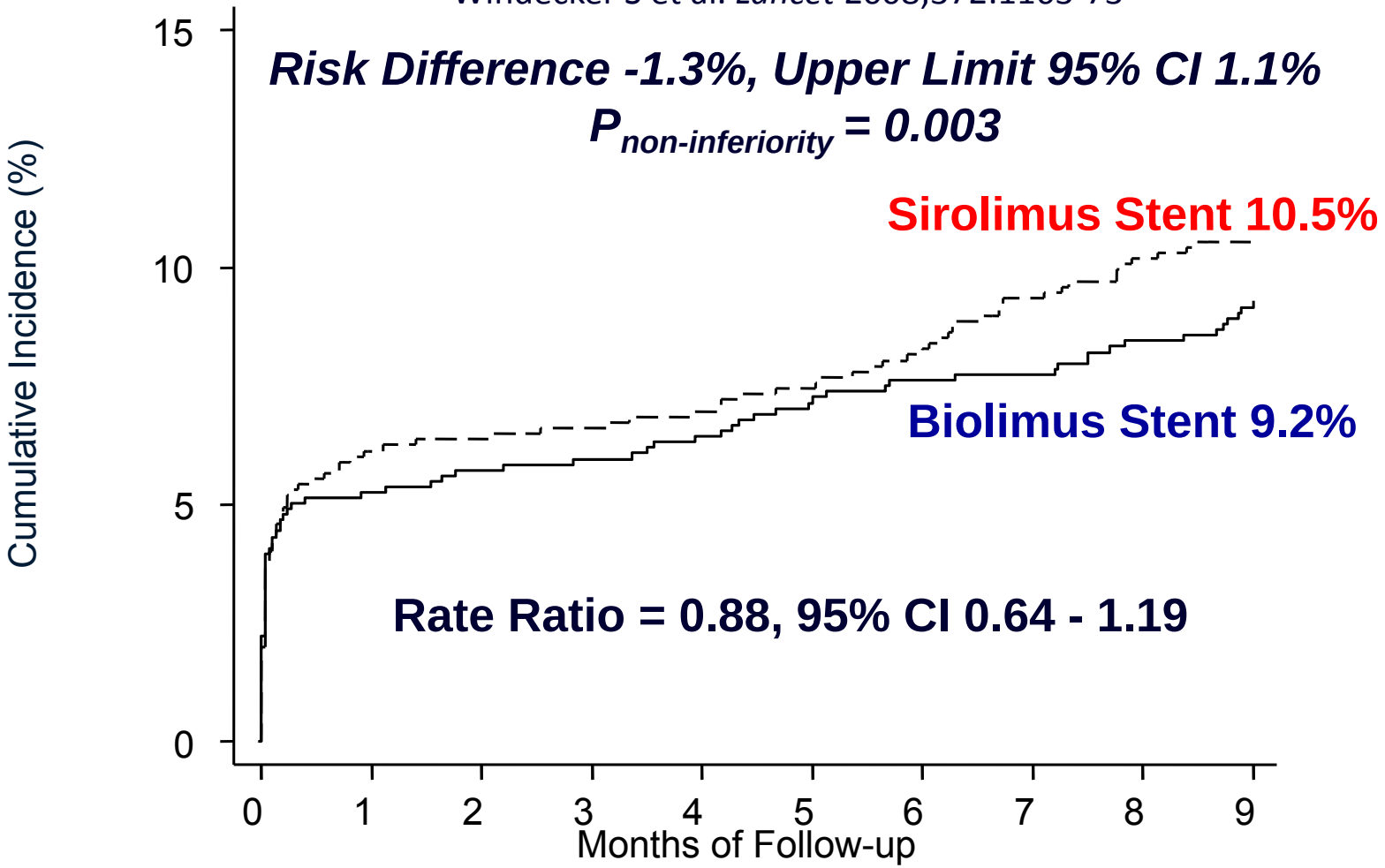


1º endpoint:	**MACE: Cardiac death, MI, clinically-indicated TVR (9 mo)**
2º endpoints:	Death, CV death, MI, TLR, TVR
	Stent thrombosis according to ARC
Angiographic study:	**In-stent % diameter stenosis (9 mo)**
	Late loss, binary restenosis
DAPT recommended for 12 months	

LEADERS – Primary Endpoint @ 9 Months

BioMatrix versus CYPHER in All-Comers

Windecker S et al. *Lancet* 2008;372:1163-73



No. at risk

BES	857	806	798	796	792	784	779	777	771	761
SES	850	791	786	784	781	777	771	758	751	746

Biosensors-Biolimus A9 Stent – Angiographic Results

BioMatrix versus CYPHER: LEADERS

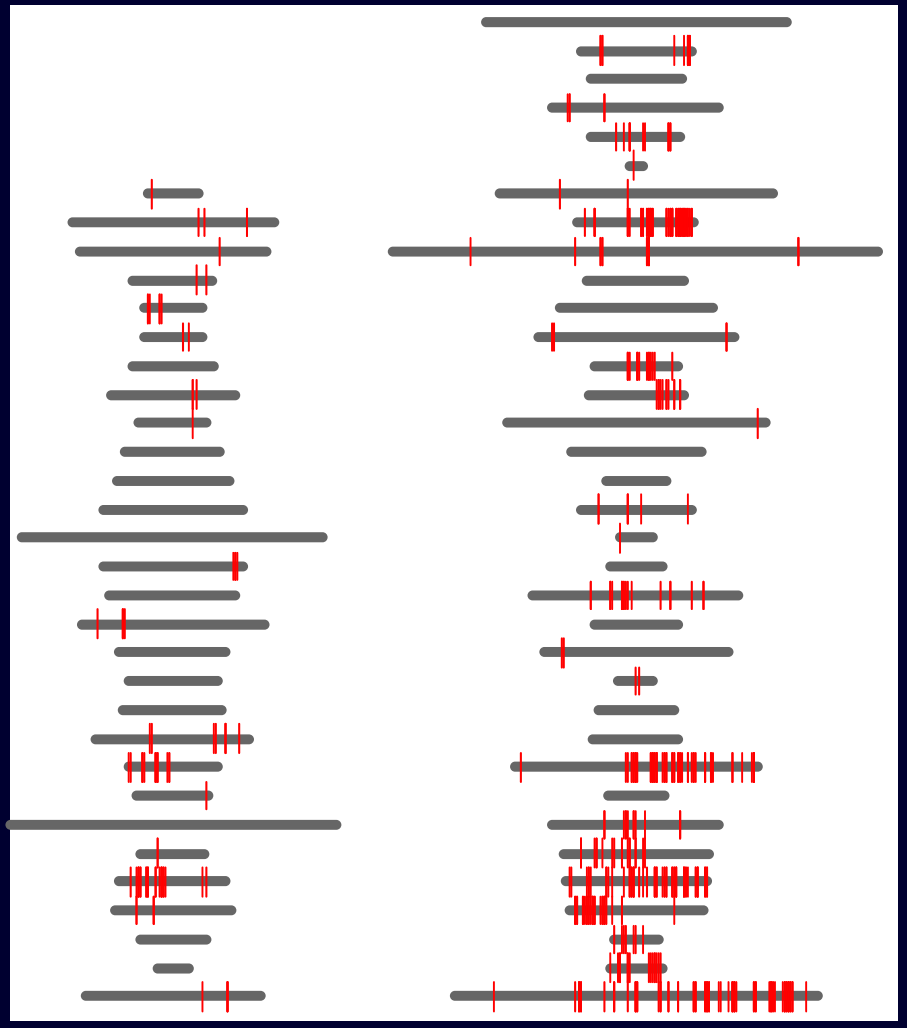
Windecker S et al. *Lancet* 2008;372:1163-73

	Biolimus Stent 255 lesions	Sirolimus Stent 233 lesions	*P**
MLD			
in-stent (mm)	2.23 ± 0.64	2.11 ± 0.70	0.08
in-segment (mm)	2.01 ± 0.59	1.87 ± 0.64	0.03
Diameter stenosis			
in-stent (%)	20.9 ± 17.5	23.3 ± 19.6	0.26
in-segment (%)	27.1 ± 16.4	29.9 ± 18.5	0.14
Late lumen loss			
in-stent (mm)	0.13 ± 0.46	0.19 ± 0.50	0.34
in-segment (mm)	0.08 ± 0.45	0.15 ± 0.46	0.12
Binary restenosis			
in-stent (%)	5.5	8.7	0.20
in-segment (%)	6.7	10.8	0.15

** P values for superiority*

Biolimus Eluted from Biodegradable Polymer versus Sirolimus Eluted from Durable Polymer

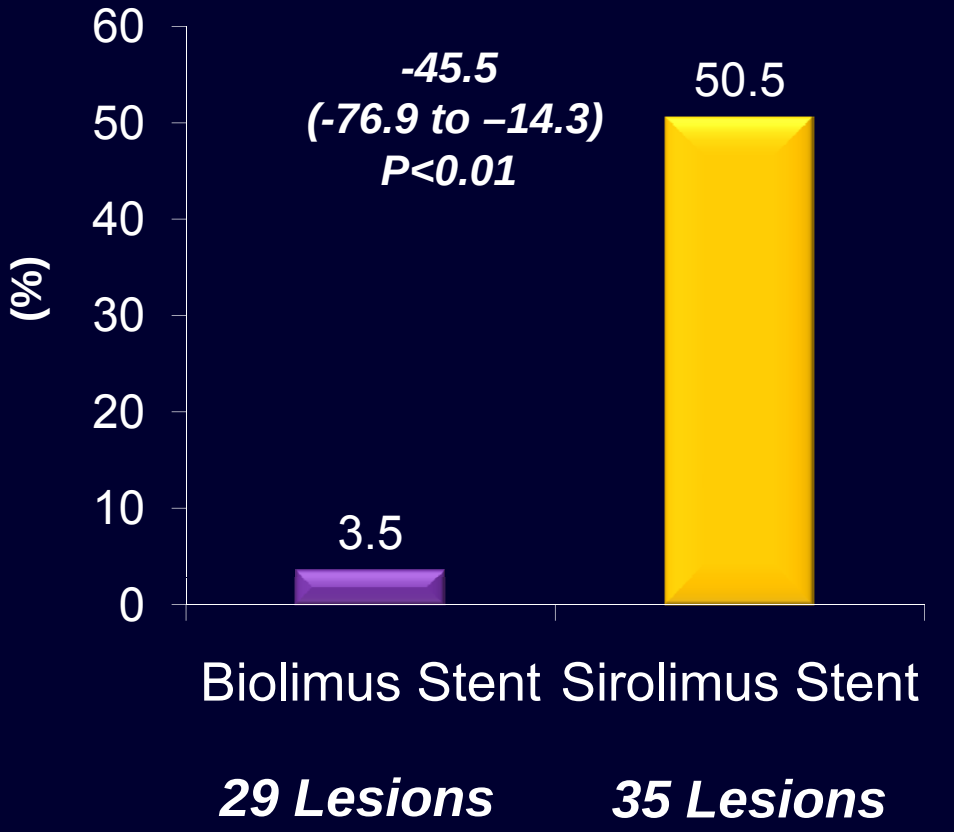
Barlis P et al. *Eur Heart J* 2010; 31:165-76



Biolimus
N=29

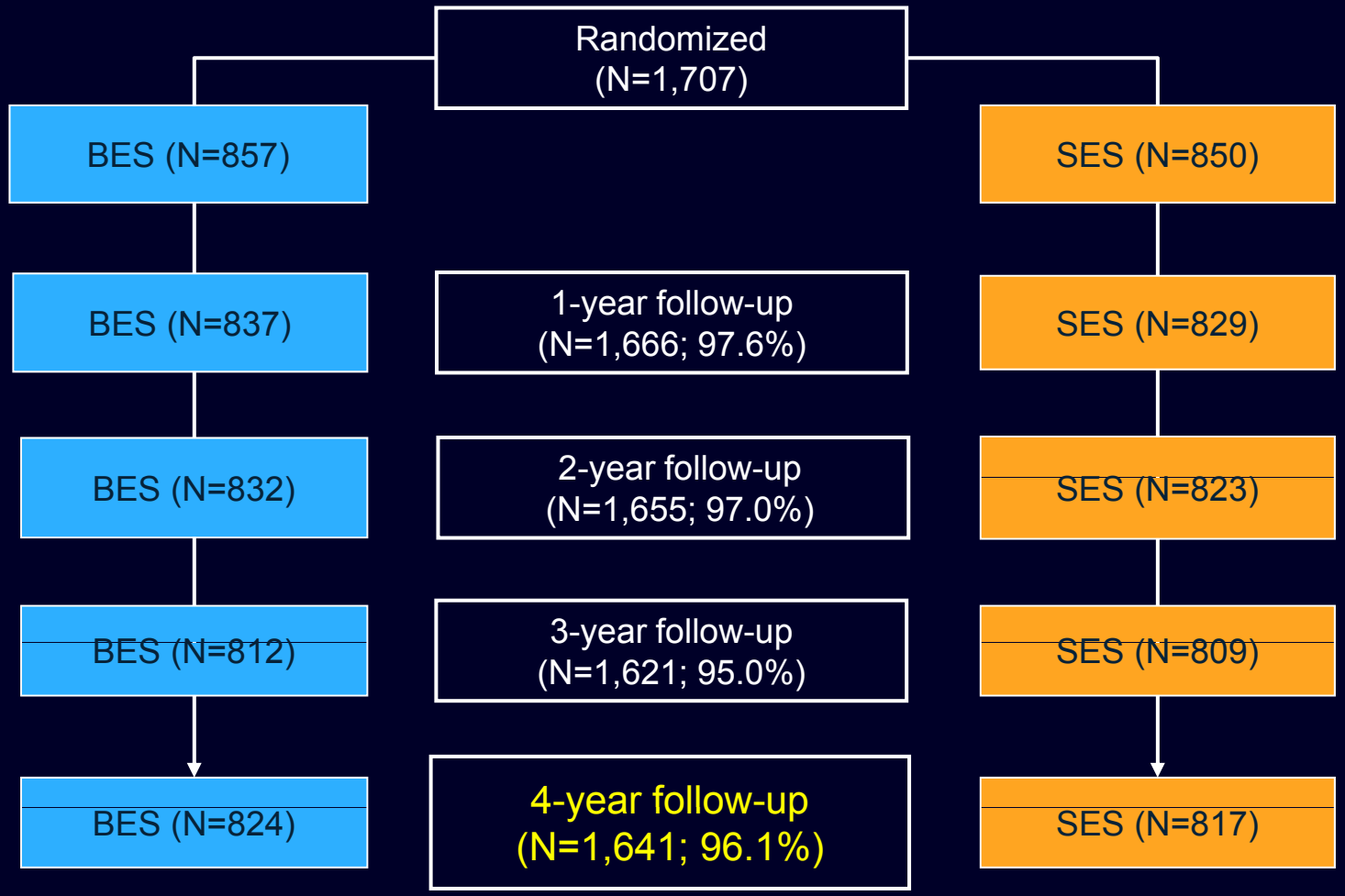
Sirolimus
N=35

Lesions With At Least 5% Uncovered Struts



29 Lesions ***35 Lesions***

LEADERS Trial – Patient Flow Through 4 Years

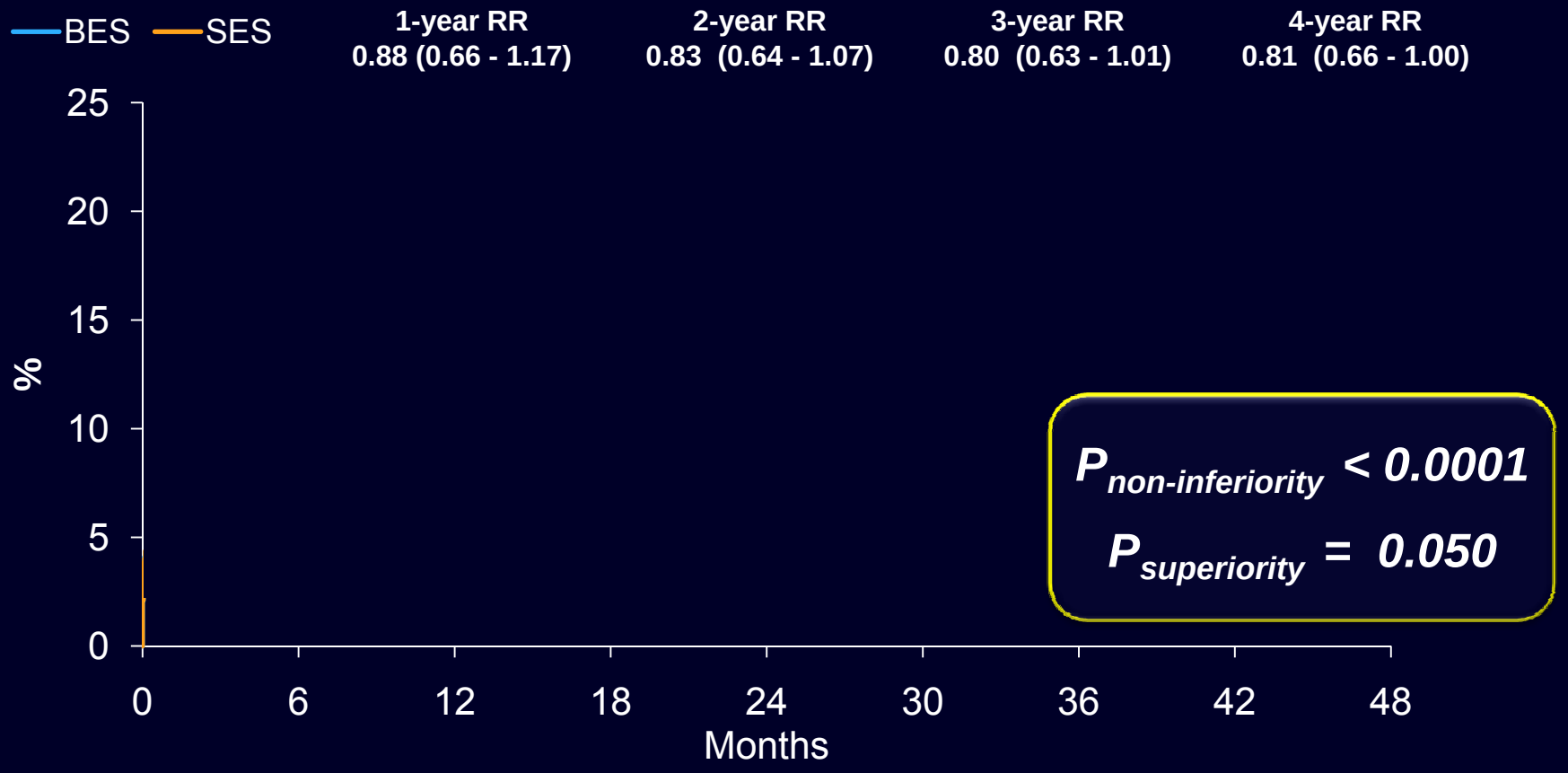


21 Lost to FU
14 lost to FU and alive
7 lost to FU and vital status unknown
12 withdrew

18 Lost to FU
10 lost to FU and alive
8 lost to FU and vital status unknown
15 withdrew

LEADERS - MACE Through 4 Years

Stefanini G et al. *Lancet* 2011; 378:1940-8



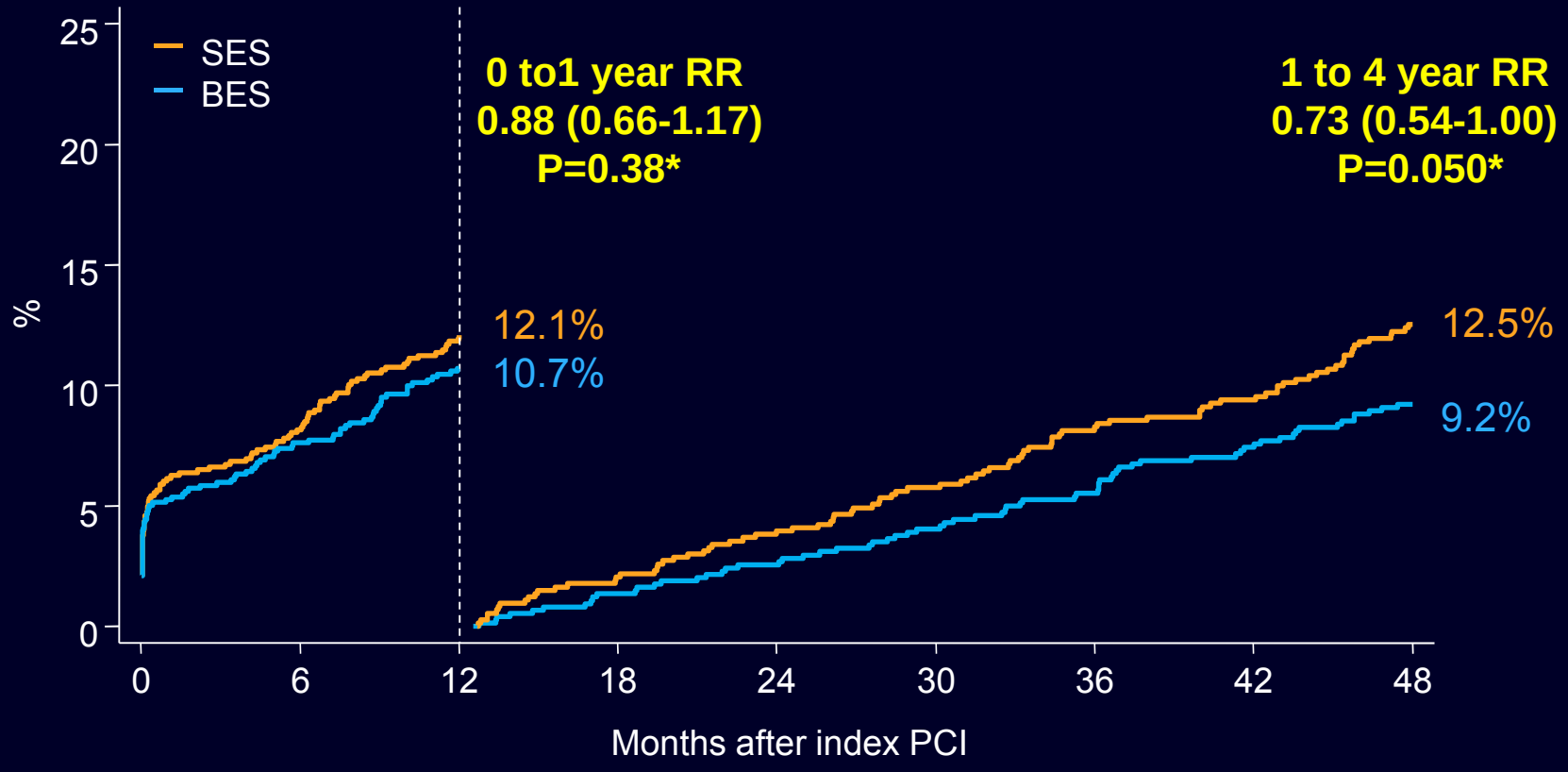
Numbers at risk

SES	850	775	738	718	702	676	656	639	614
BES	857	781	749	733	723	710	697	677	659

MACE = Cardiac death, MI, or Clinically-indicated TVR

MACE

Landmark Analysis @ 1 Year



No. at risk

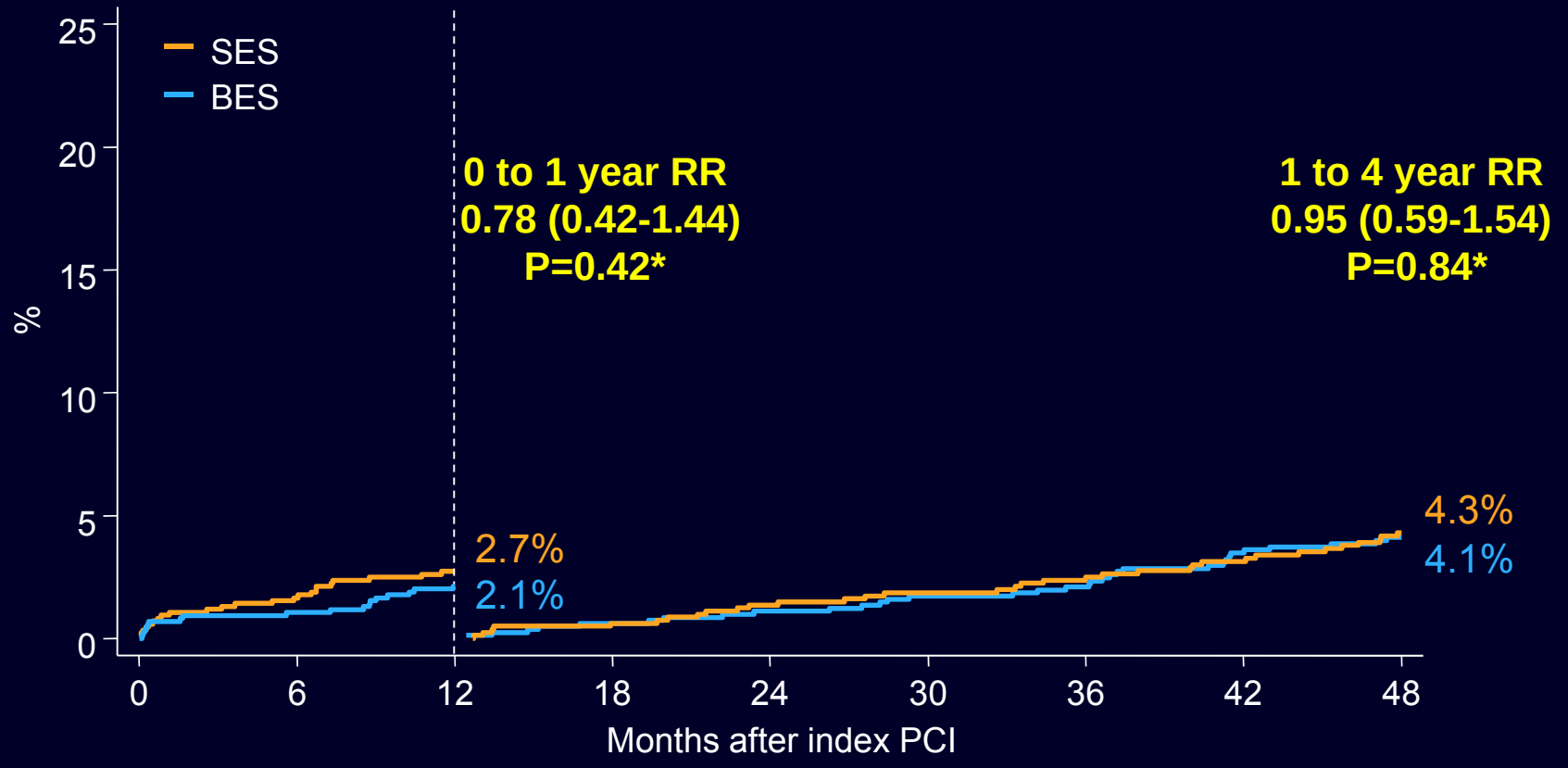
SES	850	775	738	718	702	676	656	639	614
BES	857	781	749	733	723	710	697	677	659

P for interaction=0.39

* P values for superiority

Cardiac Death

Landmark Analysis @ 1 Year



No. at risk

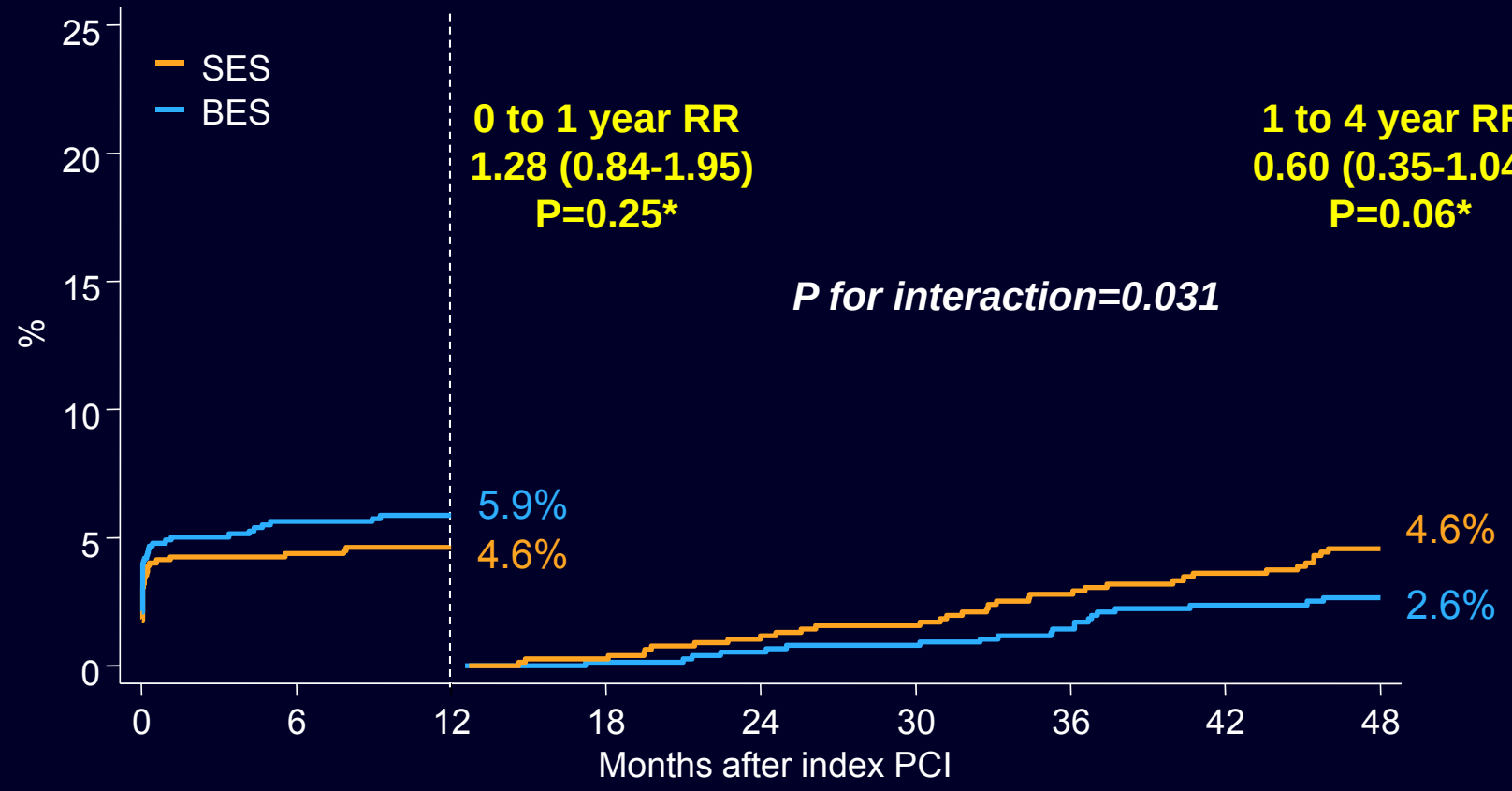
SES	850	830	814	802	793	776	768	751	739
BES	857	834	817	806	801	794	787	770	759

P for interaction=0.61

* P values for superiority

Myocardial Infarction

Landmark Analysis @ 1 Year

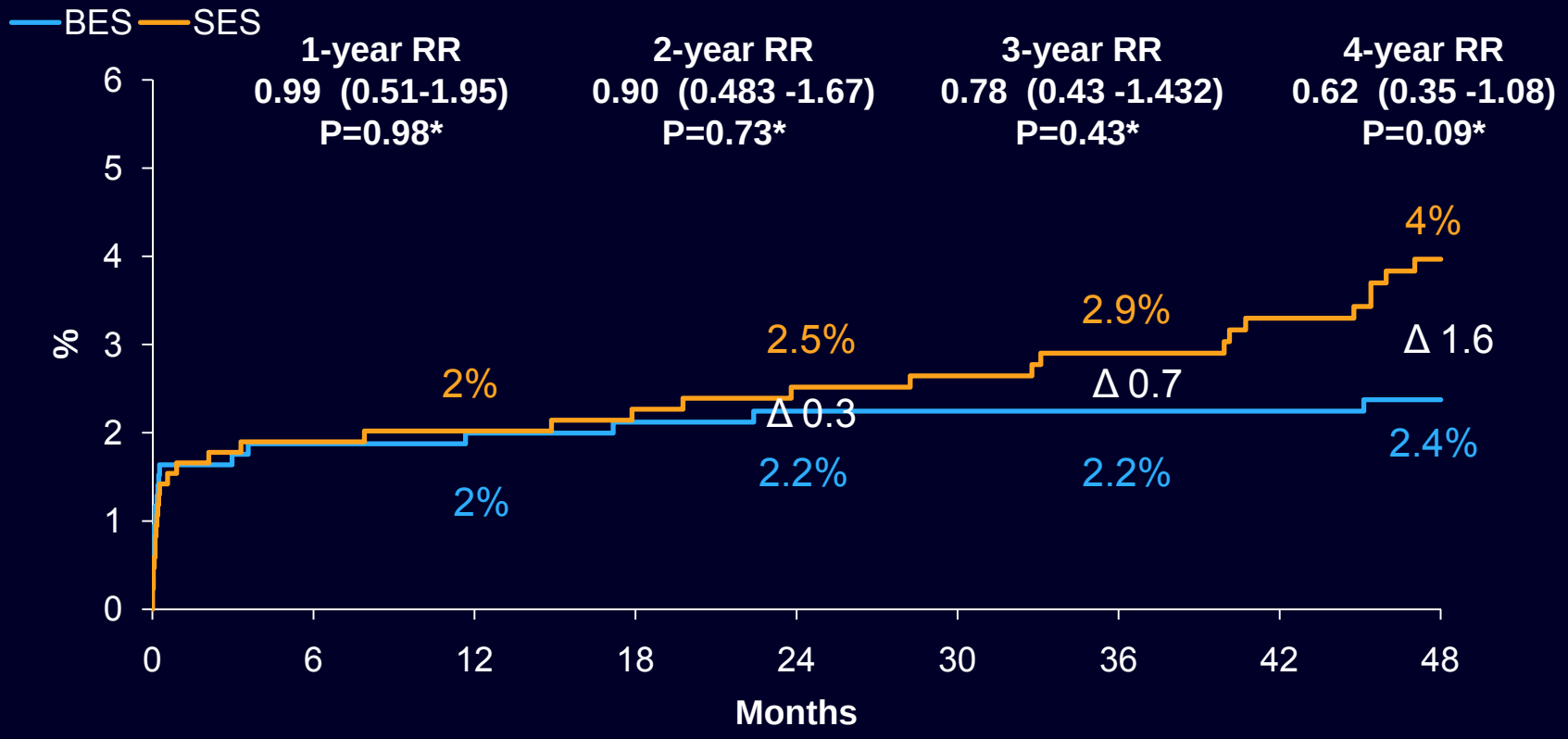


No. at risk

SES	850	797	781	767	753	733	718	699	682
BES	857	793	779	768	761	752	744	723	712

* P values for superiority

Definite Stent Thrombosis (ARC)



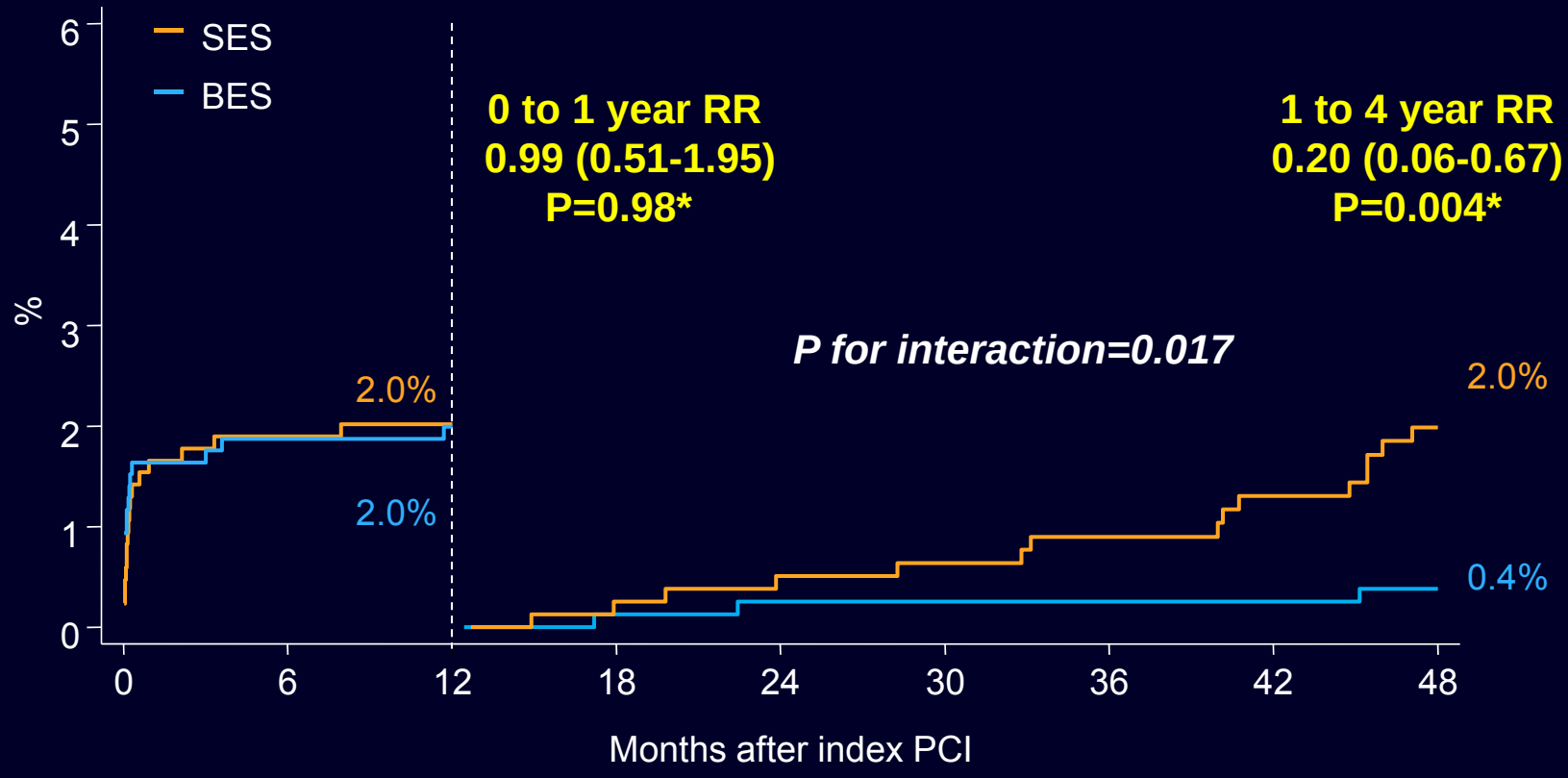
Numbers at risk

SES	850	817	801	787	776	759	750	730	714
BES	857	821	804	792	787	780	774	757	746

* P values for superiority

Definite Stent Thrombosis

Landmark Analysis @ 1 Year



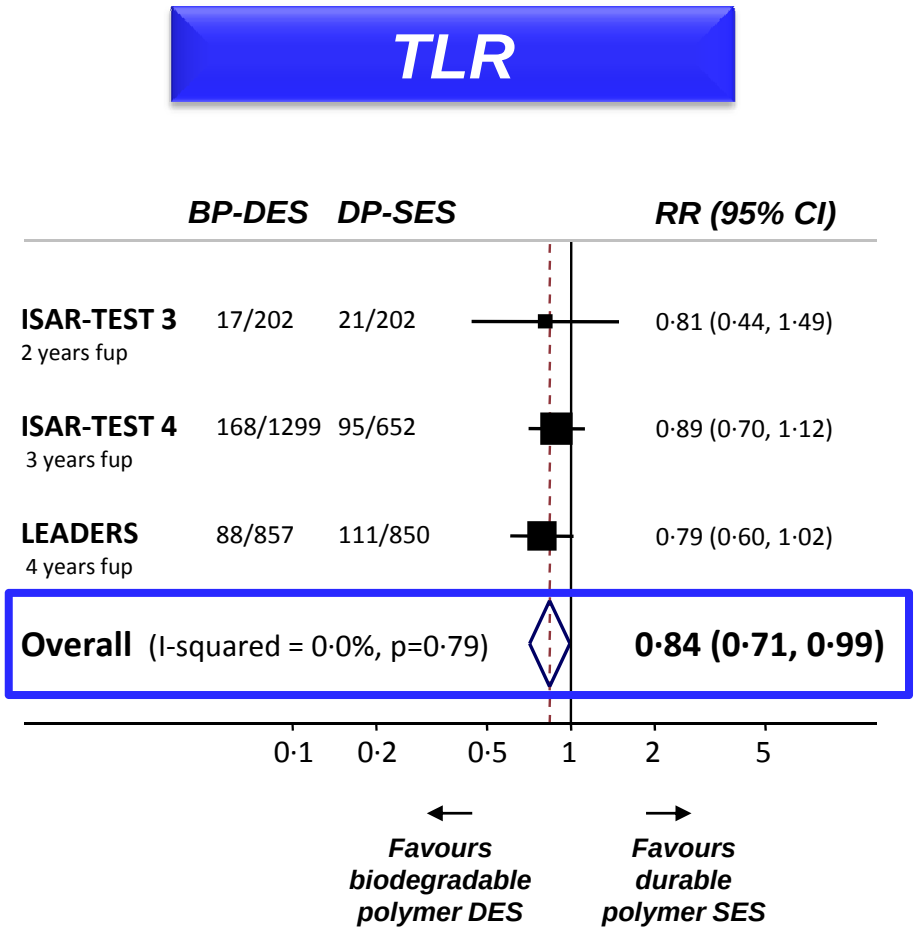
No. at risk

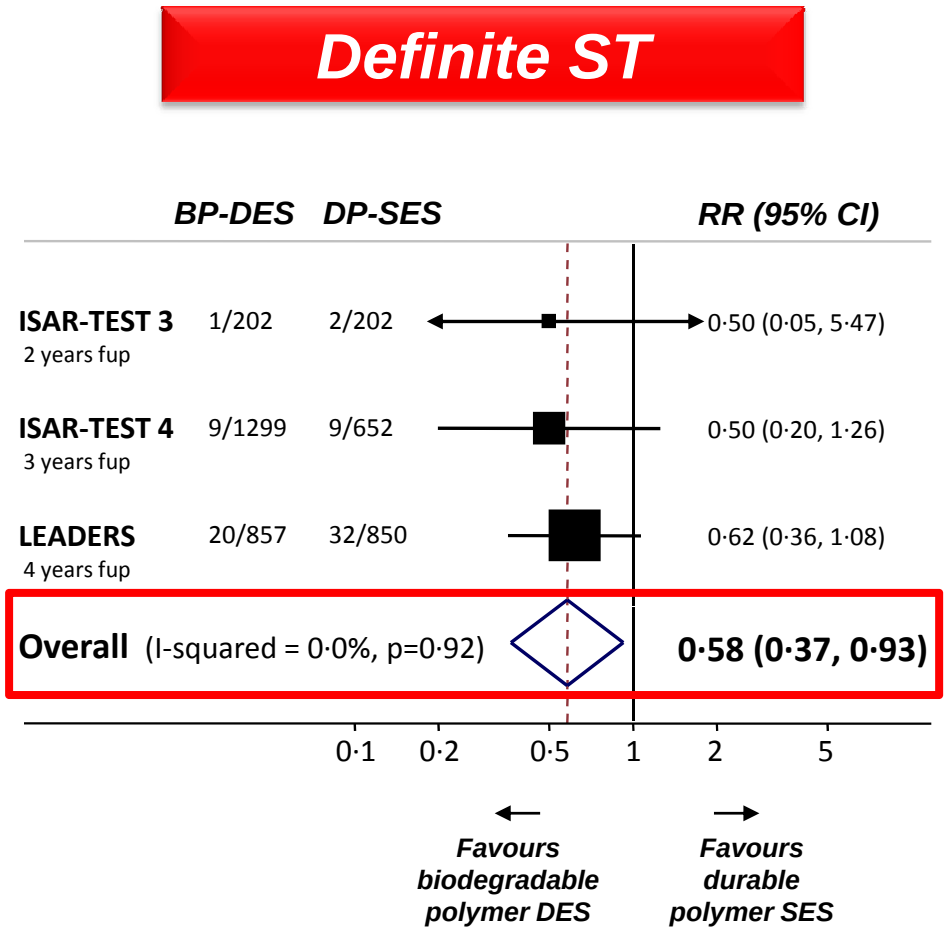
SES	850	817	801	787	776	759	750	730	714
BES	857	821	804	792	787	780	774	757	746

* P values for superiority

A Meta-Analysis of Biodegradable Polymer DES versus Durable Polymer Sirolimus Eluting Stents

Stefanini G et al. *Lancet* 2011; 378:1940-8



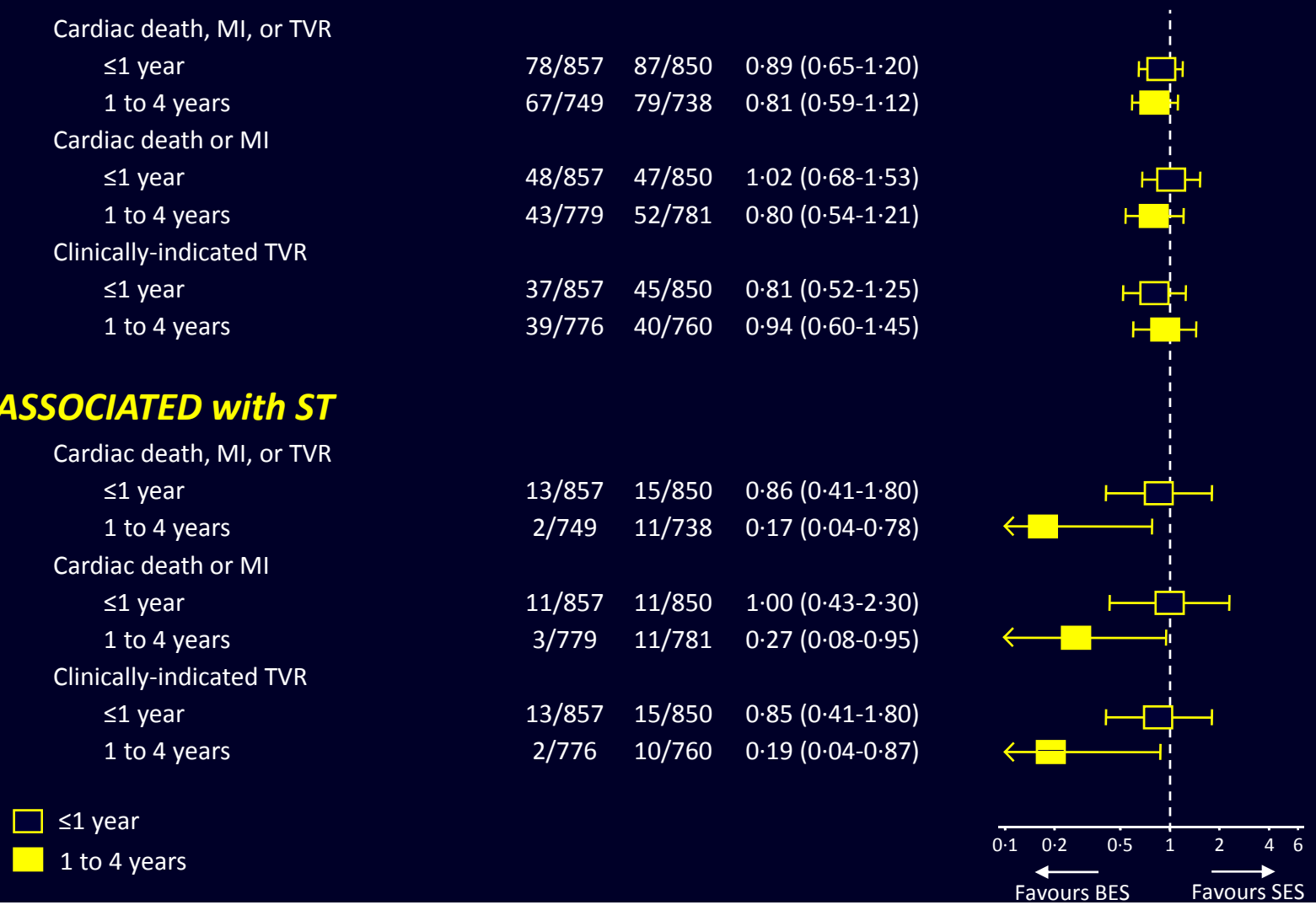


Biodegradable Polymer BES vs Durable Polymer SES

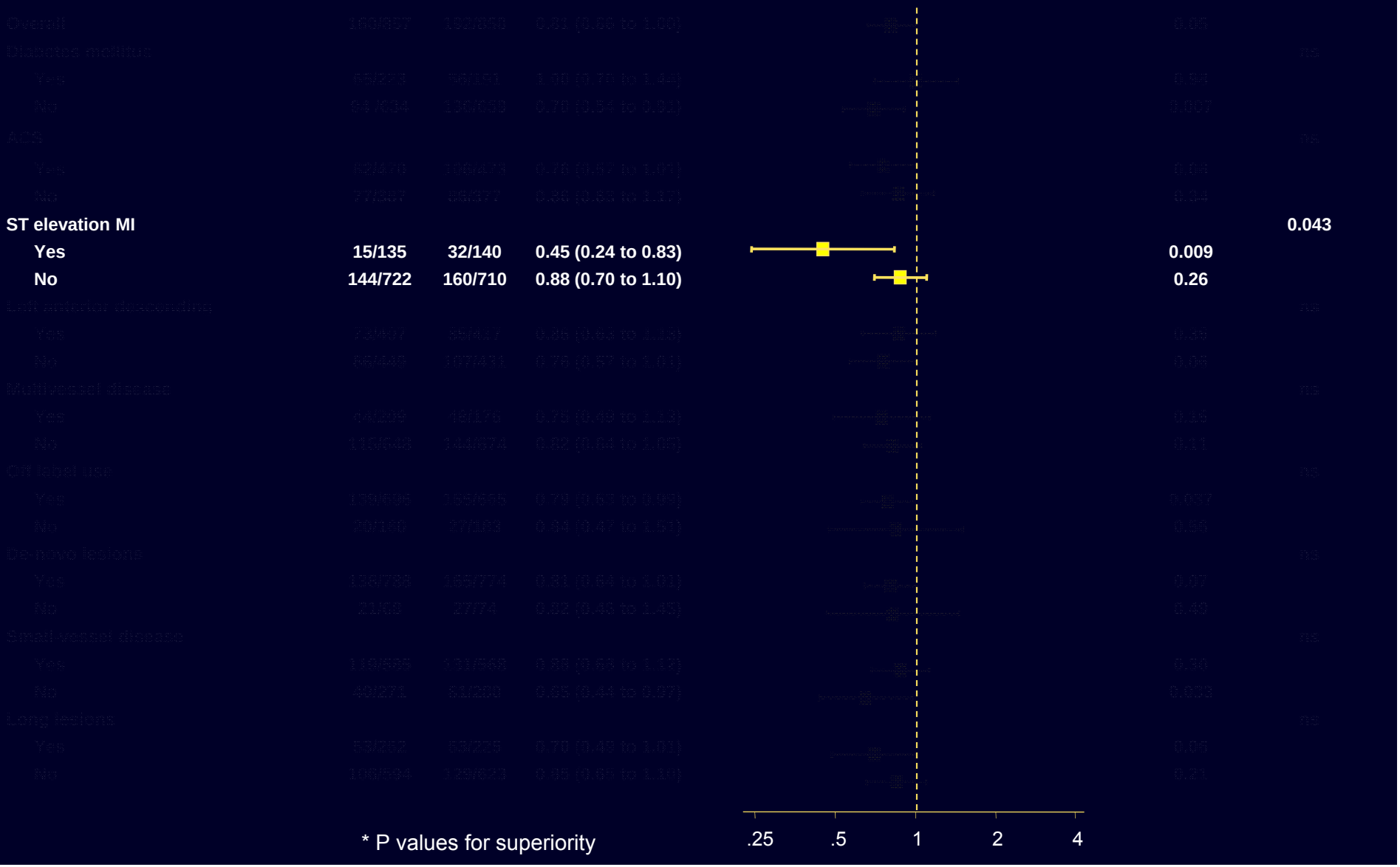
Association of Cardiac Events With Definite ST

Stefanini G et al. *Lancet* 2011;378:1940-8

	BES	SES	RR (95% CI)	P	P-inter
NOT ASSOCIATED with ST					
Cardiac death, MI, or TVR					0·70
≤1 year	78/857	87/850	0·89 (0·65-1·20)	0·44	
1 to 4 years	67/749	79/738	0·81 (0·59-1·12)	0·21	
Cardiac death or MI					0·43
≤1 year	48/857	47/850	1·02 (0·68-1·53)	0·94	
1 to 4 years	43/779	52/781	0·80 (0·54-1·21)	0·30	
Clinically-indicated TVR					0·64
≤1 year	37/857	45/850	0·81 (0·52-1·25)	0·33	
1 to 4 years	39/776	40/760	0·94 (0·60-1·45)	0·77	
ASSOCIATED with ST					
Cardiac death, MI, or TVR					0·049
≤1 year	13/857	15/850	0·86 (0·41-1·80)	0·68	
1 to 4 years	2/749	11/738	0·17 (0·04-0·78)	0·009	
Cardiac death or MI					0·08
≤1 year	11/857	11/850	1·00 (0·43-2·30)	0·99	
1 to 4 years	3/779	11/781	0·27 (0·08-0·95)	0·029	
Clinically-indicated TVR					0·07
≤1 year	13/857	15/850	0·85 (0·41-1·80)	0·68	
1 to 4 years	2/776	10/760	0·19 (0·04-0·87)	0·017	

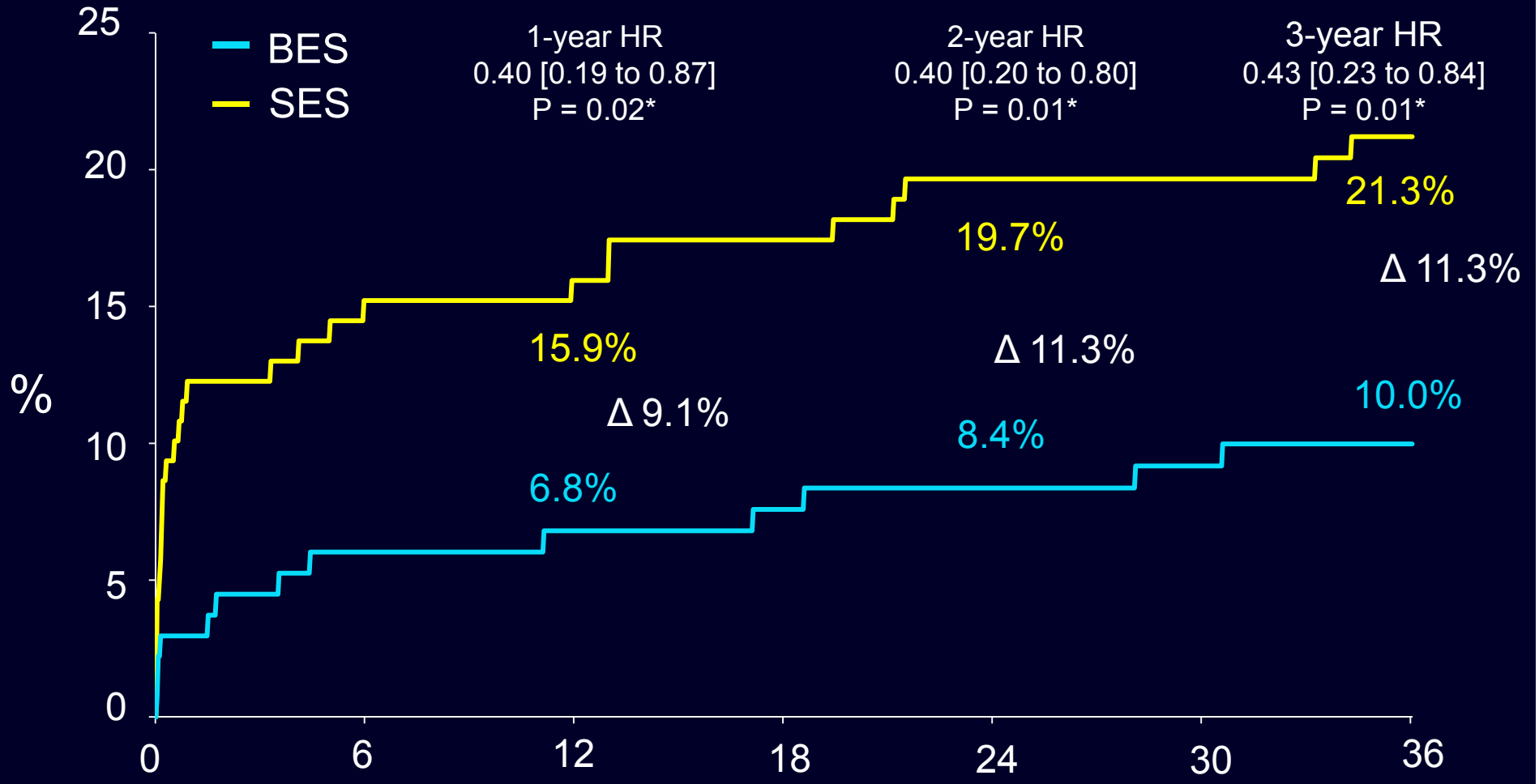


Stratified Analysis of MACE @ 4 Years



* P values for superiority

LEADERS Trial - MACE in Patients With STEMI

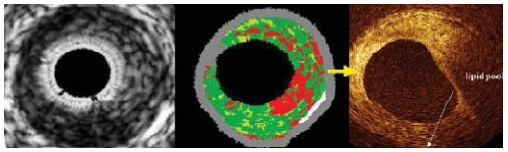


Number at risk

BES	135	132	121	120	118	116	108
SES	140	138	115	114	111	106	101

MACE = Cardiac Death, MI, or Clinically-Indicated TVR

* P values for superiority



comfortable

Comfortable AMI Trial

All Comers STEMI Population

1:1 Randomization

N = 1,100 Patients

Biolimus Eluting Stent (Biomatrix™)

Bare-metal Stent (Gazelle™)

Investigator Initiated Trial
L Räber, S Windecker, Bern University Hospital

Belgrade, Serbia (M Ostojic)
Bristol, United Kingdom (A Baumbach)
Bern, Switzerland (S Windecker)
Enschede, The Netherlands (C von Birgelen)
Geneva, Switzerland (M Roffi)
Lugano, Switzerland (G Pedrazzini)
Tel Aviv, Israel (R Kornowski)
Zurich (Triemli), Switzerland (F Eberli)
Zurich (University), Swizerland (T Lüscher)

1° Clinical Endpoint composite of CV death, target vessel MI, and ischemia driven TLR @12 months

ClinicalTrials.gov NCT00962416

LEADERS Trial - Conclusions

- Biodegradable polymer BES maintained non-inferiority and improved long-term clinical outcomes compared to SES through 4 years (P_{sup} = 0.050)
- Biodegradable polymer BES showed a 80% relative risk reduction in very late definite stent thrombosis (VLST)
- The benefit of biodegradable polymer BES emerged in the very late phase and was mainly driven by a lower risk of MACE associated with definite VLST
- The LEADERS trial provides the 1st evidence of improved clinical outcomes versus the earlier generation gold standard SES
- These findings provide the basis for the proof of concept of biodegradable polymer DES