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A Prospective, Randomised, Non-Inferiority Trial Comparing Biolimus-Eluting Stent With Biodegradable Polymer Versus Sirolimus-Eluting Stent With Durable Polymer

Clinical Result Overview

Biolimus A9™ Eluting Stent (BES)
The abluminal biodegradable polymer DES

ABLUMINAL BIODEGRADABLE COATING

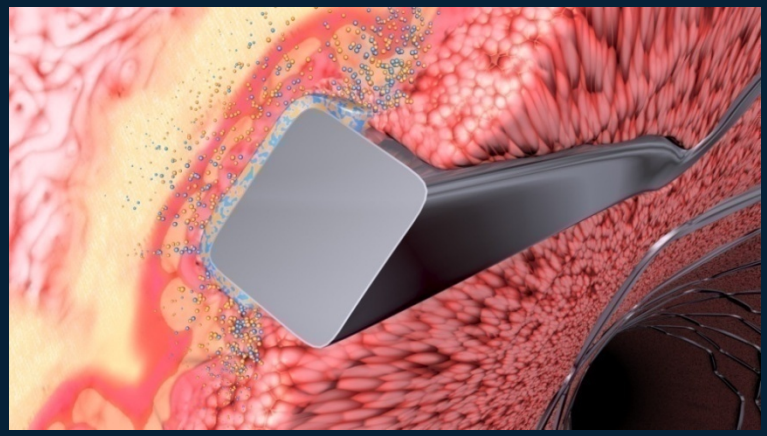
Early BMS-like endothelial coverage[1]
More targeted tissue release
Less systemic exposure

BIOLIMUS A9™ DRUG

Biosensors' proprietary rapamycin derivative
Highest lypophilicity of the common limus drugs

BIODEGRADABLE PLA

PLA biodegradation along with BA9™ elution
No PLA /BA9™ coating on the stent after 6 to 9 months*



* Data on file - molecular weight<10kDa
[1] Virmani R., Are resorbable coatings better?, oral presentation, PCR 2008

The product is not available for sale in the USA

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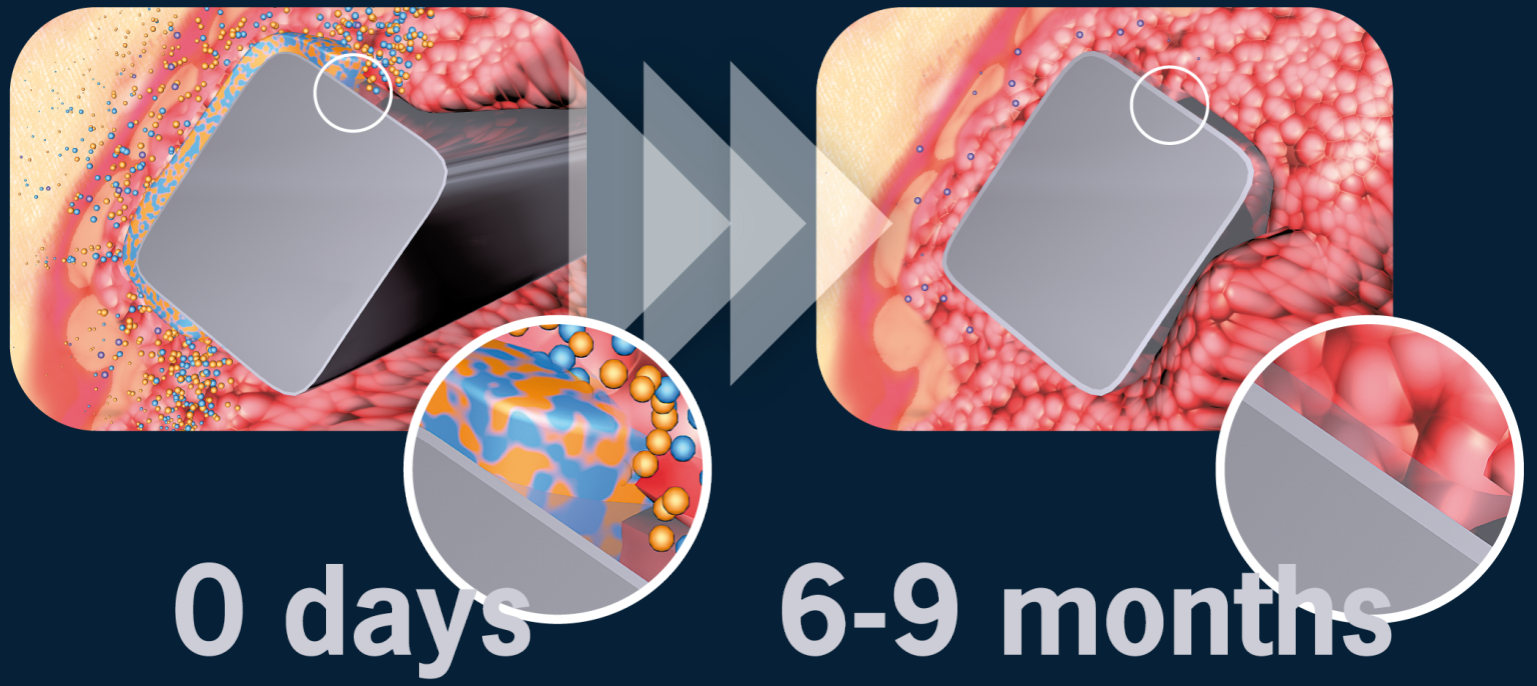
Biolimus A9™ Eluting Stent – The abluminal biodegradable polymer DES

PLA biodegradation and BA9™ elution

Abluminal biodegradable coating absorbed after 6-9 months*



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Biolimus A9™ / Biodegradable Polymer DES

Clinical Trial Program

BA9™ WITH BIODEGRADABLE PLA

From "Single de Novo" To "Real World"

STEALTH PK	STEALTH I	BEACON I	LEADERS	BEACON II	e-BioMatrix
N= 27	N= 120	N= 292	N= 1707	N= 497	N= 5000
EUROPE	EUROPE+BRAZIL	ASIA	EUROPE	ASIA	EUROPE
Single Arm Trial	Randomized Multicenter Trial vs BMS	Multicenter Registry	**All Comers Randomized Multicenter Trial vs CYPHER® SELECT™**	Multicenter Registry	Multicenter Registry PMS= 1000 PMR= 4000
Pharmacokinetic of Biolimus A9™ Concentration	**In-Stent Late Loss at 6 months**	**TVR at 6 months**	**MACE at 9 months**	**MACE at 12 months**	**MACE at 12 months**
Completed	5 year follow-up completed	Completed	2 year follow-up completed	30 day follow-up available	Currently enrolling

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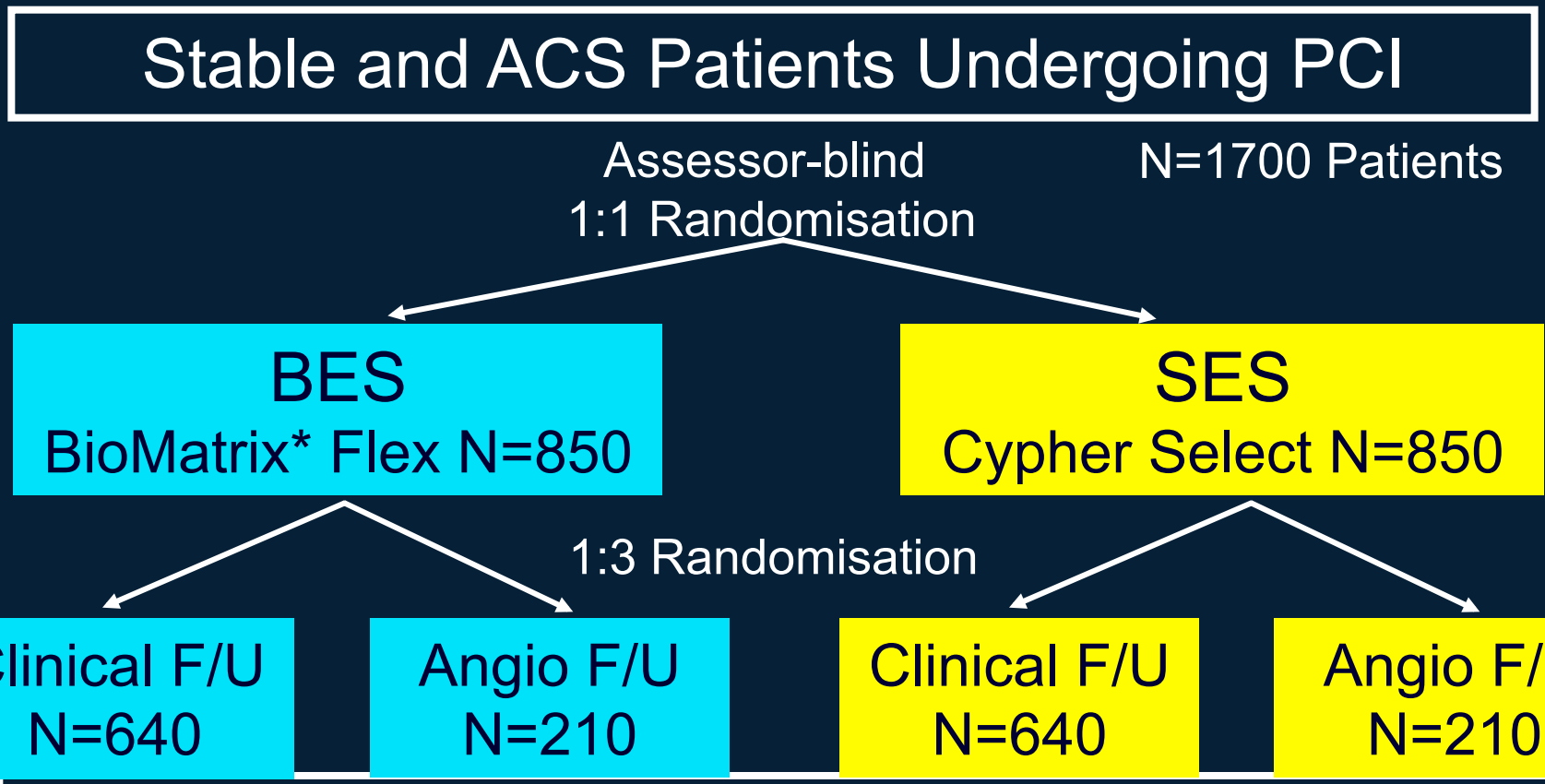
Trial Design



1º endpoint:	CV death, MI, clinically-indicated TVR (9 month)
2º endpoints:	Death, CV death, MI, TLR, TVR Stent thrombosis according to ARC
Angiographic study:	In-stent % diameter stenosis Late loss, binary restenosis

DAPT recommended for 12 months

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*The product is not available for sale in the USA

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Patient Eligibility

Inclusion Criteria

Coronary artery disease

- Stable angina
- Silent ischemia
- Acute coronary syndrome including UA, NSTEMI and STEMI

At least one lesion with

- Diameter stenosis ≥ 50%
- RVD: 2.25-3.5 mm
- Number of lesions: no limitation
- Number of vessels: no limitation
- Lesion length: no limitation

Written informed consent

Exclusion Criteria

Known allergy to

- aspirin, clopidogrel, heparin, stainless steel, sirolimus, biolimus, contrast material

Planned, elective surgery within 6 months of PCI unless dual APT could be maintained

Pregnancy

Participation in another trial

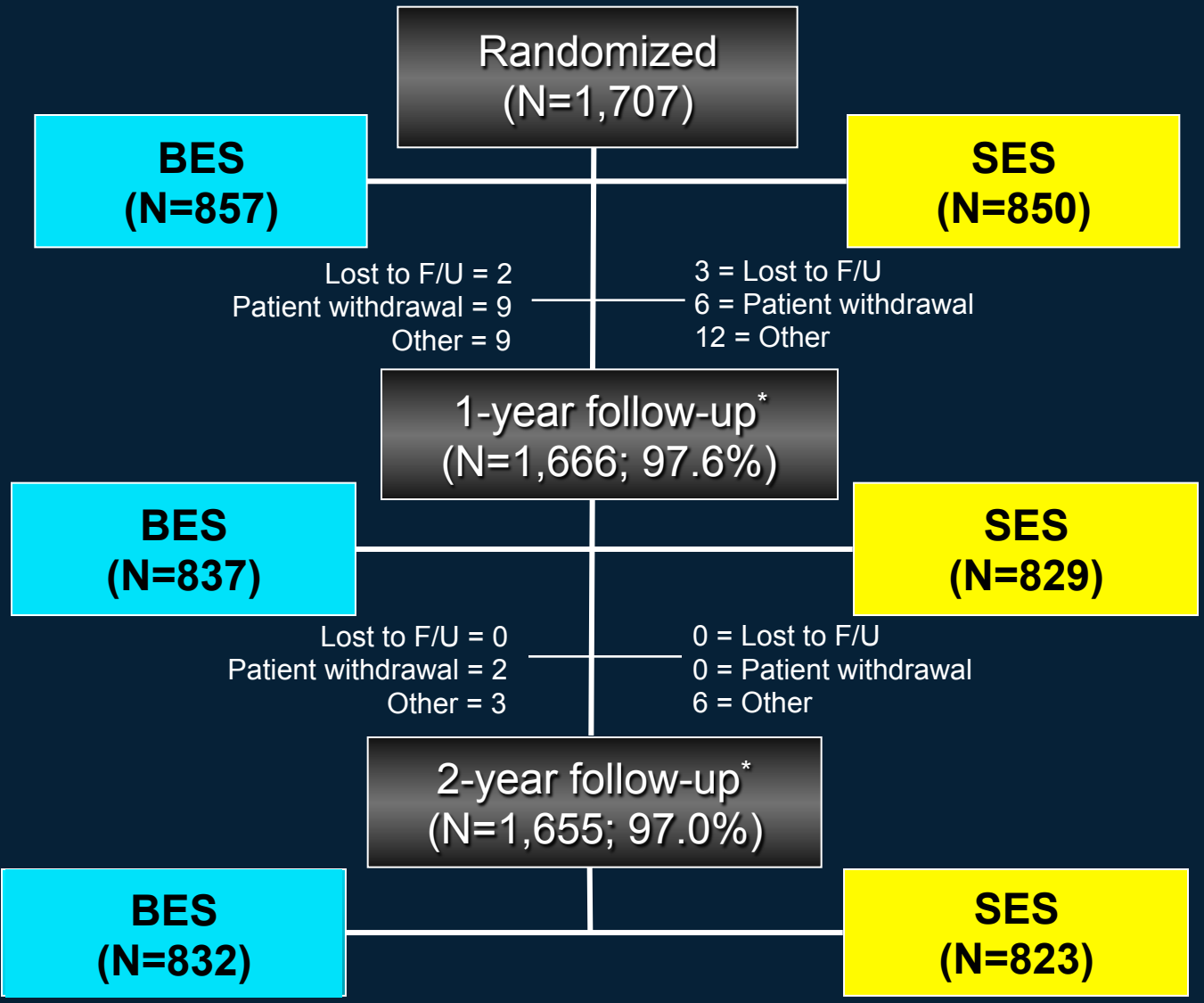
Patient Demographics

	BES 857 Patients	SES 850 Patients
Age in years	65 ± 11	65 ± 11
Male gender	75%	75%
Arterial hypertension	74%	73%
Diabetes mellitus	**26%**	**23%**
- insulin-dependent	10%	9%
Hypercholesterolemia	65%	68%
Family history	40%	44%
Smoking	24%	25%
Previous MI	**32%**	**33%**
Previous PCI	**36%**	**37%**
- with drug-eluting stent	12%	14%
Previous CABG	**11%**	**13%**
Chronic stable angina	45%	44%

Patient Characteristics

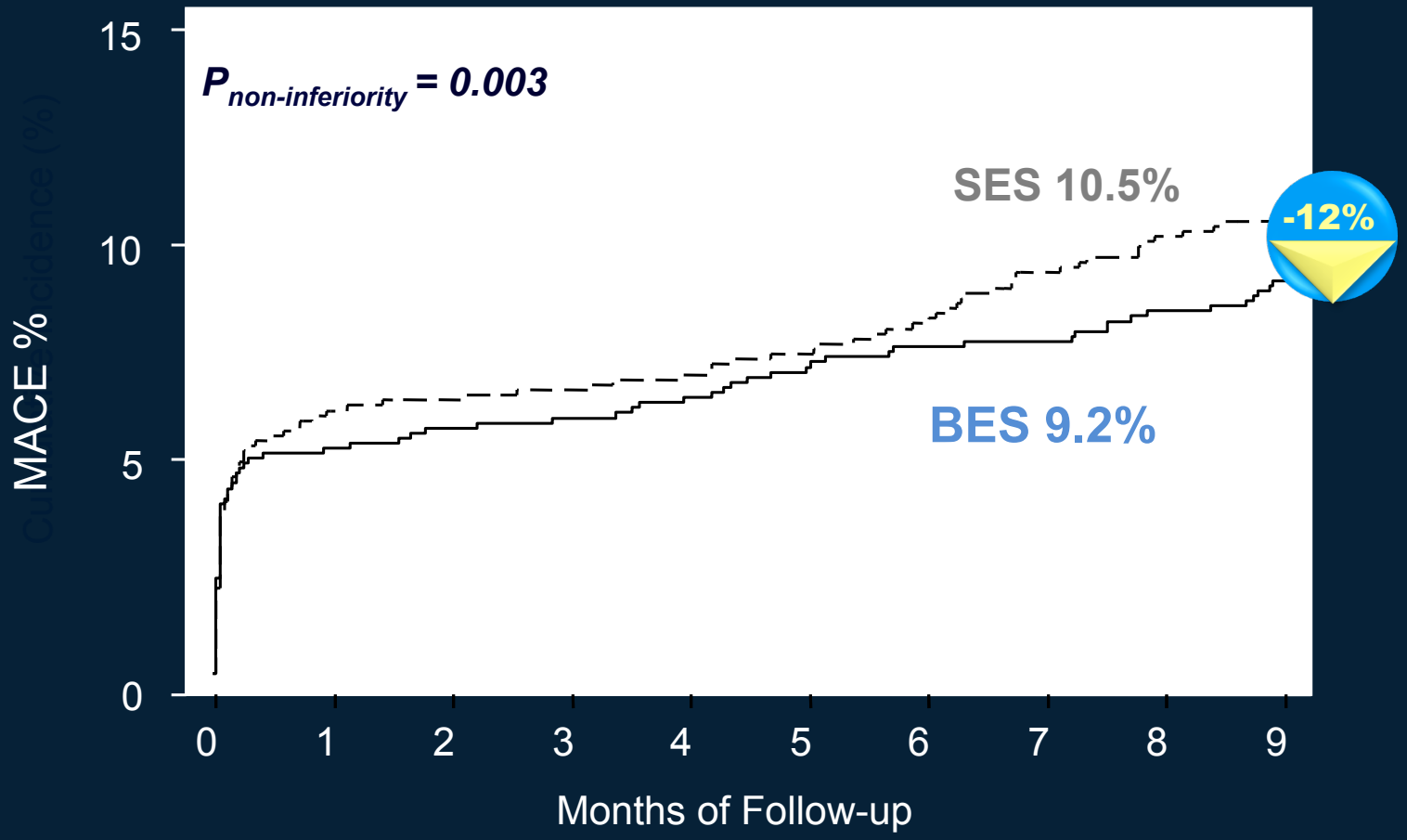
	BES 857 Patients	SES 850 Patients
Acute coronary syndrome	55%	56%
- Unstable angina	22%	21%
- Non-ST-elevation MI	17%	18%
- ST-elevation MI	16%	17%
Left ventricular ejection fraction	56 ± 11%	55 ± 12%
Number of lesions per patient	1.5 ± 0.7	1.4 ± 0.7
Lesions per patient		
- 1 lesion	63%	69%
- 2 lesions	29%	22%
- 3 lesions	7%	8%
- > 4 lesions	1%	2%
De novo lesions	92%	91%
Long lesions (>20 mm)	31%	27%
Small vessels (RVD ≤2.75 mm)	68%	69%
Off label use	81%	78%

Patient Flow - Clinical



*F/U window ±28 days

Primary Endpoint
Cardiac Death, MI and TVR @ 9 Months[2]



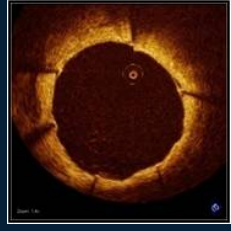
BES reached its primary endpoint

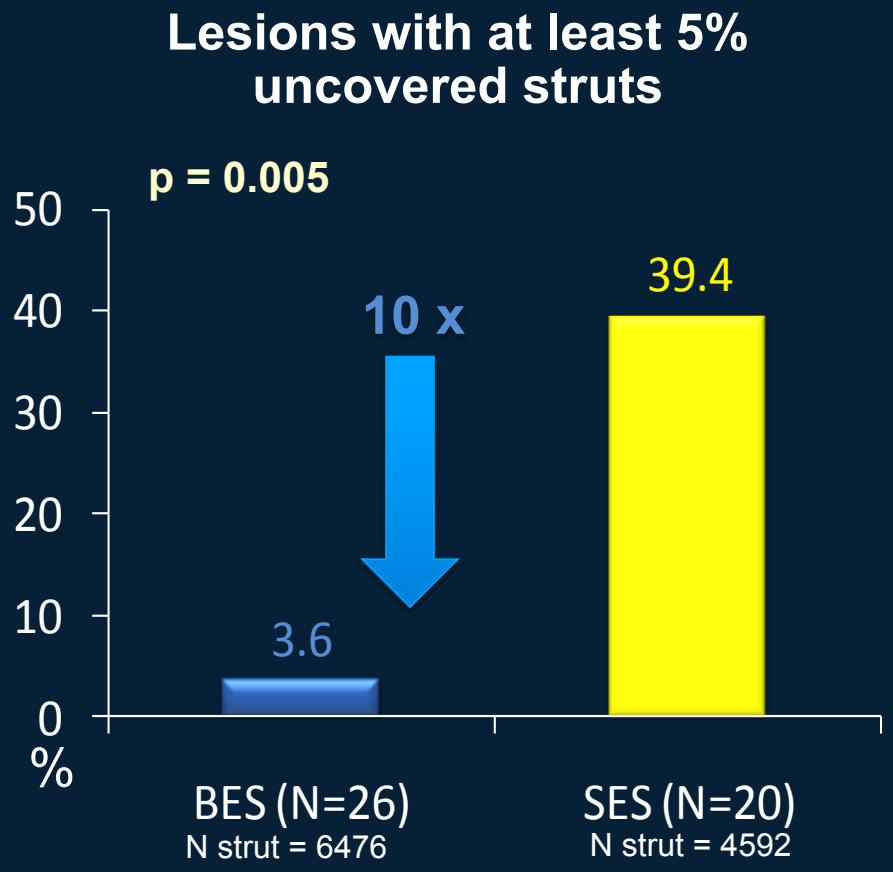
[2]Windecker S. et al., The Lancet 2008; 372 No. 9644: 1163-1173

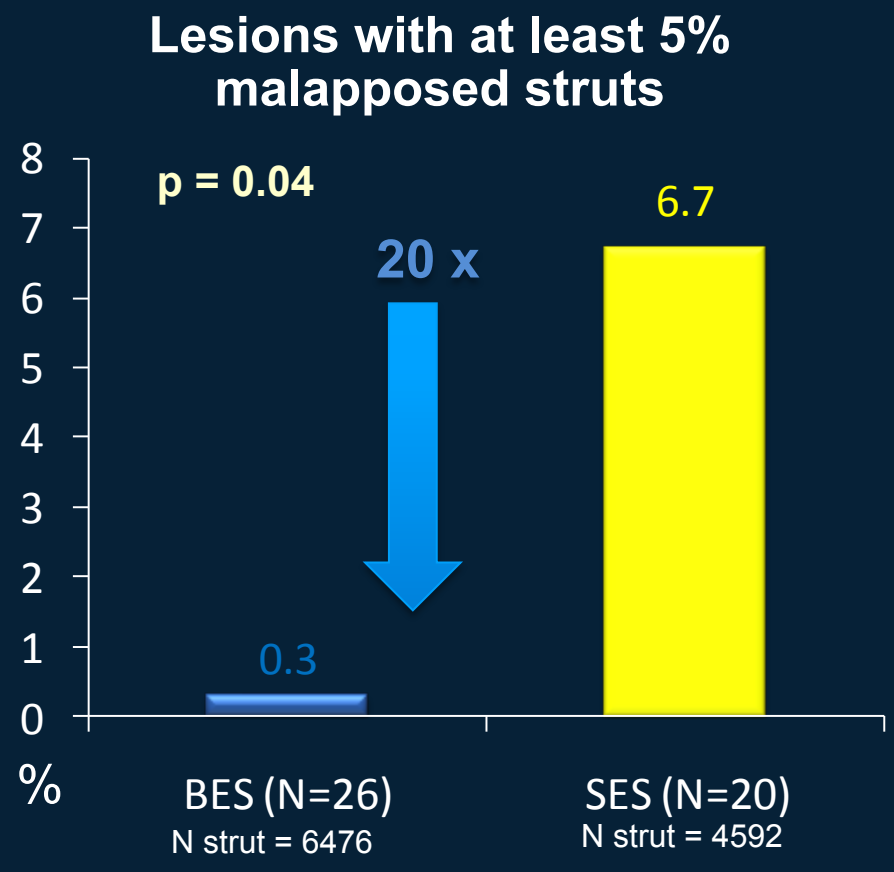
Long Term Results

Proven Safety and Efficacy

Superior Strut Coverage and Stent Apposition[3]







BES with an abluminal biodegradable polymer achieved a 10 x better strut coverage and a 20 x better stent apposition vs. SES with a symmetric durable polymer at 9 months

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[3]Di Mario C., TCT 2008

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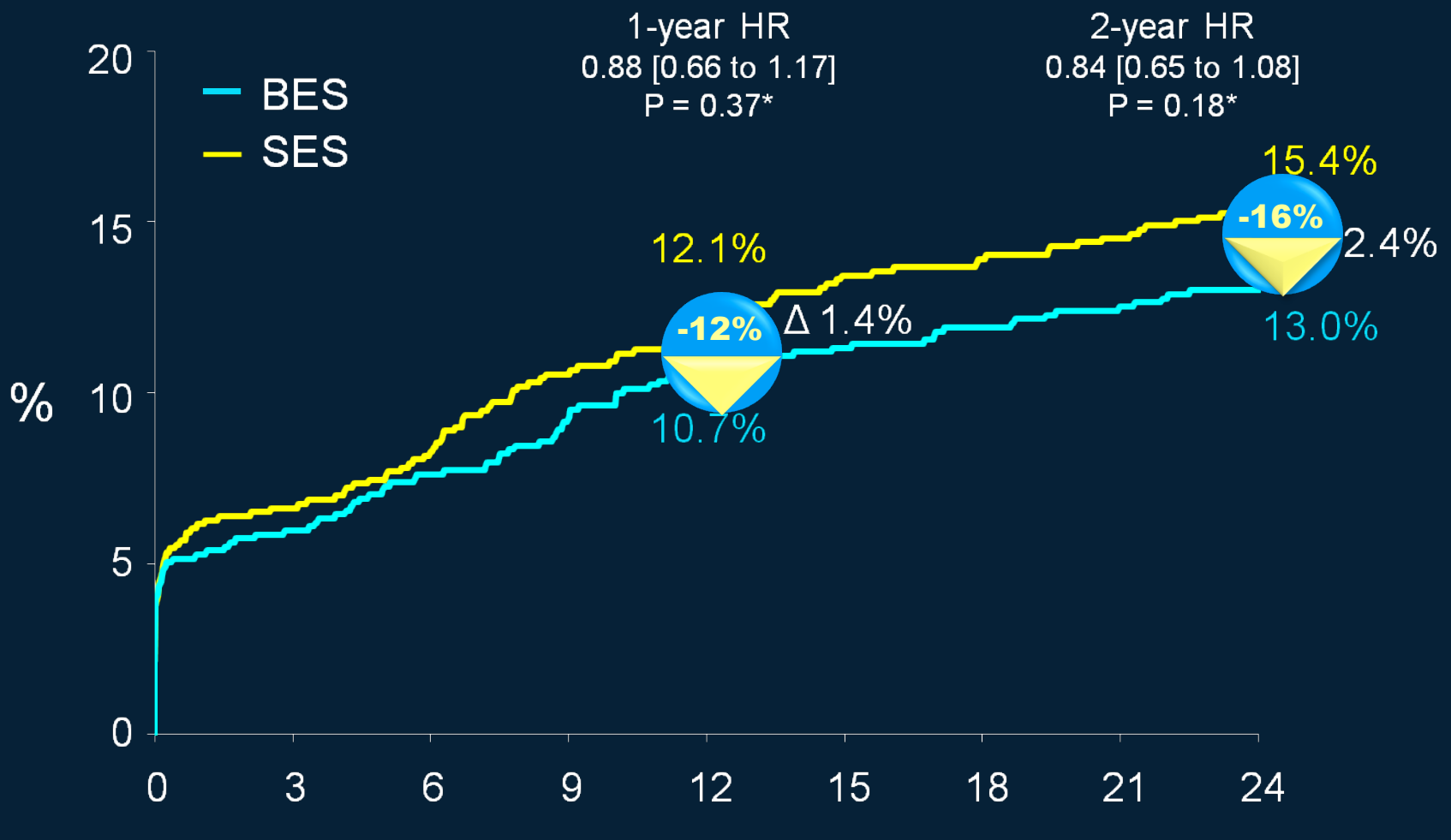
MACE[4]



Number at risk									
BES	857	804	795	777	760	742	731	725	716
SES	850	791	786	771	747	727	712	707	694

MACE = Cardiac Death, MI, or Clinically-Indicated TVR
*P values for superiority
[4] Klauss V., TCT 2009

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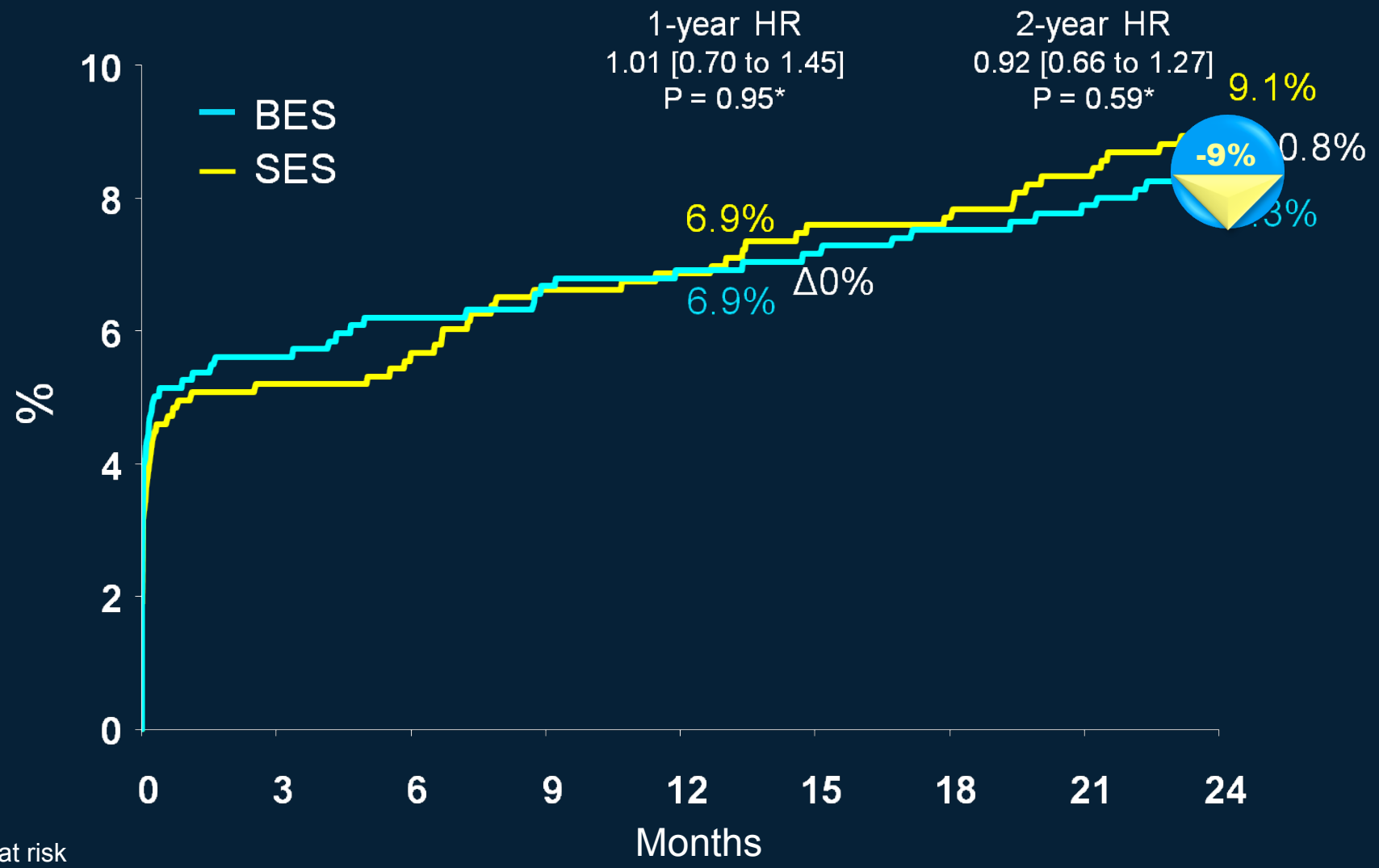
Cardiac Death or MI[4]



Number at risk									
BES	857	804	797	788	780	772	764	760	752
SES	850	801	798	793	779	770	758	755	742

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*P values for superiority

[4] Klauss V., TCT 2009

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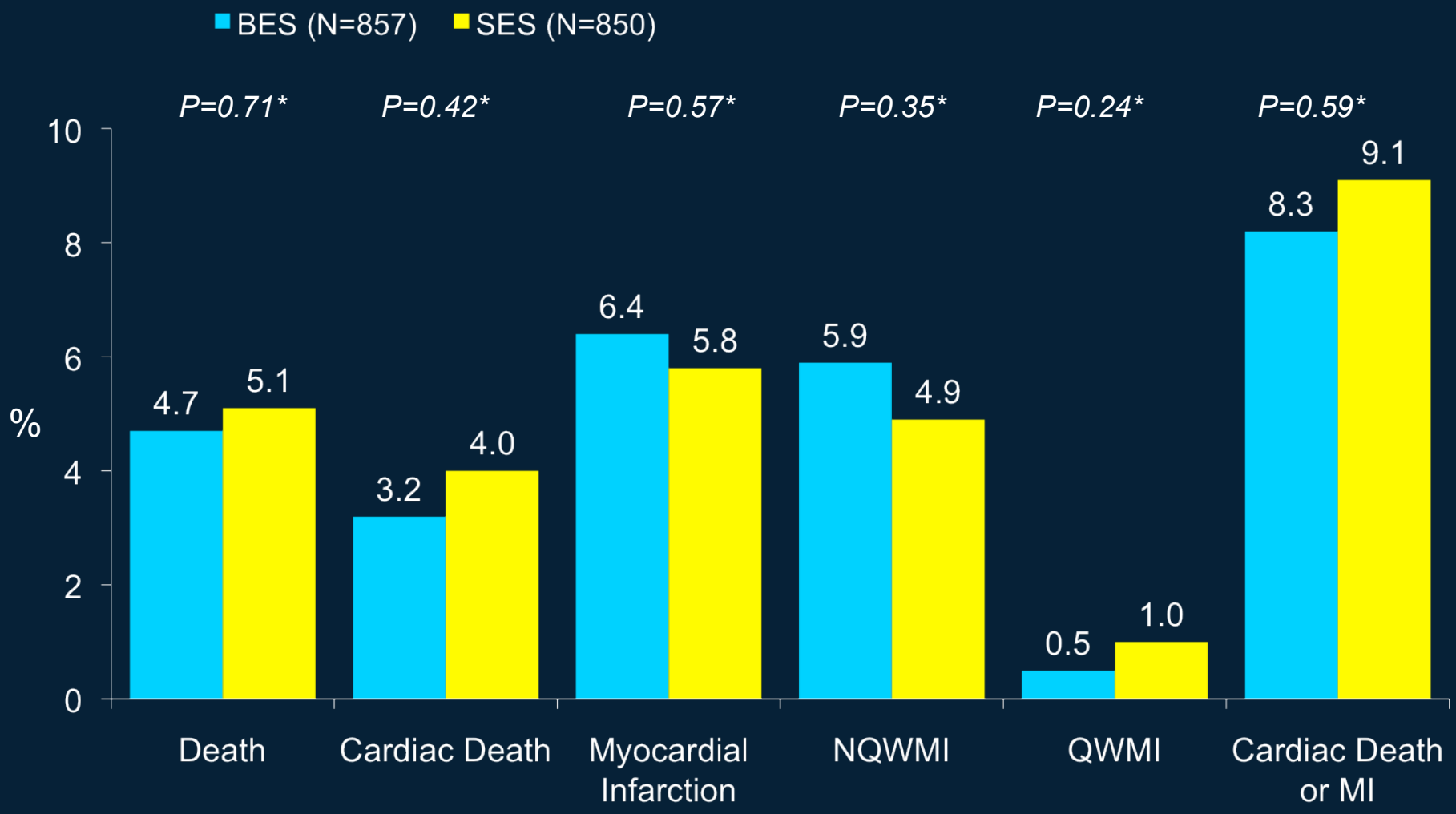
2-Year Safety Endpoints[4]



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*P values for superiority

[4] Klauss V., TCT 2009

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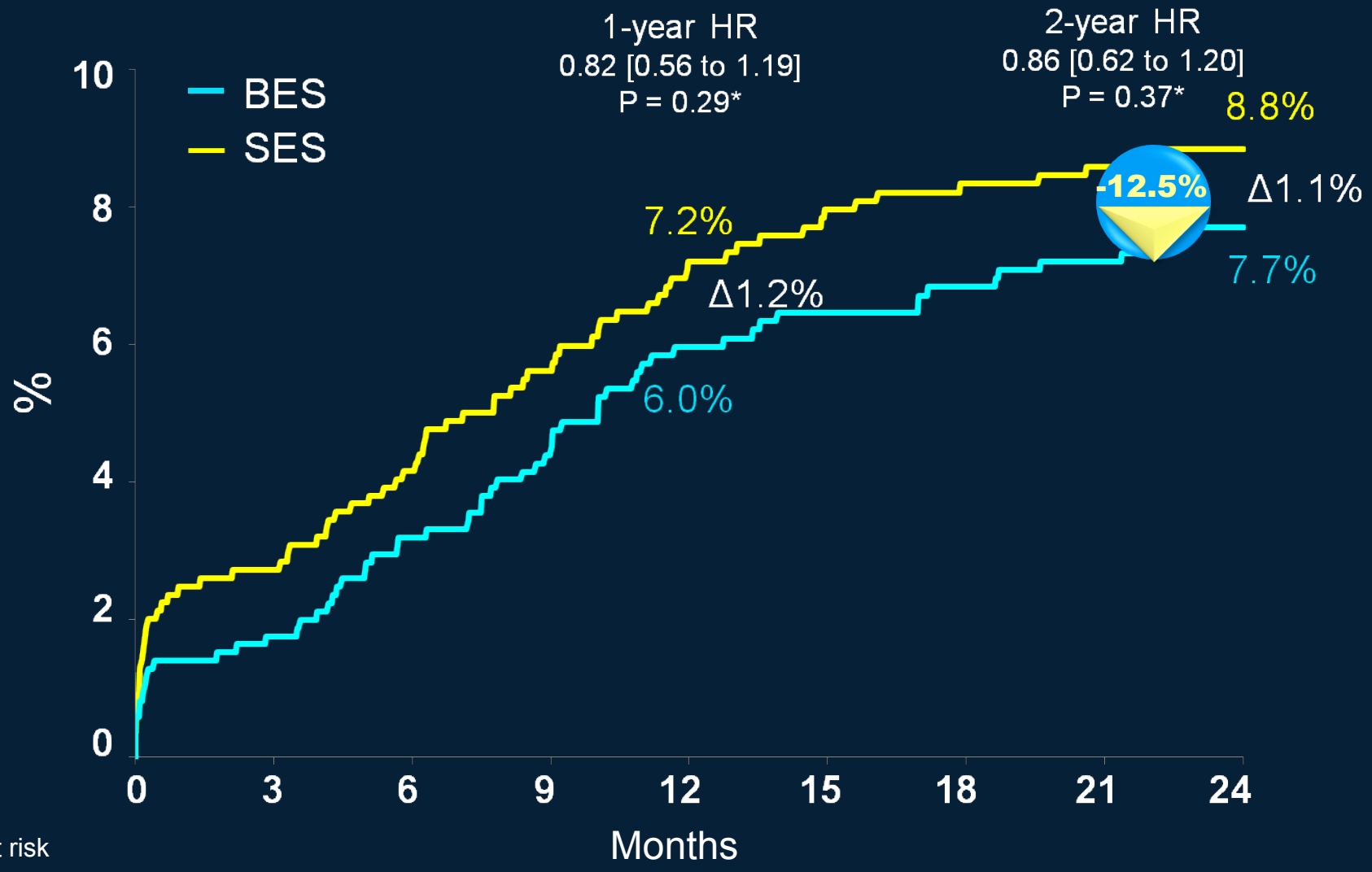
Clinically-Indicated TVR[4]



Number at risk									
BES	857	832	823	805	788	767	755	750	741
SES	850	8814	809	791	770	747	735	729	717

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*P values for superiority

[4] Klauss V., TCT 2009

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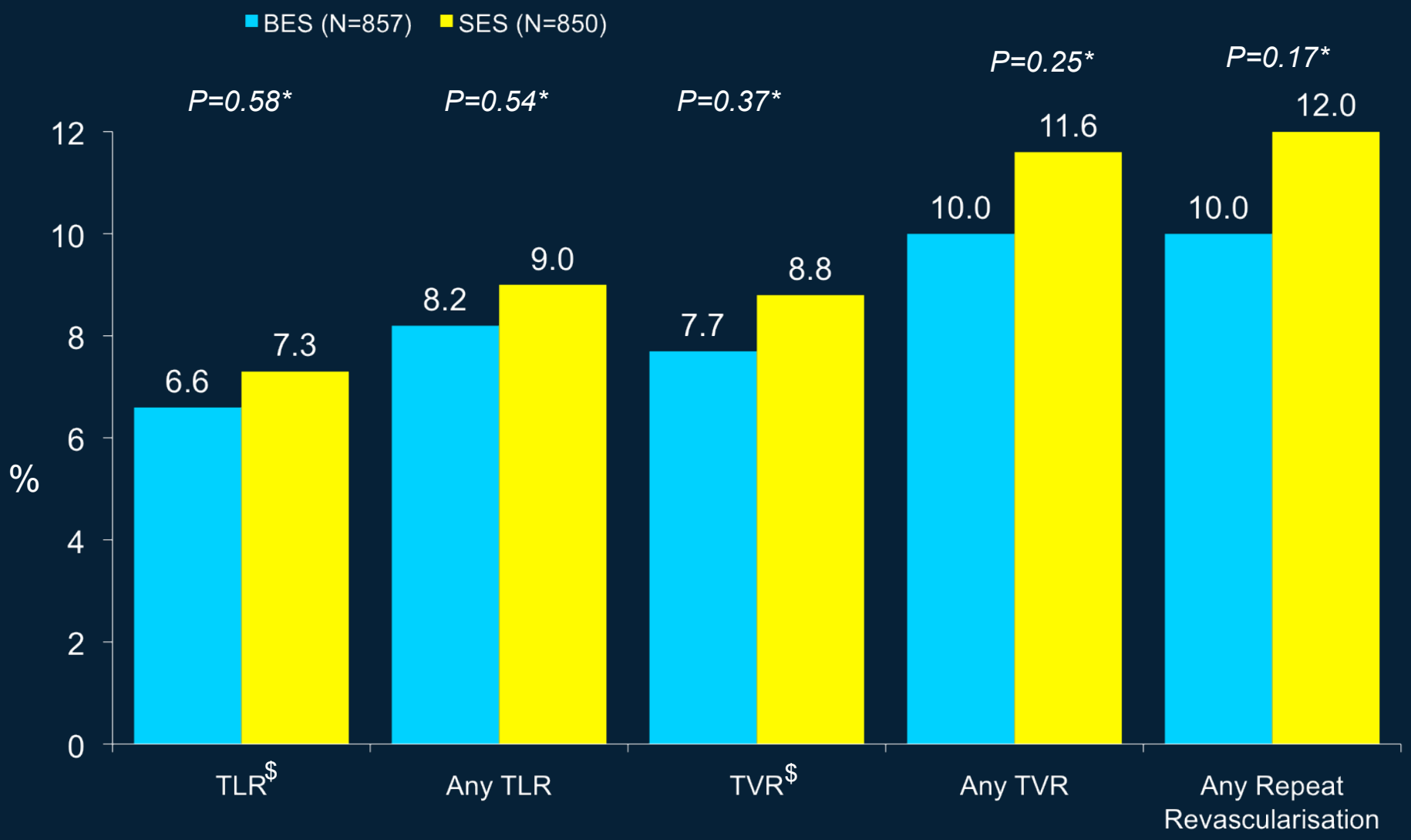
2-Year Efficacy Endpoints[4]



$Clinically Indicated
*P values for superiority
[4] Klauss V., TCT 2009

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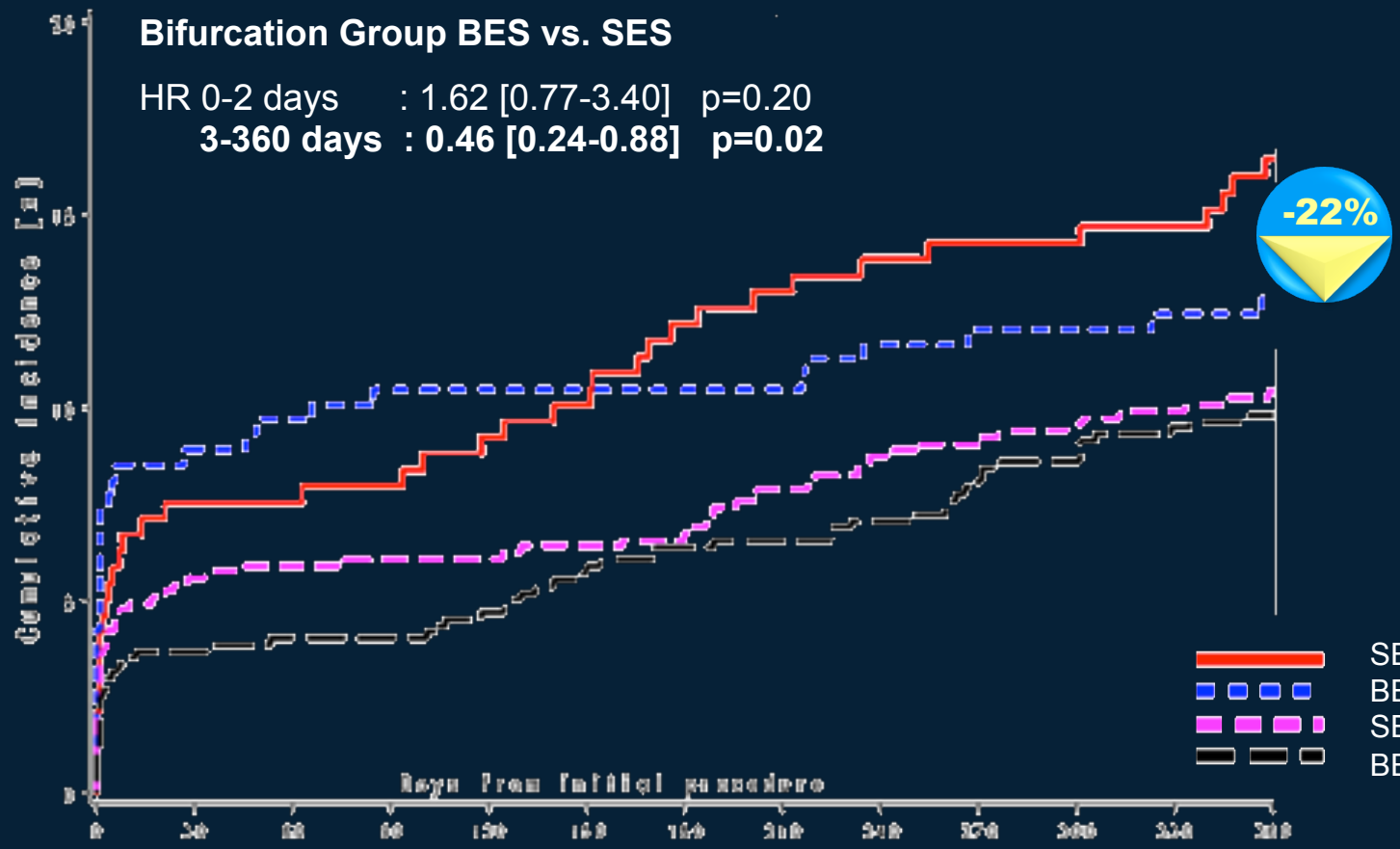
Advantage in Complex Patients

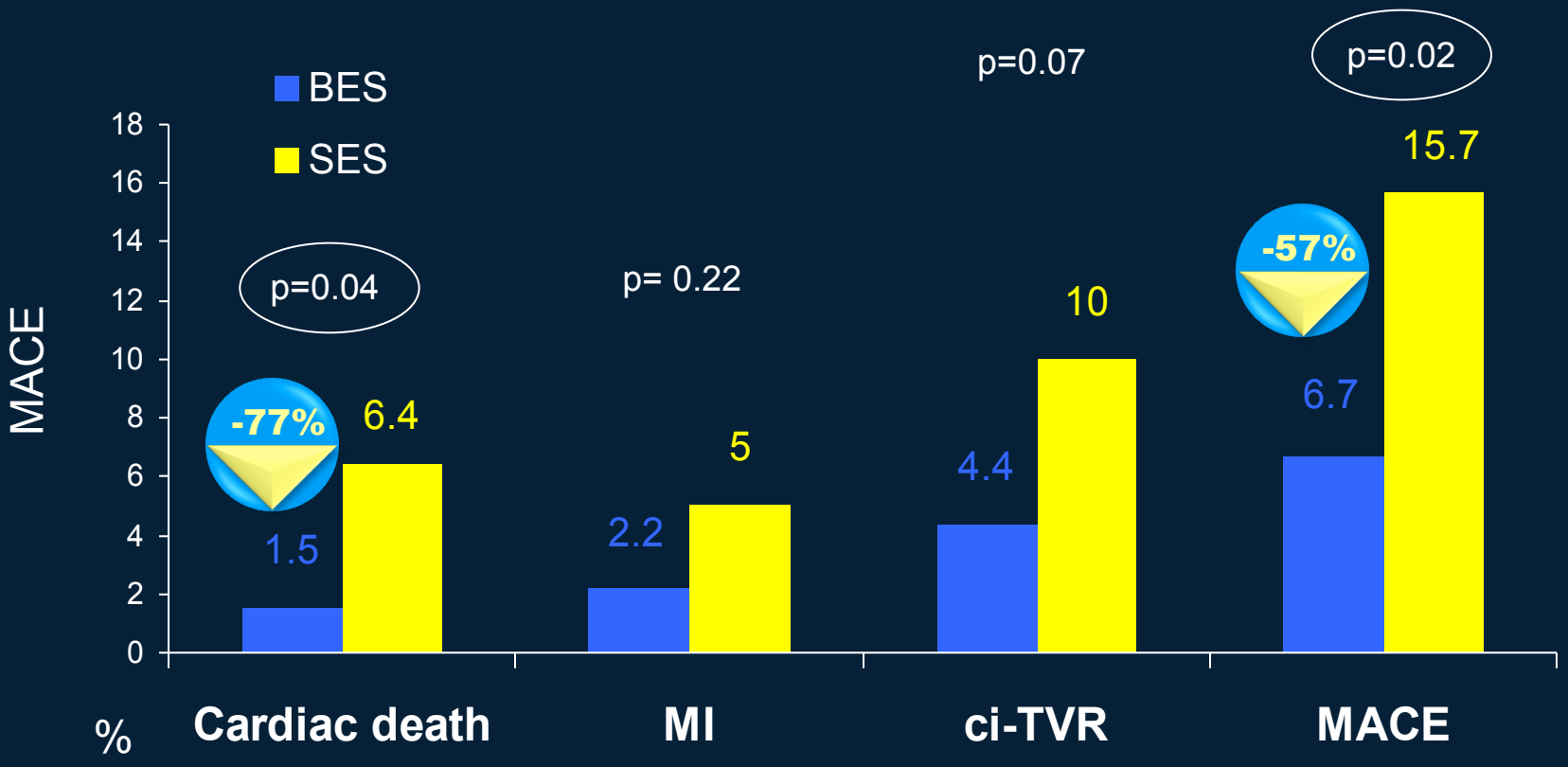
Complex Patients – Bifurcation Lesions 12 Month MACE[5]



Significant reduction in MACE for BES vs. SES in bifurcation lesions up to 12 months

[5]Garg, S., PCR 2009

Complex Patients – STEMI
12 Month MACE[6]

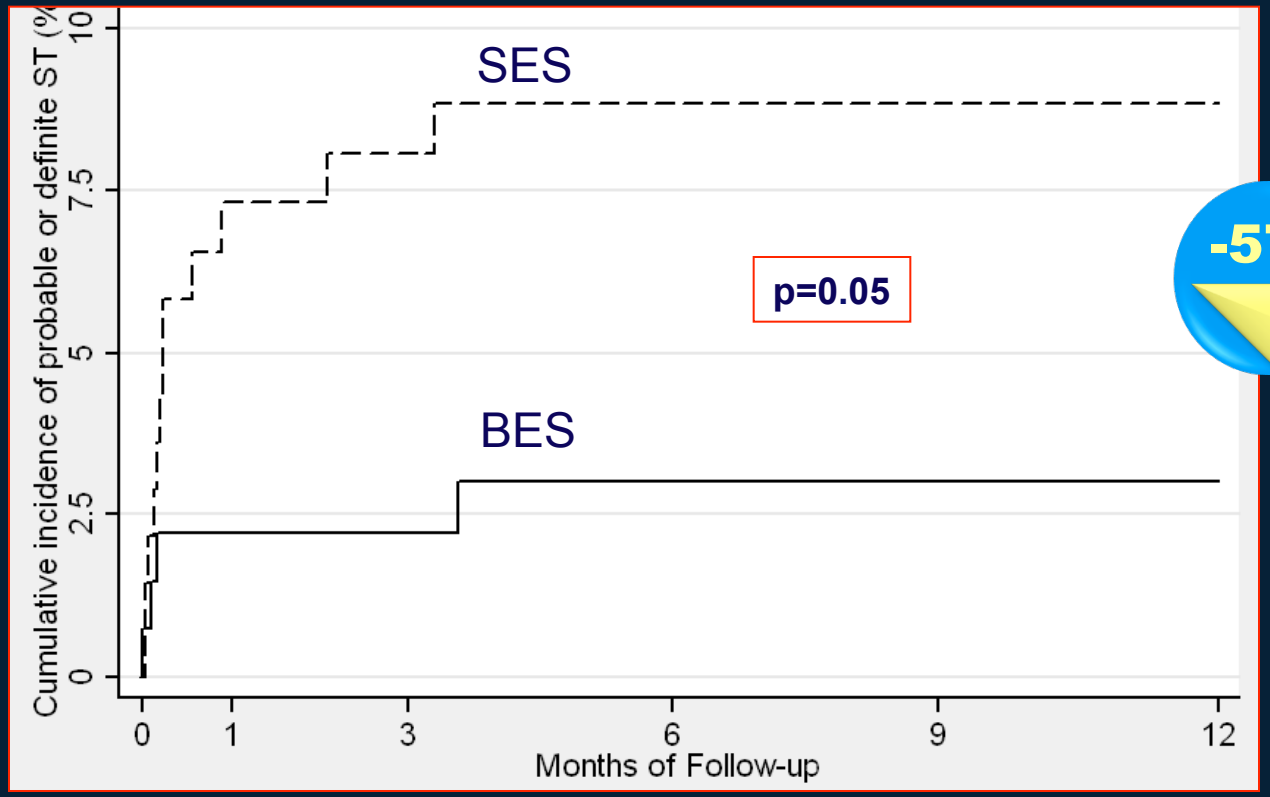


Superior clinical outcomes for the BES vs. SES up to 12 months

[6]Buszman, P., PCR 2009

Complex Patients - STEMI
12 Month Def/Prob Stent Thrombosis[6]

Probable or Definite ST

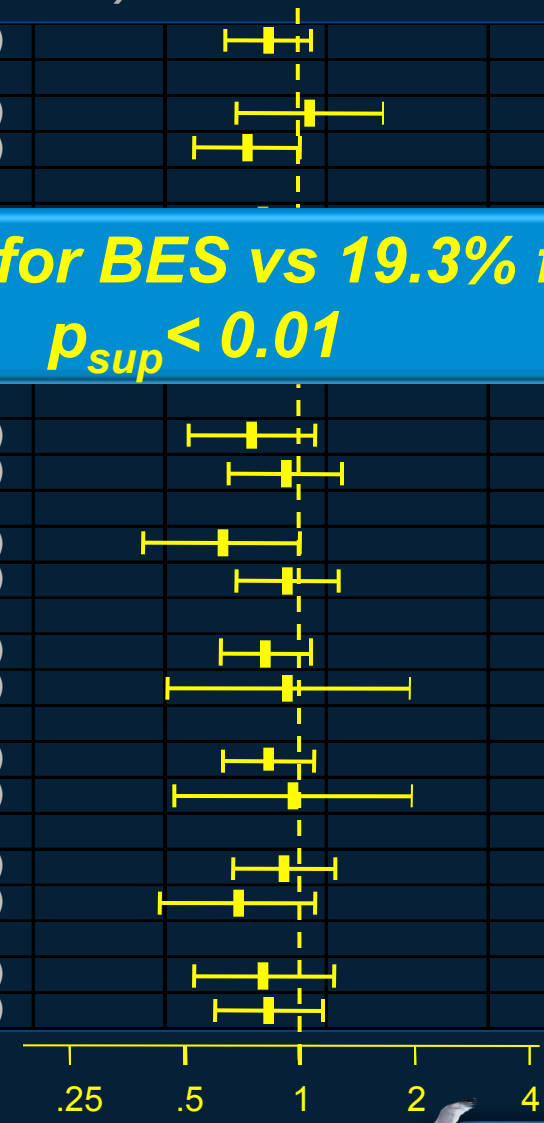


BES has significant lower rates of ST vs. SES up to 12 months

[6]Buszman, P., PCR 2009

Stratified Analysis of MACE @ 2 Years[4]

	BES	SES	Risk Ratio (95% CI)	P Value	P Int
Overall	109/857	129/850	0.83 (0.64 to 1.07)		ns
Diabetes mellitus					ns
Yes	44/223	36/191	1.06 (0.68 to 1.65)	0.79	
No	66/634	93/659	0.73 (0.53 to 1.00)	0.05	
Acute coronary					ns
Yes	56/470				
No	54/387				
ST-elevation MI					
Yes	11/135				
No	99/722				
Left anterior					ns
Yes	46/407	62/417	0.75 (0.51 to 1.10)	0.14	
No	64/449	67/431	0.92 (0.65 to 1.29)	0.62	
Multivessel disease					ns
Yes	31/209	41/176	0.63 (0.39 to 1.00)	0.05	
No	79/648	88/674	0.93 (0.68 to 1.26)	0.63	
Off-label use					ns
Yes	97/696	113/665	0.81 (0.62 to 1.07)	0.13	
No	13/160	16/183	0.93 (0.45 to 1.94)	0.85	
De-novo lesions					ns
Yes	96/788	113/774	0.83 (0.63 to 1.09)	0.18	
No	14/68	16/74	0.96 (0.47 to 1.96)	0.9	
Small-vessel disease					ns
Yes	80/585	85/568	0.91 (0.67 to 1.24)	0.57	
No	30/271	44/280	0.69 (0.43 to 1.10)	0.11	
Long lesions					ns
Yes	43/262	45/225	0.80 (0.53 to 1.23)	0.31	
No	67/594	84/623	0.83 (0.60 to 1.15)	0.26	



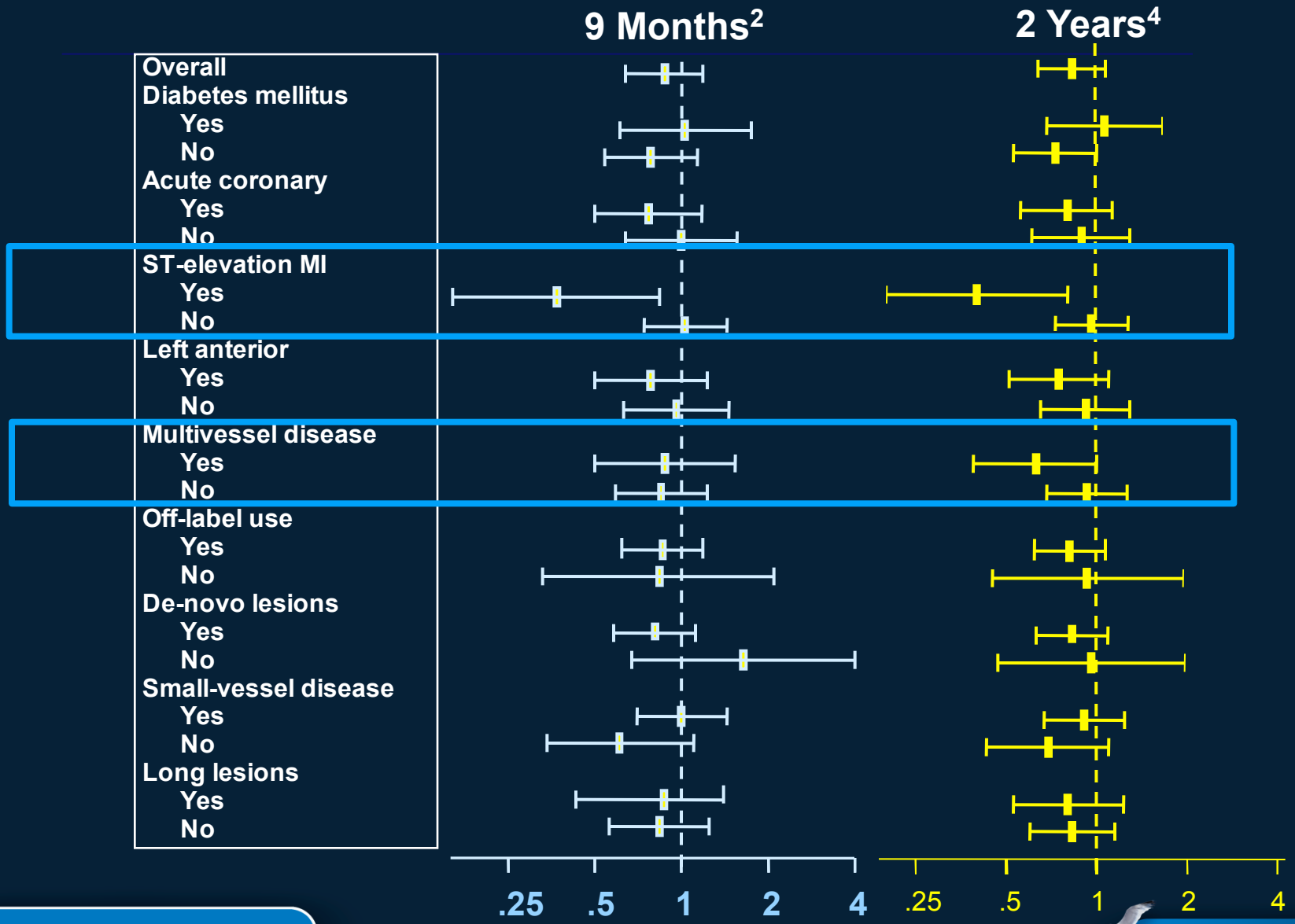
MACE 8.1% for BES vs 19.3% for SES
$p_{sup} < 0.01$

*P values for superiority

[4] Klauss V., TCT 2009

Stratified Analysis of MACE

9 Months vs. 2 Years



[2]Windecker S. et al., The Lancet 2008; 372 No. 9644: 1163-1173

[4] Klauss V., TCT 2009

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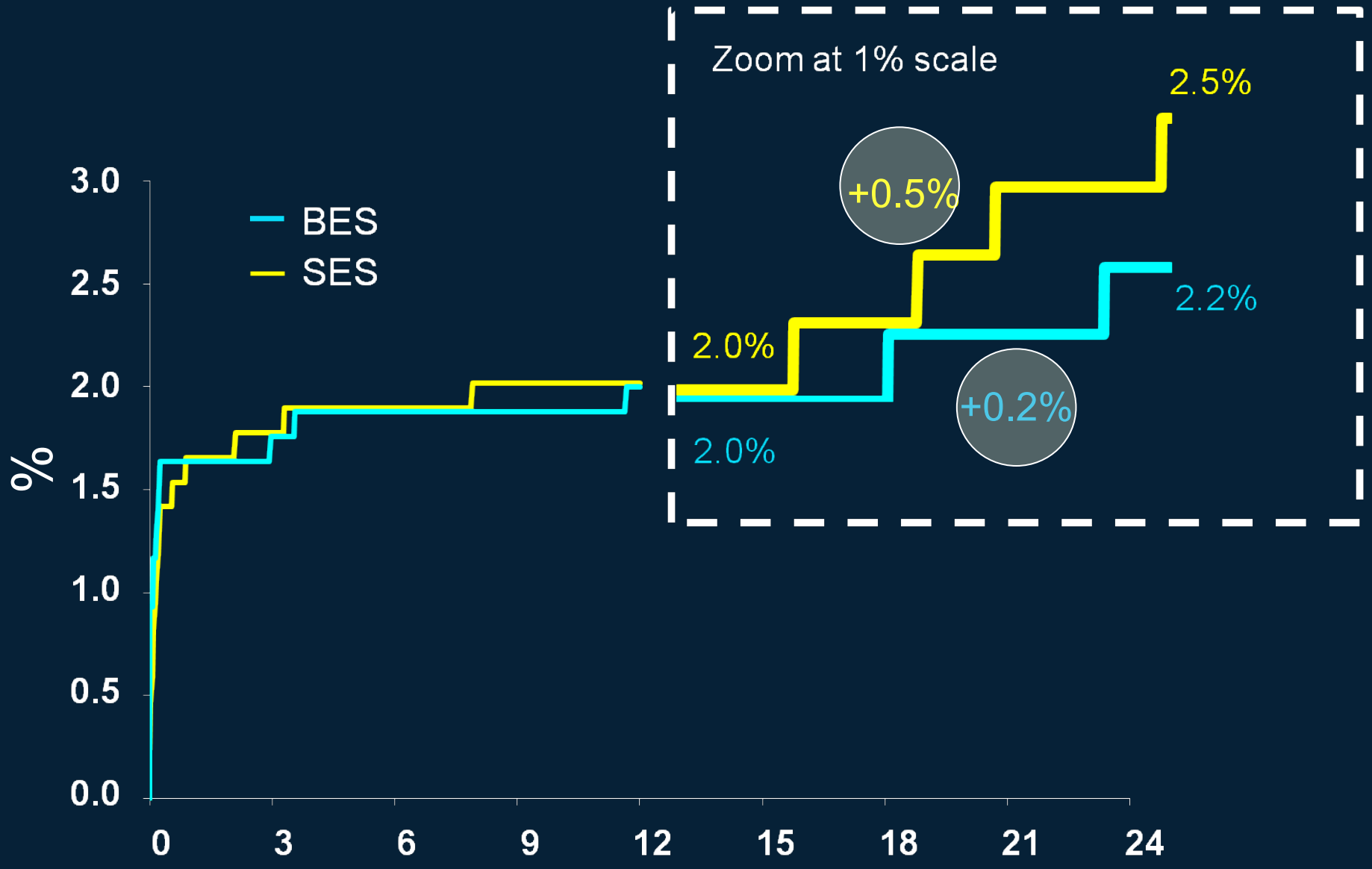
Very Late Stent Thrombosis

Signs of Safety Benefits Beyond One Year

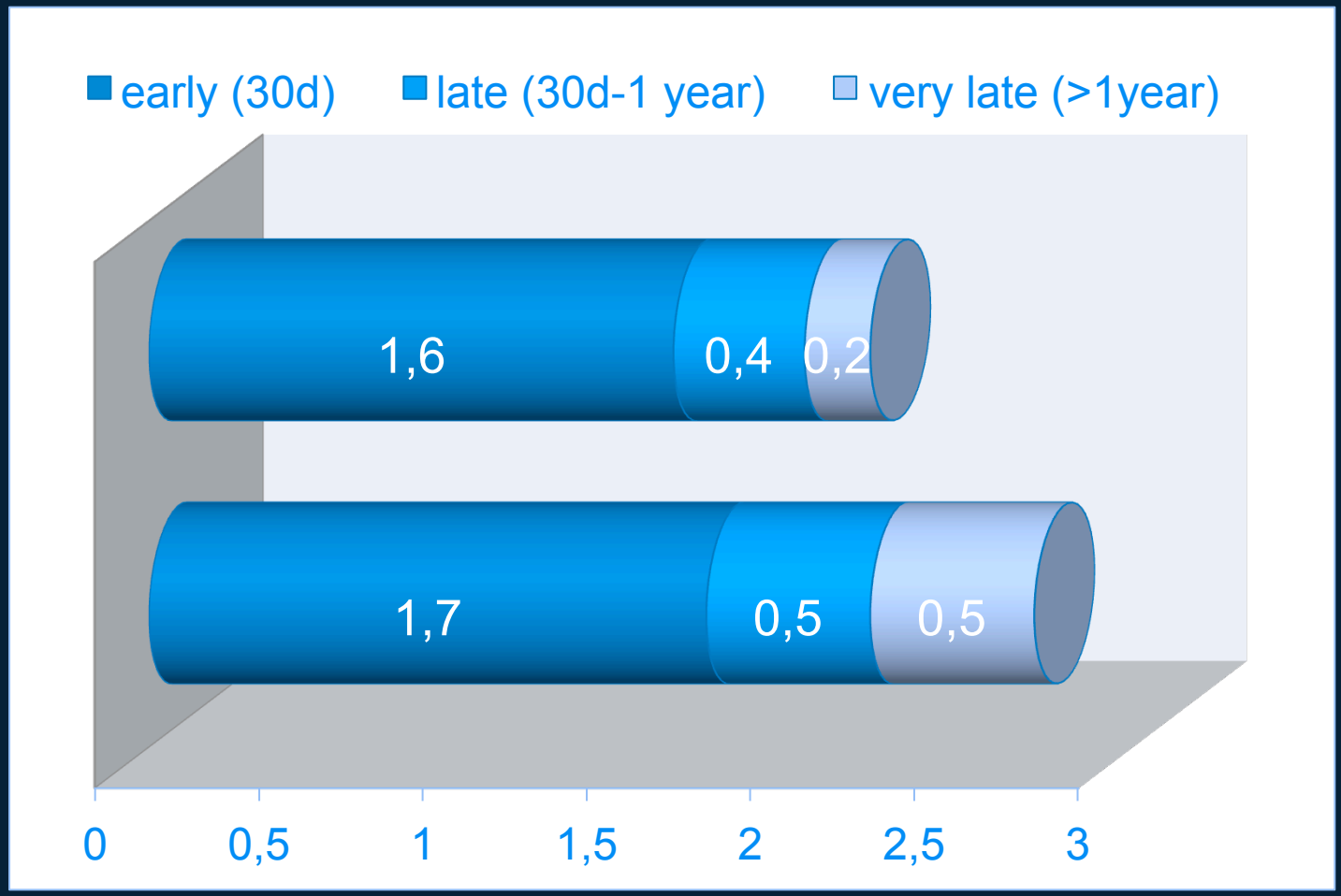
Definite ST through 2 Years[4]



*P values for superiority

[4]Klauss V., TCT 2009

Primary and Secondary Definite ST



Definite Stent Thrombosis %

According to ARC Definition

$Includes one secondary, definite ST occurring at 60 days in a patient who had early ST at 3 days

*P values for superiority

[4]Klauss V., TCT 2009

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Antiplatelet Agent Utilization[4]

	BES	SES	P value*
Aspirin			
- At 9 months	96.6% (n=818)	97.4% (n=798)	**0.39**
- At 12 months	97.0% (n=810)	96.1% (n=801)	**0.34**
- At 24 months	94.9% (n=789)	94.2% (n=778)	**0.58**
Clopidrogel/Thienopyridine			
- At 9 months	95.6% (n=818)	95.2% (n=798)	**0.81**
- At 12 months	68.1% (n=810)	66.5% (n=801)	**0.52**
- At 24 months	23.4% (n=789)	24.3% (n=778)	**0.72**

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*P values for superiority

[4]Klauss V., TCT 2009

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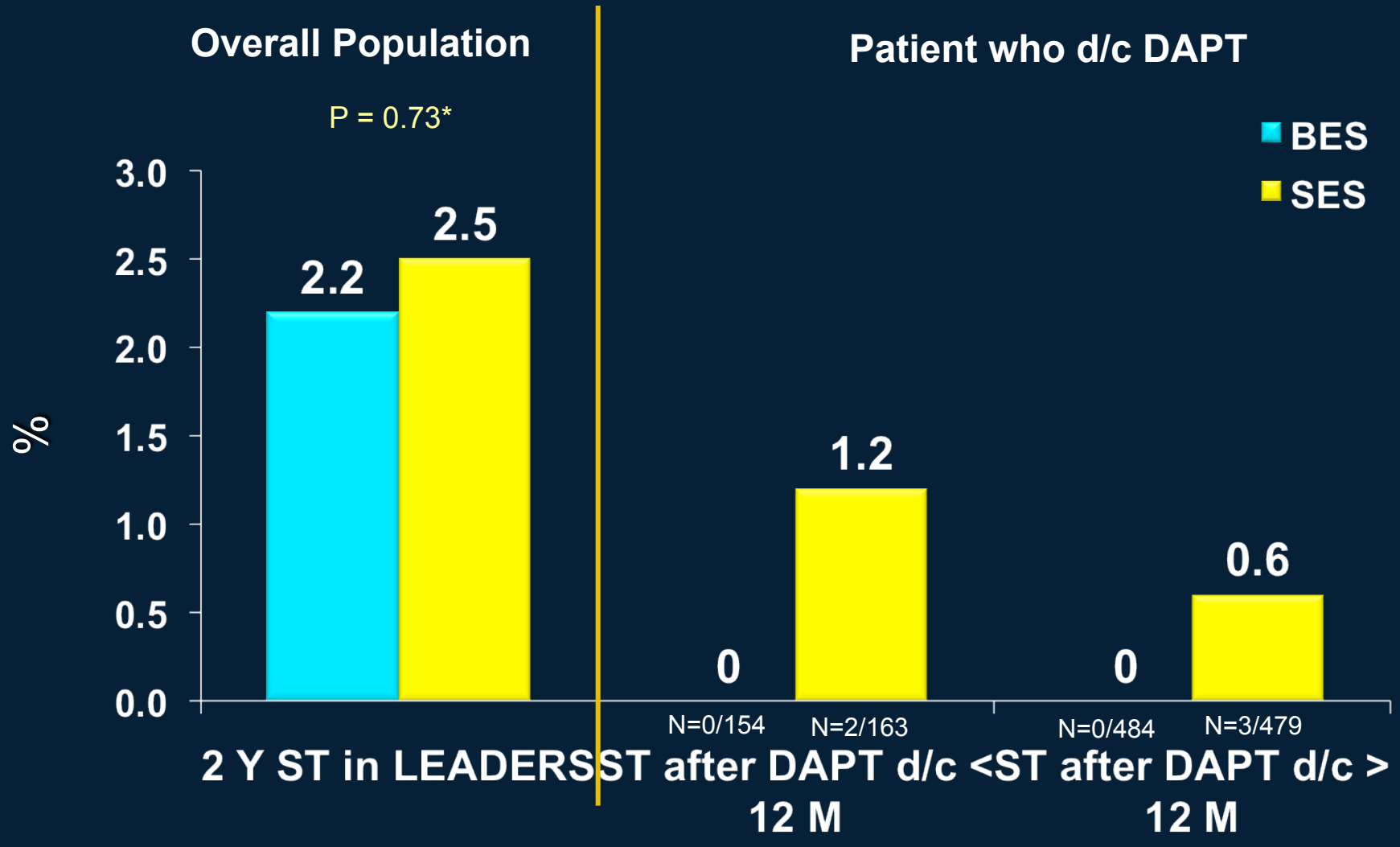
Effect of DAPT Discontinuation[4]



*P values for superiority

[4]Klauss V., TCT 2009

Conclusions

9 months follow-up

- *Primary endpoint met: non-inferior MACE rate at 9 months*
  (9.2% BES vs. 10.5% SES p=0.003)

- *BES showed superior strut coverage and stent apposition at 9 months in OCT sub-analysis*

2 years follow-up

- *Non-inferiority of BES vs. SES in an all-comers population was sustained up to 2 years*

- *BES showed superior outcomes in STEMI patients*
  (MACE was 8.1% for BES vs. 19.3% for SES $p_{sup} < 0.01$*)*

Conclusions

Very Late Stent Thrombosis

- *Although this was an all-comers study, very late stent thrombosis events were rare (BES 0.2% vs. SES 0.5% p_{sup} = 0.73)*
- *BES VLST events were limited to SVGs*
- *There were no VLST events in BES patients following discontinuation of DAPT*