BioMatrix: Learned from the Three-year LEADERS trial

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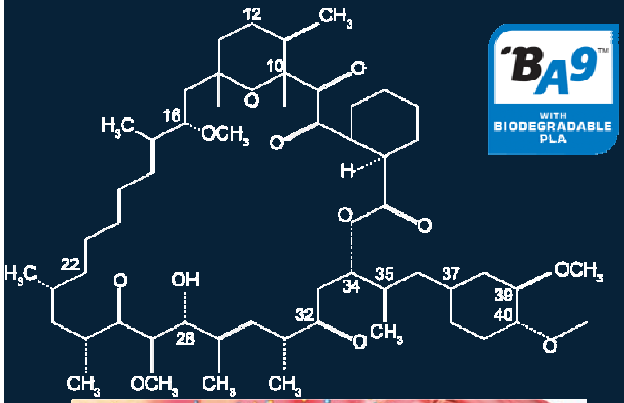
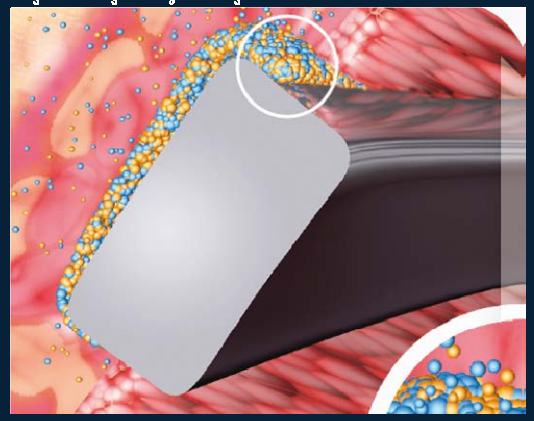
16:38-16:48 April 28

Coronary Arena, Level 1

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 120 μm with a **quadrature link** design.

Trial Design

Stable and ACS Patients Undergoing PCI

Assessor-blind
1:1 Randomisation

N=1700
Patients

BES
BioMatrix Flex N=850

SES
Cypher Select N=850

1:3 Randomisation

Clinical F/U
N=640

Angio F/U
N=210

Clinical F/U
N=640

Angio F/U
N=210

1º endpoint:	CV death, MI, clinically-indicated TVR (9 months)
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 month

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

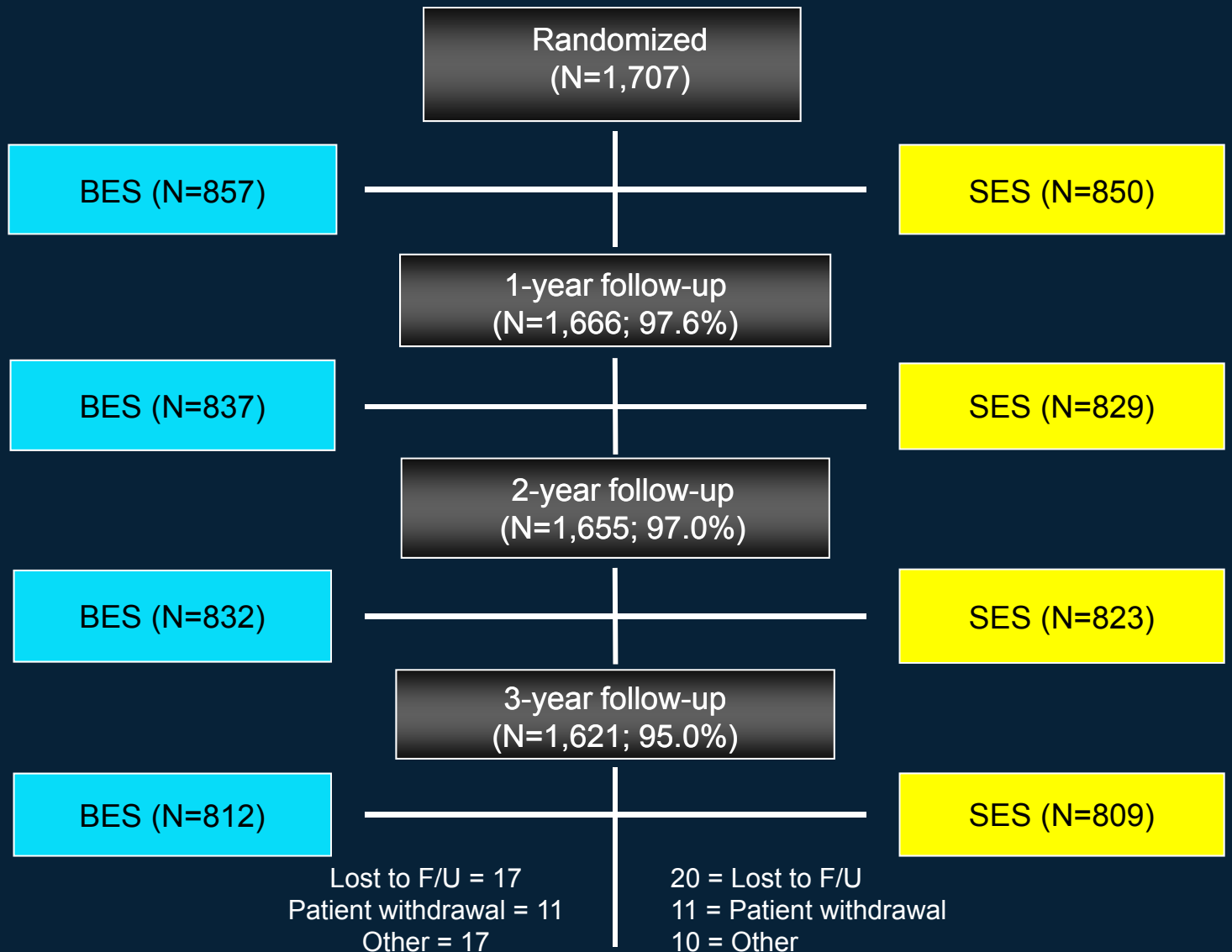
Patient Demographics

	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%

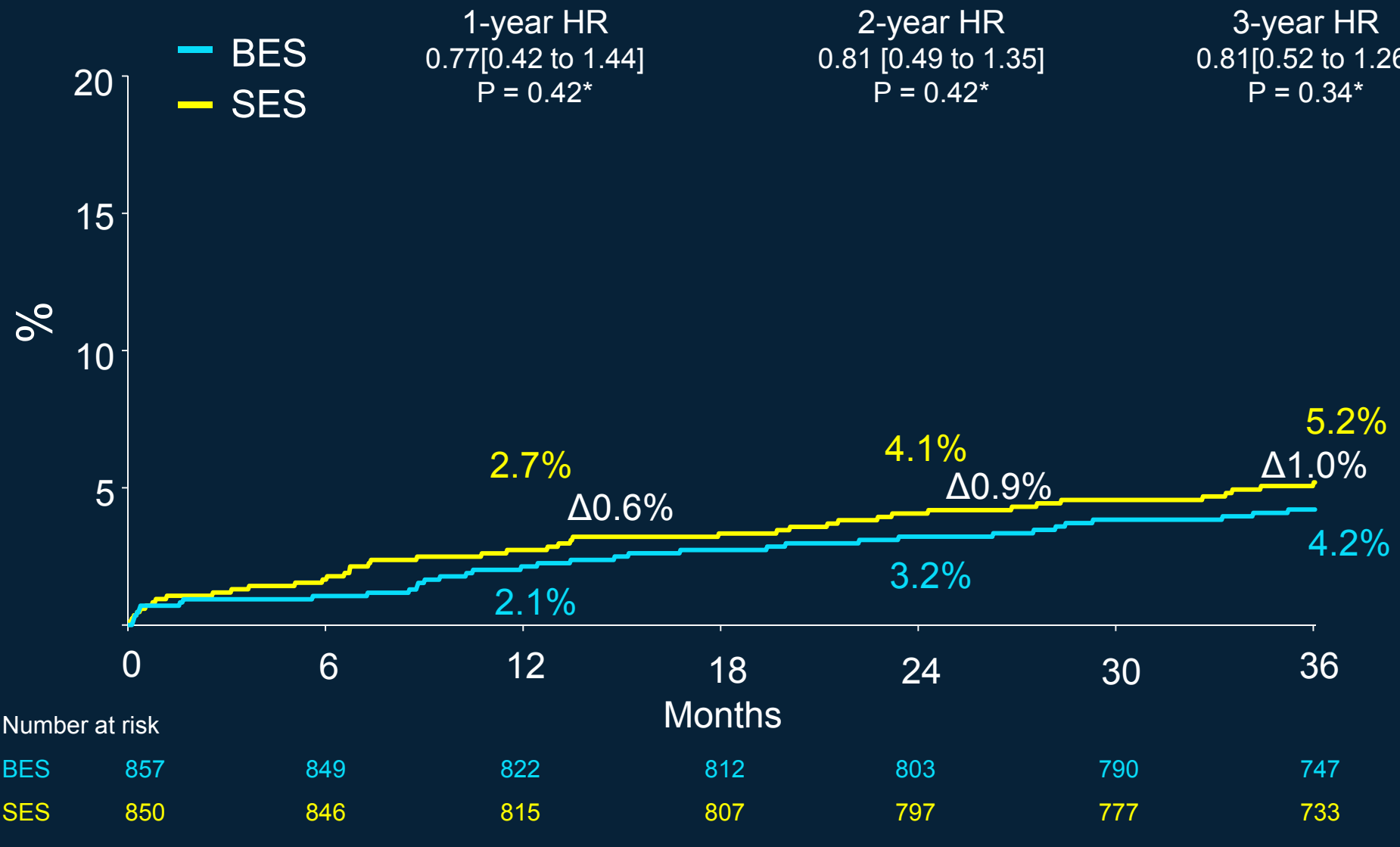
Patient Characteristics

	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%	67%
Off label use	81%	78%

Patient Flow - Clinical



Cardiac Death

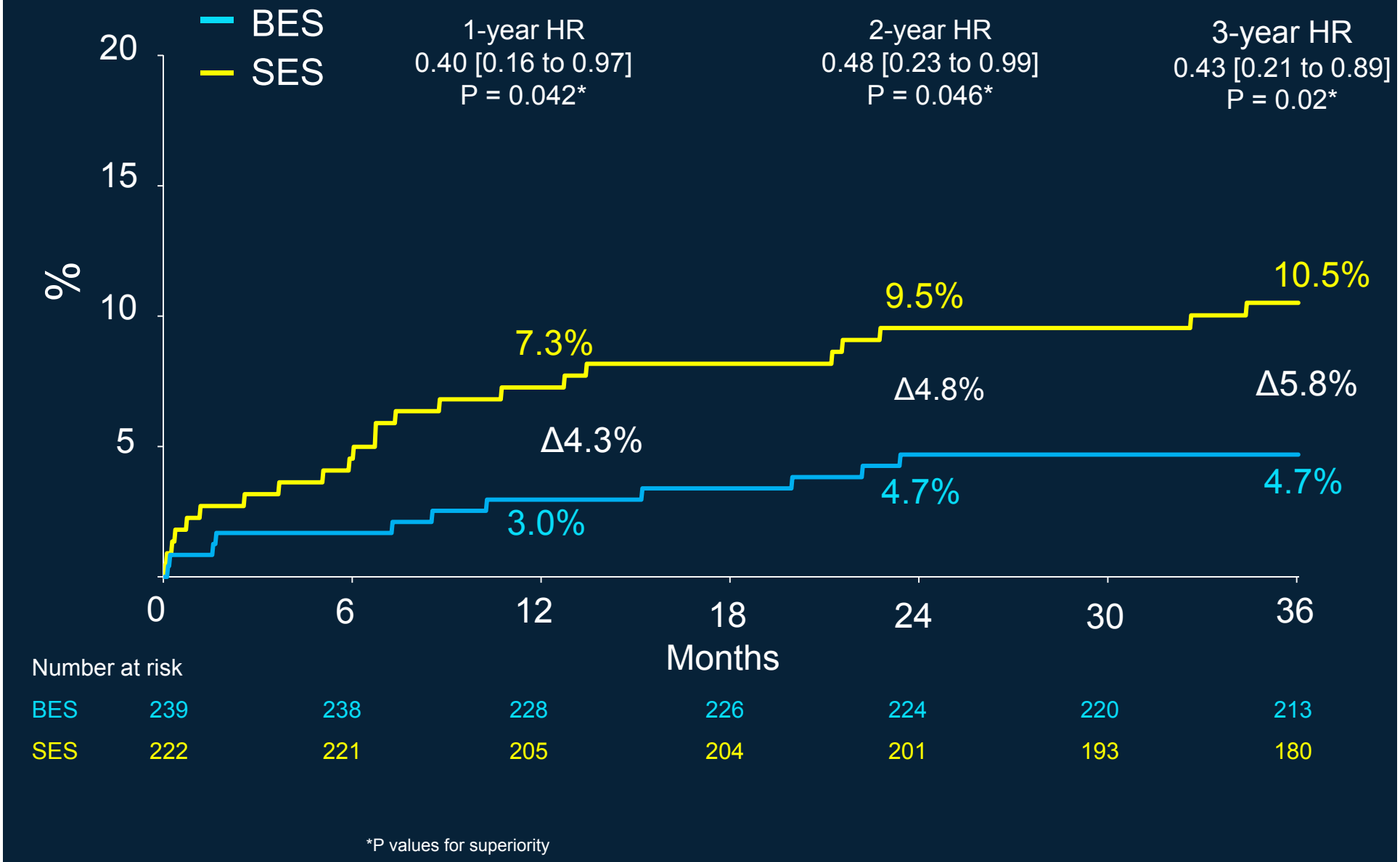


Number at risk

BES	857	849	822	812	803	790	747
SES	850	846	815	807	797	777	733

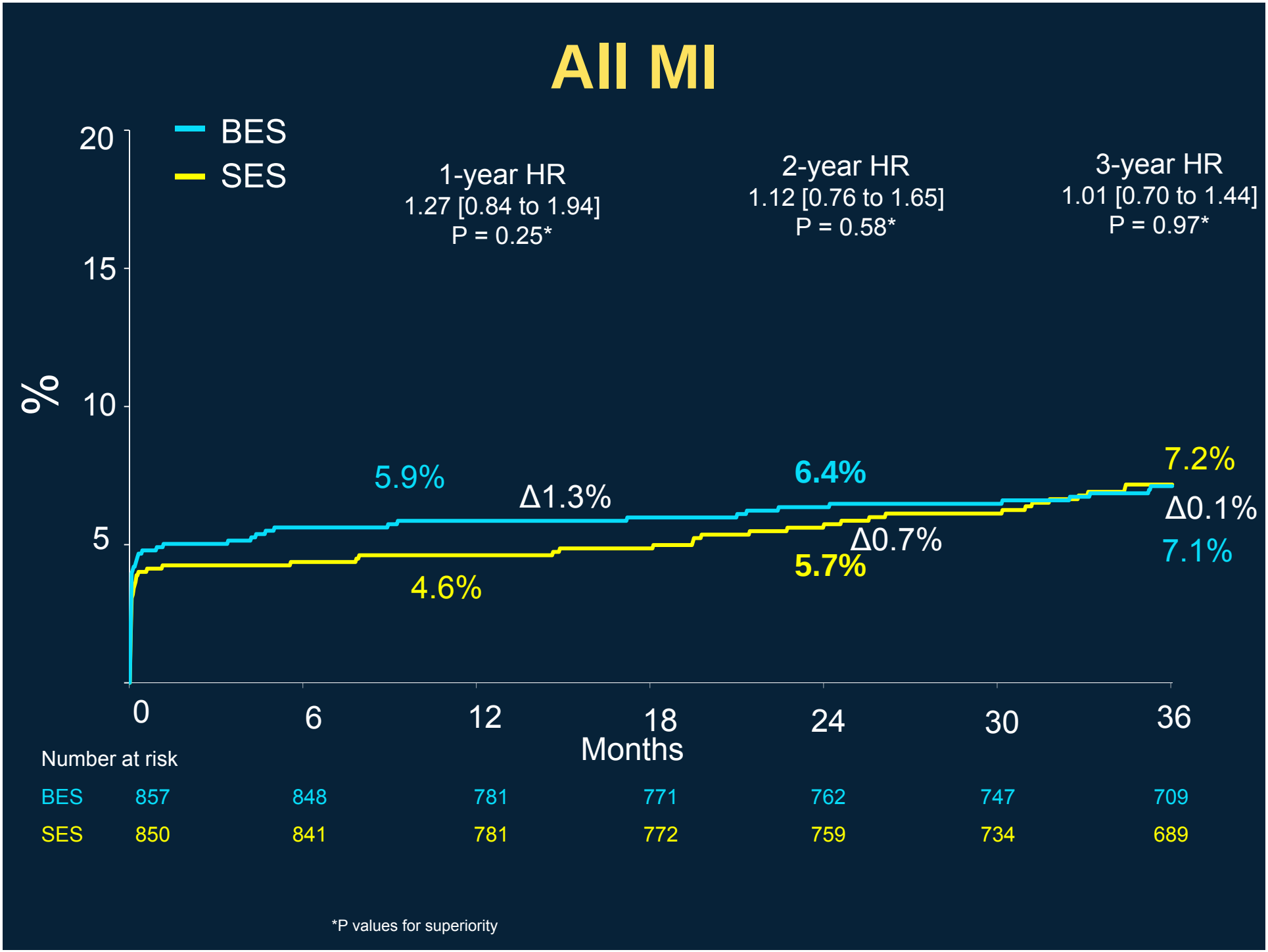
*P values for superiority

Cardiac Death
in High Syntax Score (>16)



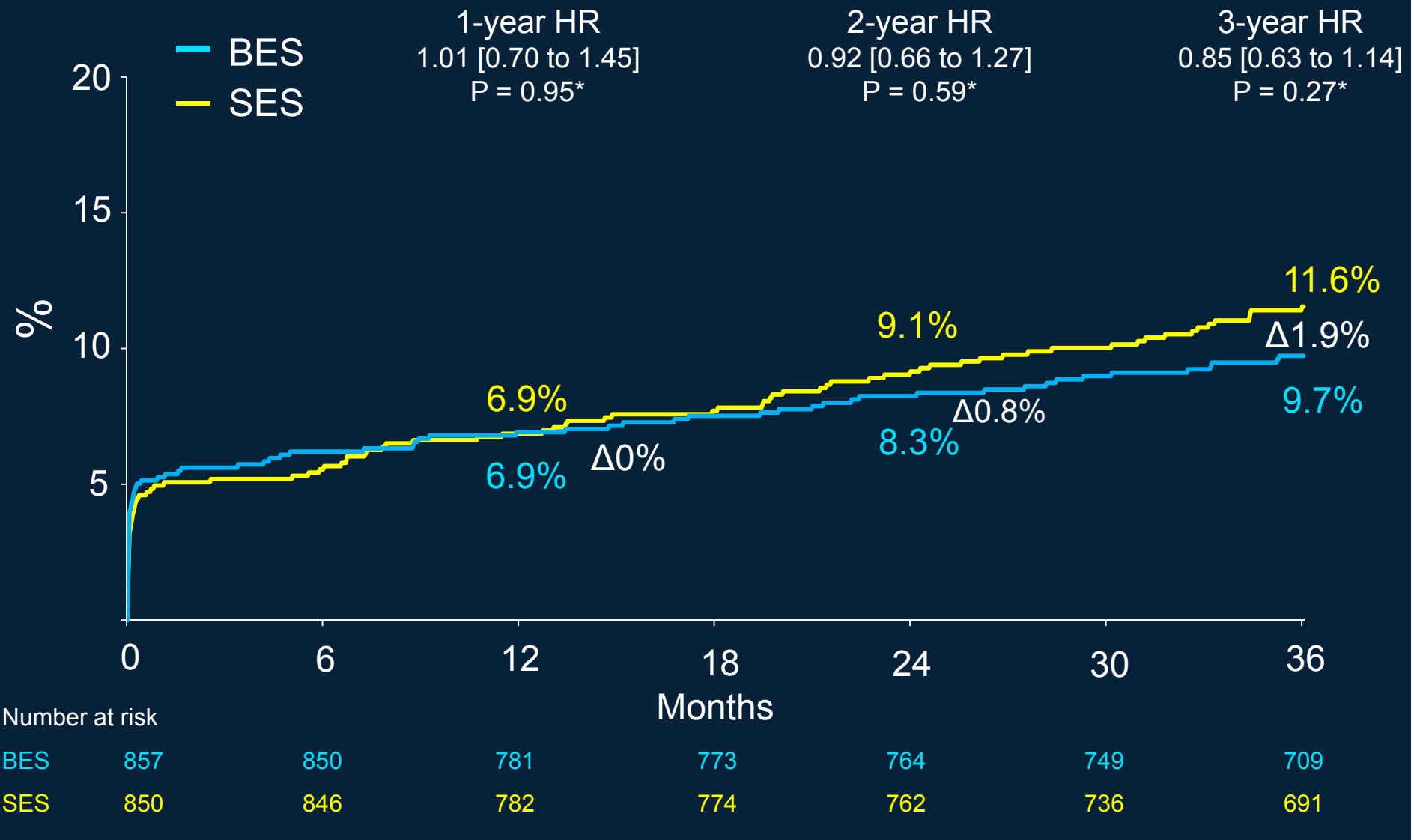
*P values for superiority

All MI



*P values for superiority

Cardiac Death or MI

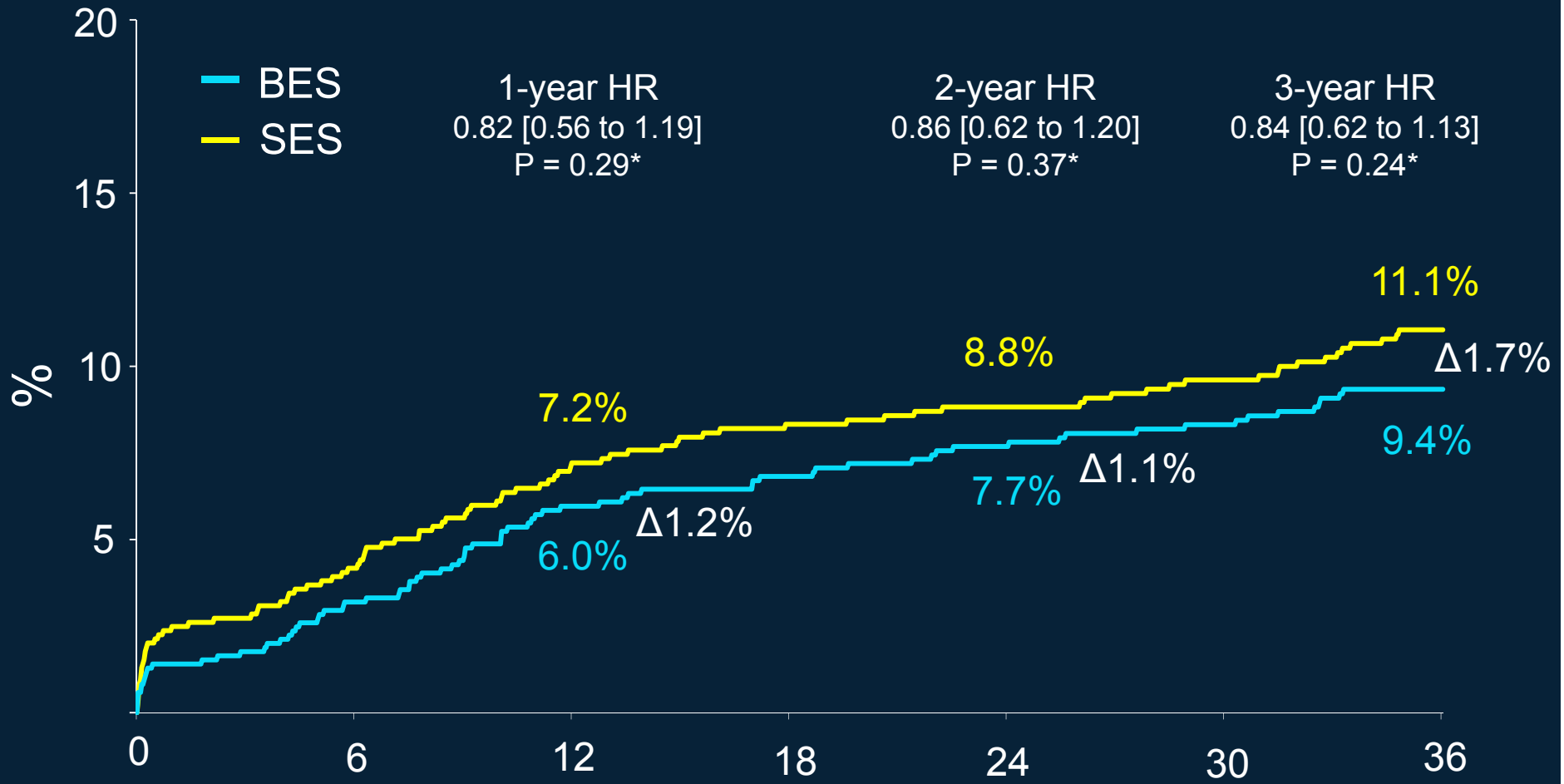


Number at risk

BES	857	850	781	773	764	749	709
SES	850	846	782	774	762	736	691

*P values for superiority

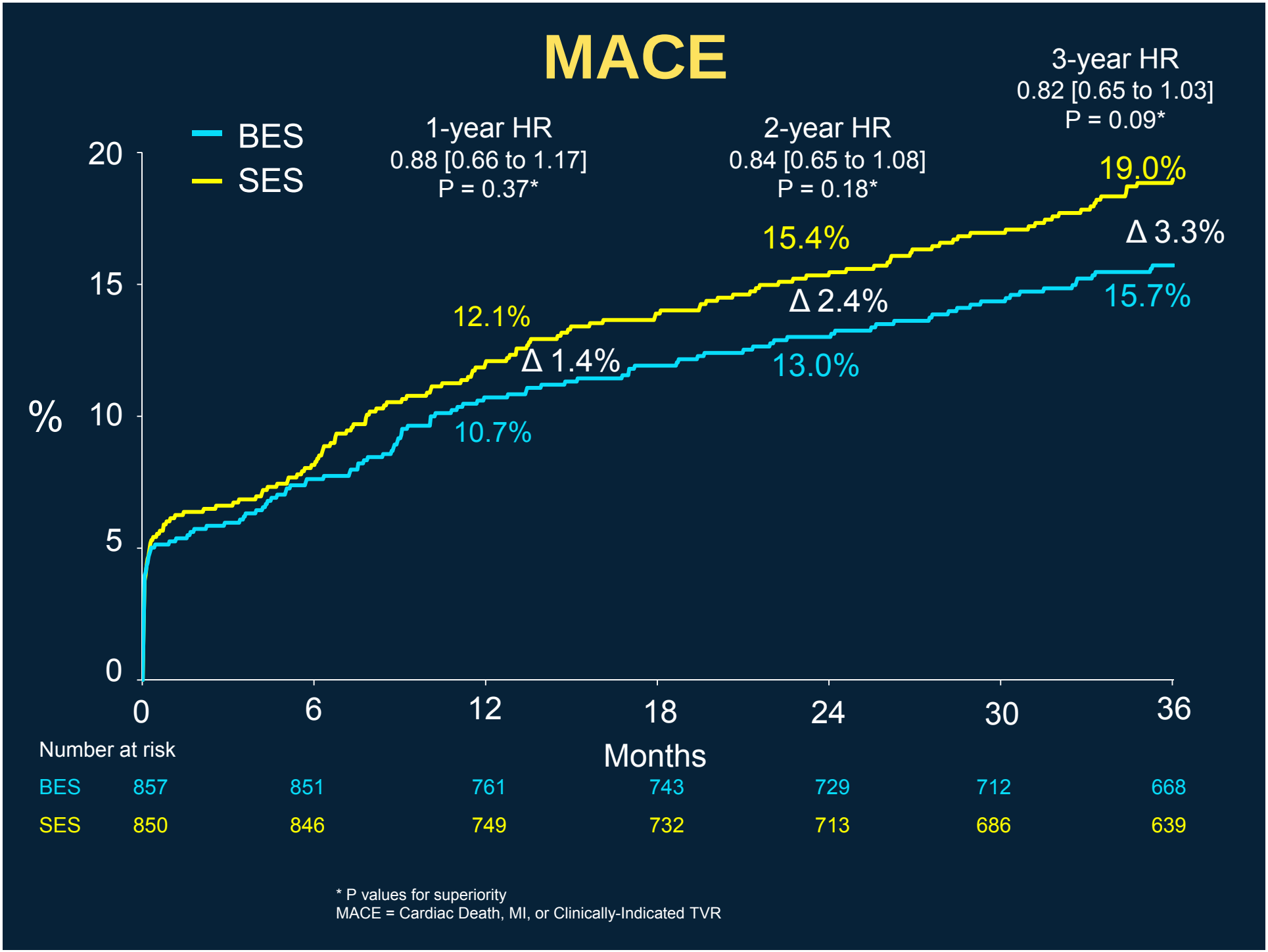
Clinically-Indicated TVR



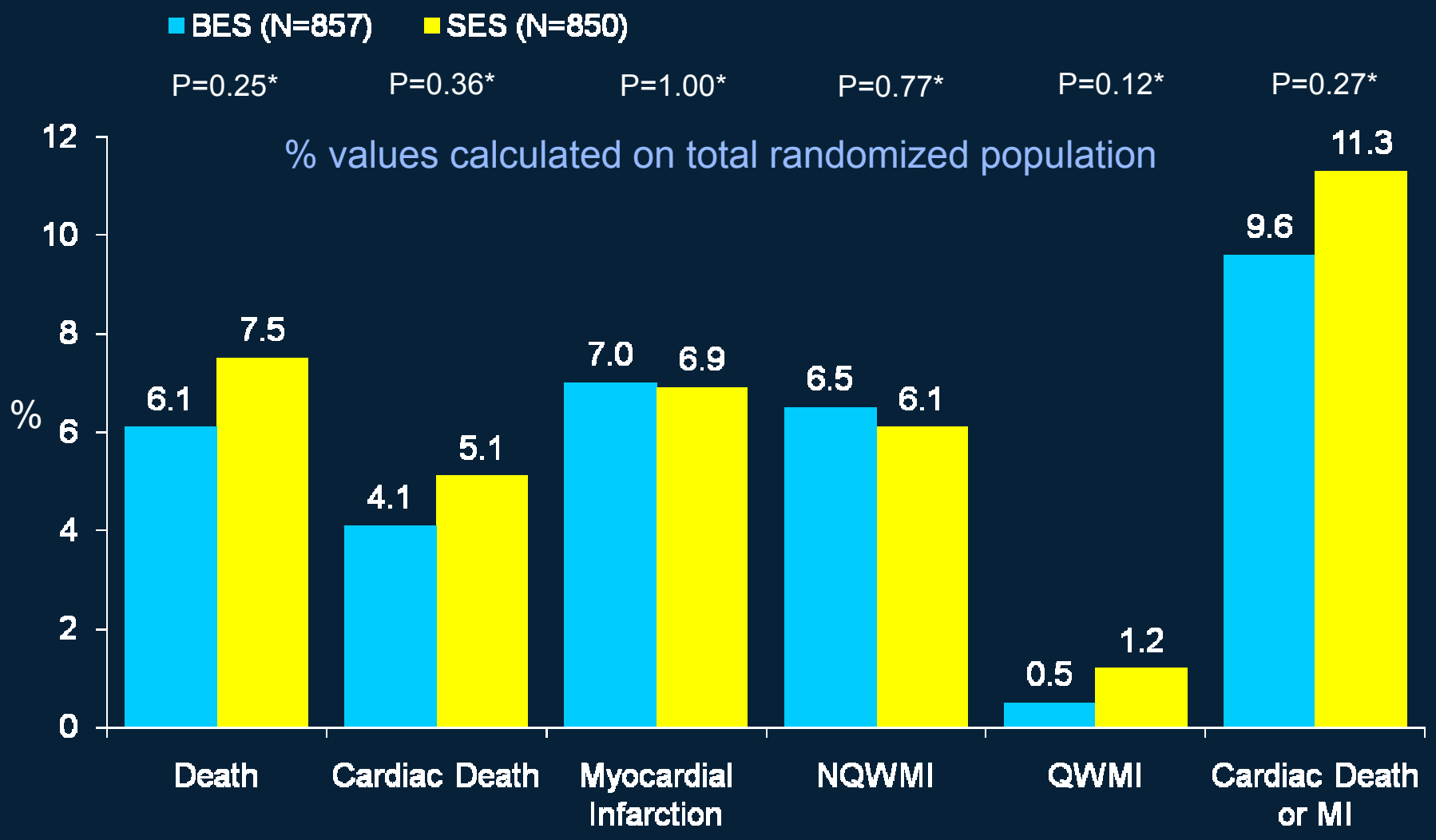
Number at risk

BES	857	847	790	769	754	735	692
SES	850	841	772	752	733	710	665

*P values for superiority

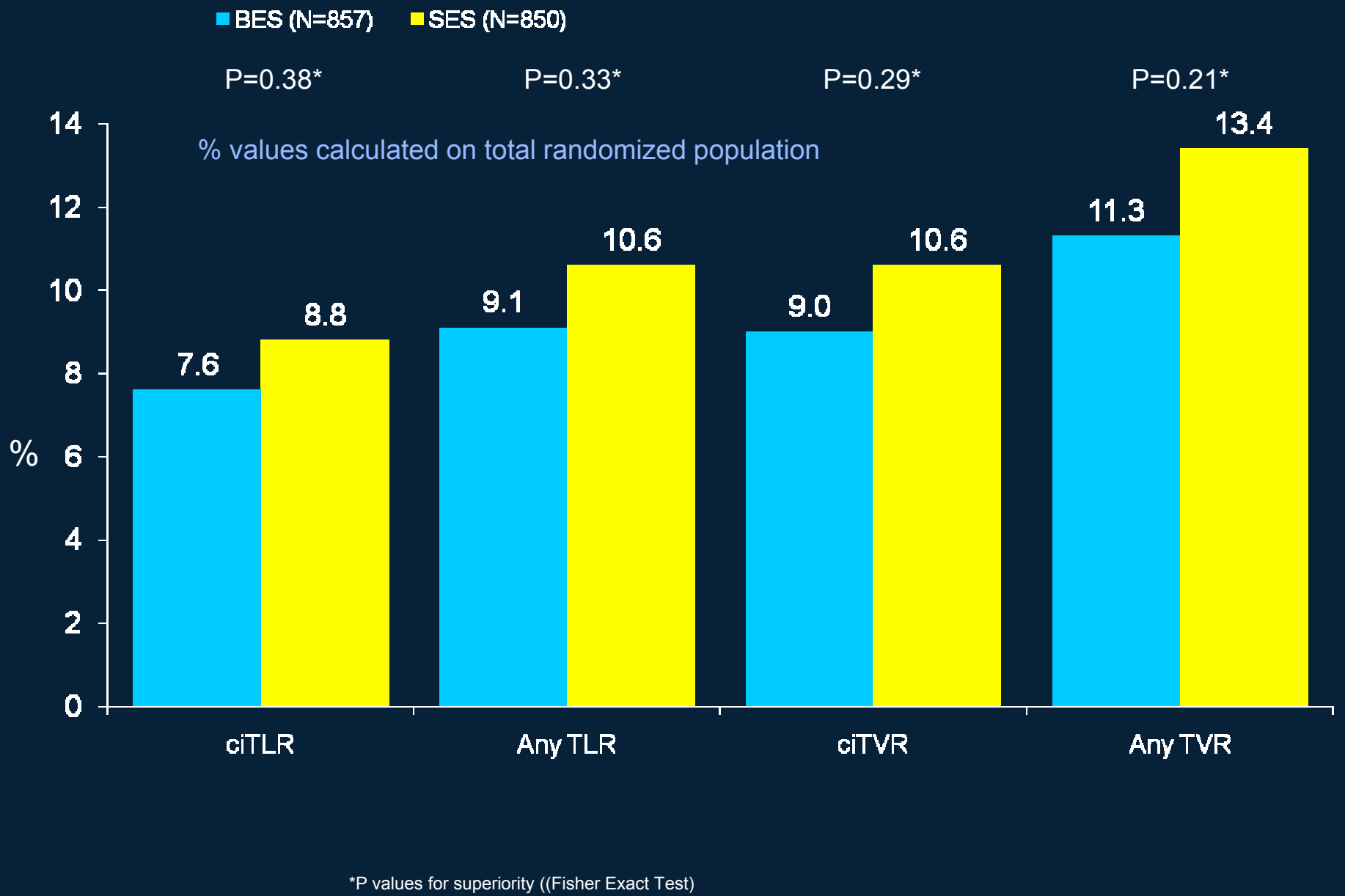

MACE
BES
SES
1-year HR
0.88 [0.66 to 1.17]
P = 0.37*
2-year HR
0.84 [0.65 to 1.08]
P = 0.18*
3-year HR
0.82 [0.65 to 1.03]
P = 0.09*
20
15
10
5
0
%
12.1%
10.7%
Δ 1.4%
15.4%
13.0%
Δ 2.4%
19.0%
15.7%
Δ 3.3%
0
6
12
18
24
30
36
Months
Number at risk
BES 857 851 761 743 729 712 668
SES 850 846 749 732 713 686 639
* P values for superiority
MACE = Cardiac Death, MI, or Clinically-Indicated TVR

3-Year Safety Endpoints



*P values for superiority ((Fisher Exact Test)

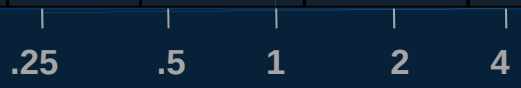
3-Year Efficacy Endpoints



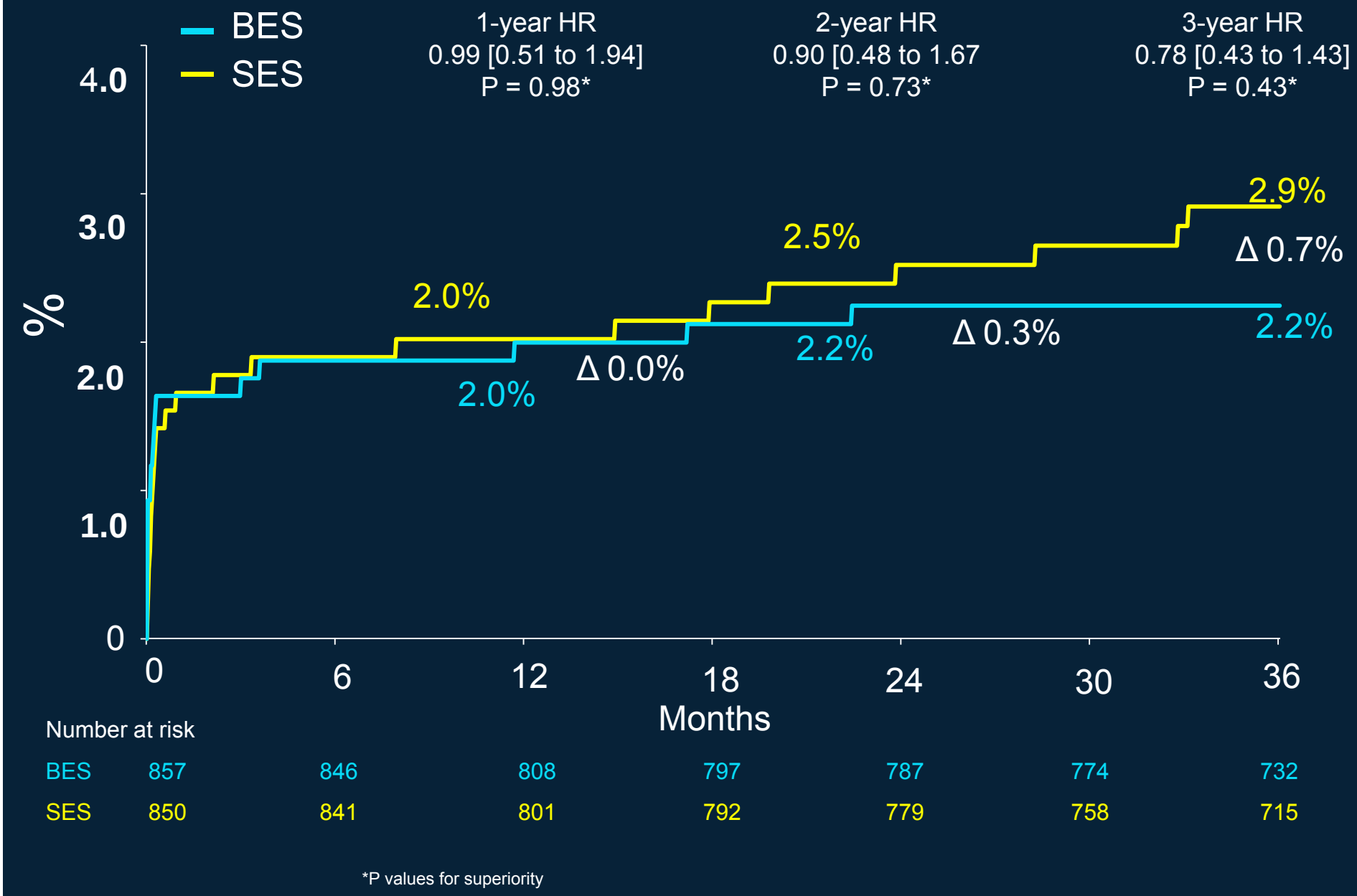
*P values for superiority ((Fisher Exact Test)

Stratified Analysis of MACE @ 3 Years

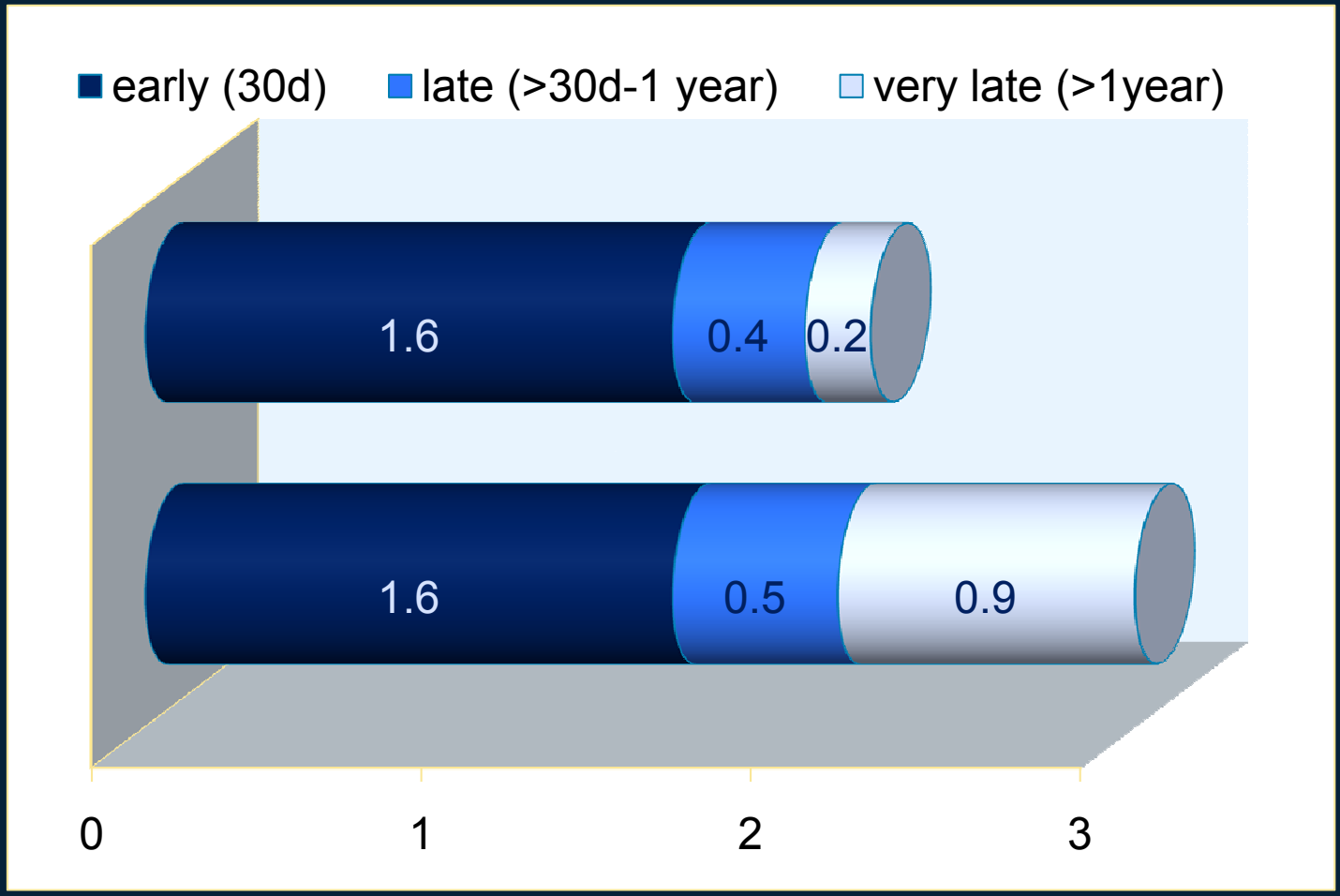
	BES	SES	*Risk Ratio (95% CI)*	P Value	P Int
Overall	132/857	157/850	0.80 (0.63 to 1.03)		ns
Diabetes mellitus					ns
Yes	53/223	45/191	1.02 (0.68 to 1.52)	0.92	
No	79/634	112/659	0.72 (0.54 to 0.96)	0.02	
Acute coronary					ns
Yes	68/470	87/473	0.77 (0.56 to 1.06)	0.11	
No	64/387	70/377	0.88 (0.63 to 1.25)	0.48	
ST-elevation MI					0.03
Yes	13/135	29/140	0.43 (0.22 to 0.83)	0.01	
No	119/722	128/710	0.91 (0.71 to 1.18)	0.48	
Left anterior					ns
Yes	59/407	71/417	0.84 (0.59 to 1.17)	0.32	
No	73/449	86/431	0.81 (0.59 to 1.11)	0.18	
Multivessel disease					ns
Yes	33/209	42/176	0.65 (0.41 to 1.03)	0.06	
No	99/648	115/674	0.89 (0.68 to 1.16)	0.39	
Off-label use					ns
Yes	116/696	135/665	0.81 (0.63 to 1.04)	0.09	
No	16/160	22/183	0.83 (0.44 to 1.59)	0.58	
De-novo lesions					ns
Yes	114/788	136/774	0.82 (0.64 to 1.05)	0.11	
No	18/68	21/74	0.92 (0.49 to 1.73)	0.79	
Small-vessel disease					ns
Yes	96/585	104/568	0.89 (0.68 to 1.18)	0.43	
No	36/271	53/280	0.68 (0.45 to 1.04)	0.08	
Long lesions					ns
Yes	46/262	52/225	0.74 (0.50 to 1.10)	0.14	
No	86/594	105/623	0.85 (0.64 to 1.13)	0.27	



Definite ST through 3 years



Definite Stent Thrombosis



Definite Stent Thrombosis %

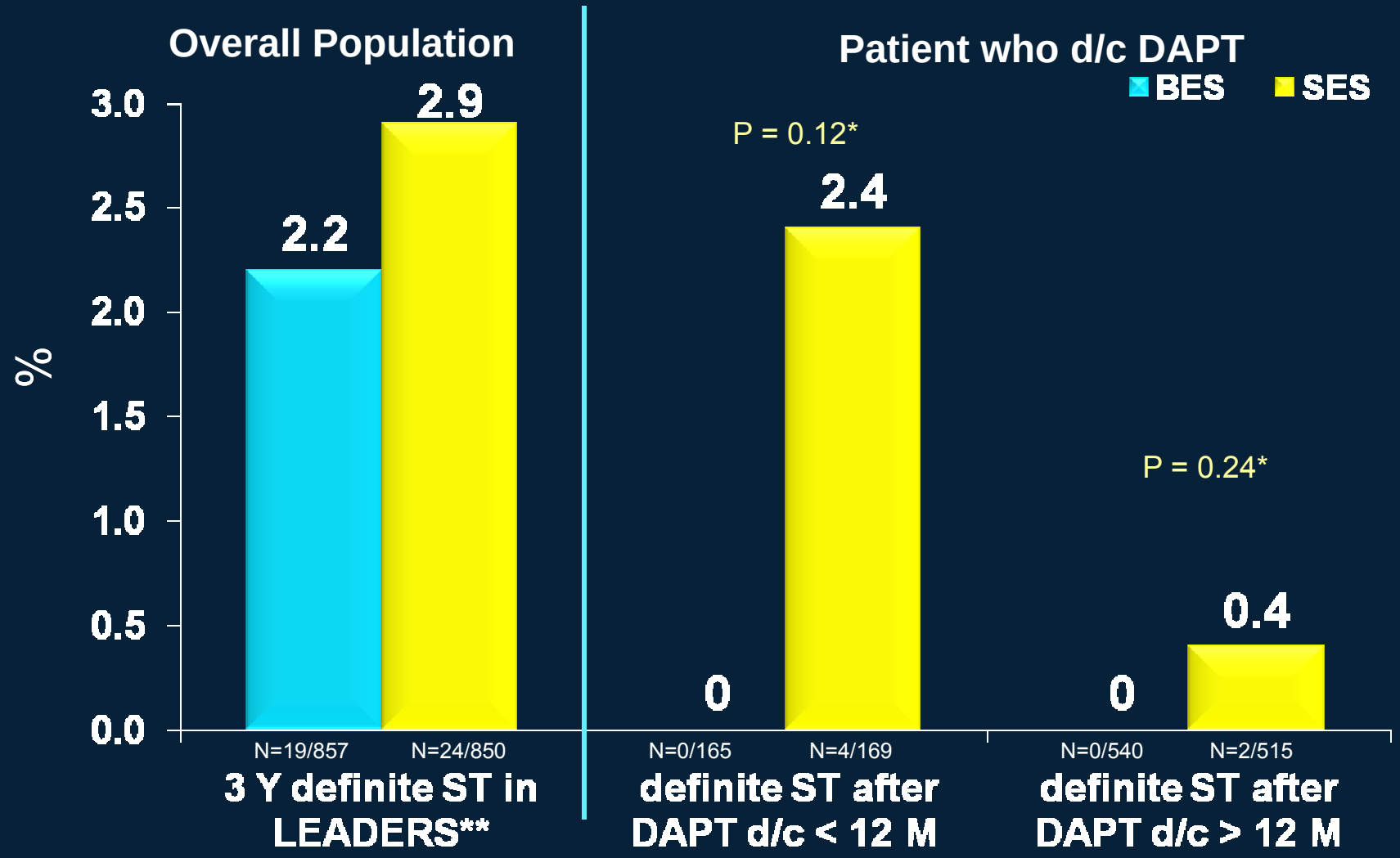
According to ARC Definition

Antiplatelet Agent Utilization

	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**
- At 36 months	94.3% (n=757)	94.8% (n=746)	**0.73**
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**
- At 36 months	19.6% (n=757)	20.4% (n=747)	**0.75**

*P values for superiority ((Fisher Exact Test)

Effect of DAPT Discontinuation



*P values for superiority (Fisher Exact Test)
** KM estimates

Summary Conclusions

1. Overall population

- *Non-inferiority of BES vs SES in an all-comers population was sustained up to 3 years*

- *In the overall LEADERS population there were similar outcomes for BES and SES with respect to MACE, Cardiac Death, MI and clinically-indicated TVR*

- *The Kaplan-Meier curves for MACE continue to diverge showing lower event rates for BES*

Summary Conclusions

2. *Subgroup analysis*

- *STEMI patients*
  - Significant reduction of MACE with BES compared to SES
    - *(9.6% vs 20.7%* $P_{sup} = 0.01$*)*

3. *Very Late Stent Thrombosis*

- *Although this was an all-comers study, definite very late stent thrombosis events were rare (BES 0.2% vs SES 0.9%* $P_{Sup} = 0.43$*)*
- *There were no VLST events in BES patients between 2 and 3 year clinical FU*
- *No VLST events in patients where a BES was implanted in native coronary arteries*