LEADERS

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

2-Year Clinical Follow-Up

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Disclosures

- Volker Klauss, MD
  - *Nothing to disclose*

Background: LEADERS at 1-Year

- **Comparison of BES with biodegradable polymer to SES with durable polymer resulted in:**
  - Non-inferior MACE rate at 9 months (primary endpoint met: 9.2% BES vs. 10.5% SES, $P_{non\text{-}inf}$ =0.003)*
  - Non-inferiority in MACE confirmed at 12 months (10.7% BES vs. 12.1% SES, $P_{non\text{-}inf}$ <0.001)
  - BES showed superior strut coverage and stent apposition at 9 months in OCT sub-analysis
  - Similar rates of stent thrombosis (ARC definition) at 12 months
- **Two year clinical outcomes have not yet been reported**

*Windecker S et al. THE LANCET 2008; 372 No 9644: 1163-1173

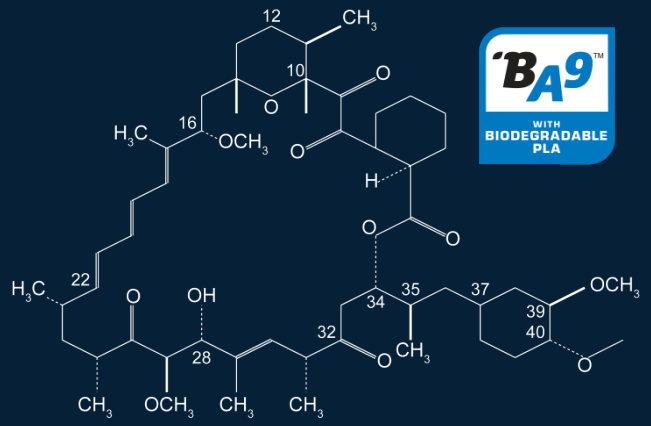
Biolimus-A9™ Eluting Stent

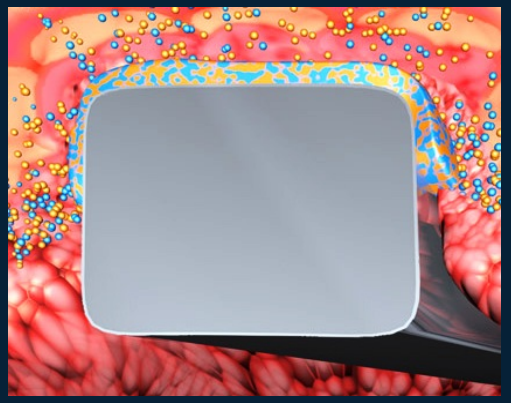
- Biolimus is a semi-synthetic sirolimus analogue with 10x higher lipophilicity and similar potency as sirolimus.

- 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.

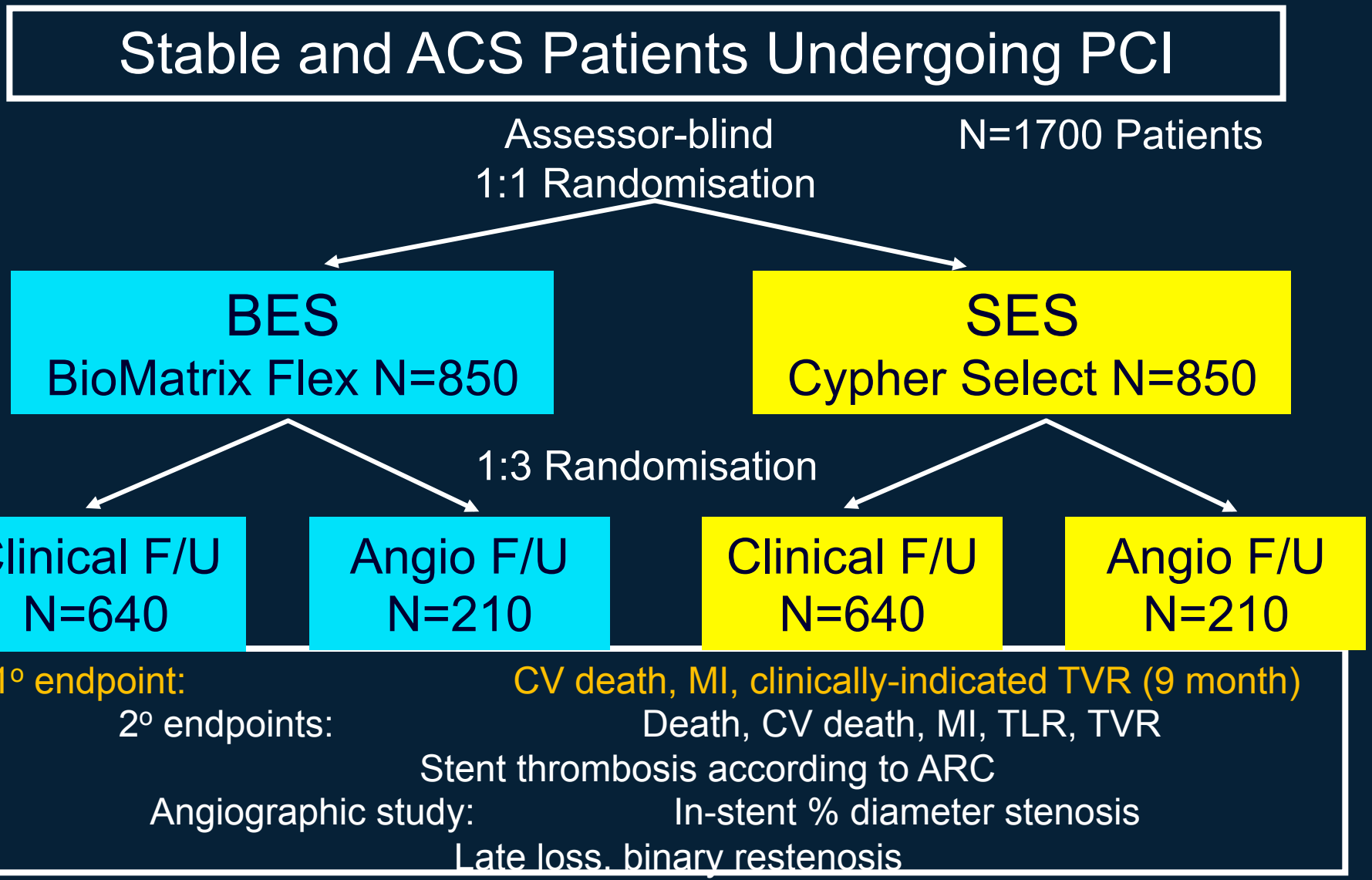
- Polylactic acid is co-released with biolimus and completely desolves into carbon dioxide and water after 6-9 months.

- The stainless steel stent platform has a strut thickness of 112 μm with a quadrature link design.





Trial Design



DAPT recommended for 12 month

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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

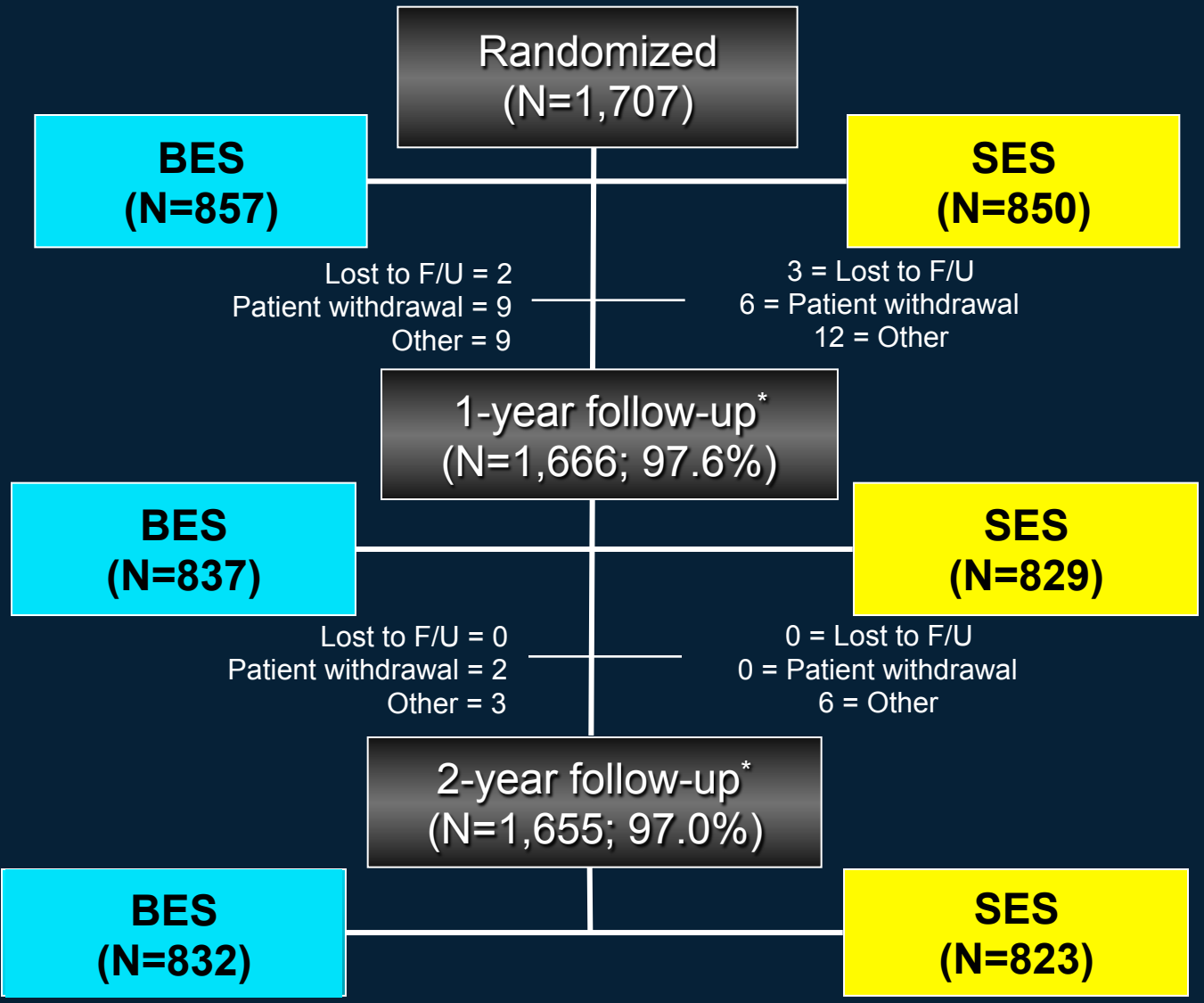
Patient Demographics

	BES	SES
	857 Patients	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	SES
	857 Patients	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



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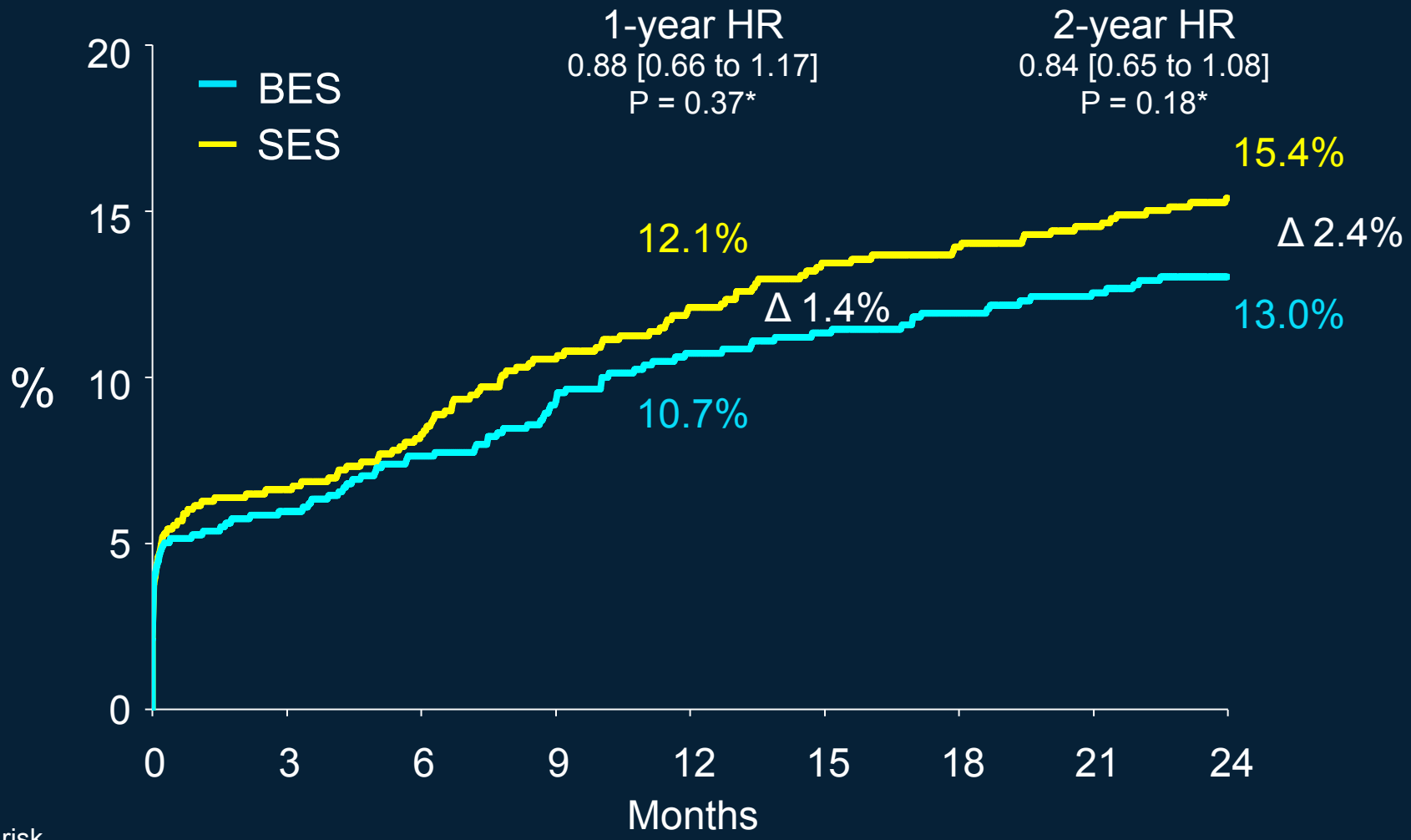
*F/U window ±28 days

MACE



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

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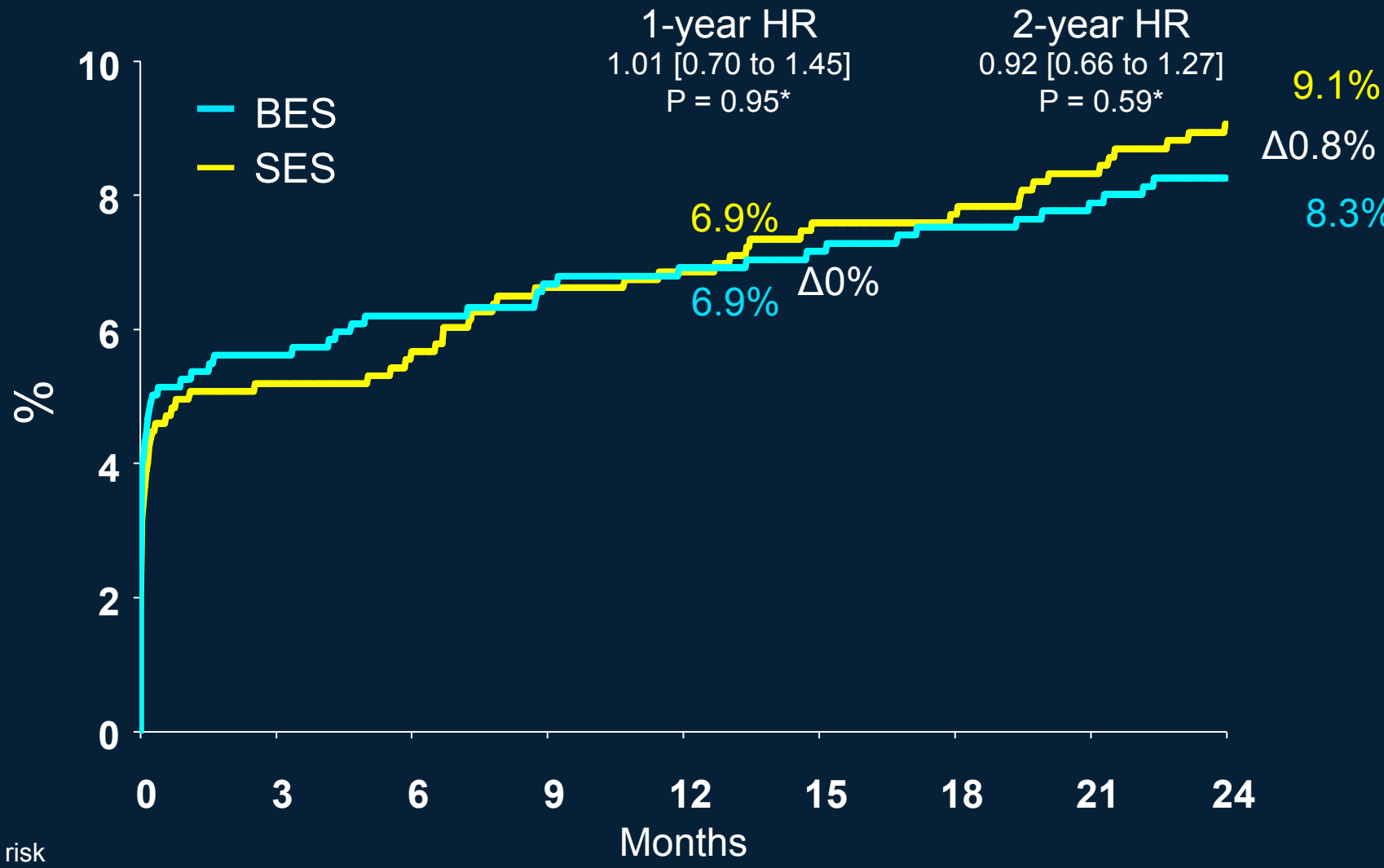
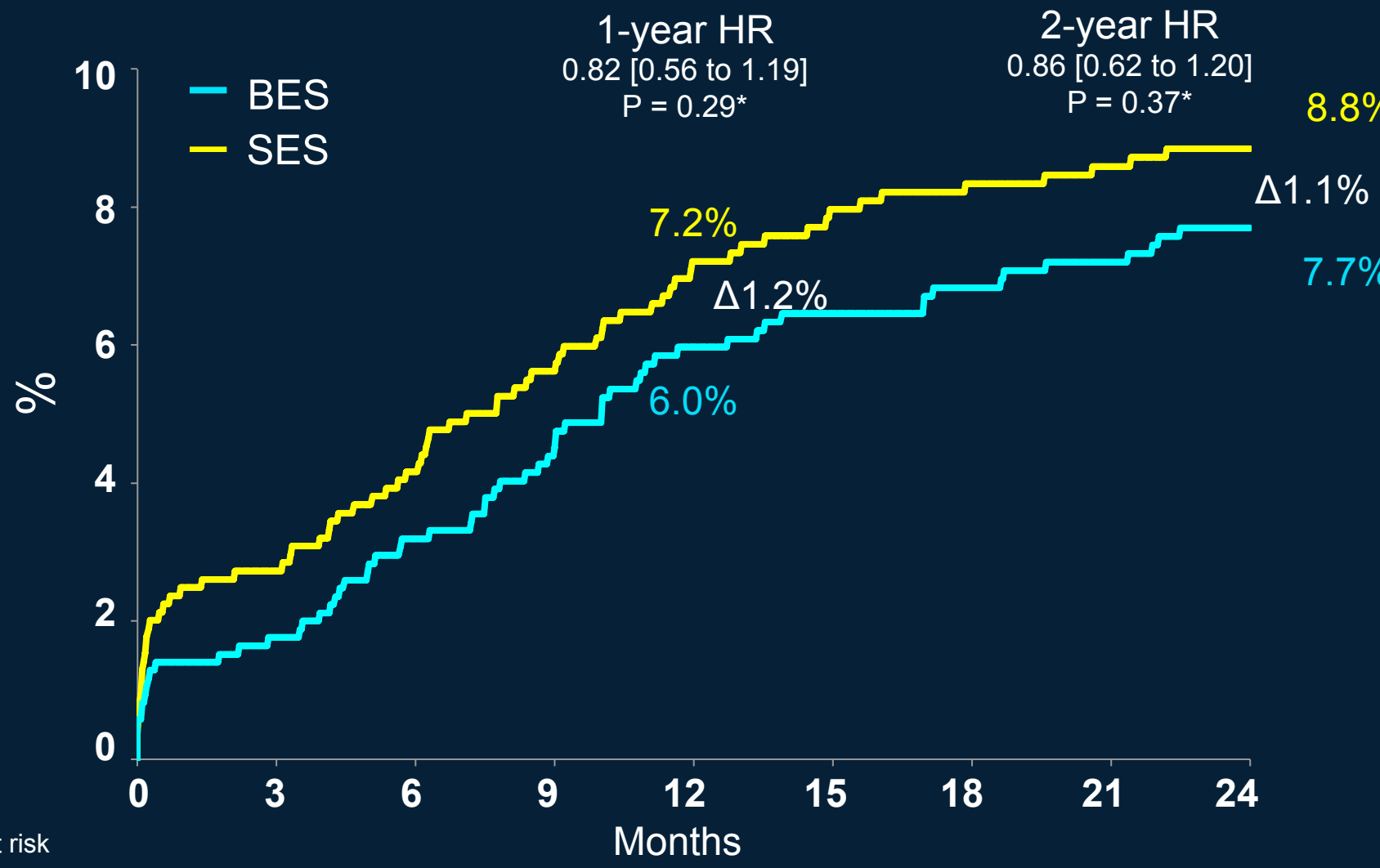
Cardiac Death or MI



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

*P values for superiority

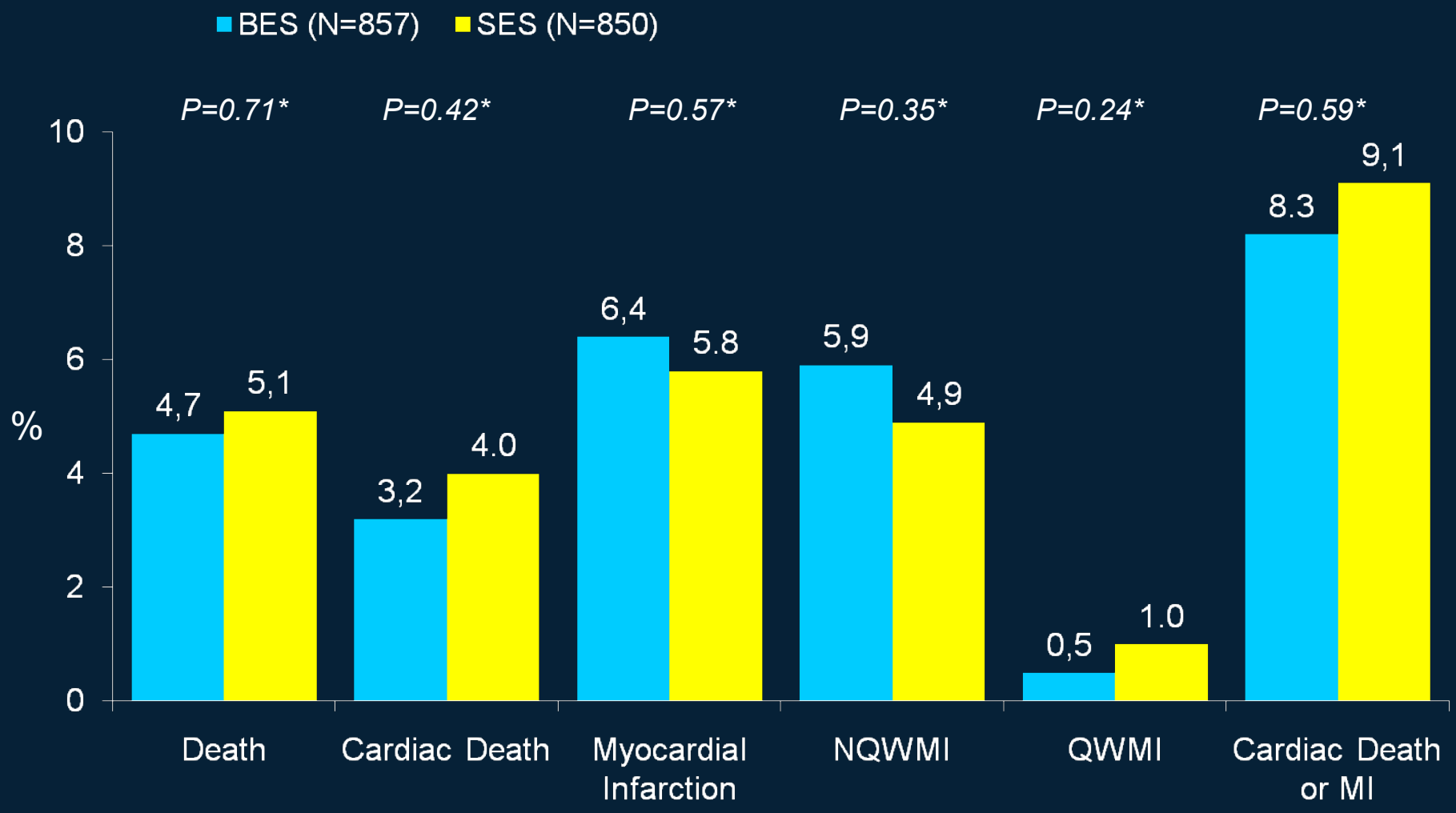
Clinically-Indicated TVR



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

*P values for superiority

2-Year Safety Endpoints



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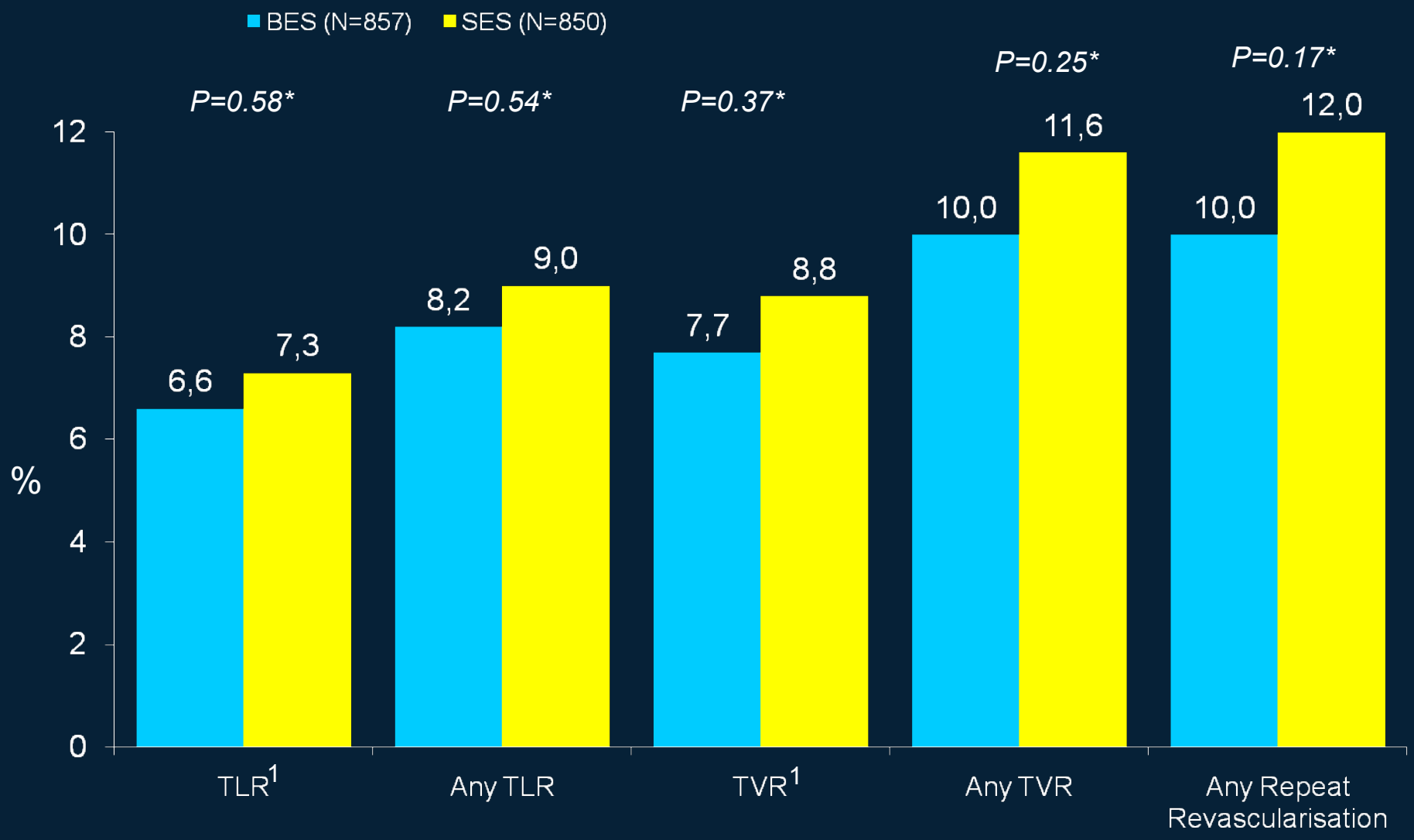
2-Year Efficacy Endpoints

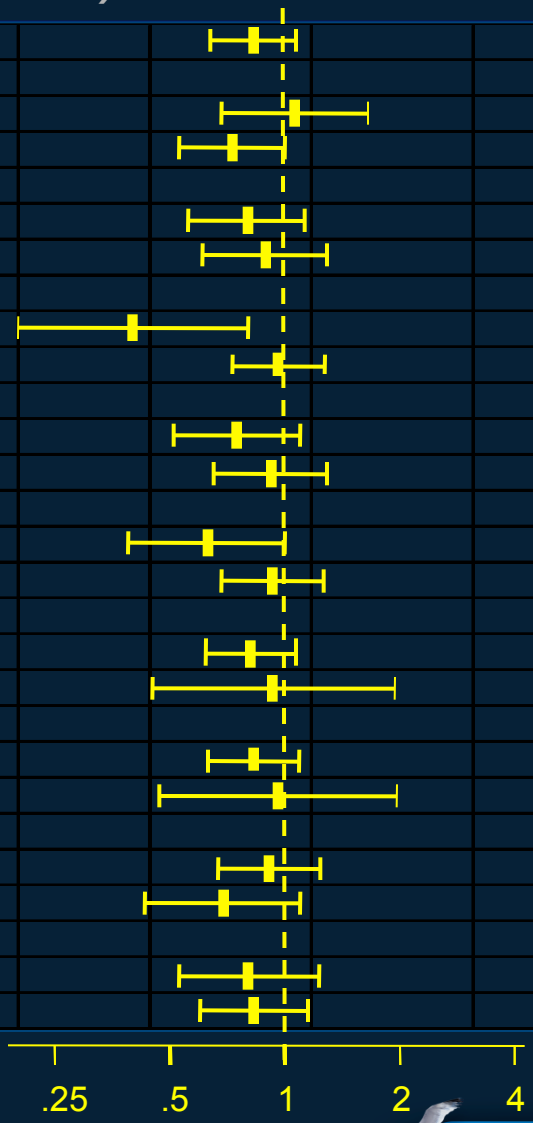


[1]Clinically Indicated

*P values for superiority

Stratified Analysis of MACE @ 2 Years

	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	70/473	0.80 (0.56 to 1.13)	0.2	
No	54/387	59/377	0.89 (0.61 to 1.29)	0.53	
ST-elevation MI					0.02
Yes	11/135	27/140	0.40 (0.20 to 0.80)	< 0.01	
No	99/722	102/710	0.96 (0.73 to 1.27)	0.76	
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	



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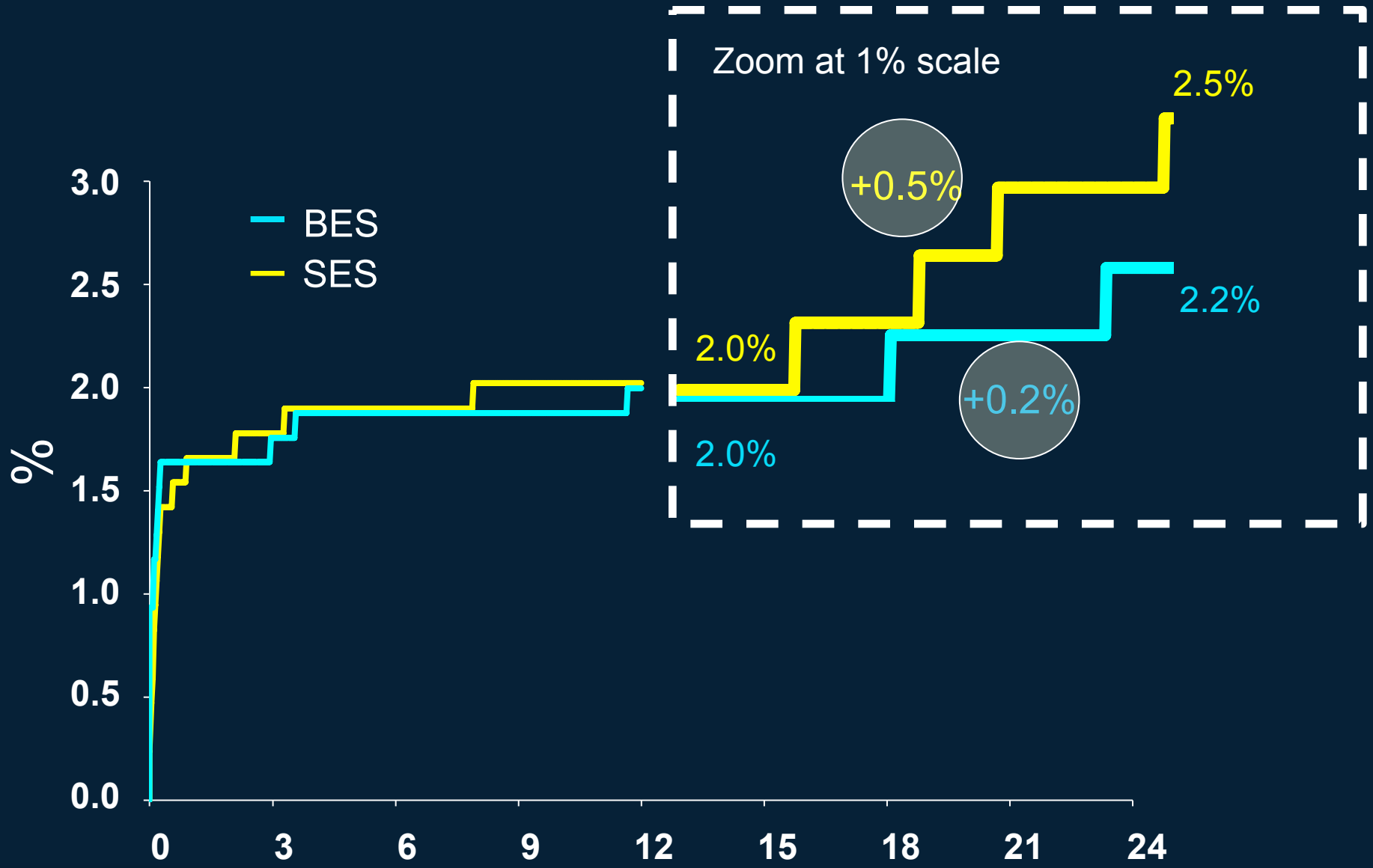
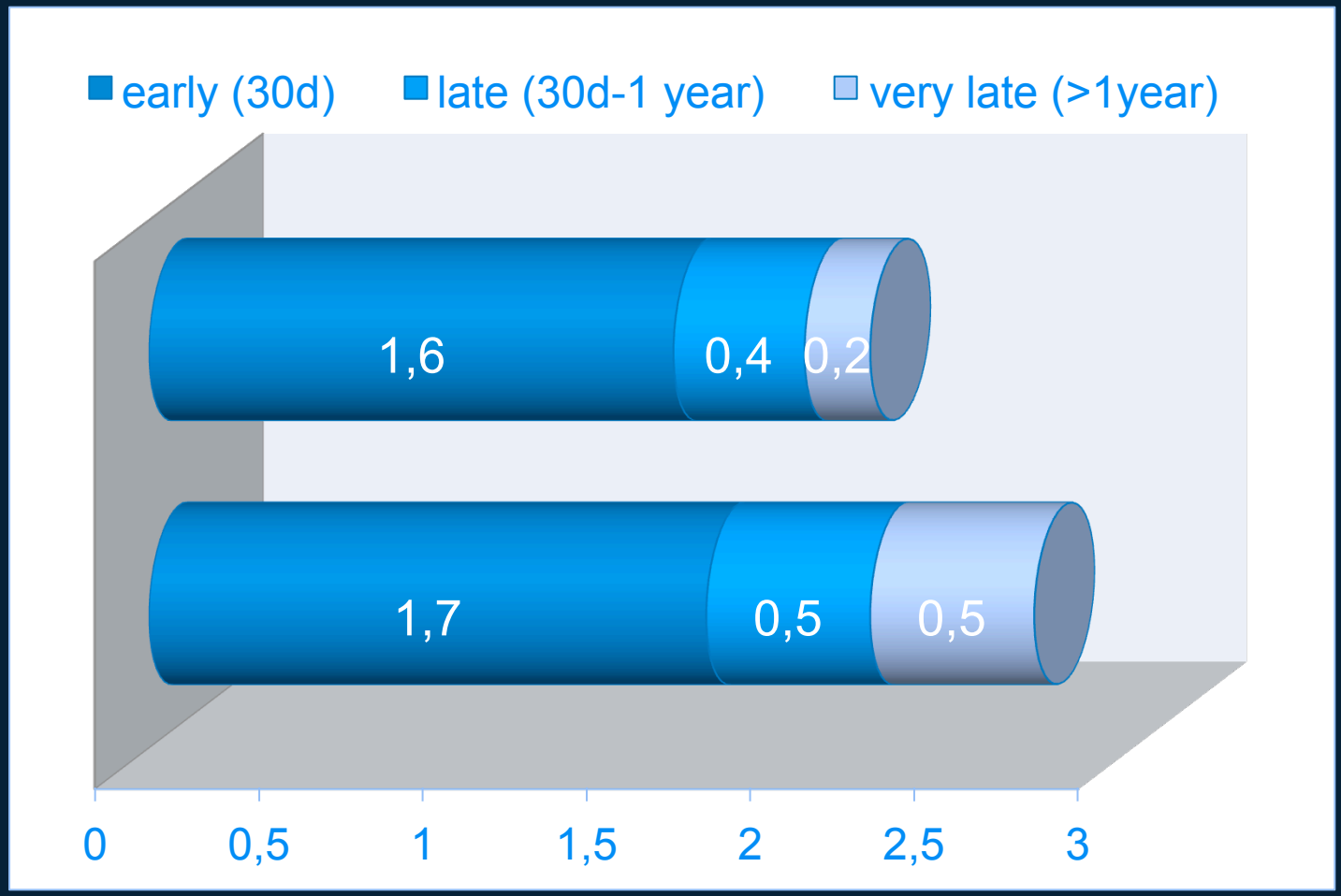
Definite ST through 2 years



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*

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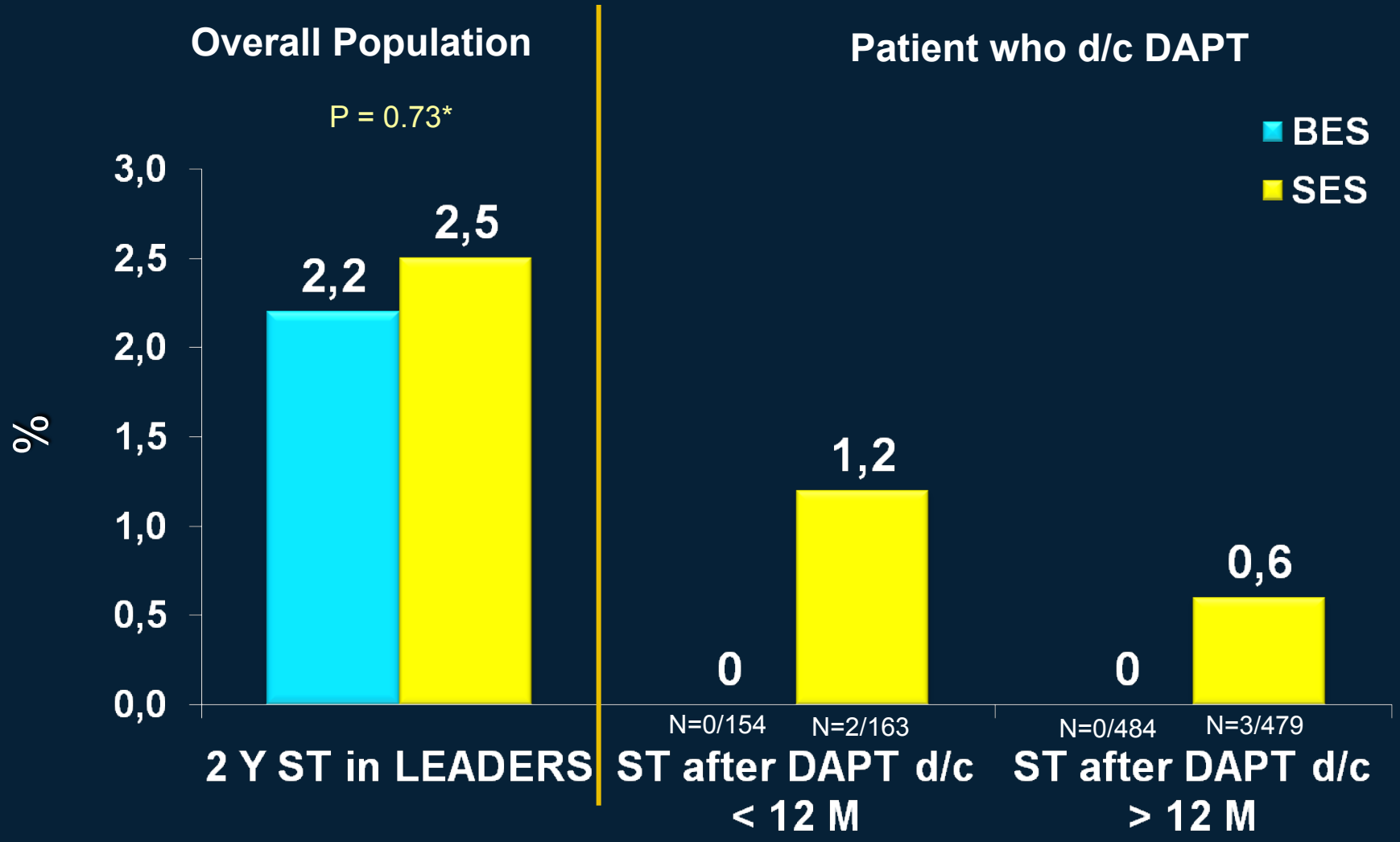
Antiplatelet Agent Utilization

	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
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

Effect of DAPT Discontinuation



*P values for superiority

Conclusions

Overall population

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

- *In the overall LEADERS population there were similar outcomes for BES and SES with respect to:*
  - MACE - BES:13% vs SES: 15.4% (P_{Sup}= 0.18)
  - Cardiac Death/MI - BES: 8.3% vs SES: 9.1% (P_{Sup}= 0.59)
  - Clinically indicated TVR – BES: 7.7% vs SES: 8.8% (P_{Sup}=0.37)

Conclusions

Subgroup analysis

- *STEMI patients*
  - improved rate of MACE with BES compared to SES
    - *(8.1% vs 19.3%* $P_{sup} < 0.01$*)*

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%* $P_{Sup} = 0.73$*)*
- *There were no VLST events in BES patients following discontinuation of DAPT*