BioMatrix Flex™

New Generation DES

Stephan Windecker

Potential conflicts of interest

Speaker's name: *Stephan Windecker*

☐ **I have the following** potential conflicts of interest to report:

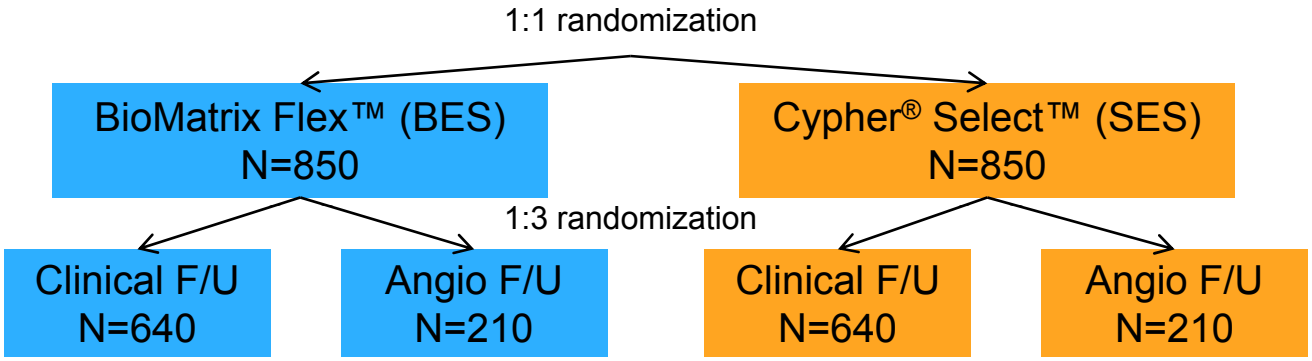
- ☐ Research contracts
- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

☐ **I do not have any potential conflict of interest**

LEADERS Trial Design

A multi-center, assessor-blind, randomized, all-comers trial

1700 stable and ACS patients in 10 European centers



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	
Inclusion criteria:	RVD: 2.25-3.5, No Limitations in # of Lesions/vessels, Lesion length
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

Endpoint Definitions

- **Pre-specified primary endpoint: MACE**
  - Composite of cardiac death, MI and clinically-indicated TVR
- **Cardiac death**
  - Any death due to immediate cardiac cause, deaths related to the procedure, unwitnessed death, and death of unknown cause
- **Myocardial infarction**
  - QWMI
    - New pathological Q waves in ≥2 contiguous leads (Minnesota code manual)
  - NQWMI
    - Peri-procedural
      - CK> 2x ULN with positive CK-MB or troponin levels or in absence of CK-MB > 3x ULN
    - Peri-procedural in setting of evolving MI
      - New CK elevation of CK > 2x ULN or rise of CK >50% above previous nadir level
- **TVR**
  - Any repeat PCI or CABG for any segment within the entire major coronary vessel proximal and distal to a target lesion, including upstream and downstream branches.
  - Clinically-indicated
    - QCA determined stenosis of at least 50% in the presence of symptoms, or
    - QCA determined stenosis of at least 70% irrespective of ischemic signs or symptoms

Statistical Analysis

- Primary Endpoint – Non-inferiority Analysis

Hypothesis for sample size calculations	Expected rate @ 9 mo
Primary Clinical endpoint (MACE)	8%
Non-inferiority margin	4%
One-sided α	0.05
Power	90%
Sample size	1700

- Subgroup Analysis

Pre-specified	Post-hoc
➢Diabetes ➢Acute coronary syndrome ➢De-novo lesions	➢STEMI ➢Multi-vessel ➢Small vessel (RVD ≤ 2.75 mm) ➢Long lesions (≥ 20 mm) ➢Bifurcations ➢Off-label use

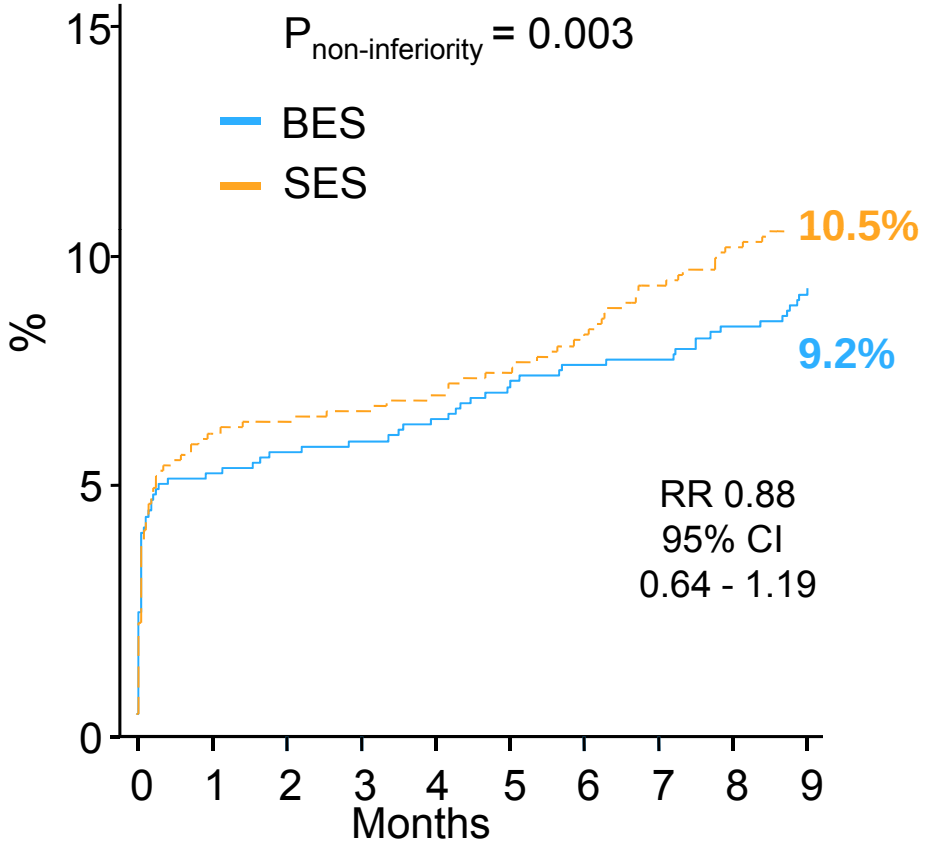
Role of Funding Source (Biosensors Int.)

- Contributed to the study design
- **No role in data collection, data monitoring, data analysis, data interpretation, or writing of the report.**
  - Independent study monitors (D-Target, CH)
  - Data stored in a central database (KIKA Medical, Fr), maintained by a contract research organization (Cardialysis, NL) in collaboration with an academic clinical trials unit (CTU Bern, CH)
  - Coronary angiograms assessed at an independent core laboratory (Cardialysis, NL), assessors blinded
  - Adjudication by a clinical event committee (assessors blinded)
  - Independent data and safety monitoring board
- **Independent data analysis by CTU Bern, with full access of data by PI**

LEADERS Results @ 9 mo

Windecker et al., Lancet 2008

Primary Endpoint
MACE* @ 9 month



* MACE: a composite endpoint of cardiac death, MI and ci-TVR

Angiographic Endpoints

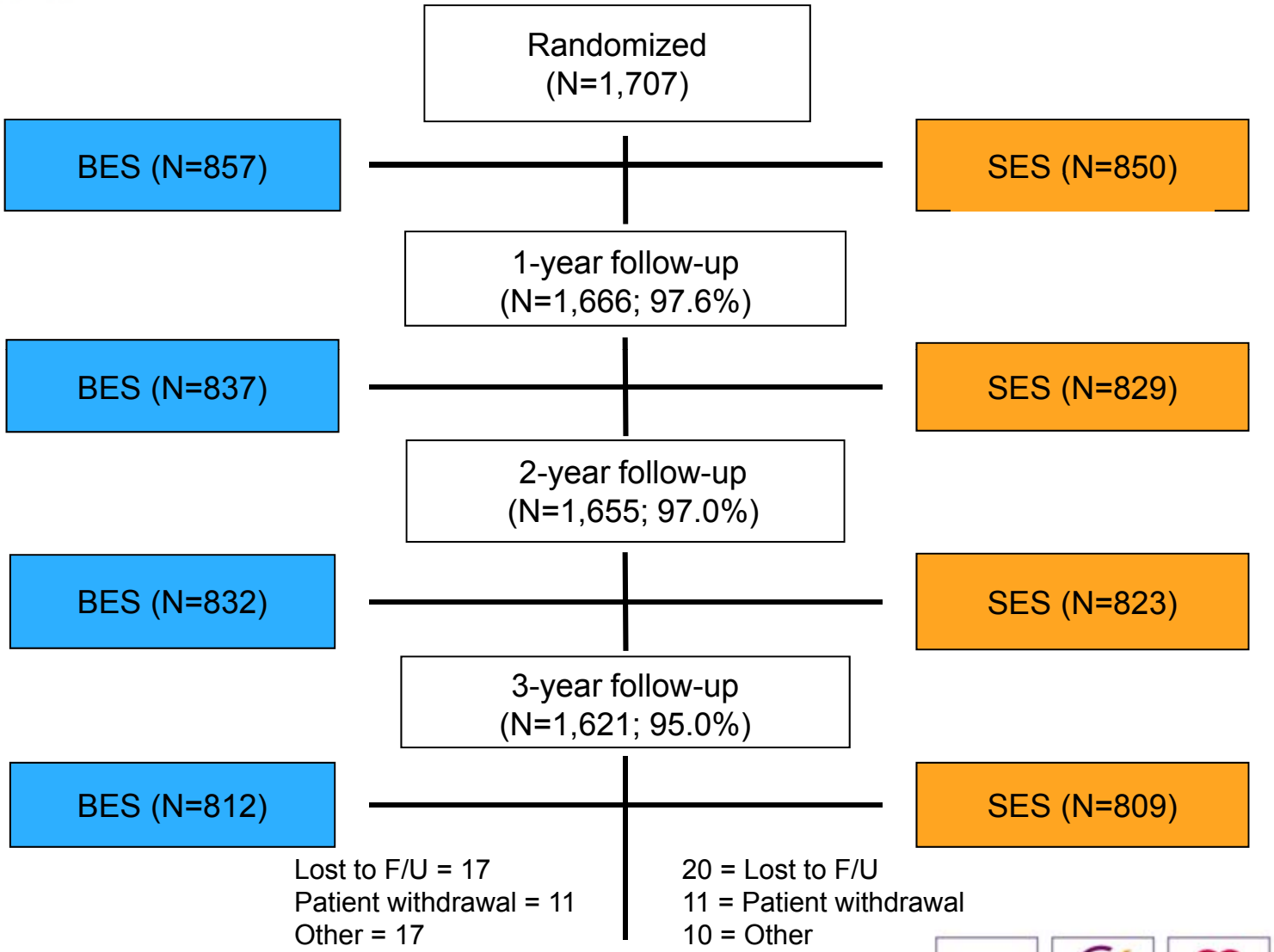
	BES 255 lesions	SES 233 lesions	P
MLD†			
in-stent (mm)	2.23 ± 0.64	2.11 ± 0.70	0.08
in-segment (mm)	2.01 ± 0.59	1.87 ± 0.64	0.03
Diameter stenosis†			
in-stent (%)	20.9 ± 17.5	23.3 ± 19.6	0.26
in-segment (%)	27.1 ± 16.4	29.9 ± 18.5	0.14
Late lumen loss‡			
in-stent (mm)	0.13 ± 0.46	0.19 ± 0.50	0.34
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

Data are mean± SD or I% (lesions/number assessed). Angiographic assessments were not possible in all lesions, therefore the number of lesions differs according to outcome

† 253 lesions assessed in the BES group and 231 in the SES group

‡ 248 lesions assessed in the BES group and 229 in the SES group

Patient Flow - Clinical



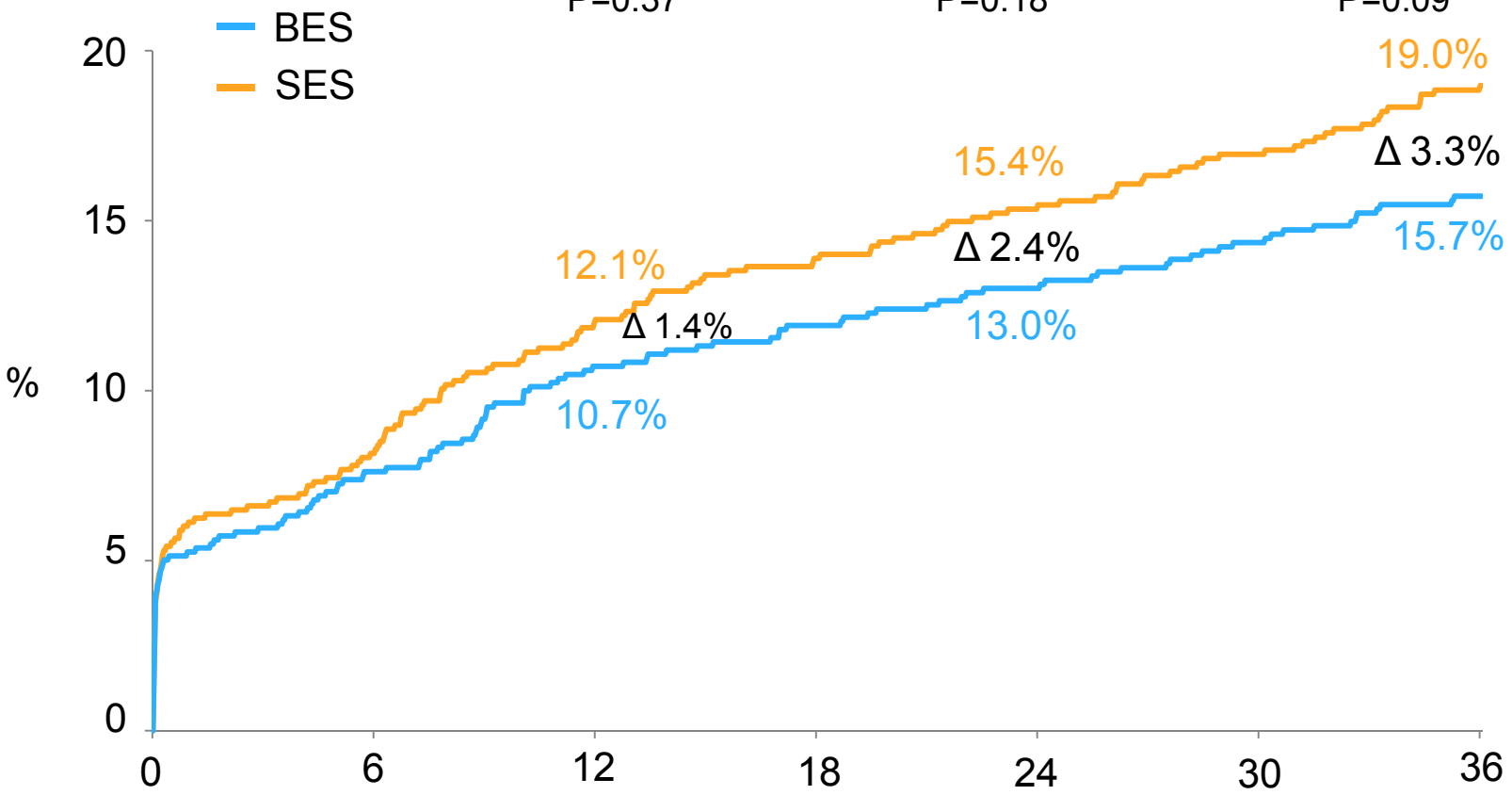
Serruys, P. W., oral presentation ,TCT 2010

MACE (CV death, MI, CI-TVR)

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*

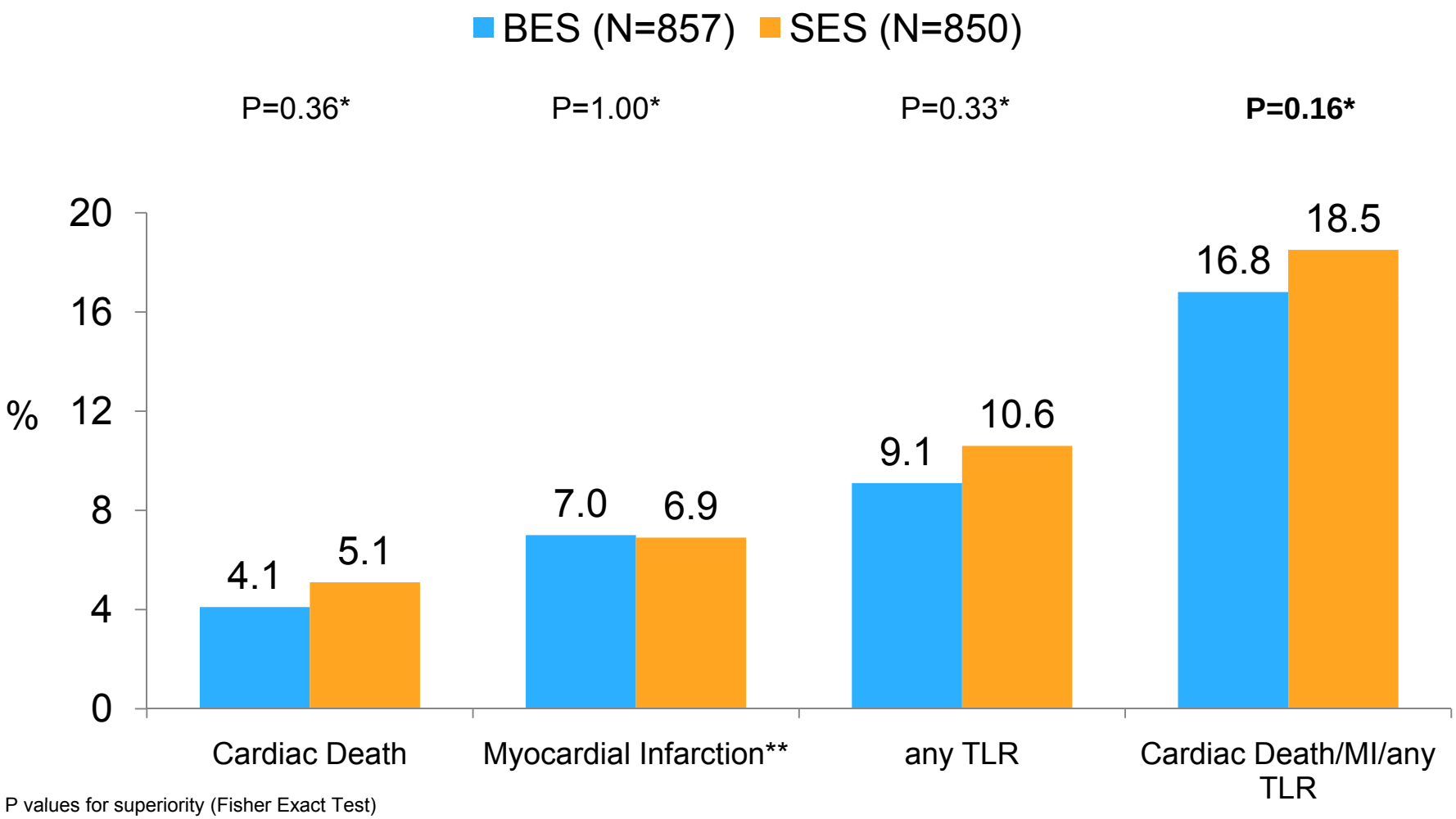
3-year HR
0.82 [0.65 to 1.03]
P=0.09*



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
Serruys, P. W., oral presentation ,TCT 2010

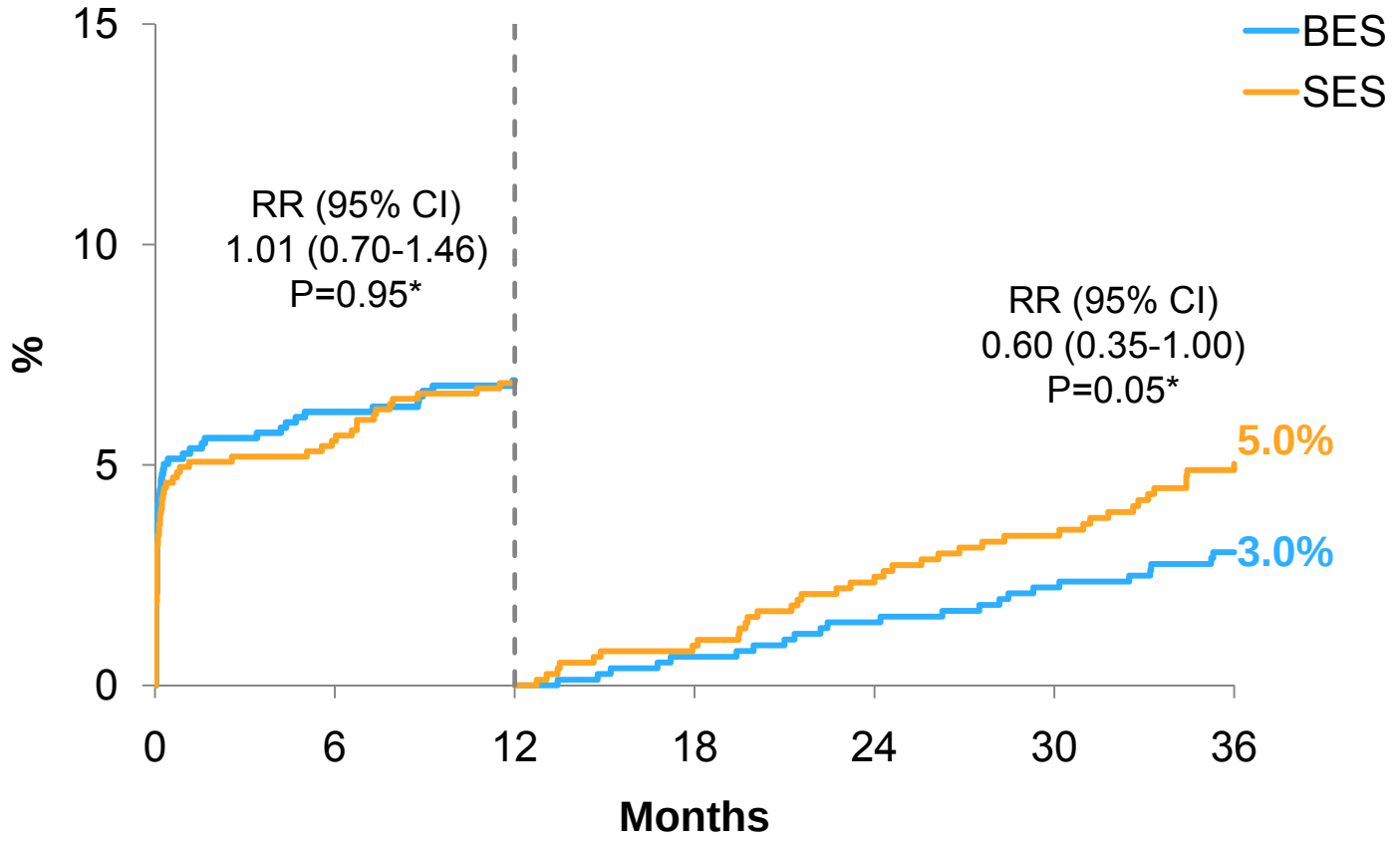
Device-Oriented 3-Year Outcomes



* P values for superiority (Fisher Exact Test)
**MI defined with the electrocardiographic criteria of the Minnesota code manual or as a measurement of Creatine Kinase concentrations> 2x normal with positive concentrations of CK-MB or troponin I or T

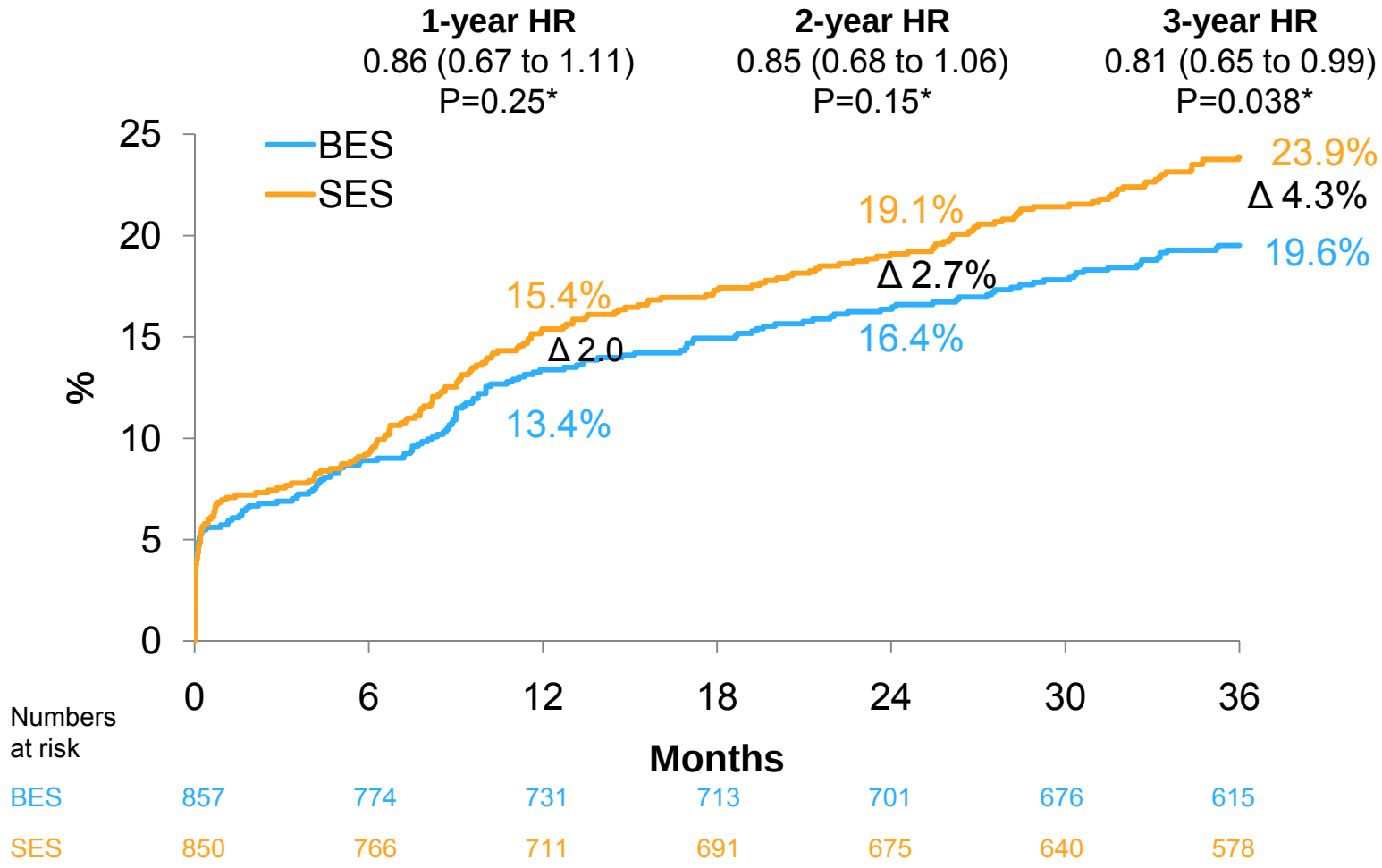
ARC defined device-oriented components include MI (not clearly attributable to a non-target vessel) which is not available in the LEADERS study. MIs indicated above are all MIs. The same holds for the composite endpoint.

Cardiac Death/MI Landmark Analysis



*P values for superiority

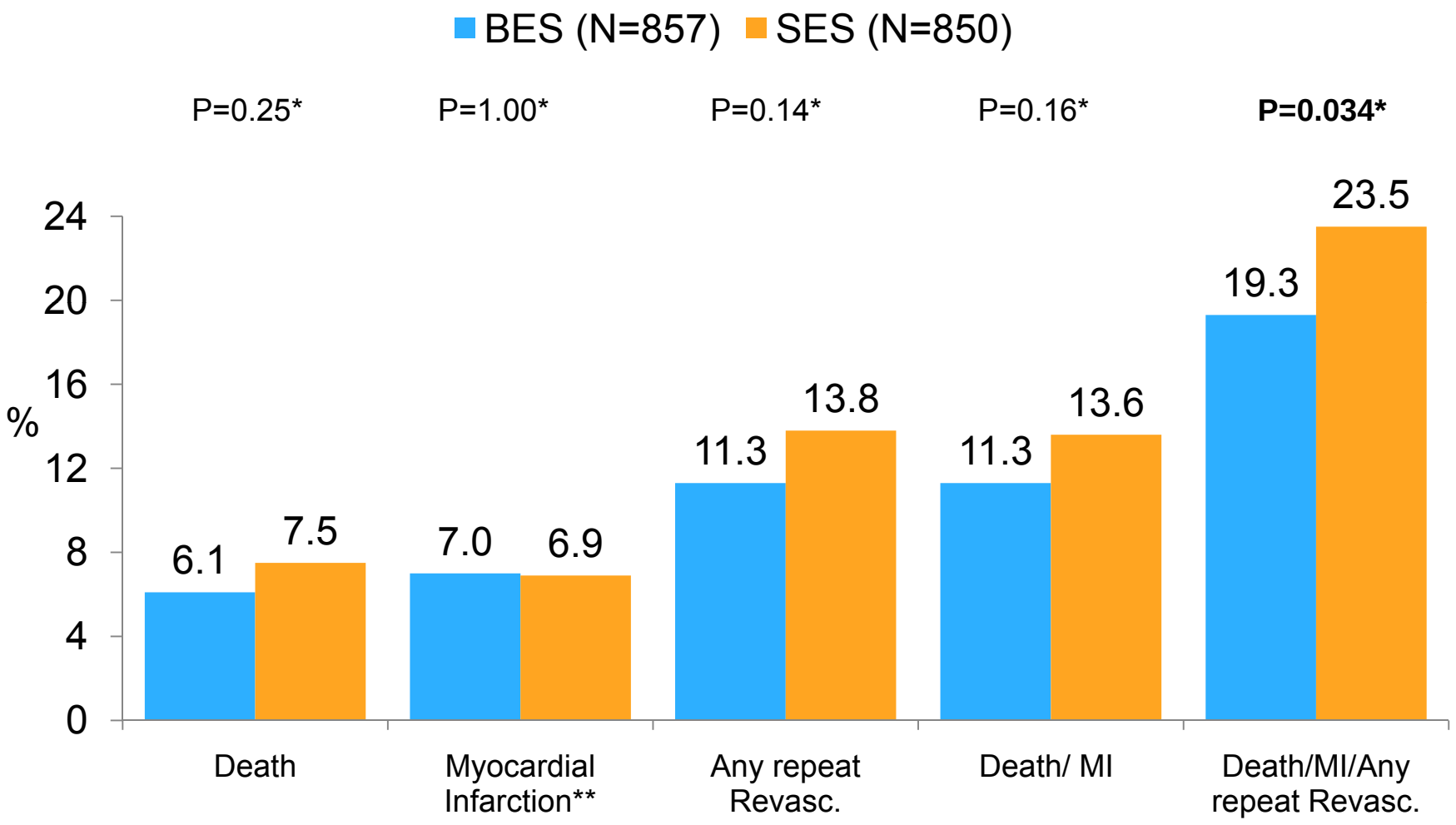
Patient-oriented Outcomes
Death/ MI**/ Any Revascularisation



Numbers at risk							
BES	857	774	731	713	701	676	615
SES	850	766	711	691	675	640	578

*P values for superiority
** MI defined with the electrocardiographic criteria of the Minnesota code manual or as a measurement of Creatine Kinase concentrations> 2x normal with positive concentrations of CK-MB or troponin I or T

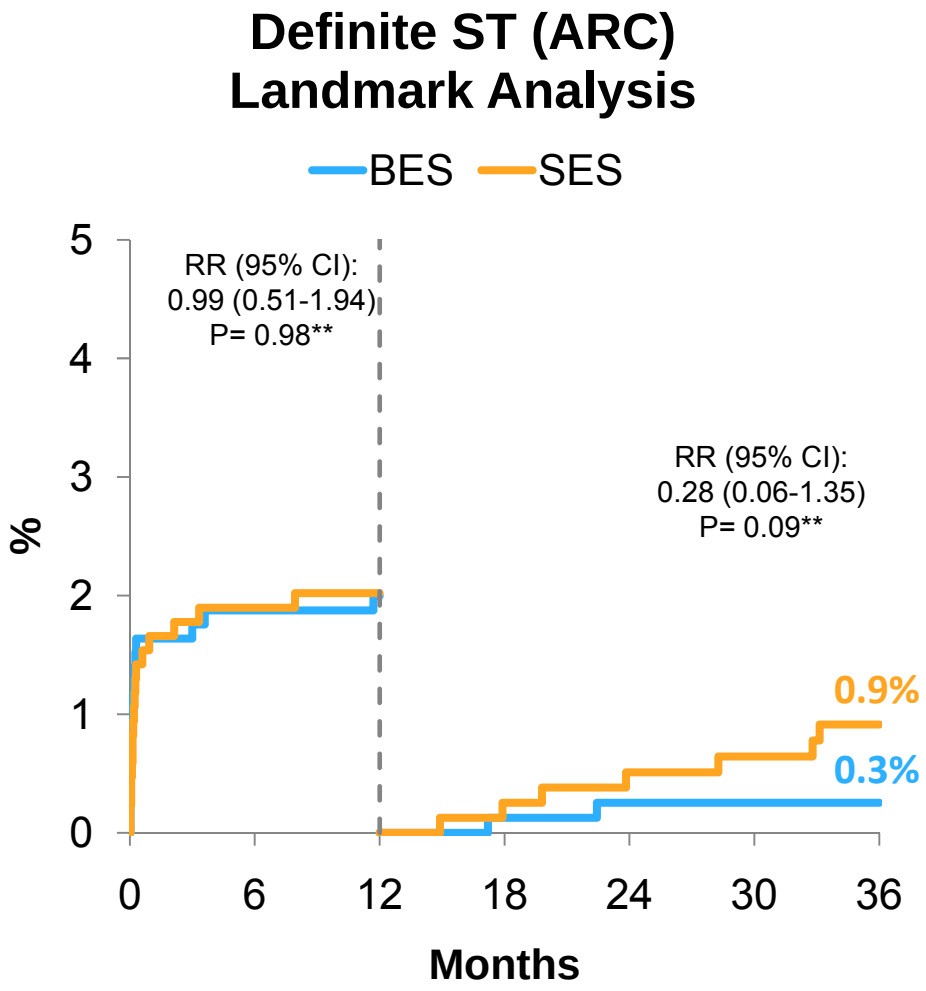
Patient-Oriented 3-Year Outcomes



* P values for superiority (Fisher Exact Test)
**MI defined with the electrocardiographic criteria of the Minnesota code manual or as a measurement of Creatine Kinase concentrations> 2x normal with positive concentrations of CK-MB or troponin I or T

Stent Thrombosis*

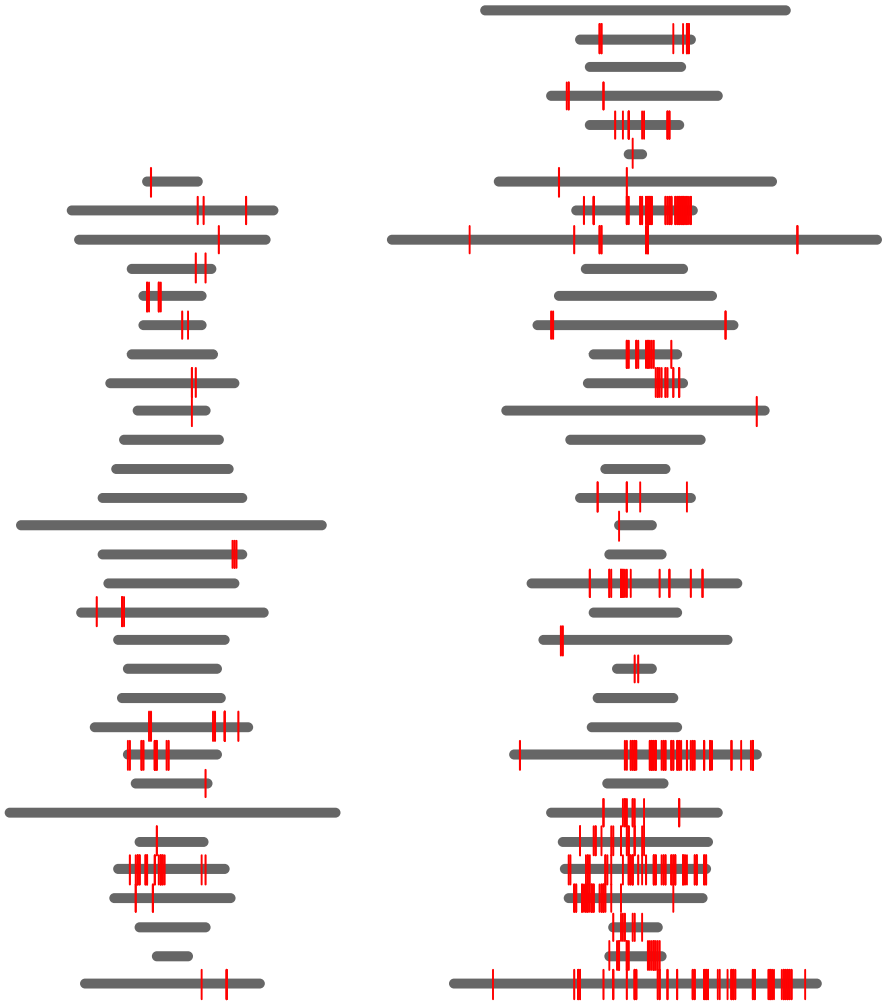
	BES (%)	SES (%)	P-value
Definite ST			
Early (0-30 days) [1]	1.6	1.6	0.98
Late (>30 days-1 y) [2]	0.4	0.5	0.69
Very late (>1-3 ys)	0.2 [3]	0.9 [3]	0.11
Probable ST			
Early (0-30 days) [1]	0.6	0.2	0.26
Late (>30 days-1 y) [2]	0.2	0	0.16
Very late (>1-3 ys) [3]	0.1 [3]	0 [3]	1.00
Possible ST			
Early (0-30 days) [1]	0	0	---
Late (>30 days-1 y) [2]	0.8	1.1	0.60
Very late (>1-3 ys)	1.6 [3]	2.0 [3]	0.59



*Stent thrombosis defined by ARC (Cutlip et al,. *Circulation, 2007)*
*** P-values for superiority*
1 : Windecker et al., Lancet, 2008. 372(9644): p. 1163-73
2: Garg, S., et al., *EuroIntervention, 2010. 6(2): p. 233-9.*
3. Serruys, oral presentation, TCT 2011

LEADERS - OCT Substudy

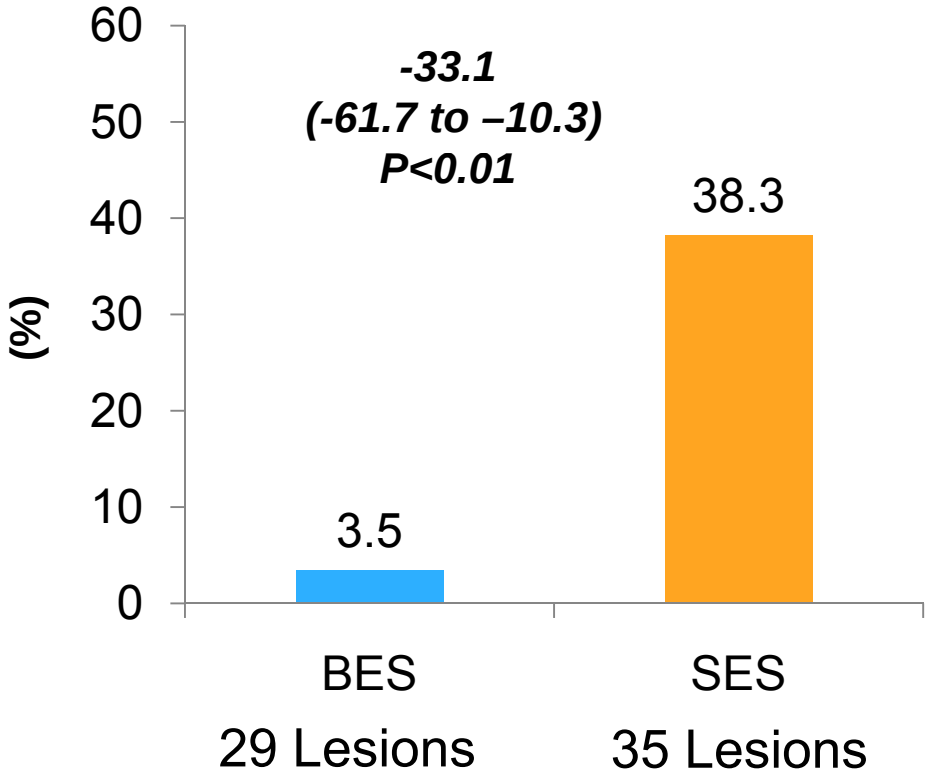
Barlis P et al. Eur Heart J 2010



BES
N=29

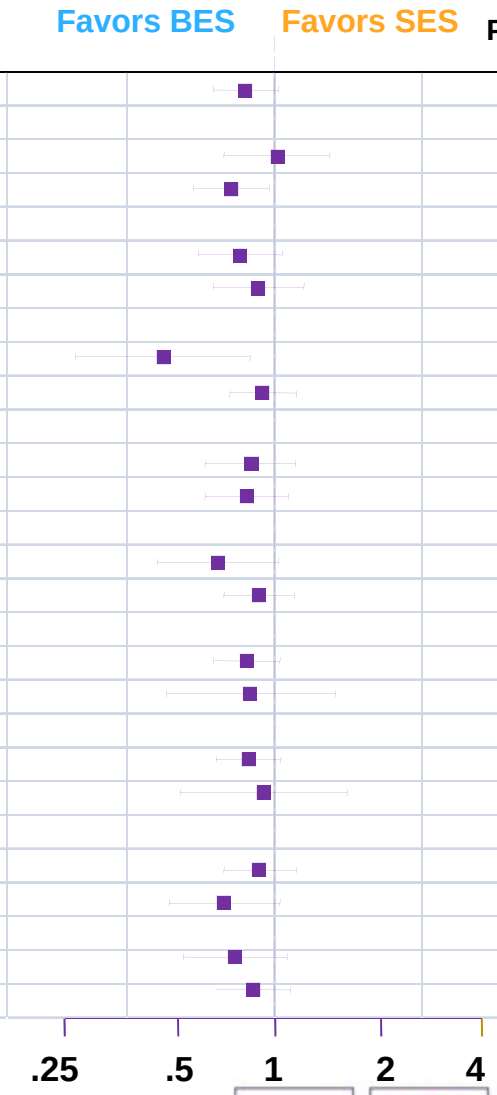
SES
N=35

Lesions With At Least 5% Uncovered Struts



Stratified Analysis of MACE

	BES	SES	Risk Ratio (95% CI)	P	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	



*P values for superiority

Serruys, P. W., oral presentation ,TCT 2010

Summary & Conclusions

- In an all-comers population, non-inferiority of BES vs SES was sustained for the primary endpoint of cardiac death/MI/ci-TVR up to 3 years
- Use of BES was associated with a lower risk in the patient-related composite endpoint of death/MI/any repeat revascularization at 3 years
- Use of BES in the subgroup of STEMI patients was associated with a lower risk in the primary endpoint at 3 years
- Although there was no difference in the overall risk of definite stent thrombosis, landmark analysis between 1 and 3 years indicates a trend towards a lower risk of this adverse event.

Ongoing Studies With BioMatrix Family Stents

Study Name	Patient Population	Study Stents	Number of Patients
COMFORTABLE AMI	STEMI	BioMatrix vs Bare Metal Stent	1,100
Team Groupo Registry	Diabetics	BioMatrix	300
EuroCTO	CTO	PCI w BioMatrix Flex vs Medical Therapy	1,200
NOBLE	LM	BioMatrix Flex vs Surgery	
Global LEADERS	All comers	BioMatrix Flex vs EES	>10,000

Thank you!