Randomized comparison of a novel, ultrathin cobalt-chromium biodegradable polymer sirolimus-eluting stent with a thin strut durable polymer everolimus-eluting stent for percutaneous coronary revascularization – final 5 year outcomes

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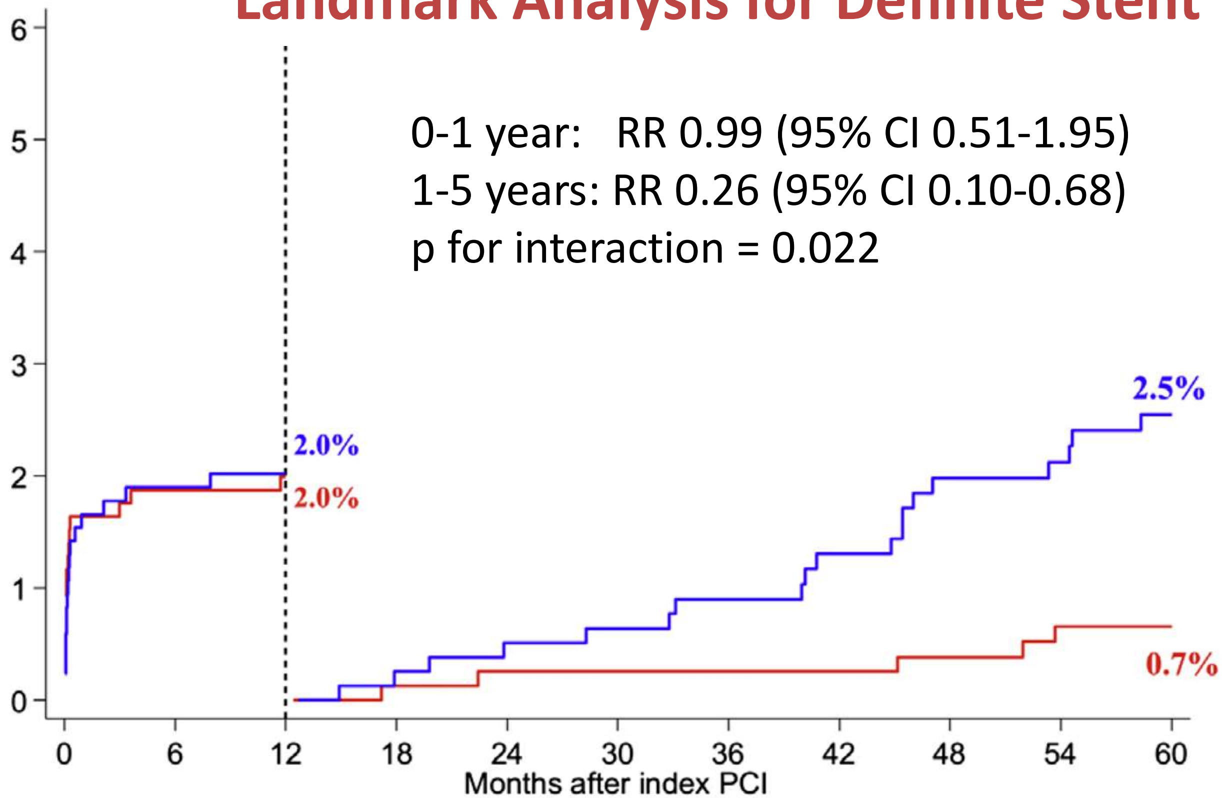
ESC Congress
Munich 2018

BIODEGRADABLE POLYMERS IN EARLIER GENERATION DES

Landmark Analysis for Definite Stent Thrombosis



Safety benefit of BP BES vs DP SES related to reduction in very late stent thrombosis (1-5 years)

WS1

LEADERS trial

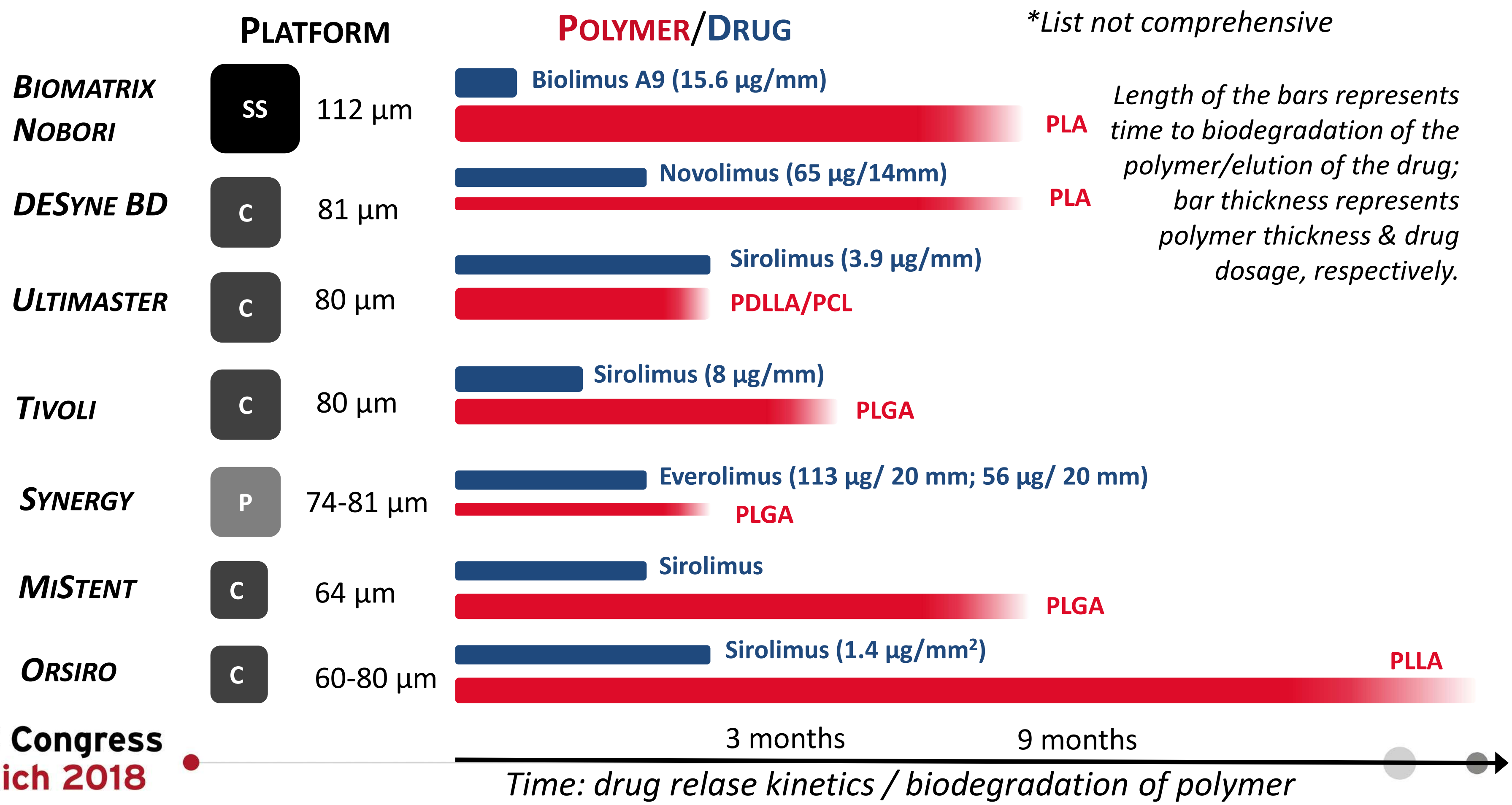
Serruys PW et al, JACC Interv 2013

Slide 2

WS1 Consider Lancet publication by Giulio which also shows impact on ST related events on CV death and MI

Windecker, Stephan, 8/2/2018

Biodegradable polymer Drug-Eluting Stents



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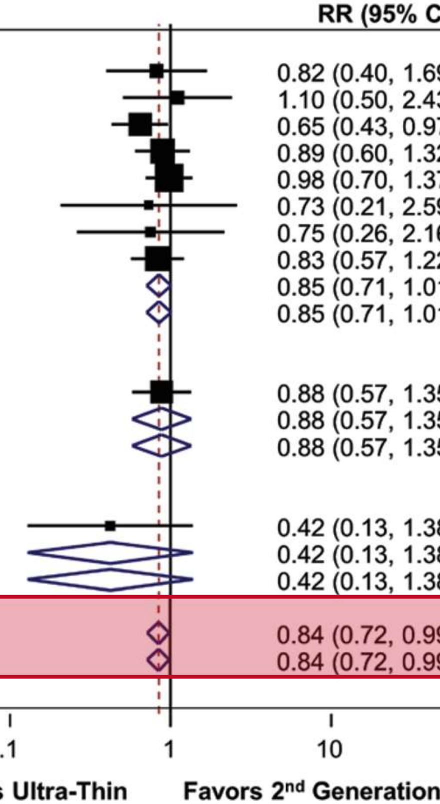
ULTRATHIN STRUT (≤65 μM) VERSUS THIN STRUT DES

Meta-Analysis of 10 RCTs including 11,658 patients

16% reduction in TLF (RR=0.84; 95% CI 0.72-0.99) driven by lower rate of MI (RR=0.80; 95% CI 0.65-0.99).

Bangalore S et al, Circulation 2018

Study	Ultra-Thin Events	Ultra-Thin N	2nd Generation Events	2nd Generation N	RR (95% CI)	% Weight (D+L)
Orsiro						
BIOFLOW II	19	298	12	154	0.82 (0.40, 1.69)	4.83
BIOFLOW IV	20	354	9	176	1.10 (0.50, 2.43)	4.08
BIOFLOW V	52	884	41	450	0.65 (0.43, 0.97)	15.07
BIORESORT	47	1169	53	1173	0.89 (0.60, 1.32)	16.37
BIOSCIENCE	69	1063	70	1056	0.98 (0.70, 1.37)	22.84
ORIENT	6	250	4	122	0.73 (0.21, 2.59)	1.58
PRISON IV	6	165	8	165	0.75 (0.26, 2.16)	2.25
SORT OUT VII	48	1261	58	1264	0.83 (0.57, 1.22)	17.26
D+L Subtotal (I-squared = 0.0%, p = 0.881)					0.85 (0.71, 1.01)	84.29
I-V Subtotal					0.85 (0.71, 1.01)	
MiStent						
DESSOLVE-III	40	703	45	695	0.88 (0.57, 1.35)	13.92
D+L Subtotal (I-squared = NA, p = NA)					0.88 (0.57, 1.35)	13.92
I-V Subtotal					0.88 (0.57, 1.35)	
BioMime						
merit-V	5	170	6	86	0.42 (0.13, 1.38)	1.79
D+L Subtotal (I-squared = NA, p = NA)					0.42 (0.13, 1.38)	1.79
I-V Subtotal					0.42 (0.13, 1.38)	
All Stents						
D+L Overall (I-squared = 0.0%, p = 0.884)					0.84 (0.72, 0.99)	100.00
I-V Overall					0.84 (0.72, 0.99)	



Stent Platforms

	Orsiro BP-SES	Xience – DP EES
Platform	Cobalt-Chromium, L-605 60 µm (≤3.0 mm) 80 µm (>3.0 mm)	Cobalt-Chromium, L-605 81 µm
Polymer	Silicon carbide layer **Biodegradable** PLLA: poly-L-lactic acid	**Durable** PBMA/PVDF-HFP
Drug	**Sirolimus** (1.4 µg/mm²)	**Everolimus** (1.0 µg/mm²)

Patient Flow Chart

2119 patients included

1063 patients allocated to **BP SES** (1594 lesions)

44 lost to follow up
25 refused follow-up

994 follow up information for clinical primary endpoint available up to 5 years
855 followed up and alive
139 followed up and died

1063 analysed for primary clinical endpoint
69 censored at time-point of refusal or loss to follow-up

1056 patients allocated to **DP EES** (1545 lesions)

27 lost to follow up
15 refused follow-up

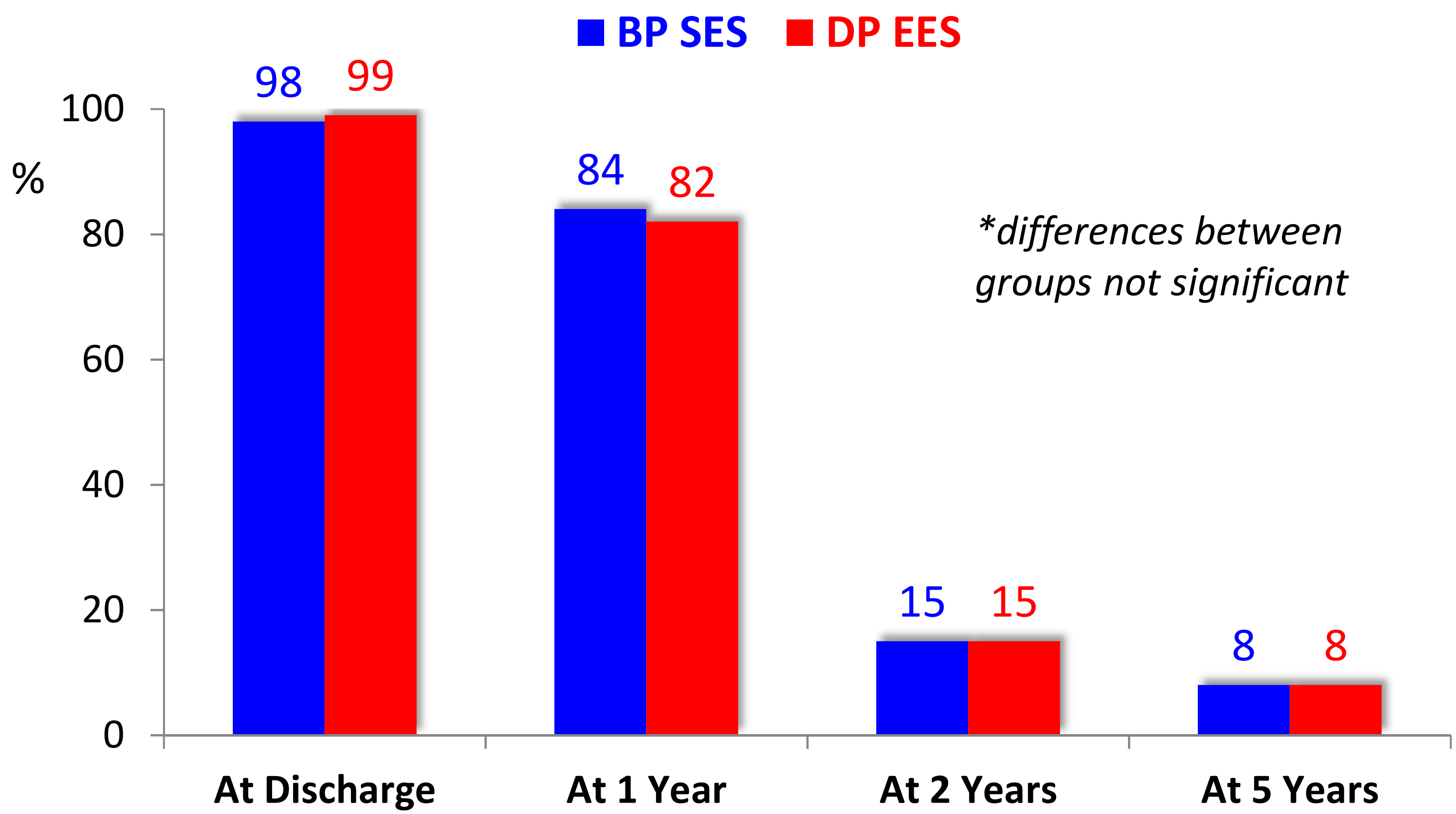
1014 follow up information for clinical primary endpoint available up to 5 years
909 followed up and alive
105 followed up and died

1056 analysed for primary clinical endpoint
42 censored at time-point of refusal or loss to follow-up

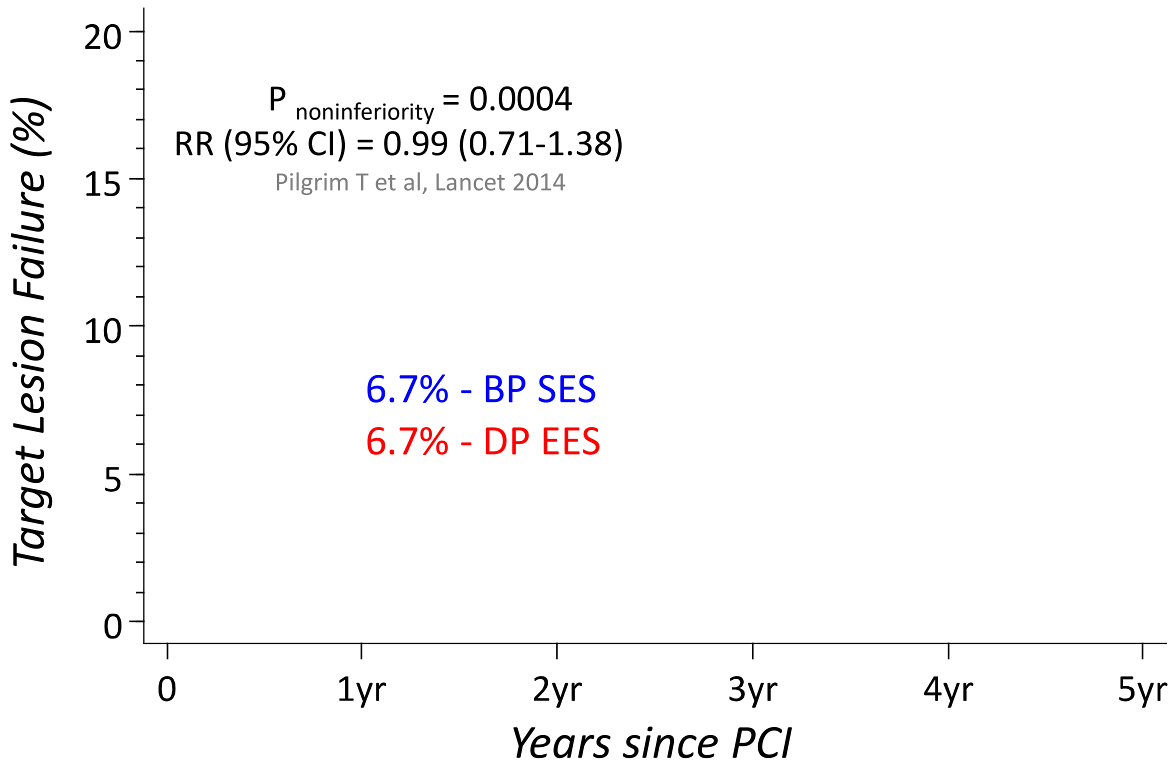
Baseline Characteristics

	BP SES (n=1,063)	DP EES (n=1,056)
Age (years) — mean ± SD	66.1 ± 11.6	65.9 ± 11.4
Male gender — n (%)	818 (77%)	816 (77%)
Diabetes mellitus — n (%)	257 (24%)	229 (22%)
Hypertension — n (%)	728 (69%)	706 (67%)
Hypercholesterolemia — n (%)	712 (67%)	716 (68%)
Renal Failure (GFR<60 ml/min) — n (%)	151 (15%)	130 (13%)
Left ventricular ejection fraction (%) — mean ± SD	55.7 ± 12.1	55.9 ± 12.6
Indication — n (%)		
Unstable angina	78 (7%)	74 (7%)
Non ST-segment elevation MI	288 (27%)	284 (27%)
ST-segment elevation MI	211 (20%)	196 (19%)
Stable angina	325 (31%)	332 (31%)

Dual Antiplatelet Treatment



Target Lesion Failure



Number at risk

	0	1yr	2yr	3yr	4yr	5yr
DP-EES	1056	966	914	866	827	797
BP-SES	1063	959	885	830	786	740

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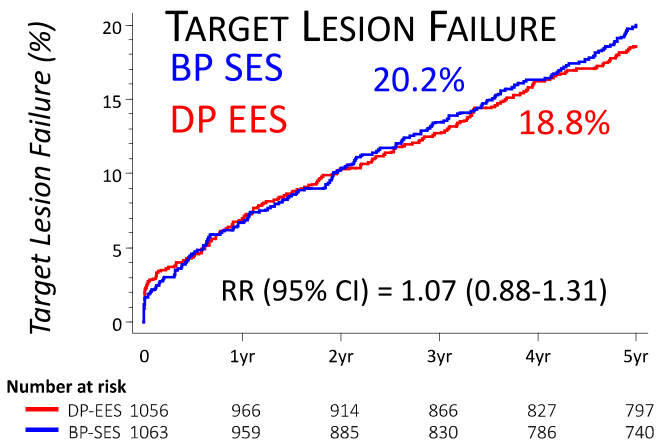
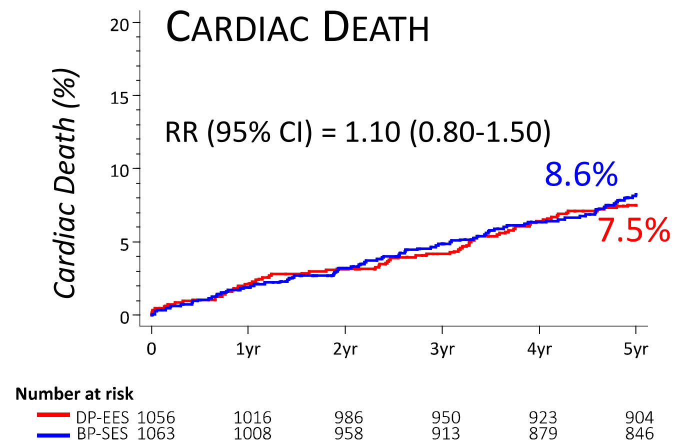
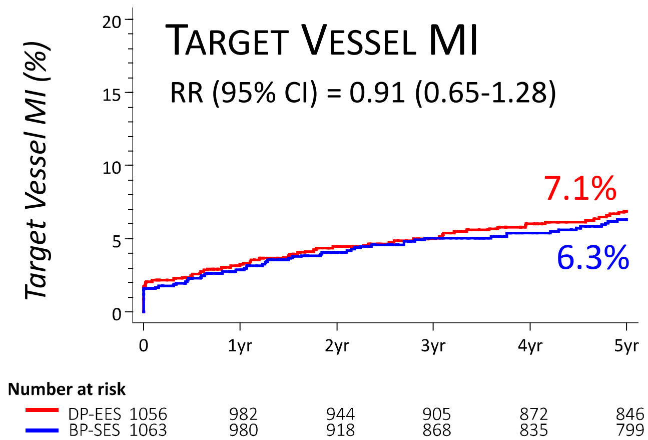
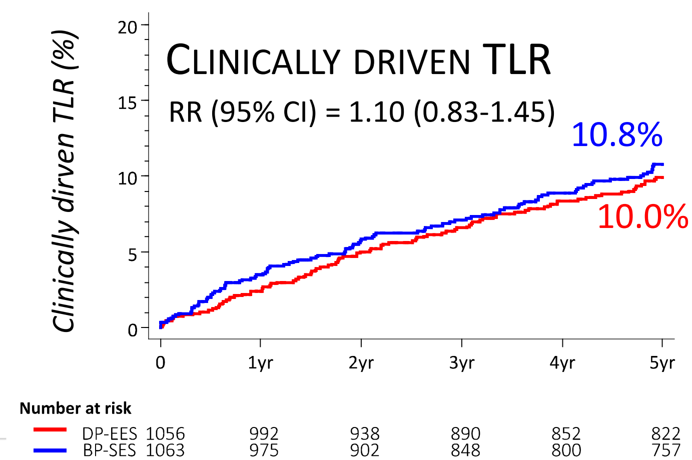
Components of the Primary Endpoint

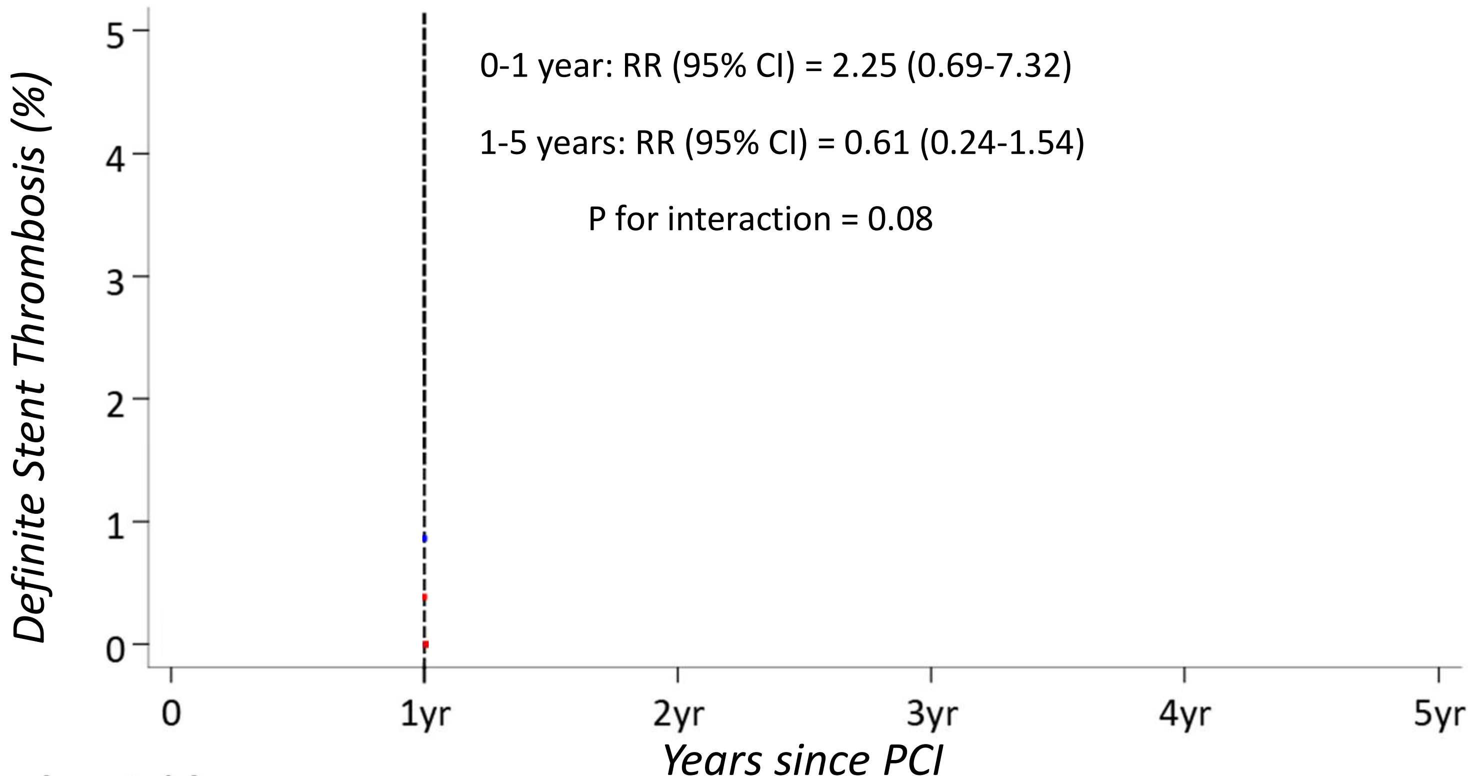








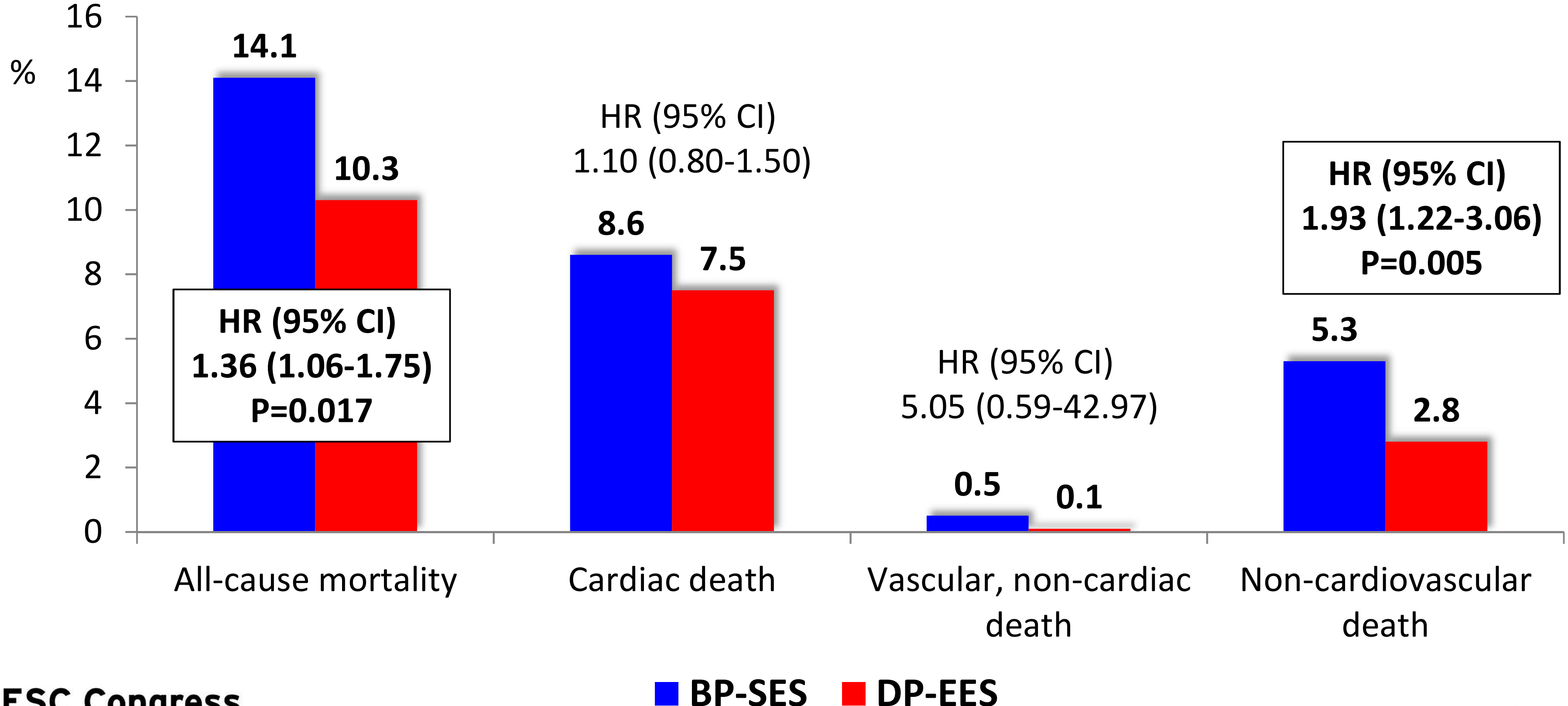
Definite Stent Thrombosis



Number at risk

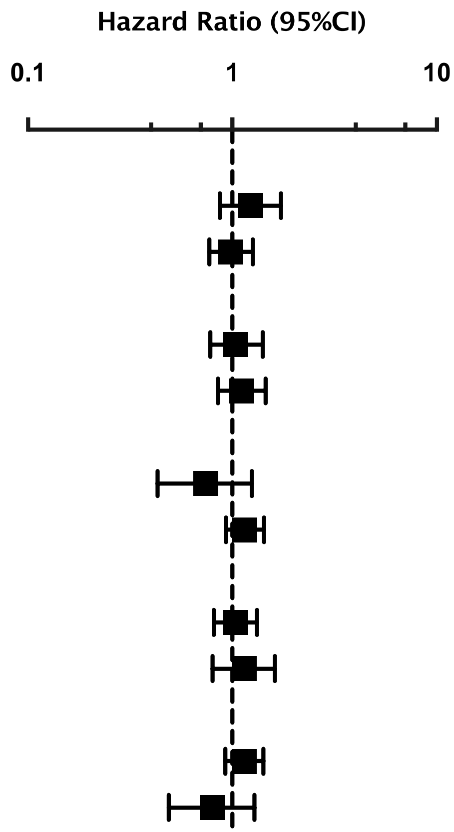
	0	1yr	2yr	3yr	4yr	5yr
DP-EES	1056	1012	979	942	914	893
BP-SES	1063	1001	949	905	870	838

All-Cause & Non-Cardiovascular Mortality



Stratified Analysis of 1° EP - Target Lesion Failure

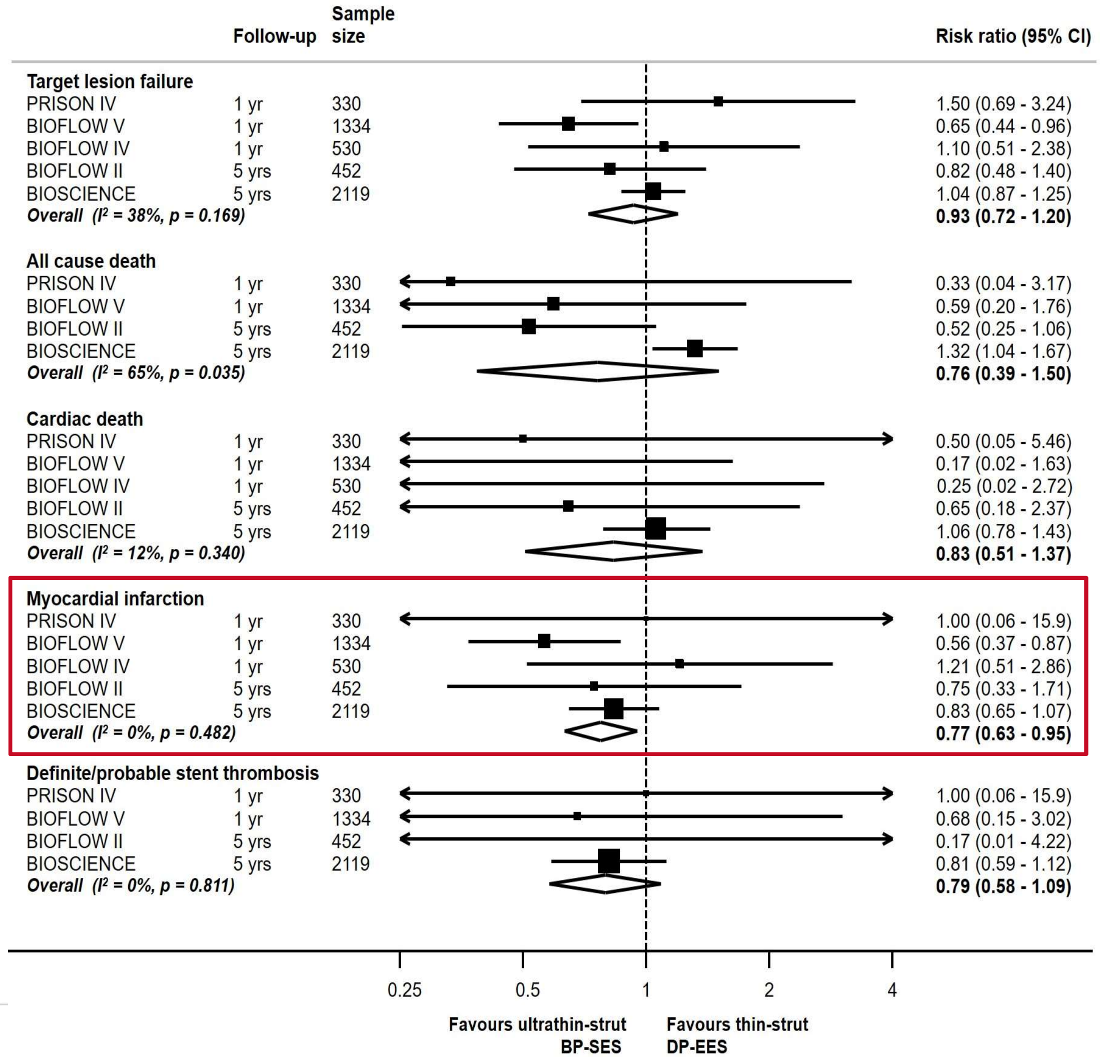
	BP-SES (N=1063) Events/ Patients	DP-EES (N=1056) Events/ Patients	Hazard Ratio (95%CI)	P-value	P-value for interaction
Diabetes					0·3070
Yes	74/257	57/229	1·23 (0·87–1·73)	0·2439	
No	124/806	132/827	0·98 (0·77–1·26)	0·9005	
ACS					0·7743
Yes	89/577	85/554	1·04 (0·78–1·41)	0·7786	
No	109/486	104/502	1·11 (0·85–1·45)	0·4604	
STEMI					0·1204
Yes	25/212	31/196	0·74 (0·43–1·25)	0·2535	
No	173/851	158/860	1·15 (0·93–1·43)	0·1936	
Off-label					0·6800
Yes	129/629	130/646	1·04 (0·81–1·32)	0·7633	
None	67/427	59/407	1·14 (0·80–1·61)	0·4764	
Small vessels					0·1796
Yes	165/812	152/828	1·14 (0·92–1·42)	0·2406	
None	31/244	37/225	0·80 (0·49–1·28)	0·3499	



META-ANALYSIS OF FIVE RCTS COMPARING ORSIRO BP SES VS. XIENCE DP EES

n = 4765 patients

23% reduction of myocardial infarction in patients treated with BP SES compared with DP EES (RR=0.77; 95% CI 0.63-0.95).



PRISON IV. Teeuven K et al, JACC Cardiovasc Interv 2017
BIOFLOW IV/V. Kandzari DE et al, Lancet 2017
BIOFLOW II. Lefèvre T et al, JACC Cardiovasc Interv 2018

CONCLUSION I

- **The final five-year outcomes of the randomized controlled BIOSCIENCE trial demonstrate comparable outcomes of ultrathin strut biodegradable sirolimus-eluting stents and thin strut durable polymer everolimus-eluting stents with regards to the composite of target lesion failure.**

Conclusion II

- **Higher rates of all-cause and non-cardiovascular mortality in patients treated with biodegradable polymer sirolimus-eluting stents warrant careful observation in ongoing studies.**

- **A trend towards a differential in timing of definite stent thrombosis may reflect an effect of the biodegradable polymer.**

- **Lower rates of myocardial infarction in a meta-analysis of BP SES versus DP EES may be related to the ultrathin strut thickness.**

Ultrathin-strut, biodegradable-polymer, sirolimus-eluting stents versus thin-strut, durable-polymer, everolimus-eluting stents for percutaneous coronary revascularisation: 5-year outcomes of the BIOSCIENCE randomised trial

Thomas Pilgrim, Raffaele Piccolo, Dik Heg, Marco Roffi, David Tüller, Olivier Muller, Igal Moarof, George C M Siontis, Stéphane Cook, Daniel Weilenmann, Christoph Kaiser, Florim Cuculi, Lukas Hunziker, Franz R Eberli, Peter Jüni, Stephan Windecker

Summary

Background Drug-eluting stents combining an ultrathin cobalt-chromium stent platform with a biodegradable polymer eluting sirolimus have been shown to be non-inferior or superior to thin-strut, durable-polymer, everolimus-eluting stents in terms of 1 year safety and efficacy outcomes.

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