

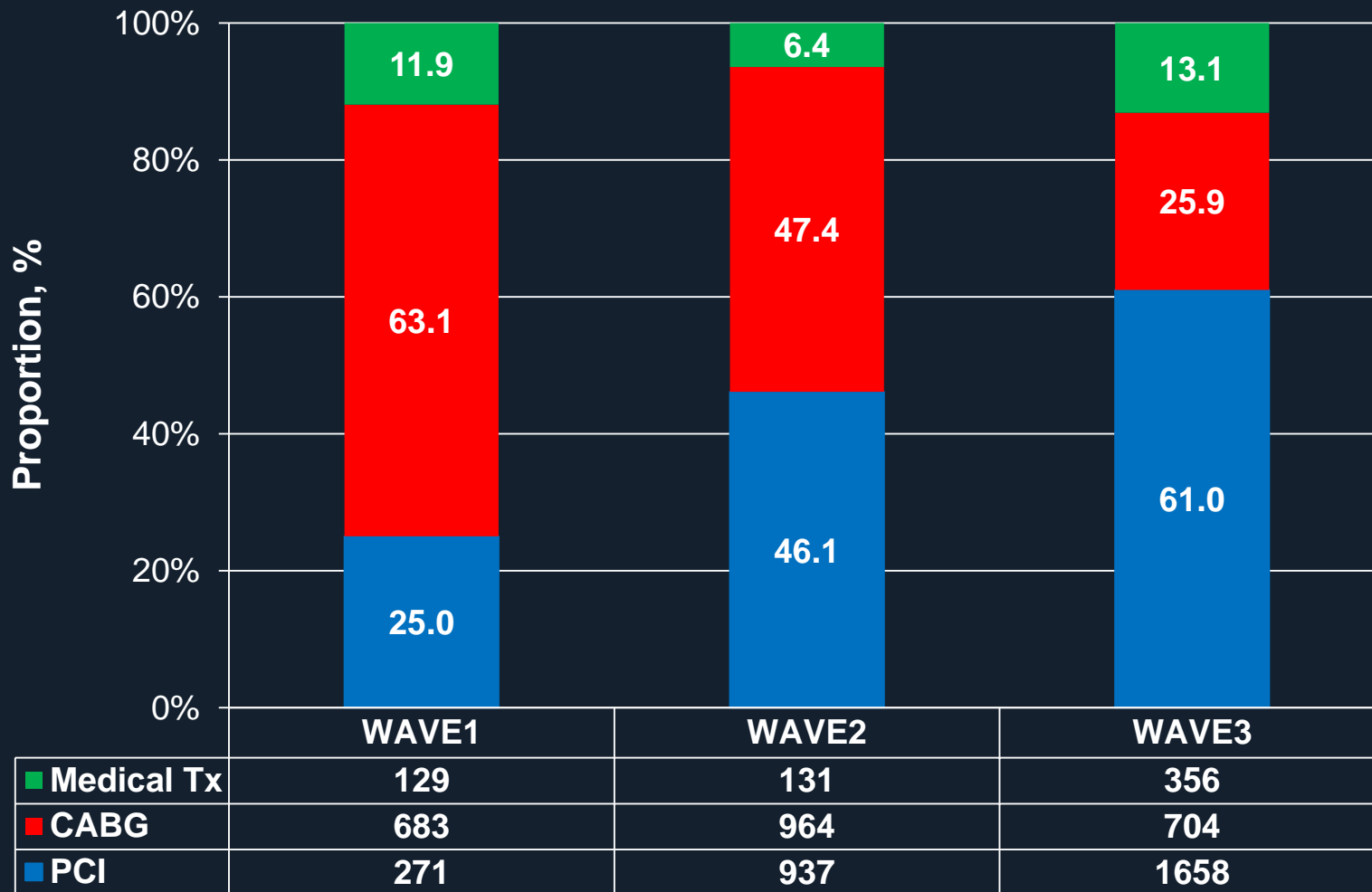
Safety and Effectiveness of Second-Generation DESs in Patients with Left Main Coronary Artery disease

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Treatment strategies for LMCAD

All comers IRIS-MAIN registry (n=5883)



Historical time periods: WAVE1: 1995 – 2002, WAVE2: 2003 – 2006, WAVE3: 2007 – 2013

Unique Features of LMCA

Ostium

- Early recoil
- Risk of protrusion
- Risk of lack of coverage
- Risk of longitudinal compression
- Radial strength
- Visibility

Shaft

- Relatively large vessel size
- Size tapering to LAD
- Often short

Sometimes lack normal segment for comparison

Distal bifurcation

- Often need complex technique
- Potentially jeopardizing a vital side branch

Does Stent Type Matter?

Randomized Trials of EES vs. 1st DES

Not a single RCT for LMCA

EES vs. SES

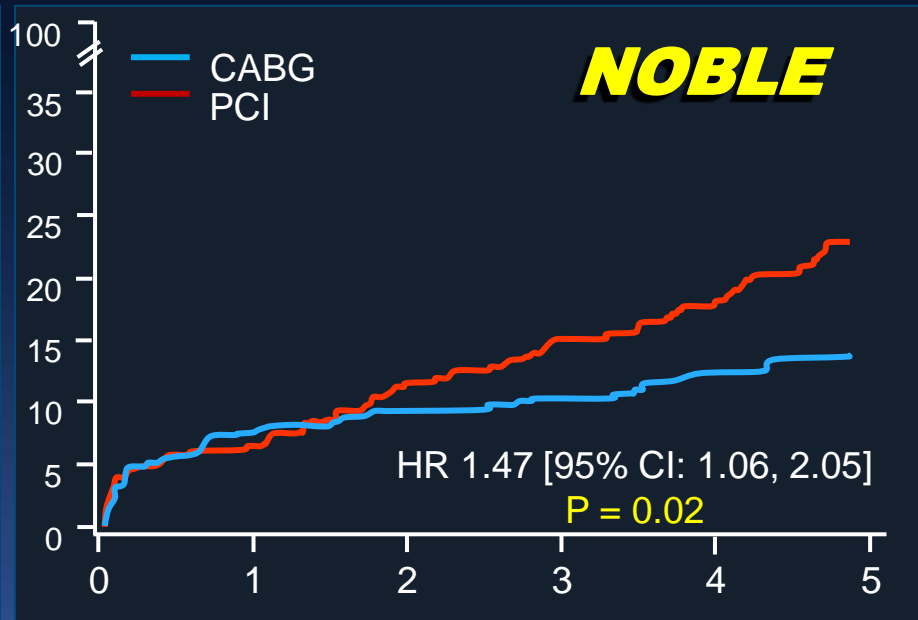
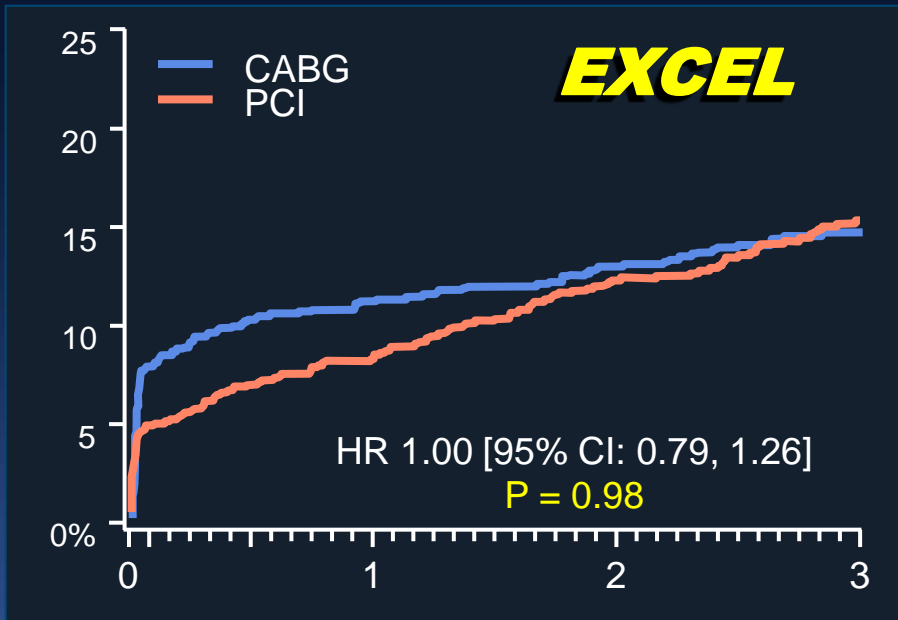
- SORT OUT 4 (n=2,777)
- ISAR-TEST-4 (n=1,304)
- EXCELLENT (n=1,372)
- BASKET-PROVE (n=1,549)
- ESSENCE-Diabetes (n=300)
- LONG-DES-III (n=450)
- RESET (n=3197)
- XAMI (n=625)
- CIBELES (n=207)
- Bifurcations (Pan et al; n=293)

EES vs. PES

- SPIRIT II (n=300)
- SPIRIT III (n=1,002)
- SPIRIT IV (n=3,687)
- SPIRIT V Diabetes (n=324)
- COMPARE (n=1,800)
- EXECUTIVE (n=200)

Different Performance Between Different Stents in LMCA?

PCI non-inferior to CABG



**PCI failed to show non-inferiority
CABG was superior to PCI**

Real World Data 2007.7 – 2015.7

Three Different Registries

- **IRIS-DES:** Multicenter (40-50 sites according to different DES arm in Korea), prospective, nonrandomized registry including PCI with several types of DES.
- **IRIS-MAIN:** Multicenter (50 sites in Asia), prospective, nonrandomized registry of LMCA disease including PCI, CABG, or medication alone.
- **PRECOMAT:** Multicenter (18-23 sites in Korea), prospective nonrandomized registry of LMCA disease including PCI with 2nd-generation DES.

DES Classification

- **CoCr-EES:** cobalt-chromium everolimus-eluting stent (Xience V, Prime, Xpedition, Alpine; Abbott Vascular, CA)
- **BP-BES:** Biodegradable polymer biolimus-eluting stent (BioMatrix; Biosensors, CA and Nobori, Terumo Clinical Supply, Japan)
- **PtCr-EES:** Platinum chromium-everolimus eluting stent (Promus Element, Premium; Boston Scientific, CA)
- **Re-ZES:** Resolute-zotarolimus eluting stent (Resolute Integrity, Medtronic Inc., CA)

The registries did not specify stent types according to clinical or anatomical features
The same type of stent was used in LMCA and in other non-LM lesions whenever necessary
The maximal available stent diameter was 4.0 mm for all kinds of DES

Study End Points

- **Primary end point**

Target-vessel failure

(cardiac death, target-vessel MI, or TVR)

- **Secondary end points**

Death (any cause, cardiac, or non-cardiac cause)

MI (periprocedural or spontaneous)

Any revascularization (TVR or non-TVR)

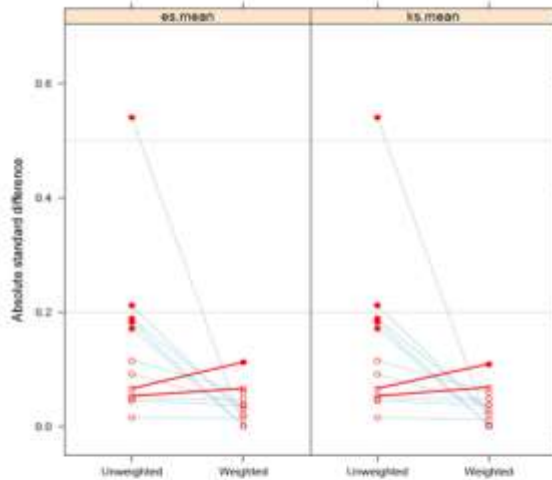
Stent thrombosis

TIMI-defined bleeding

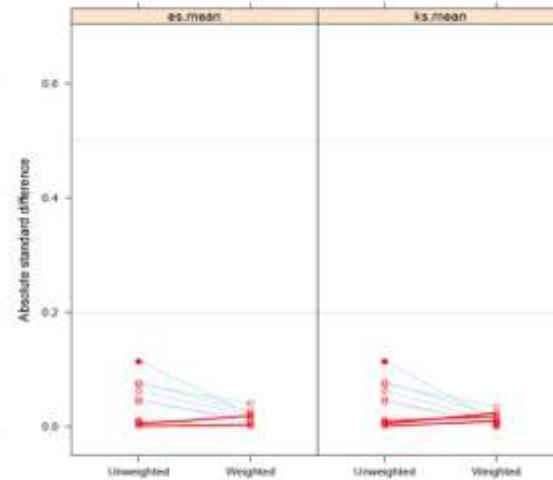
MACE (death, any MI or any revascularization)

Statistical Analysis

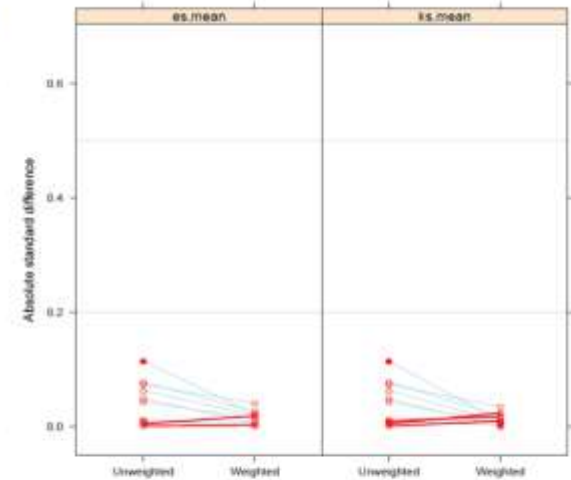
Balance of CoCr-EES versus BP-BES



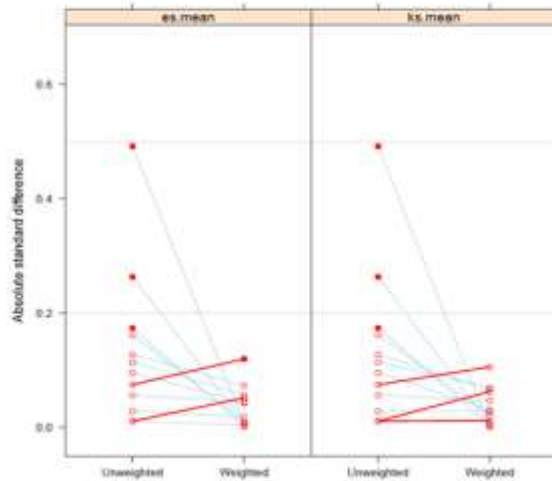
Balance of CoCr-EES versus PtCr-EES



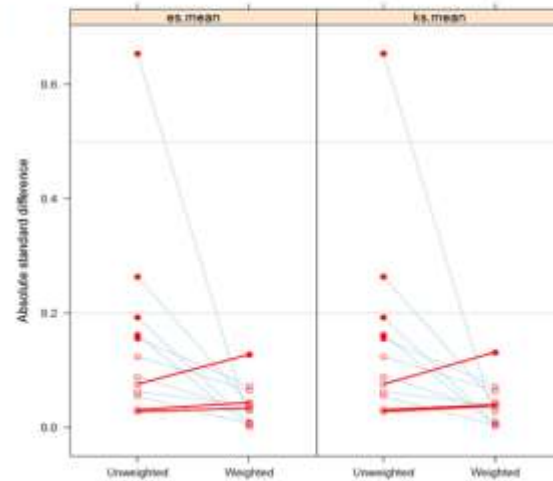
Balance of CoCr-EES versus Re-ZES



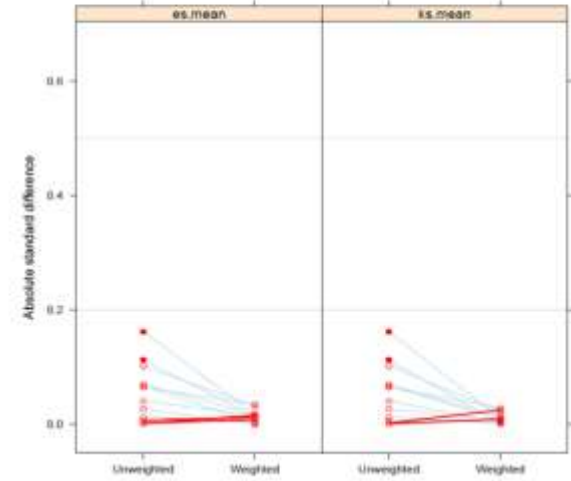
Balance of BP-BES versus PtCr-EES



Balance of BP-BES versus Re-ZES



Balance of PtCr-EES versus Re-ZES



Flow Diagram

4,470 pooled from
IRIS-MAIN, IRIS-DES, and
PRECOMBAT

1,778 excluded
675 duplicated
107 protocol violation or
withdrawal from the study
86 incomplete baseline data
786 BMSs, 1st DES
124 other 2nd DES

2,692 eligible

1,254 CoCr-EES

232 BP-BES

616 PtCr-EES

590 Re-ZES

Median follow-up
3.0 (IQR: 1.1-4.0)
years

Median follow-up
3.0 (IQR: 1.8-4.0)
years

Median follow-up
3.3 (IQR: 1.4-5.0)
years

Median follow-up
3.0 (IQR: 2.1-3.8)
years

Baseline Characteristics

	CoCr-EES (n=1,254)	BP-BES (n=232)	PtCr-EES (n=616)	Re-ZES (n=590)	P
Age (years)	64.4 ± 10.6	63.1 ± 10.8	64.3 ± 10.7	64.8 ± 10.6	0.45
Men	948 (75.6%)	177 (76.3%)	467 (75.8%)	464 (78.6%)	0.53
Body-mass index, kg/m ²	24.5 ± 3.1	24.6 ± 3.6	24.5 ± 3.0	24.4 ± 2.9	0.41
Diabetes mellitus	435 (34.7%)	86 (37.1%)	191 (31.0%)	201 (34.1%)	0.30
Hypertension	774 (61.7%)	138 (59.5%)	371 (60.2%)	393 (66.6%)	0.08
Hyperlipidemia	674 (53.7%)	145 (62.5%)	415 (67.4%)	413 (70.0%)	<0.001
Current smoker	294 (23.4%)	57 (24.6%)	136 (22.1%)	149 (25.3%)	0.61
Family history of CAD	93 (7.4%)	30 (12.9%)	44 (7.1%)	57 (9.7%)	0.02
Previous MI	82 (6.5%)	26 (11.2%)	29 (4.7%)	38 (6.4%)	0.01
Previous CHF	79 (6.3%)	17 (7.3%)	52 (8.4%)	63 (10.7%)	0.01
Previous PCI	181 (14.4%)	40 (17.2%)	97 (15.7%)	84 (14.2%)	0.62
Previous CABG	34 (2.7%)	6 (2.6%)	13 (2.1%)	7 (1.2%)	0.22

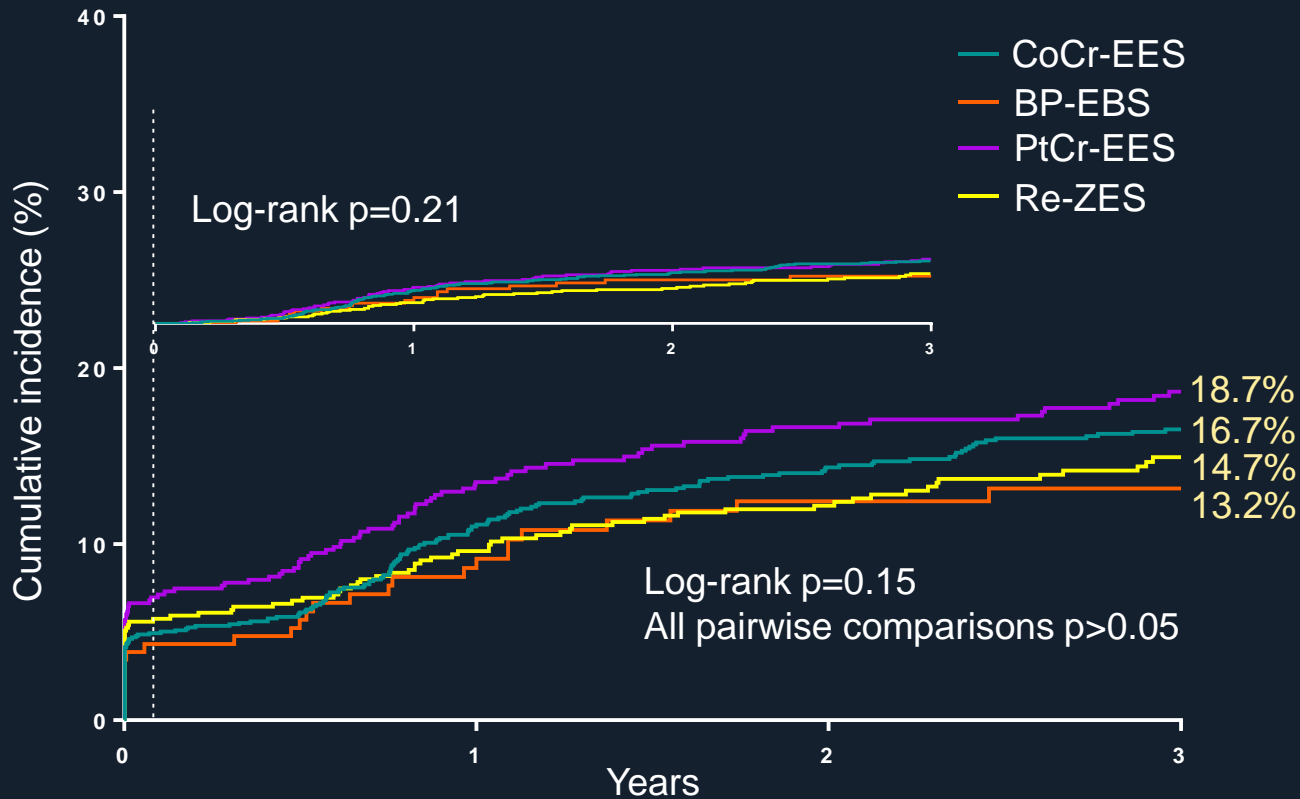
Baseline Characteristics

	CoCr-EES (n=1,254)	BP-BES (n=232)	PtCr-EES (n=616)	Re-ZES (n=590)	P
Renal failure	55 (4.4%)	7 (3.0%)	28 (4.5%)	27 (4.6%)	0.77
Cerebrovascular disease	40 (3.2%)	6 (2.6%)	26 (4.2%)	30 (5.1%)	0.16
Peripheral vascular disease	55 (4.4%)	7 (3.0%)	27 (4.4%)	27 (4.6%)	0.79
Chronic lung disease	27 (2.2%)	5 (2.2%)	15 (2.4%)	17 (2.9%)	0.81
Ejection fraction (%)	58.8 ± 9.6	58.4 ± 9.9	58.4 ± 9.6	58.2 ± 10.3	0.18
Clinical indication for PCI					0.28
Silent ischemia/ stable angina	467 (38.9%)	110 (48.0%)	237 (39.4%)	229 (39.8%)	
Unstable angina	508 (42.2%)	79 (34.5%)	257 (42.8%)	225 (39.1%)	
NSTEMI	154 (12.8%)	29 (12.7%)	74 (12.3%)	80 (13.9%)	
STEMI	72 (6.0%)	11 (4.8%)	33 (5.5%)	42 (7.3%)	

Lesion/PCI characteristics

	CoCr-EES (n=1,254)	BP-BES (n=232)	PtCr-EES (n=616)	Re-ZES (n=590)	P
Disease extent					0.40
Left main only	125 (10.0)	26 (11.2)	73 (11.9)	59 (10.0)	
Left main with 1VD	324 (25.8)	52 (22.4)	151 (24.5)	148 (25.1)	
Left main with 2VD	491 (39.2)	90 (38.8)	217 (35.2)	207 (35.1)	
Left main with 3VD	314 (25.0)	64 (27.6)	175 (28.4)	176 (29.8)	
RCA involvement	495 (39.5)	103 (44.4)	259 (42.0)	262 (44.4)	0.17
Left main lesion location					0.20
Ostium or mid-shaft	417 (33.6)	84 (36.2)	219 (35.7)	179 (30.4)	
Distal bifurcation	823 (66.4)	148 (63.8)	395 (64.3)	410 (69.6)	
Stent technique					<0.001
Left main stenting only	159 (12.7)	44 (19.0)	92 (14.9)	94 (15.9)	
Simple crossover	882 (70.3)	129 (55.6)	391 (63.5)	367 (62.2)	
2-stent technique	213 (17.0)	59 (25.4)	133 (21.6)	129 (21.9)	
Final kissing balloon	338 (27.0)	94 (40.5)	200 (32.5)	184 (31.2)	<0.001
Total stent number per patient	2.2 ± 1.2	2.4 ± 1.3	2.2 ± 1.2	2.1 ± 1.1	0.12
Total stent length per patient	52.0 ± 33.2	52.8 ± 35.1	51.2 ± 32.1	50.8 ± 33.0	0.41
Stent number in left main	1.7 ± 0.9	1.8 ± 1.1	1.6 ± 0.8	1.6 ± 0.8	0.01
Average stent diameter in left main	3.5 ± 0.4	3.3 ± 0.4	3.6 ± 0.4	3.5 ± 0.4	<0.001
Use of IVUS	975 (77.8)	127 (54.7)	466 (75.6)	487 (82.5)	<0.001
Use of Gp IIb/IIIa inhibitors	82 (6.5)	30 (12.9)	46 (7.5)	45 (7.5)	0.01

Target-Vessel Failure



No. at risk

CoCr-EES	1254	919	766	611
BP-BES	232	175	147	91
PtCr-EES	616	456	393	332
Re-ZES	590	508	442	285

Three-Year Event Rates

(%, 95% CI)

	CoCr-EES (n=1,254)	BP-BES (n=232)	PtCr-EES (n=616)	Re-ZES (n=590)	P
Target-vessel failure	16.7 (15.5–17.9)	13.2 (10.8–15.6)	18.7 (17.0–20.4)	14.7 (13.1–16.3)	0.15
Death from any cause	7.7 (6.8–8.6)	6.2 (5.5–7.9)	6.9 (5.8–8.0)	8.3 (7.1–9.5)	0.83
Cardiac	5.8 (5.1–6.5)	3.4 (2.1–4.7)	5.7 (4.7–6.7)	6.0 (4.9–7.1)	0.70
Non-cardiac	2.1 (1.6–2.6)	3.4 (2.1–4.7)	1.4 (0.9–1.9)	2.5 (1.8–3.2)	0.23
Myocardial infarction	5.4 (4.7–6.1)	5.5 (3.9–7.1)	7.0 (6.0–8.0)	6.0 (5.0–7.0)	0.55
Periprocedural	4.1 (3.5–4.7)	3.9 (2.6–5.2)	5.7 (4.8–6.6)	4.6 (3.7–5.5)	0.43
Spontaneous	1.5 (1.1–1.9)	1.7 (0.7–2.7)	1.5 (1.0–2.0)	1.4 (0.9–1.9)	0.99

Three-Year Event Rates (%, 95% CI)

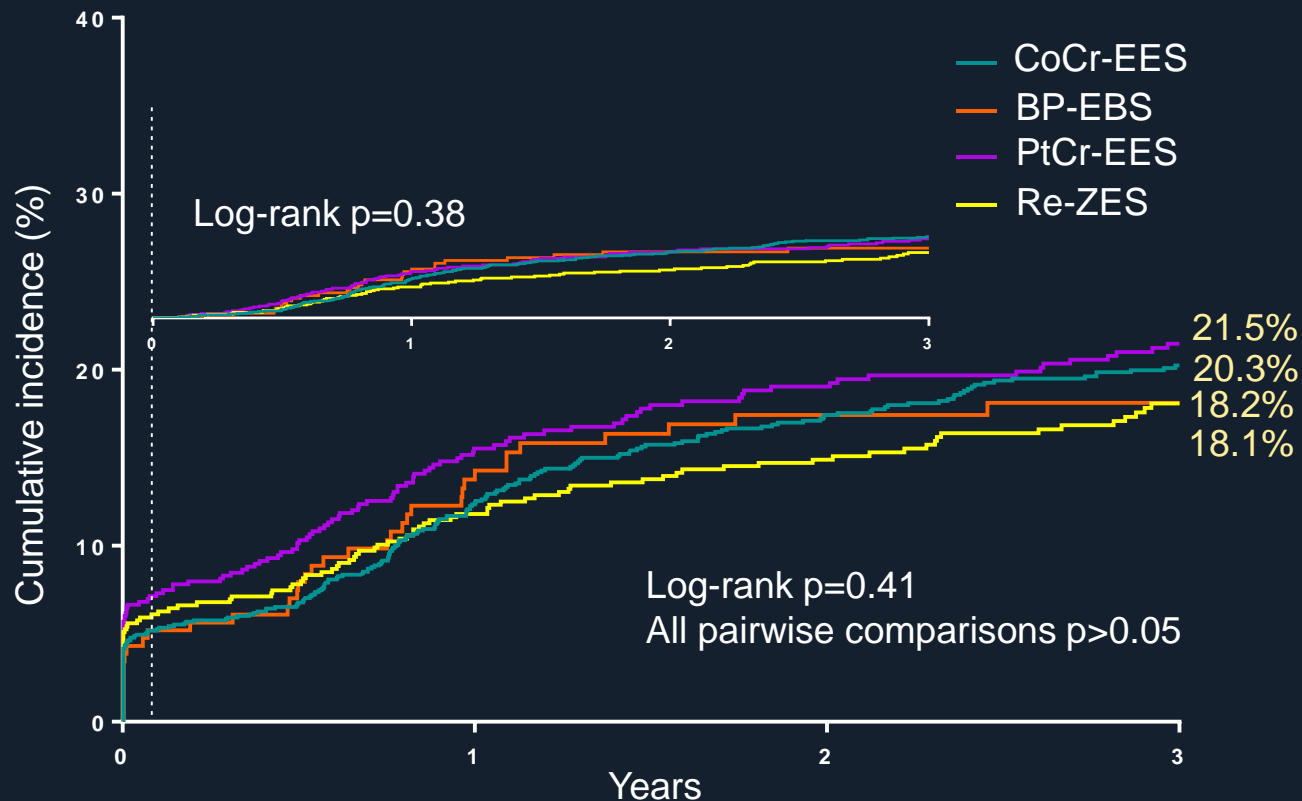
	CoCr-EES (n=1,254)	BP-BES (n=232)	PtCr-EES (n=616)	Re-ZES (n=590)	P
Any revascularization	10.1 (9.1-11.1)	10.4 (8.2-12.6)	10.2 (8.9-11.5)	7.8 (6.6-9.0)	0.43
TVR	7.8 (7.0-8.6)	8.0 (6.0-10.0)	8.0 (6.8-9.2)	5.4 (4.4-6.4)	0.34
Non-TVR	3.2 (2.6-3.8)	2.0 (1.0-3.0)	4.0 (3.2-4.8)	2.3 (1.6-4.0)	0.24
Stent thrombosis (definite or probable)	0.2 (0.1-0.3)	1.0 (0.3-1.7)	0.0 (0.0-0.0)	1.0 (0.6-1.4)	0.02*
Early, 0 to 30 days	0.2 (0.1-0.3)	0.4 (0.0-0.8)	0.0 (0.0-0.0)	0.7 (0.4-1.0)	0.10†
Late, 30 days to 1 yr	0.1 (0.0-0.2)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.4 (0.1-0.7)	0.30
Very late, 1 to 3 yrs	0.0 (0.0-0.0)	0.6 (0.0-1.2)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.01‡

*The pairwise comparisons were significant between CoCr-EES and Re-ZES (P=0.03), BP-BES and PtCr-EES (P=0.02), PtCr-EES and Re-ZES (P=0.01)

†The pairwise comparisons were significant between PtCr-EES and Re-ZES (P=0.04)

‡The pairwise comparisons were significant between CoCr-EES and BP-BES (P=0.02)

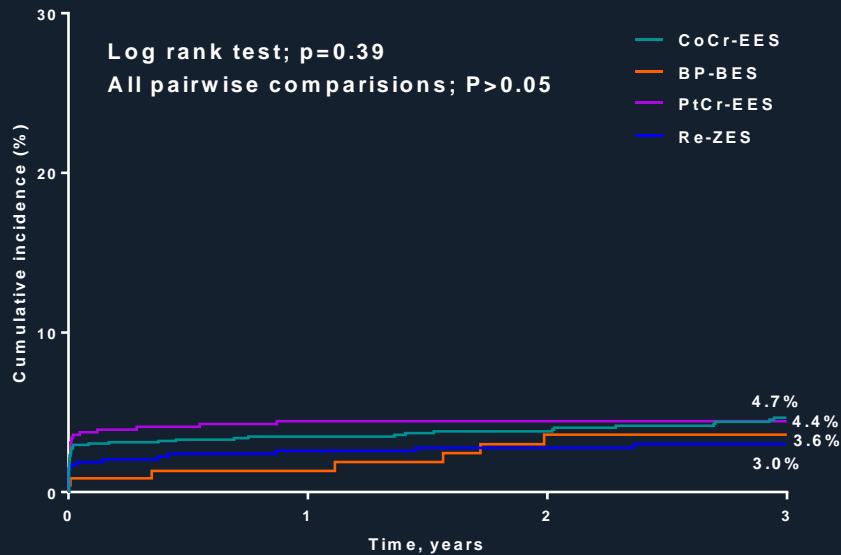
Major Adverse Cardiac Event



No. at risk				
CoCr-EES	1254	913	752	598
BP-BES	232	171	143	90
PtCr-EES	616	447	384	324
Re-ZES	590	503	437	280

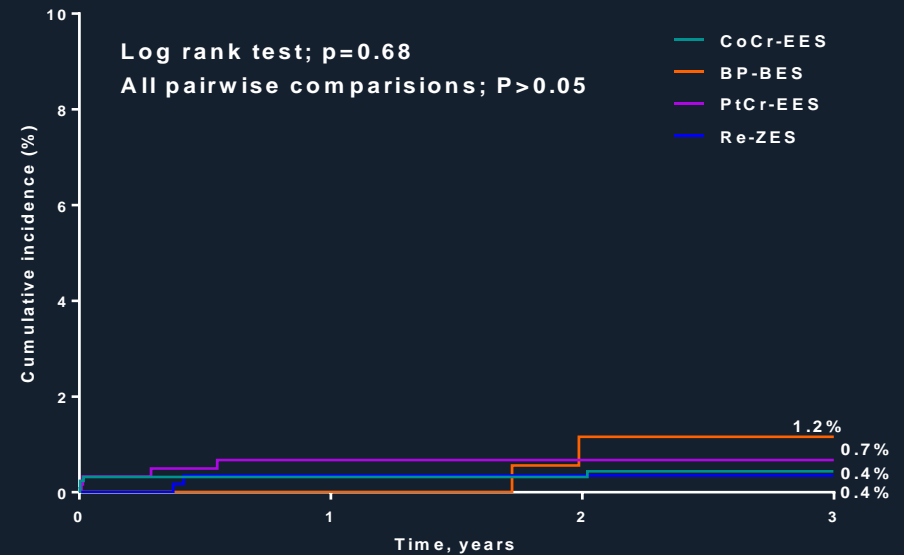
TIMI-Bleeding

Any bleeding



No. at risk	0	1	2	3
CoCr-EES	1254	980	841	669
BP-BES	232	186	159	100
PtCr-EES	616	488	430	365
Re-ZES	590	531	469	307

Major bleeding



No. at risk	0	1	2	3
CoCr-EES	1254	1005	865	694
BP-BES	232	189	163	104
PtCr-EES	616	505	442	376
Re-ZES	590	543	481	316

Restenosis pattern

according to stent type and stenting technique

	Total N=2692			CoCr-EES N=1254			BP-BES N=232			PtCr-EES N=616			Re-ZES N=590			
LM restenosis	120 (4.5)			53 (4.2)			10 (4.3)			33 (5.4)			24 (4.1)			
Angiography available	113 (4.2)			50 (4.0)			9 (3.9)			31 (5.0)			23 (3.9)			
Stenting technique	Two-stent 57	Cross-over 49†	LM-only 7	Two-stent 23	Cross-over 25†	LM-only 2	Two-stent 2	Cross-over 5‡	LM-only 2	Two-stent 19	Cross-over 9	LM-only 3	Two-stent 13	Cross-over 10§	LM-only 0	
Location of restenosis																
LM ostium	3 (5.3)	7 (14.3)	2 (28.6)	1 (4.3)	3 (12.0)	0	0	0	2 (100)	1 (5.3)	2 (22.2)	0	1 (7.7)	2 (20.0)	-	
LM shaft/distal	12 (21.1)	11 (22.4)	3 (42.9)	4 (17.4)	7 (28.0)	2 (100)	0	2 (40.0)	0	4 (21.1)	0	1 (33.3)	4 (30.8)	2 (20.0)	-	
LAD	15 (26.3)	21 (42.9)	2 (28.6)	6 (26.1)	11 (44.0)	0	1 (50)	2 (40.0)	0	5 (26.3)	3 (33.3)	2 (66.7)	3 (23.1)	5 (50.0)	-	
LCX	53 (93.0)	27 (55.1)	0	21 (91.3)	13 (52.0)	0	1 (50)	5 (100)	0	18 (94.7)	4 (44.4)	0	12 (92.3)	5 (50.0)	-	

Values are number (%)

† In 5 cases, stent was implanted from LM to LCX.

‡ In 1 case, stent was implanted from LM to LCX.

§ In 2 cases, stent was implanted from LM to LCX

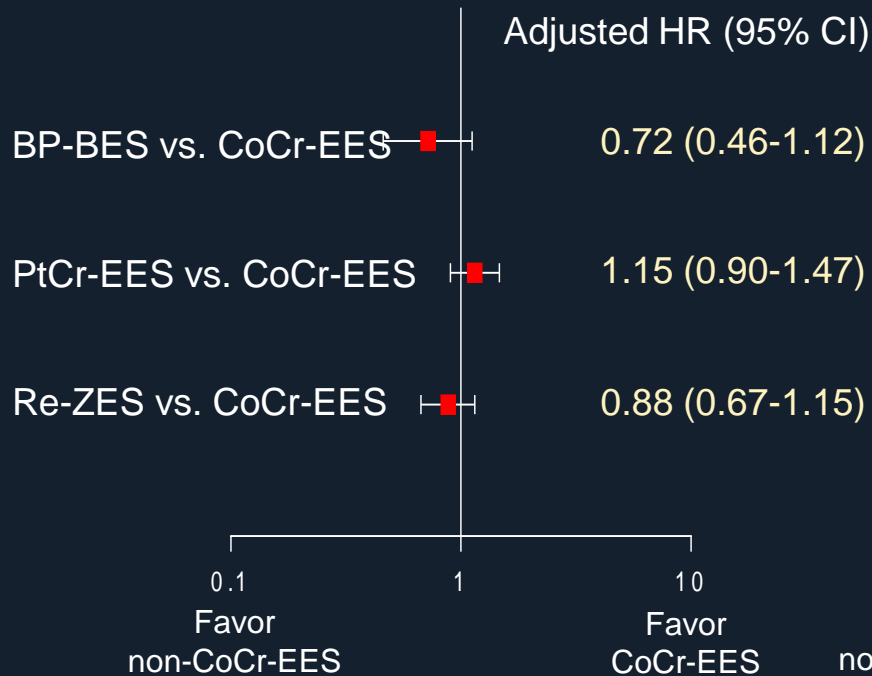
Adjusted Hazard Ratios in the Multigroup Propensity-Score Analyses

	TVF	Death	MI	TVR	MACE
BP-BES vs. CoCr-EES	0.72 (0.46-1.12) P=0.62	0.62 (0.33-1.17) P=0.14	1.02 (0.53-1.95) P=0.95	0.95 (0.52-1.74) P=0.87	0.85 (0.58-1.23) P=0.38
PtCr-EES vs. CoCr-EES	1.15 (0.90-1.47) P=0.28	0.88 (0.59-1.32) P=0.55	1.36 (0.92-2.02) P=0.13	1.00 (0.69-1.47) P=0.98	1.08 (0.86-1.36) P=0.50
Re-ZES vs. CoCr-EES	0.88 (0.67-1.15) P=0.35	1.13 (0.77-1.67) P=0.53	1.11 (0.73-1.71) P=0.62	0.68 (0.44-1.04) P=0.08	0.91 (0.71-1.16) P=0.43
PtCr-EES vs. BP-BES	1.60 (1.01-2.54) P=0.046	1.43 (0.72-2.84) P=0.30	1.33 (0.68-2.63) P=0.41	1.05 (0.56-1.99) P = 0.87	1.28 (0.86-1.90) P=0.23
Re-ZES vs. BP-BES	1.23 (0.76-1.98) P=0.40	1.83 (0.93-3.60) P=0.08	1.09 (0.54-2.20) P=0.80	0.71 (0.36-1.39) P = 0.31	1.07 (0.71-1.61) P=0.74
Re-ZES vs. PtCr-EES	0.77 (0.57-1.04) P=0.08	1.28 (0.81-2.02) P=0.29	0.82 (0.51-1.31) P=0.41	0.67 (0.42-1.09) P=0.11	0.84 (0.64-1.10) P=0.21

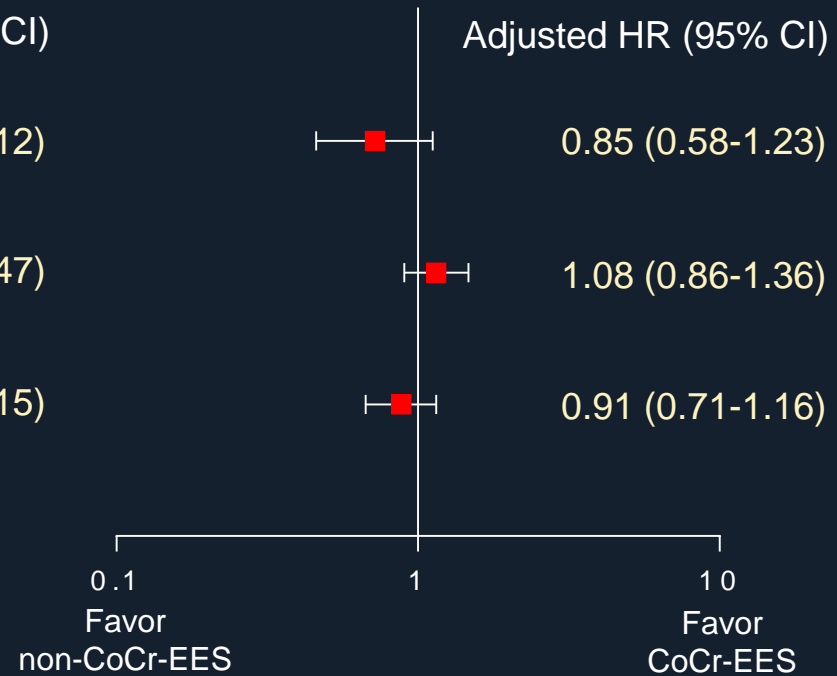
*Values are adjusted hazard ratio (95% confidence interval).

Adjusted Hazard Ratios in the Multigroup Propensity-Score Analyses

TVF



MACE



Conclusions

- Our result confirms the expected low adverse event rates at 3 years of 2nd-generation stent in LM trials and registries.
- The 2-year clinical outcomes after PCI of LMCA disease between second-generation DESs were otherwise similar, except that PtCr-EES were associated with a higher risk of TVF than BP-BES.
- Patient and lesion selection and optimal technique may be more important than the stent platform to determine early and late outcomes in LM stenting.



Thank You !!

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