Current status of DES
: Clinical evidences of Ultimaster

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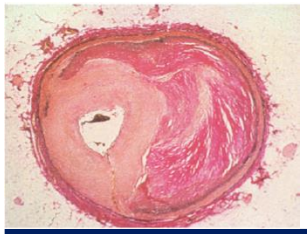
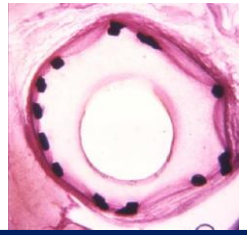
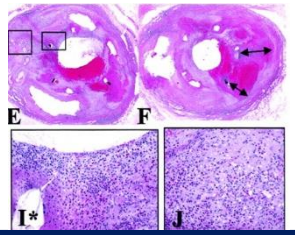
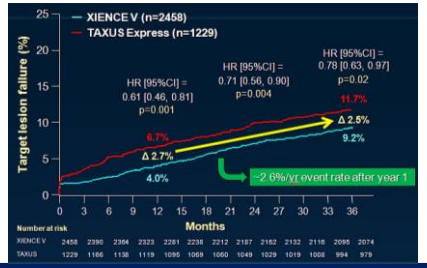
Evolution of Coronary Stent Innovation

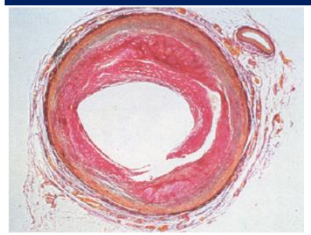








BMS → DP-DES → BP-DES → BRS ??



- With risk of impaired vascular healing
  - chronic local inflammatory reaction & restriction of vascular vasomotion

- Late stent failures
  - in-stent restenosis (ISR)
  - Late stent thrombosis (LST)

In stent restenosis

- Higher degree of vessel injury with stent increased the extent of NIH
  - Dominant cause of restenosis after stent implantation.
- Inflammatory response to vessel wall injury
  - fibroblast growth and smooth muscle cell hyperplasia.
- Mechanistically contributing factors to ISR
  - Acute or subacute prolapse of the disrupted plaque
  - Elastic recoil of the vessel wall
  - Constrictive remodeling
  - Neointimal hyperplasia (due to ECM deposition and SMC hyperplasia)
  - De novo in-stent atherosclerosis (neoatherosclerosis)
- Angiographic restenosis
  - re-narrowing of > 50% of the vessel diameter as determined by coronary angiography
- Clinical restenosis
  - restenosis accompanied by requirement for re-treatment (Sx or sign of ischaemia)

From DP-ZES vs BP-BES (SORT OUT VI) trial…

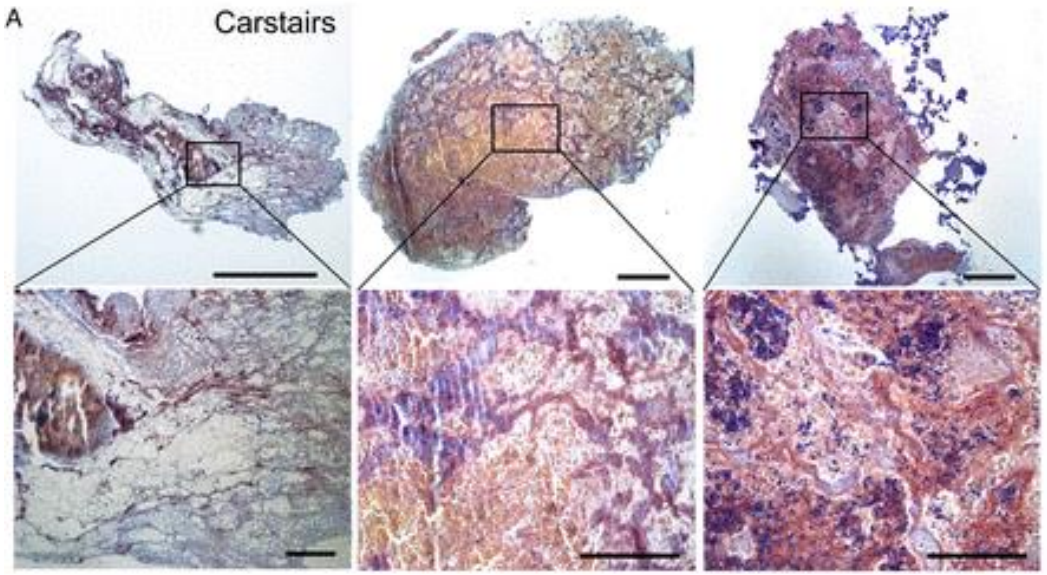
	Durable-polymer zotarolimus-eluting stent (n=1502)	Biodegradable-polymer biolimus-eluting stent (n=1497)	Risk difference (95% CI)	p value
Events at 12 months				
Composite primary endpoint*	79 (5·3%)	75 (5·0%)	0·3% (–1·3 to 1·9)	0·72
All-cause mortality	50 (3·3%)	40 (2·7%)	0·7% (–0·5 to 1·9)	0·28
Cardiac mortality	22 (1·5%)	26 (1·7%)	–0·3% (–1·2 to 0·6)	0·58
Composite secondary endpoint†	206 (13·8%)	215 (14·3%)	–0·6% (–0·3 to 1·9)	0·67
Myocardial infarction	31 (2·1%)	30 (2·0%)	0·1% (–0·9 to 1·1)	0·89
Target-vessel revascularisation	67 (4·5%)	71 (4·7%)	–0·3% (–1·8 to 1·2)	0·75
Target-lesion revascularisation	52 (3·5%)	47 (3·1%)	0·3% (–0·9 to 1·6)	0·60
Stent thrombosis‡				
Definite	9 (0·6%)	6 (0·4%)	0·2% (–0·3 to 0·7)	0·44
Acute (<24 h)	1 (0·1%)	0 (0·0%)	0·1% (–0·1 to 0·2)	0·32
Subacute (24 h to 30 days)	4 (0·3%)	1 (0·1%)	0·2% (–0·1 to 0·6)	0·10
Late (31 days to 12 months)	4 (0·3%)	5 (0·3%)	–0·1% (–0·5 to 0·3)	0·74
Probable	3 (0·2%)	1 (0·1%)	0·1% (–0·1 to 0·4)	0·32
Definite or probable	12 (0·8%)	7 (0·5%)	0·3% (–0·2 to 0·9)	0·25
Possible	7 (0·5%)	14 (0·9%)	–0·5% (–1·1 to 0·1)	0·13

- **Clinical restenosis**

Lancet 2015;385:1527

Stent thrombosis

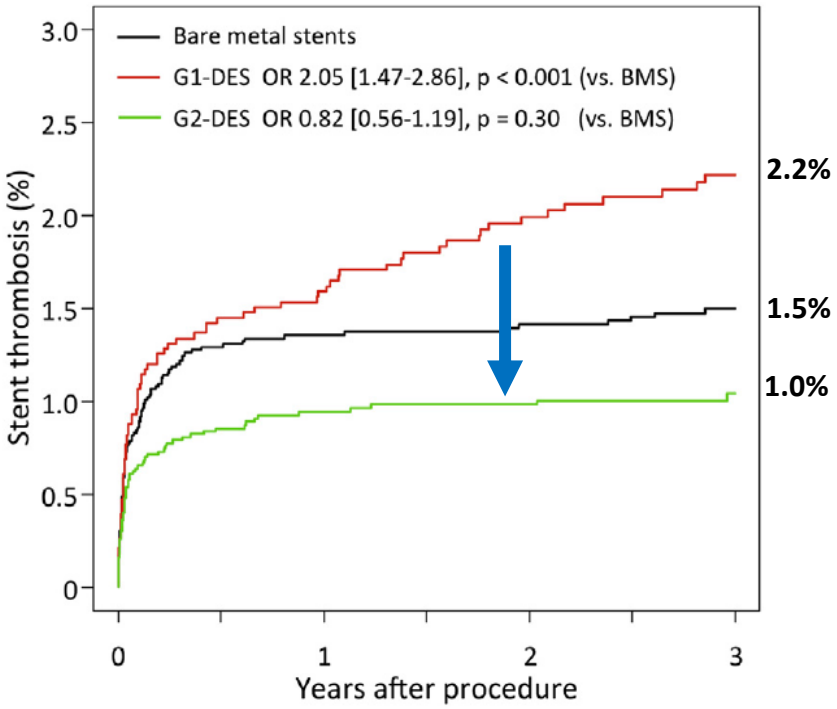
- **Characterized by angiographic or postmortem evidence of recently formed thrombus in a previously stented segment**
- **Mix of thrombotic and inflammatory components including platelet-rich thrombus, fibrin fragments, and leukocytes of both neutrophil and eosinophil lineage.**



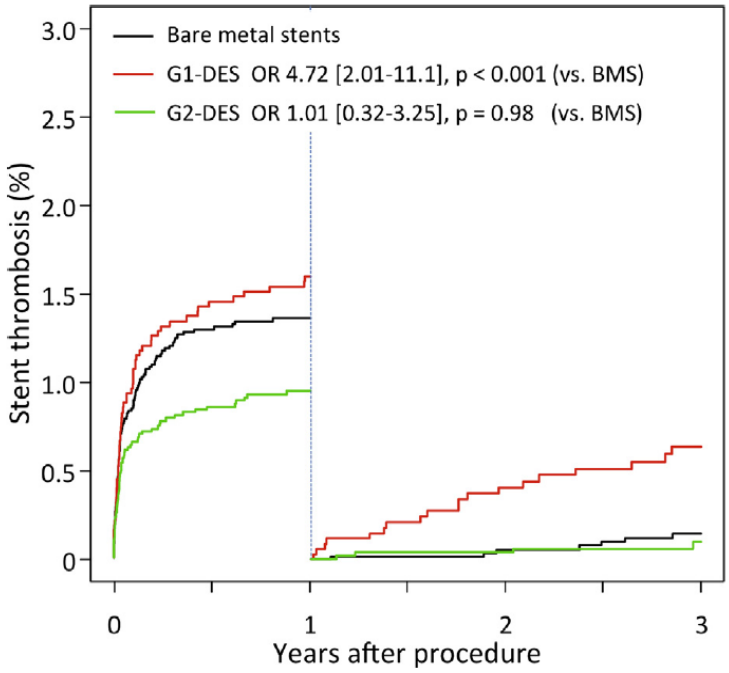
Eur Heart J. 2016;37:1538

Incidence of ST

- **18,334 patients undergoing PCI from 1998 to 2011 at 2 centers in Germany**
- **Treatment with BMS, G1-DES, and G2-DES**



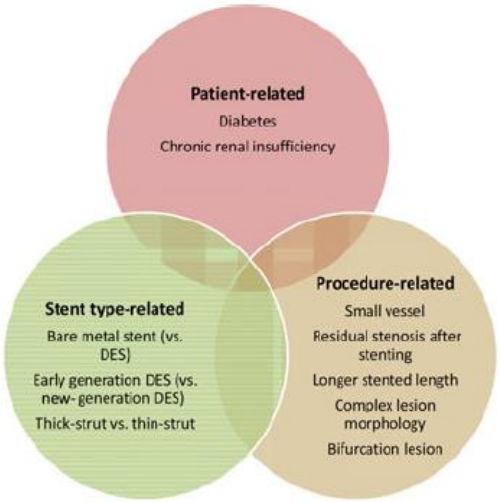
N at risk				
Bare metal stent	7410	6058	4932	4582
G1-DES	3831	3417	2967	2426
G2-DES	7093	5497	5021	2708



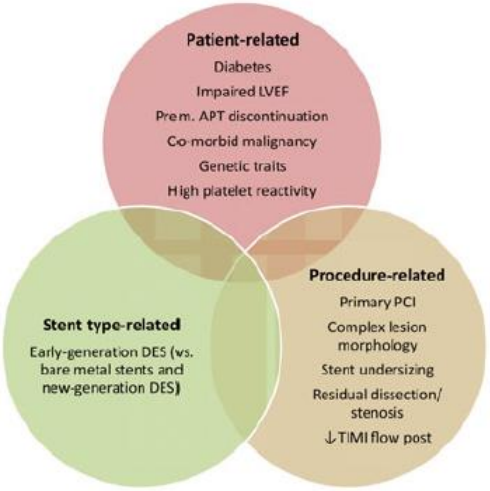
Landmark Analysis of ST

J Am Coll Cardiol Intv 2013;6:1267

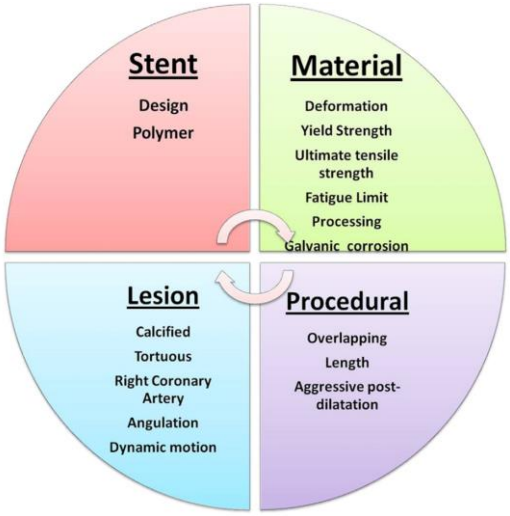
Risk factors of stent failure



ISR



ST



Stent fracture

Neoatherosclerosis as a common pathway in stent failure !!

IVUS findings in stent thrombosis
- RI & malapposition

	ST (n = 18)	Control Subjects (n = 36)	p Value
Reference segment			
Mean EEM CSA, mm^2	13.6 ± 3.9	13.7 ± 3.5	0.50
Mean lumen CSA, mm^2	6.9 ± 1.7	6.9 ± 1.8	0.96
Stent segment			
Mean EEM, mm^2	19.4 ± 5.8	15.1 ± 4.6	0.003
Remodeling index	1.24 (1.06–1.43)	0.99 (0.90–1.11)	<0.001
Mean stent CSA, mm^2	7.8 ± 1.6	7.6 ± 1.4	0.42
Minimal stent CSA, mm^2	5.7 ± 1.4	5.9 ± 1.4	0.99
Minimal stent CSA < 4 mm^2	3 (16.7)	3 (8.3)	0.38
Stent expansion index	0.87 ± 0.3	0.91 ± 0.3	0.69
ISA	14 (77.8)	15 (41.7)	0.01
Maximal ISA CSA, mm^2	4.11 ± 2.3	1.16 ± 1.5	0.001

JACC Cardiovasc Interv. 2012;5:12

OCT findings in stent thrombosis
- Strut coverage & malapposition

	ST (n = 18 Lesions; 4,407 Struts)	Control Subjects (n = 36 Lesions; 9,064 Struts)	p Value
Cross-section level analysis			
Analyzed cross-sections/patient, n	27 ± 12	30 ± 13	0.47
Struts analyzed/cross-section, n	6.78 ± 1.22	6.74 ± 1.41	0.93
Frequency of cross-sections with uncovered struts, %	33.30 (11.82–53.00)	0.00 (0.00–7.80)	0.003
Frequency of cross-sections with >30% uncovered struts, %	21.59 (0.00–43.70)	0.00 (0.00–6.09)	0.002
Maximum length of segments with uncovered struts, mm	3.30 (1.35–4.13)	0.90 (0.00–1.55)	<0.001
Maximum length of segments with malapposed struts, mm	1.40 (0.68–1.93)	0.00 (0.00–0.00)	0.001
Maximum malapposition distance, mm	0.35 (0.00–0.75)	0.00 (0.00–0.62)	0.002
Area of malapposition, mm^2	1.02 (0.00–1.92)	0.00 (0.00–0.32)	0.002
Minimum stent area, mm^2	5.04 ± 1.23	5.50 ± 1.27	0.26
Mean stent area, mm^2	7.24 ± 0.97	7.69 ± 1.61	0.20
Mean neointimal area, mm^2	1.57 ± 0.68	1.68 ± 0.71	0.41
Strut-level analysis			
Number of struts analyzed/patient	244 ± 131	251 ± 86	0.81
Number of uncovered struts/patient	25.00 (8.25–52.25)	9.00 (4.25–14.00)	0.006
Frequency of uncovered struts/patient, %	12.27 (5.50–23.33)	4.14 (3.00–6.22)	0.001
Number of malapposed struts/patient	10.00 (2.25–21.75)	4.00 (0.00–7.00)	0.02
Frequency of malapposed struts/patient, %	4.60 (1.85–7.19)	1.81 (0.00–2.99)	0.001
Neointimal thickness of covered struts, mm	0.23 ± 0.15	0.17 ± 0.09	0.28

JACC Cardiovasc Interv. 2012;5:12

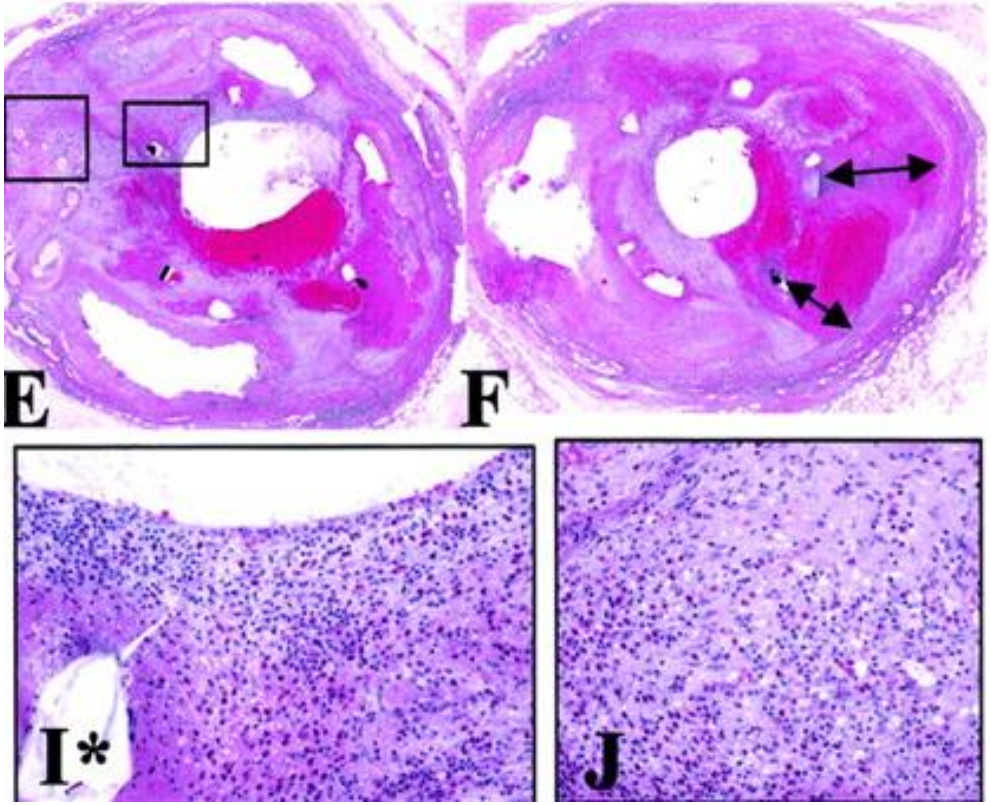
Key mechanisms of DES failure

- **Stent underexpansion**
- **Malapposition**
- **Incomplete lesion/stent coverage**
- **In-stent neoatherosclerosis**

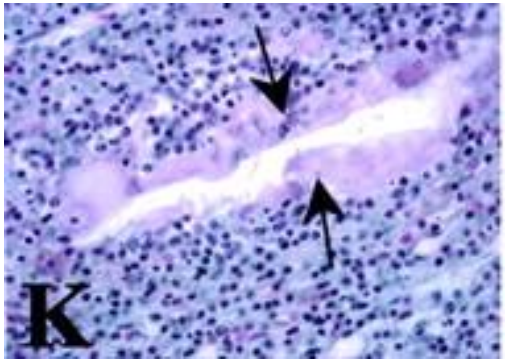
Stent Thrombosis of 1st G. DES :

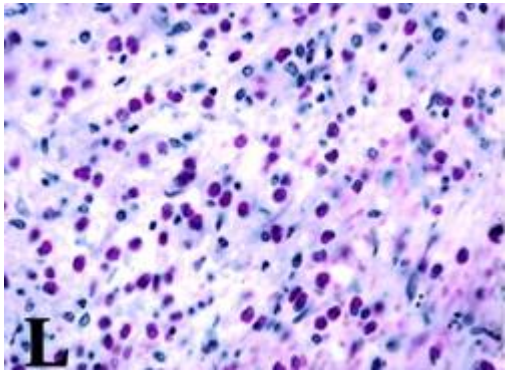
Hypersensitivity reaction to polymer

…. concerns about the potential for late stent thrombosis with DES related to hypersensitivity reaction to polymer and delayed vessel healing ….



Extensive inflammation with a focal giant cell reaction around stent strut (*) and surrounding polymer

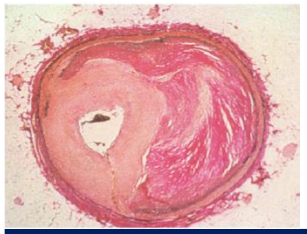


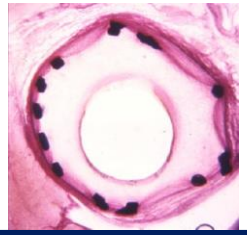


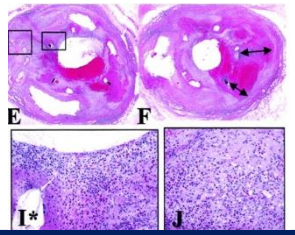
giant cells (arrowheads) around a polymer remnant that has separated from stent strut and numerous eosinophils within arterial wall.

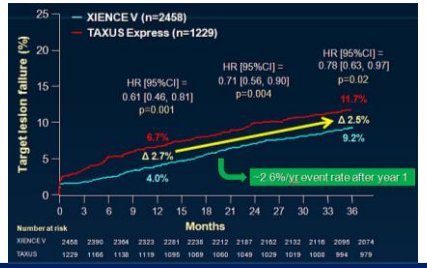
Virmani et at. *Circulation* 2004

Evolution of Coronary Stent Innovation

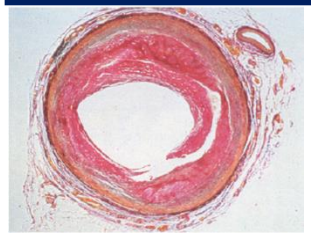








BMS → DP-DES → **BP-DES** → BRS ??



- **With risk of impaired vascular healing**
  - **chronic local inflammatory reaction & restriction of vascular vasomotion**

- **Late stent failures**
  - **in-stent restenosis (ISR)**
  - **Late stent thrombosis (LST)**

HATTRICK-OCT Trial

- Early neointimal coverage (OCT) and vasodilator response (invasive thermodilution-derived CFR at 3M)
- BP-SES vs. DP-ZES in 44 ACS pts.
- Primary endpoints :
  % uncovered struts & CFR

Variable	BP-SES group (n=22)	DP-ZES group (n=22)	P-value
Cross-sectional analysis			
No. cross-sections analyzed	425	425	1.0
Struts per cross-section	11.5±0.66	12.9±1.2	<0.001
Stent area (mm^2)	6.8±1.6	7.5±1.7	0.09
Lumen area (mm^2)	6.5 [2.2]	7.1 [2.6]	0.06
NIH area (μm^2)	380 [410]	460 [550]	0.11
% NIH area	5.7 [5.9]	5.7 [7.6]	0.69
Strut-level analysis			
Total no. struts analyzed	4,897	5,467	0.13
NIH thickness (μm)	69.1±58.2	76.5±82.9	0.15
Uncovered struts	189 (3.9)	495 (8.9)	<0.001
Malapposed struts	101 (2.1)	292 (5.3)	<0.001
Stent-level analysis			
% Uncovered struts	3.9±3.2	8.9±6.9	0.019
Stents with >5% uncovered struts	7 (31.8)	14 (63.6)	0.069
% Malapposed struts	2.2±3.7	4.3±9.5	0.33
Intra-stent thrombus	2 (9.1)	1 (4.5)	1.0

Variable	BP-SES group (n=18)	DP-ZES group (n=16)	P-value
Fractional flow reserve	0.87±0.07	0.87±0.06	0.93
Coronary flow reserve	3.0±1.3	3.2±1.0	0.56
Coronary flow reserve <2.5	8 (44.4)	2 (12.5)	0.06
Index of microcirculatory resistance	19.2±8.1	22.7±13.0	0.32

Circ J 2015; 79: 360

BP- vs DP-DES for late loss

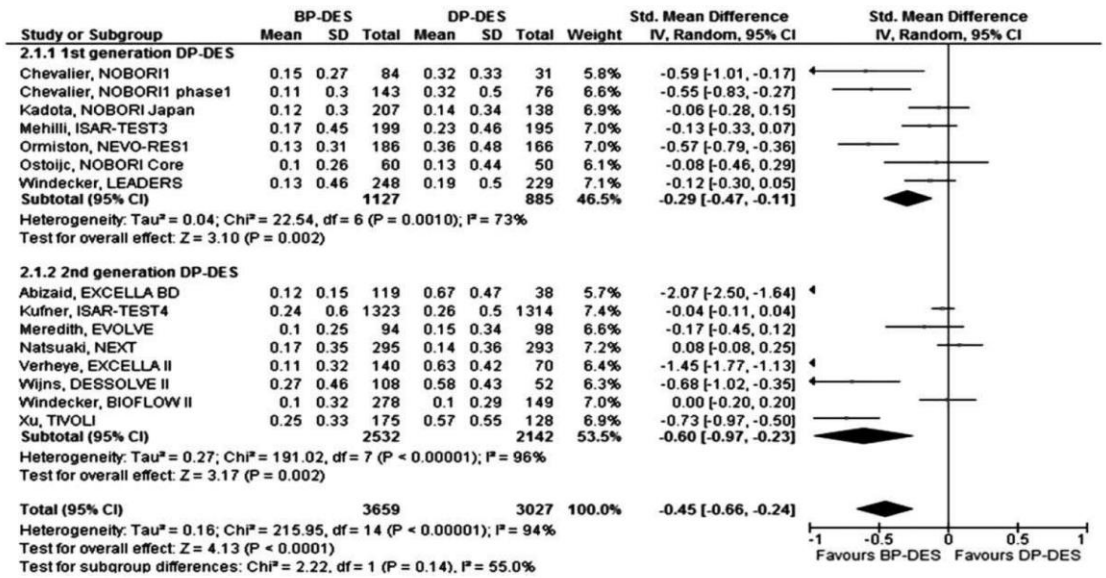
- **Meta-analysis including 20 studies w/ 20,005 pts (median clinical fup of 1 year)**

Author	Study	Year	Journal	Data reported	Pts number	Randomization	BPDES TYPE	DPDES TYPE	BPDES TYPE	DPDES TYPE
Windecker	BIOFLOW II	2013	EuroPCR	9 months clinical + angiographic follow-up	452	yes (2:1)	SES	EES	Orsiro™	Xience V™
Smits	COMPARE II	2013	Lancet	1 year clinical follow-up	2,707	yes (2:1)	BES	EES	Nobori™	Xience V™
Kruckoff	COSTAR II	2008	JACC	1 year clinical follow-up	1,675	yes (3:2)	PES	PES	CoStar™	Taxus Espress™
Wijns	DESSOLVE II	2012	JACC	1 year clinical + angiographic follow-up	181	yes (2:1)	SES	ZES	Elixir DESyne™	Endeavor™
Ge	EVOLUTION	2012	EuroPCR	1 year clinical follow-up	1,909	yes (2:1)	SES	SES	Excel™	Cypher Select™
Meredith	EVOLVE	2012	JACC	1 year clinical + angiographic follow-up	190	yes (1:1)	EES	EES	Promus Element™	Synergy™
Abizaid	EXCELLA BD	2012	JACC	1 year clinical + angiographic follow-up	146	yes (3:1)	NES	ZES	Elixir DESyne™	Endeavor™
Verheye	EXCELLA II	2012	JACC	1 year clinical + angiographic follow-up	210	yes (2:1)	NES	ZES	Elixir DESyne™	Endeavor™
Mehilli	ISAR TEST3	2008	Eur Heart J	1 year clinical + angiographic follow-up	404	yes (1:1)	SES	SES	BP 0.4% rapamycin stent	Cypher Select™
Byrne I	ISAR TEST3	2009	Heart	2 year clinical + angiographic follow-up	404	yes (1:1)	SES	SES	BP 0.4% rapamycin stent	Cypher Select™
Kufner	ISAR TEST4	2011	CCI	6 months angiographic follow-up	2,016	yes (2:1:1)	SES	SES/EES	BP 0.4% rapamycin stent	Cypher Select™, Xience™
Byrne III	ISAR TEST4	2011	JACC	3 years clinical follow-up	2,603	yes (2:1:1)	SES	SES/EES	BP 0.4% rapamycin stent	Cypher Select™, Xience™
Windecker	LEADERS	2008	Lancet	9 months clinical + angiographic follow-up	1,707	yes (1:1)	BES	SES	BioMatrix Flex™	Cypher Select™
Stefanini	LEADERS	2011	Lancet	4 year clinical follow-up	1,707	yes (1:1)	BES	SES	BioMatrix Flex™	Cypher Select™
Xu	na	2011	Chinese Med J	1 year clinical + angiographic follow-up	324	no	SES	ZES	Tivoli™	Endeavor™
Lee	na	2012	JACC	1 year clinical follow-up	604	no	BES	ZES/EES	Nobori™	Resolute™, Xience™
Ormiston	NEVO RES-1	2010	Circ Cardiovasc Int	1 year clinical + angiographic follow-up	394	yes (1:1)	SES	PES	Nevo™	Cypher Select™
Abizaid II	NEVO RES-1	2013	Eurointervention	2 year clinical + angiographic follow-up	394	yes (1:1)	SES	PES	Nevo™	Cypher Select™
Natsuaki	NEXT	2013	ACC	1 year clinical + angiographic follow-up	3,235	yes (1:1)	BES	EES	Nobori™	Xience V™ or Promus™
Ostojic	NOBORI CORE	2008	Eurointervention	1 year clinical + angiographic follow-up	107	no	BES	SES	Nobori™	Cypher Select™
Kadota	NOBORI JAPAN	2011	CCI	1 year clinical + angiographic follow-up	326	yes (3:2)	BES	SES	Nobori™	Cypher Select™
Kimura	NOBORI JAPAN	2012	JACC	3 years clinical follow-up	326	yes (3:2)	BES	SES	Nobori™	Cypher Select™
Chevalier I	NOBORI1	2007	Eurointervention	1 year clinical + angiographic follow-up	120	yes (2:1)	BES	PES	Nobori™	Taxus Liberté™
Chevalier II	NOBORI1 Phase1	2009	Circ Cardiovasc Int	1 year clinical + angiographic follow-up	243	yes (2:1)	BES	PES	Nobori™	Taxus Liberté™
Christiansen	SORT-OUT V	2013	Lancet	1 year clinical follow-up	2,468	yes (1:1)	BES	SES	Nobori™	Cypher Select™

Catheter Cardiovasc Interv. 2014;83:E193

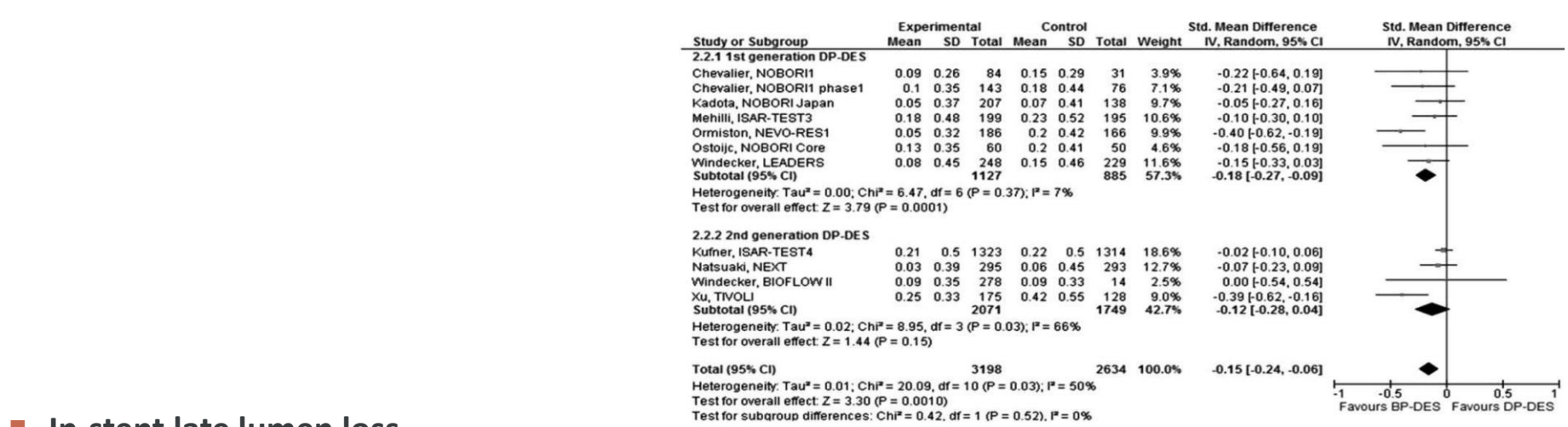
BP- vs DP-DES for late loss

- In-stent late lumen loss



Study or Subgroup	BP-DES Mean	SD	Total	DP-DES Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.1.1 1st generation DP-DES								
Chevalier, NOBORI1	0.15	0.27	84	0.32	0.33	31	5.8%	-0.59 [-1.01, -0.17]
Chevalier, NOBORI1 phase1	0.11	0.3	143	0.32	0.5	76	6.6%	-0.55 [-0.83, -0.27]
Kadota, NOBORI Japan	0.12	0.3	207	0.14	0.34	138	6.9%	-0.06 [-0.28, 0.15]
Mehilli, ISAR-TEST3	0.17	0.45	199	0.23	0.46	195	7.0%	-0.13 [-0.33, 0.07]
Ormiston, NEVO-RES1	0.13	0.31	186	0.36	0.48	166	7.0%	-0.57 [-0.79, -0.36]
Ostoijc, NOBORI Core	0.1	0.26	60	0.13	0.44	50	6.1%	-0.08 [-0.46, 0.29]
Windecker, LEADERS	0.13	0.46	248	0.19	0.5	229	7.1%	-0.12 [-0.30, 0.05]
Subtotal (95% CI)			**1127**			**885**	**46.5%**	**-0.29 [-0.47, -0.11]**
Heterogeneity: Tau² = 0.04; Chi² = 22.54, df = 6 (P = 0.0010); I² = 73%								
Test for overall effect: Z = 3.10 (P = 0.002)								
2.1.2 2nd generation DP-DES								
Abizaid, EXCELLA BD	0.12	0.15	119	0.67	0.47	38	5.7%	-2.07 [-2.50, -1.64]
Kufner, ISAR-TEST4	0.24	0.6	1323	0.26	0.5	1314	7.4%	-0.04 [-0.11, 0.04]
Meredith, EVOLVE	0.1	0.25	94	0.15	0.34	98	6.6%	-0.17 [-0.45, 0.12]
Natsuaki, NEXT	0.17	0.35	295	0.14	0.36	293	7.2%	0.08 [-0.08, 0.25]
Verheye, EXCELLA II	0.11	0.32	140	0.63	0.42	70	6.4%	-1.45 [-1.77, -1.13]
Wijns, DESSOLVE II	0.27	0.46	108	0.58	0.43	52	6.3%	-0.68 [-1.02, -0.35]
Windecker, BIOFLOW II	0.1	0.32	278	0.1	0.29	149	7.0%	0.00 [-0.20, 0.20]
Xu, TIVOLI	0.25	0.33	175	0.57	0.55	128	6.9%	-0.73 [-0.97, -0.50]
Subtotal (95% CI)			**2532**			**2142**	**53.5%**	**-0.60 [-0.97, -0.23]**
Heterogeneity: Tau² = 0.27; Chi² = 191.02, df = 7 (P < 0.00001); I² = 96%								
Test for overall effect: Z = 3.17 (P = 0.002)								
Total (95% CI)			**3659**			**3027**	**100.0%**	**-0.45 [-0.66, -0.24]**
Heterogeneity: Tau² = 0.16; Chi² = 215.95, df = 14 (P < 0.00001); I² = 94%								
Test for overall effect: Z = 4.13 (P < 0.0001)								
Test for subgroup differences: Chi² = 2.22, df = 1 (P = 0.14), I² = 55.0%								

- In-segment late lumen loss



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.2.1 1st generation DP-DES								
Chevalier, NOBORI1	0.09	0.26	84	0.15	0.29	31	3.9%	-0.22 [-0.64, 0.19]
Chevalier, NOBORI1 phase1	0.1	0.35	143	0.18	0.44	76	7.1%	-0.21 [-0.49, 0.07]
Kadota, NOBORI Japan	0.05	0.37	207	0.07	0.41	138	9.7%	-0.05 [-0.27, 0.16]
Mehilli, ISAR-TEST3	0.18	0.48	199	0.23	0.52	195	10.6%	-0.10 [-0.30, 0.10]
Ormiston, NEVO-RES1	0.05	0.32	186	0.2	0.42	166	9.9%	-0.40 [-0.62, -0.19]
Ostoijc, NOBORI Core	0.13	0.35	60	0.2	0.41	50	4.6%	-0.18 [-0.56, 0.19]
Windecker, LEADERS	0.08	0.45	248	0.15	0.46	229	11.6%	-0.15 [-0.33, 0.03]
Subtotal (95% CI)			**1127**			**885**	**57.3%**	**-0.18 [-0.27, -0.09]**
Heterogeneity: Tau² = 0.00; Chi² = 6.47, df = 6 (P = 0.37); I² = 7%								
Test for overall effect: Z = 3.79 (P = 0.0001)								
2.2.2 2nd generation DP-DES								
Kufner, ISAR-TEST4	0.21	0.5	1323	0.22	0.5	1314	18.6%	-0.02 [-0.10, 0.06]
Natsuaki, NEXT	0.03	0.39	295	0.06	0.45	293	12.7%	-0.07 [-0.23, 0.09]
Windecker, BIOFLOW II	0.09	0.35	278	0.09	0.33	14	2.5%	0.00 [-0.54, 0.54]
Xu, TIVOLI	0.25	0.33	175	0.42	0.55	128	9.0%	-0.39 [-0.62, -0.16]
Subtotal (95% CI)			**2071**			**1749**	**42.7%**	**-0.12 [-0.28, 0.04]**
Heterogeneity: Tau² = 0.02; Chi² = 8.95, df = 3 (P = 0.03); I² = 66%								
Test for overall effect: Z = 1.44 (P = 0.15)								
Total (95% CI)			**3198**			**2634**	**100.0%**	**-0.15 [-0.24, -0.06]**
Heterogeneity: Tau² = 0.01; Chi² = 20.09, df = 10 (P = 0.03); I² = 50%								
Test for overall effect: Z = 3.30 (P = 0.0010)								
Test for subgroup differences: Chi² = 0.42, df = 1 (P = 0.52), I² = 0%								

Catheter Cardiovasc Interv. 2014;83:E193

BP- vs DP-DES for harder endpoints

- **Weighted Mean Differences & Odds Ratios for Various Endpoints**

	Study number	BP-DES pt/ lesion number	DP-DES pt/ lesion number	WMD or OR	95% CI	*P* level for overall effect
In stent LLL	15	3,659	3,027	−0.45	−0.66 to −0.24	<0.0001
In segment LLL	11	3,198	2,796	−0.15	−0.24 to −0.06	0.001
Overall death	17	9,323	8,113	0.94	0.80 to 1.11	0.48
Cardiac death	16	8,052	6,431	0.90	0.71 to 1.14	0.39
MI	18	10,806	8,884	01:08	0.92 to 1.28	0.34
TLR	17	8,718	7,598	0.82	0.65 to 1.04	0.10
TVR	15	10,138	8,372	1.04	0.84 to 1.27	0.74
Acute/subacute ST	16	9,238	7,371	1.23	0.80 to 1.90	0.34
Late/very late ST	17	9,359	7,431	0.51	0.30 to 0.86	0.01

Catheter Cardiovasc Interv. 2014;83:E193

BP-DES vs 2nd G. DP-DES

- **Meta-analysis including 16 RCTs w/ 19,886 pts (mean duration 26 months).**

Study/First Author (Ref. #)	Number of Patients (N)		DAPT Duration (Months)	Follow-Up (Months)	BP-DES Characteristics		
	BP-DES	DP-DES			Stent	Strut Thickness (μm)	Drug
BASKET-PROVE II (20)	765	765	12	24	Nobori	120	Biolimus
BIOFLOW II (21)	298	154	>6	12	Orsiro	60	Sirolimus
BIOSCIENCE (22)	1063	1056	12	24	Orsiro	60	Sirolimus
CENTURY II (23)	551	550	>6	9	Ultimaster	80	Sirolimus
COMPARE II (24)	1,795	912	12	36	Nobori	120	Biolimus
DESSOLVE II (25)	123	61	6 to 12	9	MiStent	64	Sirolimus
EVERBIO II (26)	80	80	>6	9	BioMatrix Flex	112	Biolimus
EVOLVE FHU (27)	193	98	>6	24	Synergy	74	Everolimus
EVOLVE II (28)	846	838	>6	12	Synergy	74	Everolimus
ISAR-TEST 4 (29)	1,299	1,304	>6	60	Yukon choice PC	87	Sirolimus
LONG-DES V (30)	245	255	>12	12	Nobori	120	Biolimus
NEXT (31)	1,617	1,618	>3	36	Nobori	120	Biolimus
Separham et al. (32)	100	100	>12	12	BioMatrix	112	Biolimus
SORT OUT VI (33)	1,497	1,502	>12	12	BioMatrix Flex	112	Biolimus
TARGET I (34)	227	231	>12	12	Firehawk	86	Sirolimus
Xu et al. (35)	168	156	6	24	Tivoli	80	Sirolimus

TABLE 1 Continued

Study/First Author (Ref. #)	BP-DES Characteristics			DP-DES Characteristics			
	Scaffold Material	Drug Release (Months)	Polymer Biodegradation (Months)	Stent	Strut Thickness (μm)	Drug	Scaffold Material
BASKET-PROVE II (20)	SS	6-9	12	Xience Prime	81	Everolimus	Co-Cr
BIOFLOW II (21)	Co-Cr	12	14	Xience Prime	81	Everolimus	Co-Cr
BIOSCIENCE (22)	Co-Cr	12	14	Xience Prime	81	Everolimus	Co-Cr
CENTURY II (23)	Co-Cr	4	4	Xience V	81	Everolimus	Co-Cr
COMPARE II (24)	SS	6-9	12	Xience V/ Prime	81	Everolimus	Co-Cr
DESSOLVE II (25)	Co-Cr	9	3	Endeavor	91	Zotarolimus	Co-Cr
EVERBIO II (26)	SS	6-9	6-9	Promus Element	81	Everolimus	Pl-Cr
EVOLVE FHU (27)	Pl-Cr	3	4	Promus Element	81	Everolimus	Pl-Cr
EVOLVE II (28)	Pl-Cr	3	4	Promus Element	81	Everolimus	Pl-Cr
ISAR-TEST 4 (29)	SS	1	2-3	Xience V	81	Everolimus	Co-Cr
LONG-DES V (30)	SS	6-9	12	Promus Element	81	Everolimus	Pl-Cr
NEXT (31)	SS	6-9	12	Xience/Promus	81	Everolimus	Co-Cr/Pl-Cr
Separham et al. (32)	SS	6-9	12	Xience V	81	Everolimus	Co-Cr
SORT OUT VI (33)	SS	6-9	6-9	Resolute Integrity	91	Zotarolimus	Co-Cr
TARGET I (34)	Co-Cr	1	6-9	Xience V	81	Everolimus	Co-Cr
Xu et al. (35)	Co-Cr	1	6	Endeavor	91	Zotarolimus	Co-Cr

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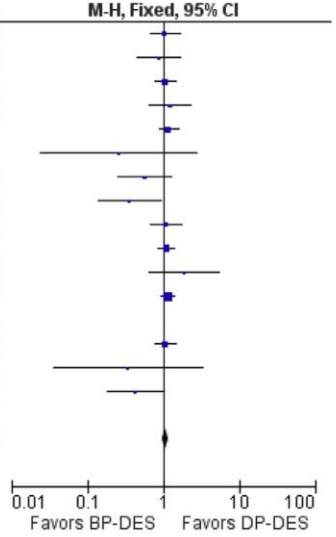
BP-DES vs 2nd G. DP-DES

- **TVR**

Study or Subgroup	BP-DES Events	BP-DES Total	DP-DES Events	DP-DES Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BASKET-PROVE II	38	765	36	765	5.7%	1.06 [0.68, 1.65]
BIOFLOW-II	22	298	13	154	2.7%	0.87 [0.45, 1.69]
BIOSCIENCE	81	1063	75	1056	11.9%	1.07 [0.79, 1.45]
CENTURY II	21	551	17	550	2.7%	1.23 [0.66, 2.31]
COMPARE II	137	1795	59	912	12.4%	1.18 [0.88, 1.58]
DESSOLVE II	1	117	2	60	0.4%	0.26 [0.02, 2.77]
EVERBIO	8	80	14	80	2.2%	0.57 [0.25, 1.29]
EVOLVE FHU	7	191	10	98	2.1%	0.36 [0.14, 0.91]
EVOLVE II	32	846	29	838	4.6%	1.09 [0.67, 1.79]
ISAR-TEST 4	170	1299	77	652	16.3%	1.11 [0.86, 1.43]
LONG-DES V	9	245	5	255	0.8%	1.87 [0.64, 5.51]
NEXT	177	1617	155	1618	24.6%	1.14 [0.93, 1.40]
SEPARHAM et al	0	100	0	100		Not estimable
SORT OUT VI	71	1497	67	1502	10.6%	1.06 [0.77, 1.47]
TARGET I	1	227	3	231	0.5%	0.34 [0.04, 3.24]
XU et al	7	168	15	156	2.5%	0.43 [0.18, 1.03]
Total (95% CI)		**10859**		**9027**	**100.0%**	**1.06 [0.96, 1.18]**
Total events	782		577			

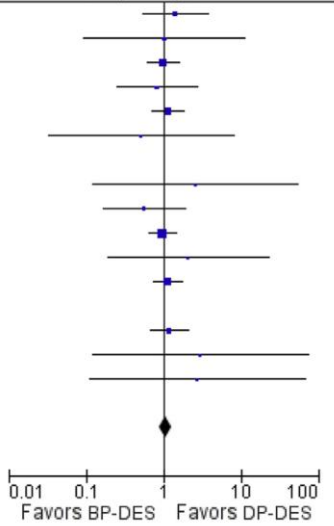
Heterogeneity: Chi² = 16.56, df = 14 (P = 0.28); I² = 15%
Test for overall effect: Z = 1.17 (P = 0.24)



- **Cardiac death**

Study or Subgroup	BP-DES Events	BP-DES Total	DP-DES Events	DP-DES Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BASKET-PROVE II	10	765	7	765	3.6%	1.43 [0.55, 3.73]
BIOFLOW-II	2	298	1	154	0.7%	1.03 [0.09, 11.31]
BIOSCIENCE	33	1063	33	1056	17.2%	0.99 [0.62, 1.60]
CENTURY II	5	551	6	550	3.1%	0.83 [0.26, 2.71]
COMPARE II	52	1795	23	912	15.8%	1.15 [0.71, 1.86]
DESSOLVE II	1	117	1	60	0.7%	0.51 [0.03, 8.06]
EVERBIO	0	80	0	80		Not estimable
EVOLVE FHU	2	191	0	98	0.3%	2.58 [0.12, 53.18]
EVOLVE II	4	846	7	838	3.6%	0.57 [0.17, 1.93]
ISAR-TEST 4	64	1299	33	652	22.8%	0.97 [0.65, 1.47]
LONG-DES V	2	245	1	255	0.5%	2.08 [0.19, 22.81]
NEXT	43	1617	38	1618	19.7%	1.13 [0.74, 1.74]
SEPARHAM et al	0	100	0	100		Not estimable
SORT OUT VI	26	1497	22	1502	11.4%	1.19 [0.68, 2.08]
TARGET I	1	227	0	231	0.3%	3.05 [0.13, 74.54]
XU et al	1	168	0	156	0.3%	2.79 [0.11, 67.91]
Total (95% CI)		**10859**		**9027**	**100.0%**	**1.08 [0.89, 1.31]**
		172				

13 (P = 0.99); I² = 0%
P = 0.46)



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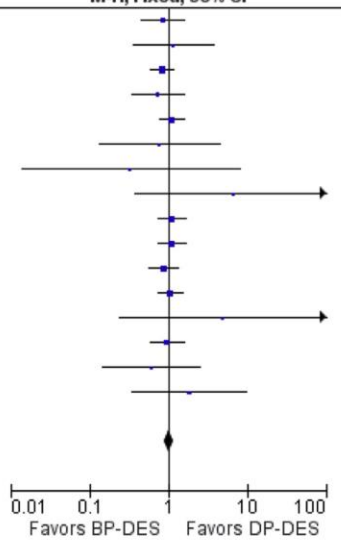
BP-DES vs 2nd G. DP-DES

- MI

Study or Subgroup	BP-DES Events	BP-DES Total	DP-DES Events	DP-DES Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BASKET-PROVE II	18	765	21	765	5.3%	0.86 [0.46, 1.60]
BIOFLOW-II	9	298	4	154	1.3%	1.16 [0.36, 3.72]
BIOSCIENCE	62	1063	73	1056	18.5%	0.84 [0.61, 1.17]
CENTURY II	11	551	15	550	3.8%	0.73 [0.34, 1.58]
COMPARE II	93	1795	42	912	14.1%	1.13 [0.79, 1.61]
DESSOLVE II	3	117	2	60	0.7%	0.77 [0.13, 4.48]
EVERBIO	0	80	1	80	0.4%	0.33 [0.01, 8.06]
EVOLVE FHU	6	191	0	98	0.2%	6.70 [0.38, 117.77]
EVOLVE II	45	846	40	838	10.2%	1.11 [0.74, 1.69]
ISAR-TEST 4	70	1299	32	652	10.8%	1.10 [0.73, 1.65]
LONG-DES V	34	245	40	255	9.9%	0.88 [0.58, 1.35]
NEXT	64	1617	60	1618	15.2%	1.07 [0.76, 1.51]
SEPARHAM et al	2	100	0	100	0.1%	5.00 [0.24, 102.85]
SORT OUT VI	30	1497	31	1502	7.8%	0.97 [0.59, 1.60]
TARGET I	3	227	5	231	1.3%	0.61 [0.15, 2.52]
XU et al	4	168	2	156	0.5%	1.86 [0.34, 10.00]
Total (95% CI)		**10859**		**9027**	**100.0%**	**1.00 [0.87, 1.15]**
Total events	454		368			

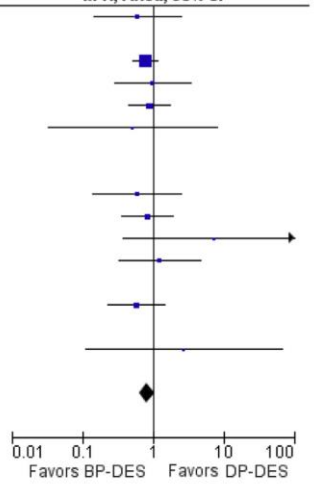
Heterogeneity: Chi² = 7.64, df = 15 (P = 0.94); I² = 0%
Test for overall effect: Z = 0.03 (P = 0.98)



- ST

Study or Subgroup	BP-DES Events	BP-DES Total	DP-DES Events	DP-DES Total	Weight	Risk Ratio M-H, Fixed, 95% CI
BASKET-PROVE II	3	765	5	765	4.4%	0.60 [0.14, 2.50]
BIOFLOW-II	0	298	0	154		Not estimable
BIOSCIENCE	40	1063	50	1056	44.5%	0.79 [0.53, 1.19]
CENTURY II	5	551	5	550	4.4%	1.00 [0.29, 3.43]
COMPARE II	23	1795	13	912	15.3%	0.90 [0.46, 1.77]
DESSOLVE II	1	117	1	60	1.2%	0.51 [0.03, 8.06]
EVERBIO	0	80	0	80		Not estimable
EVOLVE FHU	0	191	0	98		Not estimable
EVOLVE II	3	846	5	838	4.5%	0.59 [0.14, 2.48]
ISAR-TEST 4	15	1299	9	652	10.6%	0.84 [0.37, 1.90]
LONG-DES V	3	245	0	255	0.4%	7.28 [0.38, 140.30]
NEXT	5	1617	4	1618	3.5%	1.25 [0.34, 4.65]
SEPARHAM et al	0	100	0	100		Not estimable
SORT OUT VI	7	1497	12	1502	10.6%	0.59 [0.23, 1.48]
TARGET I	0	227	0	231		Not estimable
XU et al	1	168	0	156	0.5%	2.79 [0.11, 67.91]
Total (95% CI)		**10859**		**9027**	**100.0%**	**0.83 [0.64, 1.09]**
Total events	106		104			

Heterogeneity: Chi² = 4.26, df = 10 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.32 (P = 0.19)



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BP-DES vs 2nd G. DP-DES
- beyond 1 year

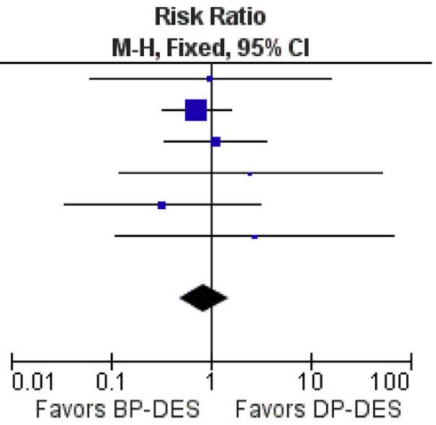
- **Landmark analysis for cardiac outcomes**

Analysis (No. of Trials Included)	TVR RR (95% CI)	Cardiac Death RR (95% CI)	MI RR (95% CI)	Definite/Probable ST RR (95% CI)
Outcomes at 1 yr (12)	1.08 (0.94-1.23)	1.05 (0.82-1.36)	1.02 (0.87-1.20)	0.82 (0.59-1.12)
Outcomes at the longest follow-up (16)	1.06 (0.96-1.18)	1.08 (0.89-1.31)	1.00 (0.87-1.15)	0.83 (0.64-1.09)
Landmark analysis beyond 1 yr (6)	1.12 (0.93-1.35)	1.13 (0.82-1.56)	0.95 (0.71-1.29)	0.87 (0.49-1.53)

- **VLST**

	BP-DES		DP-DES			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI
BASKET-PROVE II	1	765	1	765	3.9%	1.00 [0.06, 15.96]
BIOSCIENCE	11	1063	15	1056	58.9%	0.73 [0.34, 1.58]
COMPARE II	9	1795	4	912	20.8%	1.14 [0.35, 3.70]
ISAR-TEST 4	2	1299	0	652	2.6%	2.51 [0.12, 52.24]
NEXT	1	1617	3	1618	11.7%	0.33 [0.03, 3.20]
XU et al	1	168	0	156	2.0%	2.79 [0.11, 67.91]
Total (95% CI)		**6707**		**5159**	**100.0%**	**0.87 [0.49, 1.53]**
Total events	25		23			

Heterogeneity: Chi² = 2.09, df = 5 (P = 0.84); I² = 0%
Test for overall effect: Z = 0.49 (P = 0.62)



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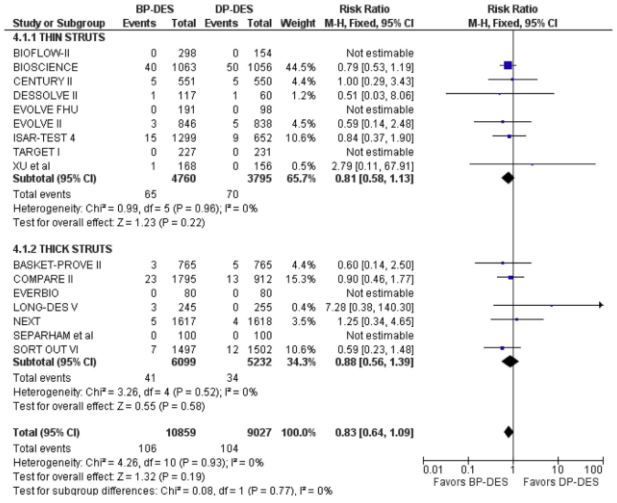
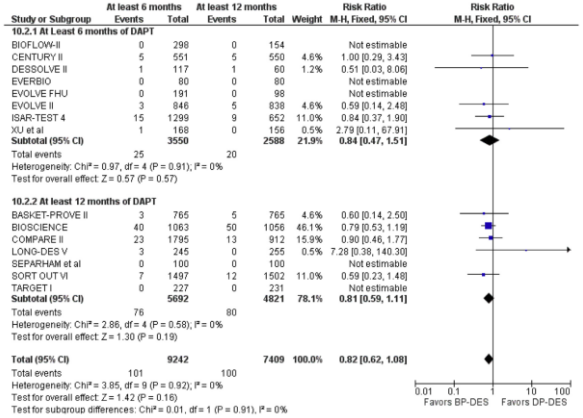
BP-DES vs 2nd G. DP-DES
- subgroup analysis

Analysis (No. of Trials Included)	TVR RR (95% CI)	Cardiac Death RR (95% CI)	MI RR (95% CI)	Definite/Probable ST RR (95% CI)
BP eluting drug				
Biolimus (7)	1.11 (0.97–1.28)	1.18 (0.90–1.54)	1.02 (0.84–1.23)	0.88 (0.56–1.39)
Sirolimus (7)	1.02 (0.86–1.22)	0.99 (0.74–1.32)	0.92 (0.73–1.16)	0.83 (0.59–1.17)
BP-DES strut thickness				
Thin struts (9)	1.00 (0.85–1.17)	0.97 (0.73–1.28)	0.98 (0.81–1.20)	0.81 (0.58–1.13)
Thick struts (7)	1.11 (0.97–1.28)	1.18 (0.90–1.54)	1.02 (0.84–1.23)	0.88 (0.56–1.39)
BP-DES scaffold				
Alloy (8)	0.94 (0.76–1.15)	0.96 (0.65–1.42)	0.95 (0.76–1.20)	0.81 (0.56–1.16)
Stainless steel (8)	1.11 (0.99–1.26)	1.12 (0.89–1.40)	1.03 (0.87–1.22)	0.87 (0.58–1.30)
BP-DES drug release				
<6 months	0.99 (0.81–1.21)	0.96 (0.67–1.38)	1.08 (0.83–1.40)	0.86 (0.47–1.57)
>6 months	1.09 (0.97–1.24)	1.13 (0.89–1.42)	0.97 (0.83–1.14)	0.83 (0.61–1.12)
Polymer degradation				
<6 months	0.99 (0.81–1.21)	0.93 (0.65–1.34)	1.09 (0.84–1.42)	0.84 (0.47–1.51)
>6 months	1.09 (0.97–1.24)	1.14 (0.90–1.43)	0.97 (0.83–1.14)	0.83 (0.61–1.13)
DP eluting drug				
Everolimus (13)	1.09 (0.97–1.21)	1.06 (0.86–1.31)	1.00 (0.87–1.15)	0.86 (0.65–1.14)
Zotarolimus (3)	0.92 (0.68–1.24)	1.18 (0.69–2.03)	1.01 (0.64–1.59)	0.66 (0.29–1.52)
DAPT duration				
≥6 months (8)	0.95 (0.79–1.15)	0.94 (0.66–1.33)	1.09 (0.84–1.42)	0.84 (0.47–1.51)
≥12 months (7)	1.13 (0.99–1.28)	1.14 (0.87–1.50)	0.94 (0.77–1.14)	0.81 (0.59–1.11)





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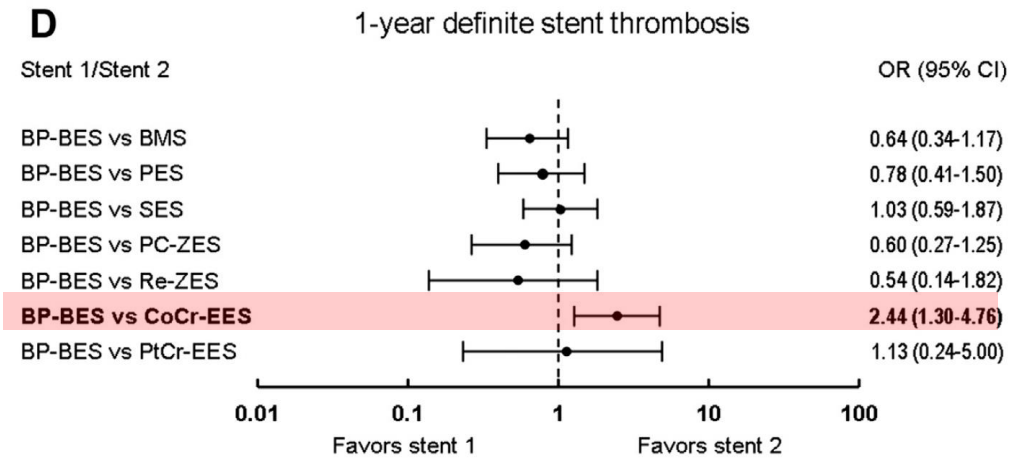
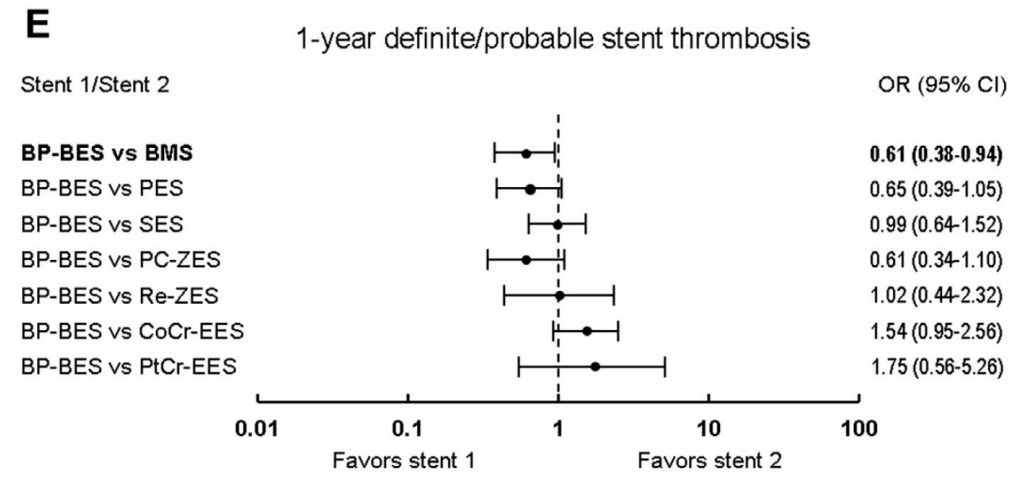
BMS vs DP-DES vs BP-BES for clinical outcomes

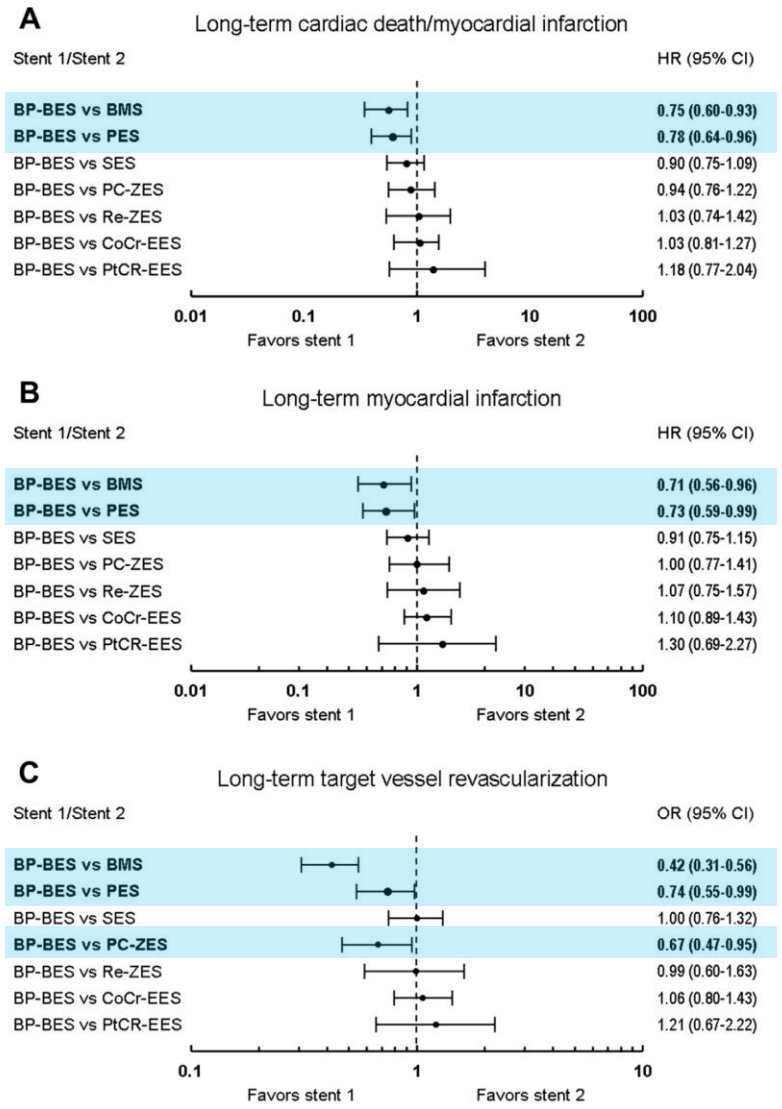
- Network meta-analysis using 89 trials w/ 85,490 pts (BMS, DP-DES, & BP-BES)
- Principal endpoint : definite or probable ST within 1 year.

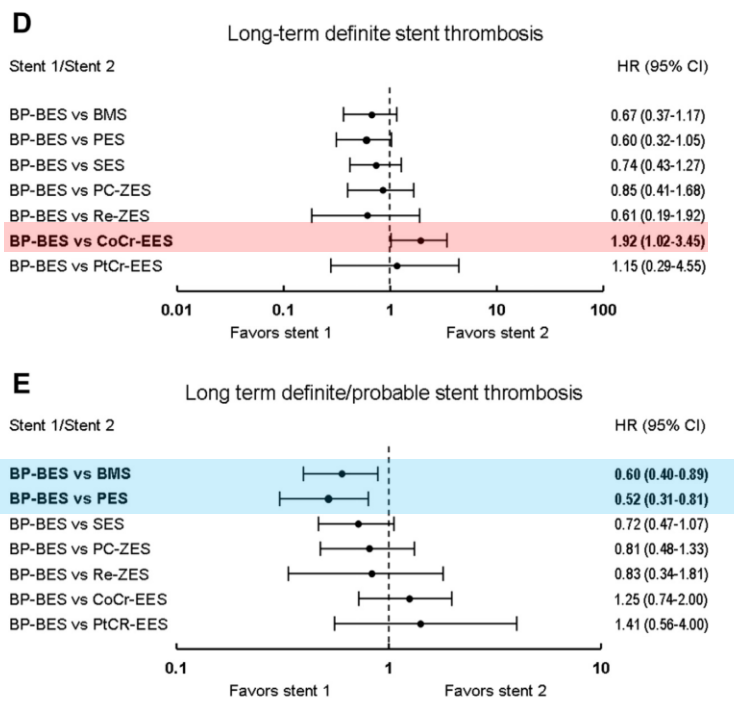




J Am Coll Cardiol 2014;63:299

BMS vs DP-DES vs BP-BES for late (> 1 year) outcomes



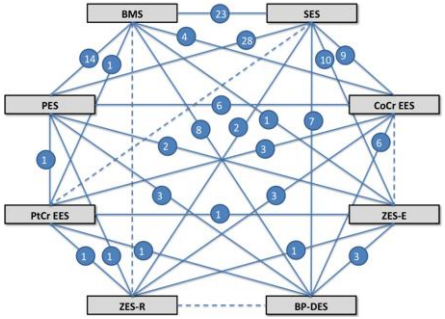


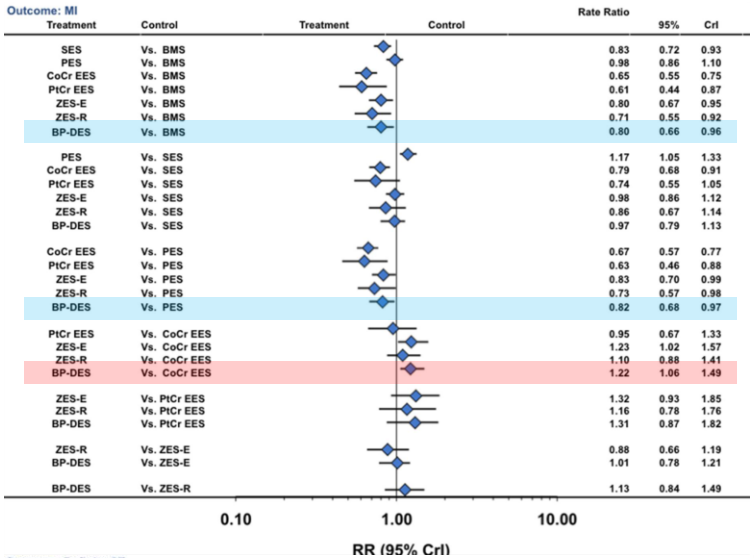
J Am Coll Cardiol 2014;63:299

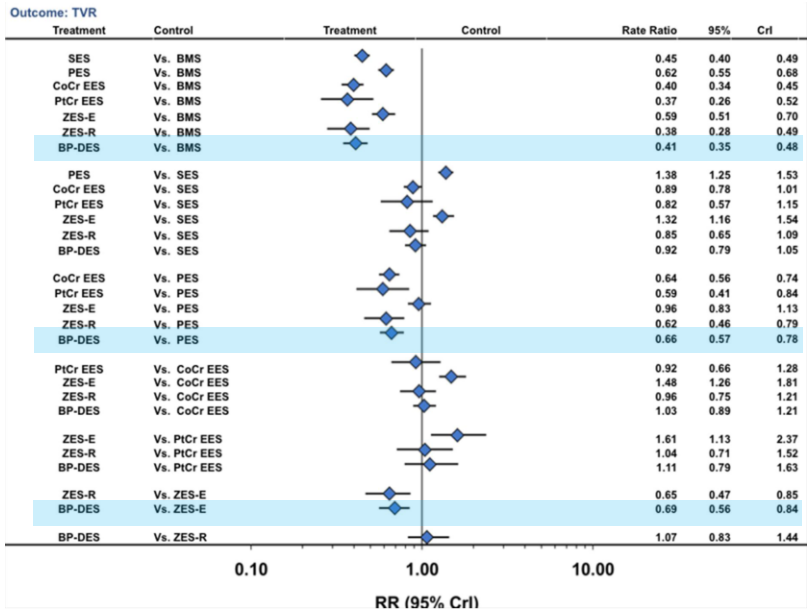
BMS vs DP-DES vs BP-BES

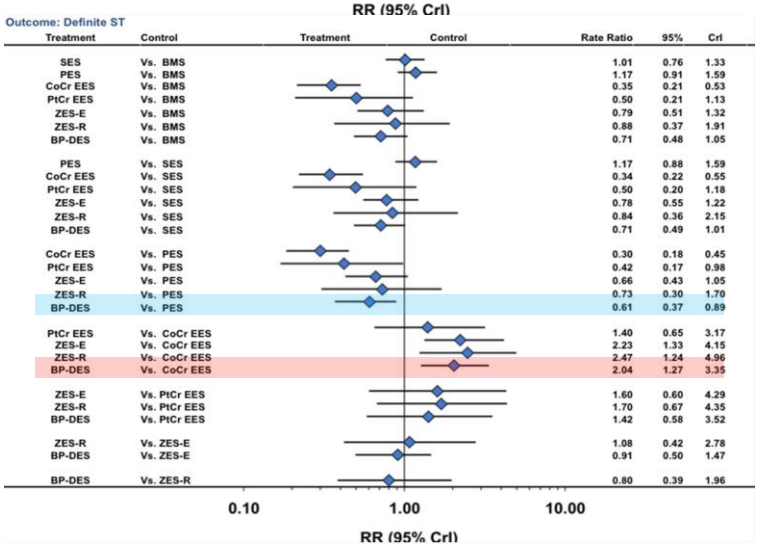
- mixed treatment comparison meta-analysis

- 126 randomized trials & 258,544 pt years of fup
- Long term efficacy (TVR, TLR) & safety (death, MI, ST)
- Landmark analysis





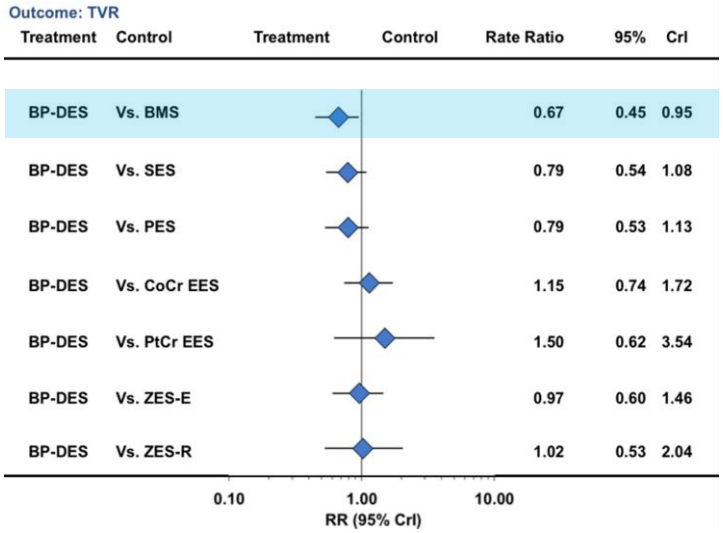


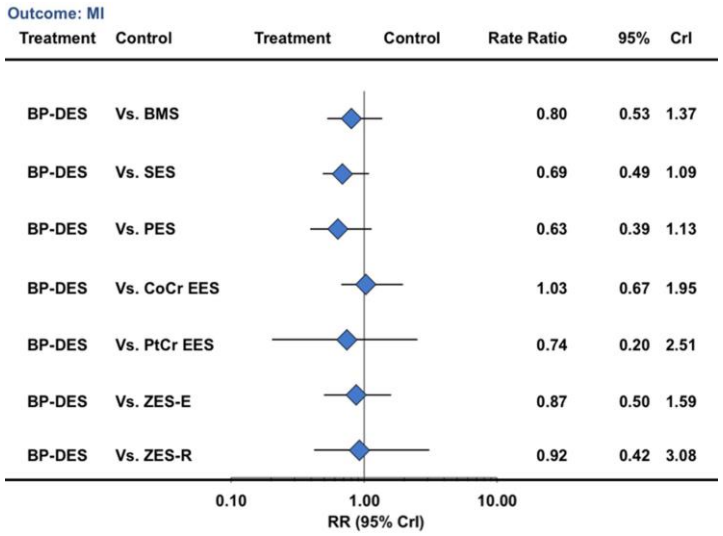


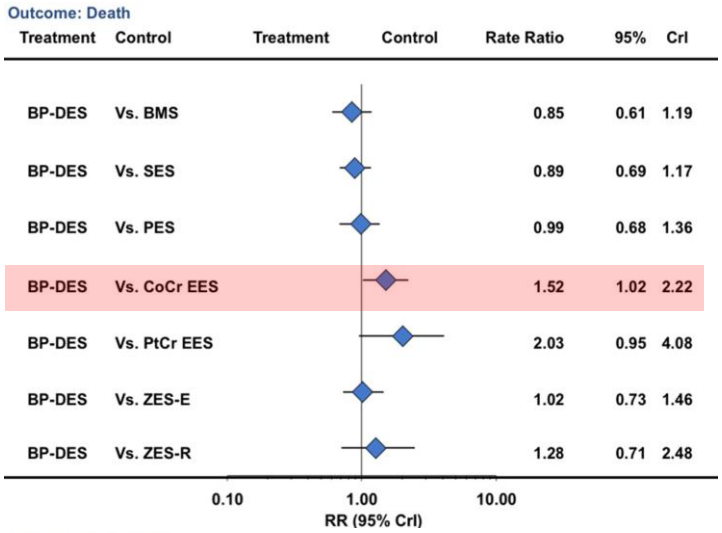
BMJ. 2013 Nov 8;347:f6625

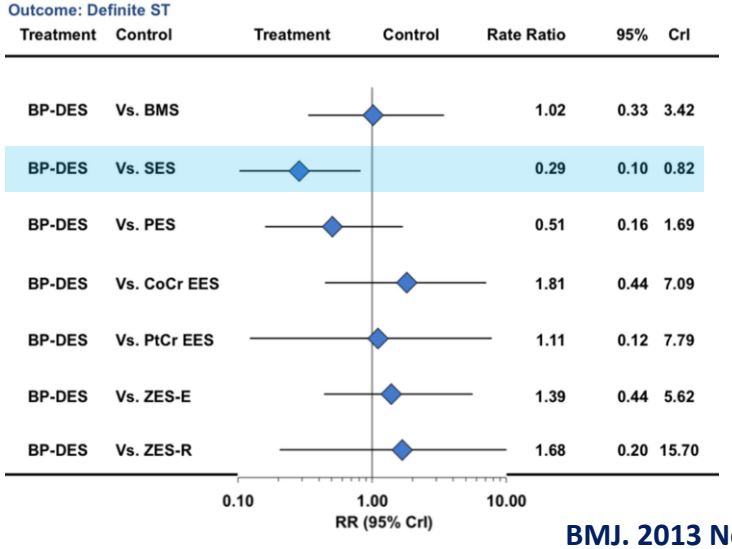
BMS vs DP-DES vs BP-BES

- Landmark analysis beyond 1 year









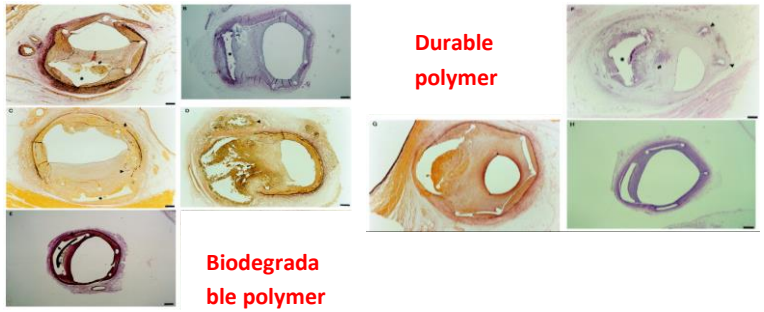
BMJ. 2013 Nov 8;347:f6625

Porcine coronary model

3M histomorphometric analysis

Measurements	EES n=6	BES n=5	SES n=6	*p*-value
EEL area (mm²)	7.50±0.66	8.21±0.89	8.47±2.09	0.46
Stent area (mm²)	6.19±0.50	6.83±0.77	6.74±1.50	0.52
Lumen area (mm²)	3.31±0.88	3.07±1.34	1.67±0.73*	0.03
Neointimal area (mm²)	2.88±0.47	3.76±0.91	5.07±1.54**	0.01
Area stenosis (%)	47.23±10.77	56.00±16.87	75.91±9.80*	0.0047
Neointimal thickness (mm)	0.39±0.09	0.50±0.22	0.80±0.24*	0.0083
Injury score	0.45±0.22	0.78±0.59	1.64±0.57*	0.0022
Fibrin score	0.33±0.35	0.75±0.79	0.31±0.29	0.29
Struts with granuloma (%)	2.32±3.49	5.05±7.31	45.47±34.06*	0.0033
Inflammatory score	0.50±0.42	0.80±0.88	2.92±1.42*	0.0014
Giant cells (%)	1.98±2.08	2.08±0.85	43.65±22.67*	0.0001

*Significantly different from EES and BES. **Significantly different from EES. EEL: external elastic lamina



6M histomorphometric analysis

Measurements	EES n=6	BES n=6	SES n=6	*p*-value
EEL area (mm²)	7.02±0.93	8.01±1.07	7.30±1.87	0.44
Stent area (mm²)	5.93±0.74	6.79±0.85	5.86±1.23	0.21
Lumen area (mm²)	2.40±1.47	2.91±1.40	1.83±0.68	0.34
Neointimal area (mm²)	3.53±1.00	3.88±0.70	4.04±0.66	0.54
Area stenosis (%)	60.99±20.52	58.62±14.73	69.44±6.29	0.44
Neointimal thickness (mm)	0.53±0.23	0.48±0.14	0.58±0.05	0.56
Injury score	0.87±0.65	0.97±0.34	1.71±0.71*	0.05
Fibrin score	0.03±0.7	0	0	0.39
Struts with granuloma (%)	1.57±2.49	0.25±0.61	27.09±36.94	0.08
Inflammatory score	0.39±0.60	0.28±0.29	1.63±1.53*	0.049
Giant cells (%)	3.56±7.22	0.25±0.62	27.73±37.86	0.09

*Significantly different from EES and BES. EEL: external elastic lamina

EuroIntervention. 2014;10:717

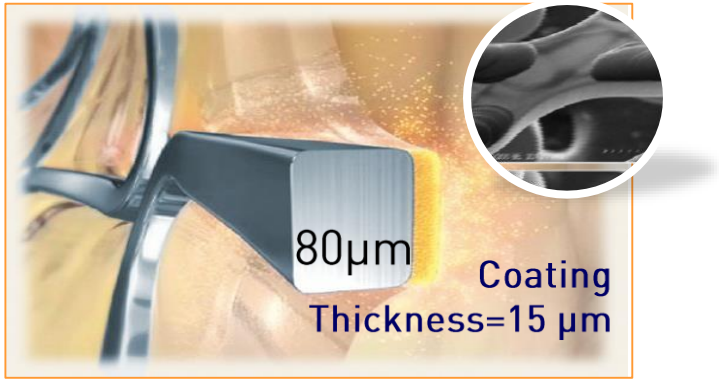
OCT substudy of NEXT trial

- 91 pts (55 EES-treated lesions in 48 patients and 51 BES-treated lesions in 43 patients)
- 8–12 months follow-up OCT imaging

	EES	BES	P-value
Stent struts			
No. struts	8,996	8,745	
Well-apposed and covered struts	8,762 (97.4)	7,920 (90.6)	<0.001
Well-apposed and uncovered struts	217 (2.4)	712 (8.1)	<0.001
Malapposed and covered struts	2 (0.02)	25 (0.3)	<0.001
Malapposed and uncovered struts	15 (0.2)	88 (1.0)	<0.001
Stent-treated lesions			
No. stent-treated lesions	55	51	
Neointimal coverage over stent struts			
Uncovered struts (%)	3±7	9±10	<0.001
Lesions with any uncovered struts	28 (51)	42 (82)	<0.001
Frames with >30% uncovered struts (%)	4±10	6±11	0.375
Maximum length of segments with uncovered struts (mm)	1.0±1.4	3.1±3.2	<0.001
Stent malapposition			
Malapposed struts (%)	0.2±0.8	1.3±2.8	0.006
Lesions with any malapposed struts	6 (11)	14 (27)	0.028
Maximum length of segments with stent malapposition (mm)	0.1±0.3	0.3±0.5	0.030
Intra-stent thrombus	2 (4)	5 (10)	0.258
Morphometry			
Minimum lumen area (mm^2)	5.20±2.19	5.69±2.05	0.242
Minimum stent area (mm^2)	6.13±2.24	6.41±2.20	0.515
Maximum neointima area (mm^2)	1.56±0.66	1.31±0.75	0.069
Maximum stent malapposition area (mm^2)	0.16±0.60	0.30±0.69	0.275
Lumen volume (mm^3)	108.07±53.74	115.96±40.50	0.398
Stent volume (mm^3)	123.54±61.05	128.47±46.44	0.643
Neointima volume (mm^3)	15.79±11.54	13.09±12.58	0.253
Stent malapposition volume (mm^3)	0.31±1.28	0.58±1.57	0.336

Circ J 2014; 78: 2408

Ultimaster



- Thin strut CoCr stent
- Abluminal gradient coating with bioresorbable and elastic polymer
- Bioabsorbtion in 3-4 months
- Sirolimus 3.9 µg/mm stent

– ULTIMASTER® is a new reduced dose sirolimus-eluting stent using an abluminal bioabsorbable coating (Ultimaster; Terumo, Tokyo, Japan), which has a potential to obtain a different arterial healing than early generation of permanent polymer-based DES.

- However, the time course of early vascular healing has not been fully elucidated in STEMI and SAP, which hampers an understanding of "mechanisms" of the risk reduction for stent thrombosis.

Various clinical programs covered by Ultimaster®

Approximately 45,000pts worldwide planned in studies with Ultimaster DES

Worldwide

TCD-10023 PK	CENTURY	CENTURY II	MASTER
20 pts	105 pts	1,123 pts	500 pts
Single arm	Single arm	Randomised 1:1vsPP-EES	Randomised 3:1vsBMS
Pharmaco-kinetics	Selected patients (CE mark approved)	Real world global study	STEMI
Published	Published	Published	PCR2016

DISCOVERY 1TO3	e-Ultimaster	MASTER DAPT
60 pts	Approximately 37,000pts	4,300pts
Single arm	Single arm	Randomised 1:1
Multivessel disease OFDI strut coverage	All-comers	1 month DAPT for High Bleeding Risk patients
PCR2016	On-going	On-going

Japan

MODEL U-SES	CENTURY JSV
1,500pts	70pts
Single arm	Single arm
3 months DAPT	Stents Φ2.25mm
On-going	PCR2016

MECHANISM-Ultimaster AMI	MECHANISM-Ultimaster Elective
100pts	100pts
Single arm	Single arm
Early OFDI strut coverage for AMI patients	Early OFDI strut coverage for Elective patients
On-going	On-going

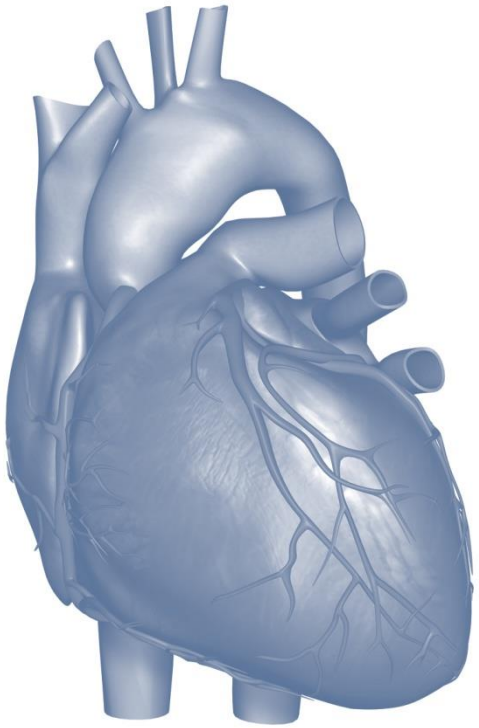
Barbato E et al. EuroIntervention. 2015;11:541–8; Saito S et al. Eur Heart J 2014;35:2021–31; Stojkovic S et al. Fundam Clin Pharmacol 2015;29:95–105; Barbato E. Presented at EuroPCR 2015, abstract OP047; Stankovic G. Presented at EuroPCR 2015; Smits P. Presented at EuroPCR 2015; Data on file at Terumo Corporation

CENTURY II series

CENTURY II
NSTEMI subgroup/
MASTER

CENTURY II
Long lesion subgroup

CENTURY II
Diabetes subgroup



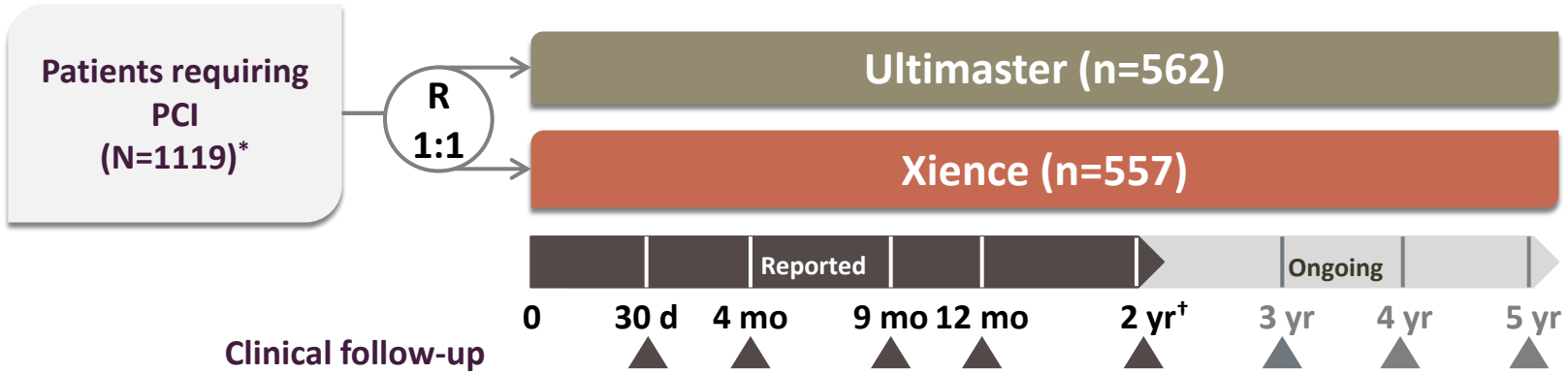
CENTURY II
Bifurcation subgroup

CENTURY II
Multivessel disease
subgroup

CENTURY II
Small vessel
subgroup

CENTURY II: Head-to-head study vs Xience

A large, prospective, multicentre, intercontinental study has directly studied Ultimaster vs Xience



Primary endpoint : Freedom from TLF at 9 months

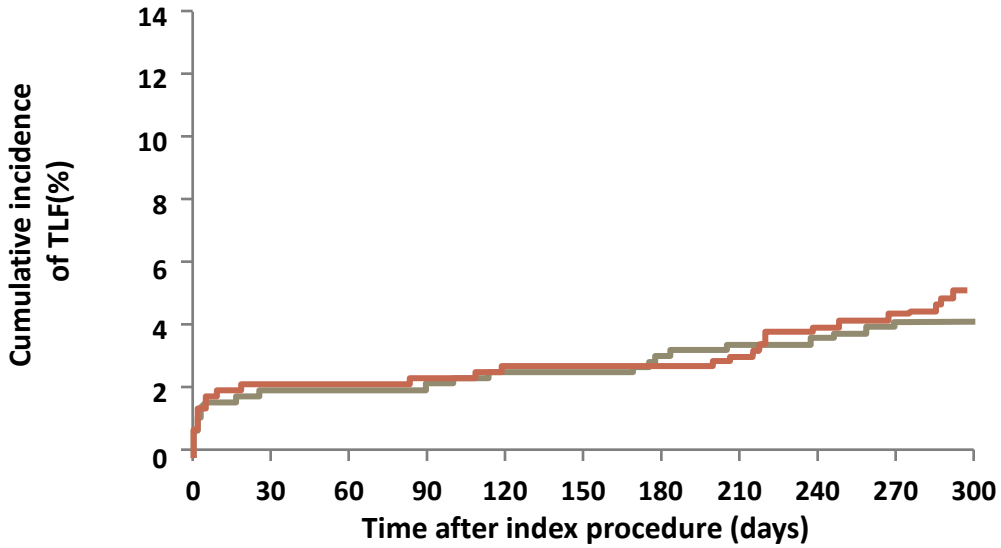
*1123 enrolled, 1119 in intention-to-treat population; †2-year data reported for key subgroups; TLF, target lesion failure

Saito S et al. Eur Heart J 2014;35:2021–31; Lesiak M. Presented at EuroPCR 2015, abstract OP016; Merkely B. Presented at EuroPCR 2015, abstract OP 135; Iniguez R. Presented at EuroPCR 2015, abstract OP071; Valdés M. Presented at EuroPCR 2015, abstract OP043.

CENTURY II: Head-to-head study vs Xience

Favourable outcomes in a randomized study vs Xience

Primary endpoint was met. Ultimaster showed similar freedom from TLF to Xience in first 9 months.



No. patients at risk

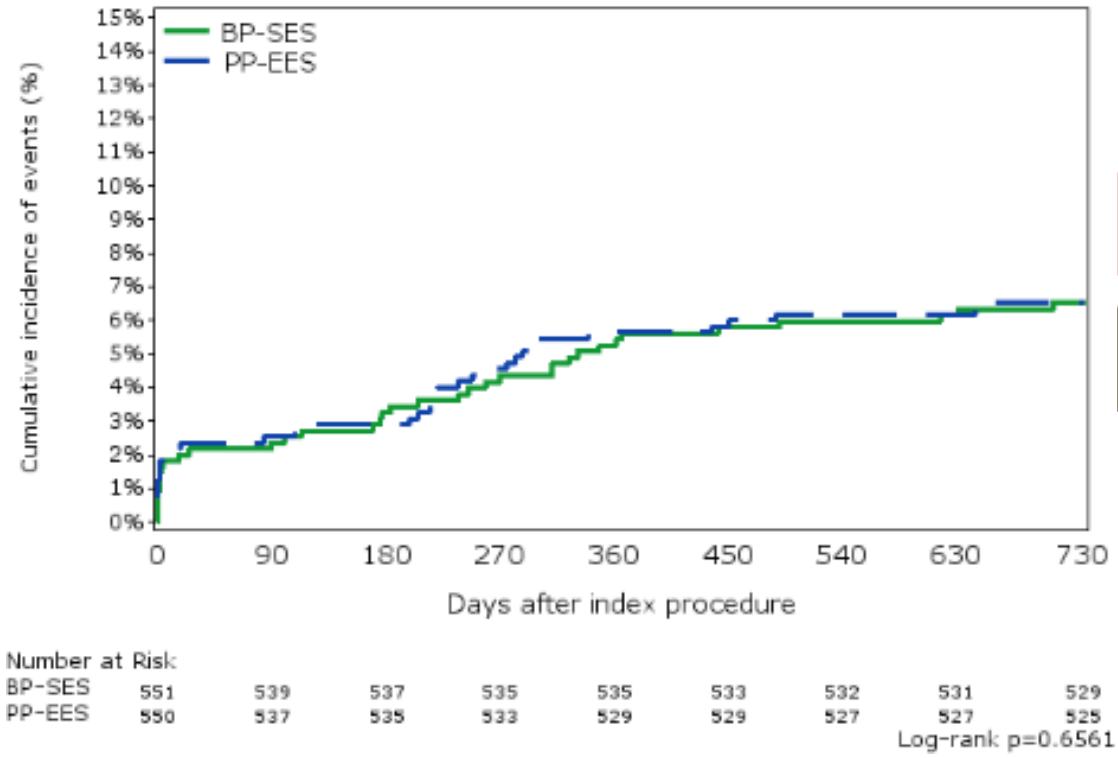
Ultimaster	551	539	539	538	536	536	533	531	530	527	527
Xience	550	537	537	536	534	534	534	532	527	525	521

p=0.9873

Eur Heart J 2014;35:2021–31

CENTURY II: Head-to-head study vs Xience

TLF rate remained similar for Ultimaster and Xience for up to 2 years



Xience
6.6%
(95% CI: 4.8 to 9.0%)

Ultimaster
6.5%
(95% CI: 4.8 to 8.9%)

- **presented at TCT2015**

CENTURY II: Head-to-head study vs Xience

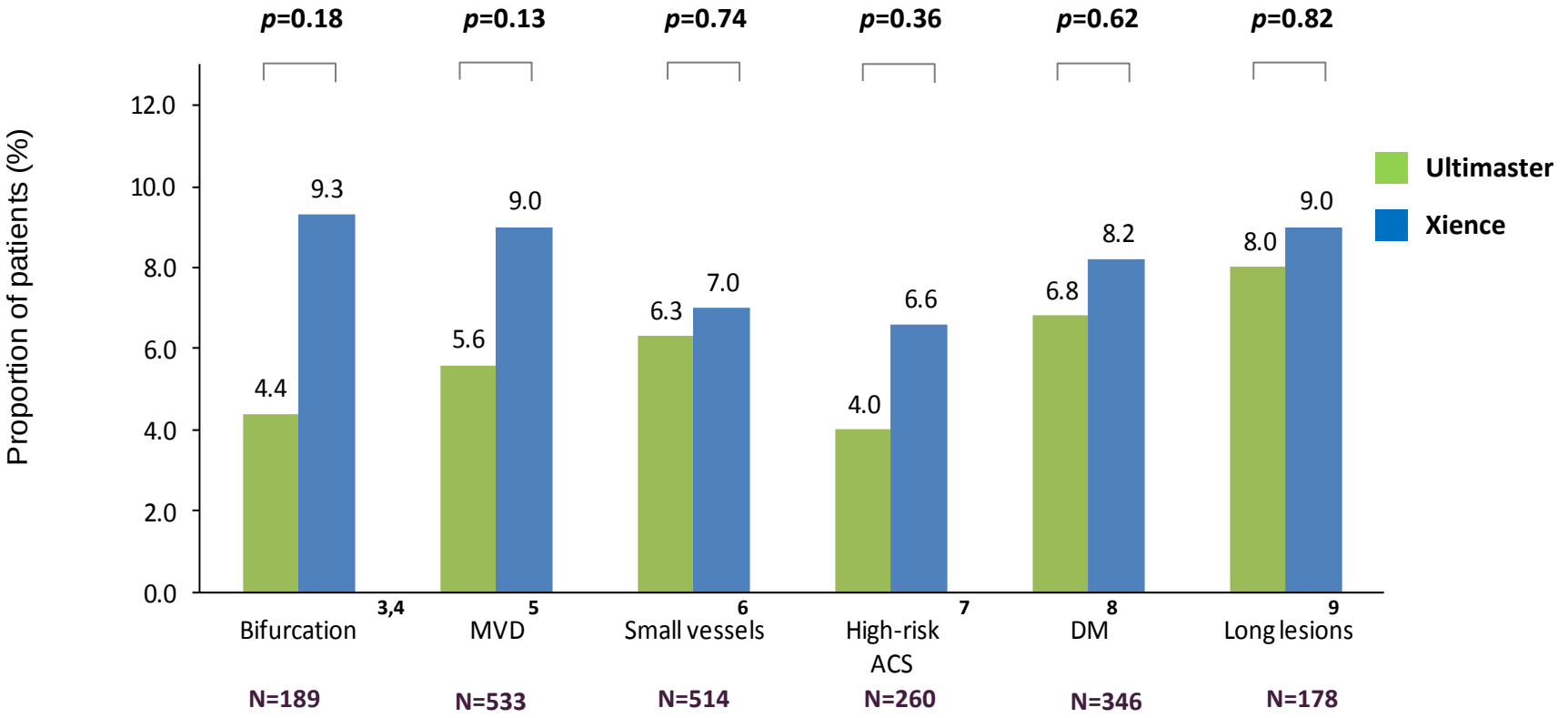
There are no VLST reported between 12 and 24 months for Ultimaster, which further demonstrated good safety profile for this stent.

	Ultimaster Npt=551	Xience Npt=550	P-value
Stent thrombosis, Def+prob	6 (1.1)	6 (1.1)	0.99
early, n (%)	3 (0.54)	3 (0.55)	
late, n (%)	3 (0.54)	3 (0.54)	
very late, n (%)	0 (0.0)	0 (0.0)	
DAPT,			
12 months, %	66.1	64.9	0.68
24 months, %	31.1	29.2	0.50
Any bleeding, %			
12 months, %	8.0	10.7	0.12
24 months, %	9.8	11.5	0.37
Any angina			
12 months, %	5.8	5.3	0.74
24 months, %	5.5	7.4	0.23

- Saito S presented at TCT2015.

Safety & efficacy confirmed in high-risk patients

Death and MI at 2 years remained low and comparable to Xience:[1,2]

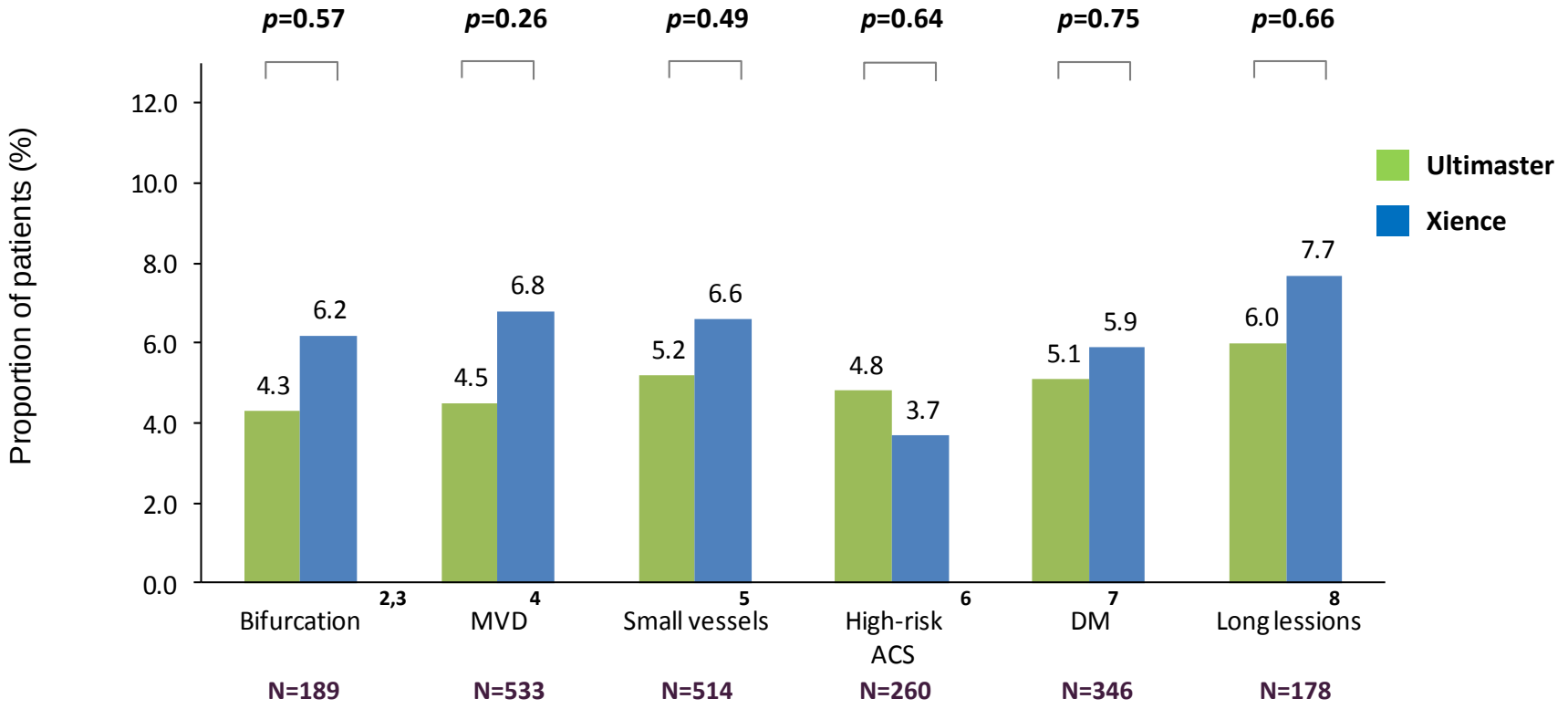


- 1. Based on ST rates from CENTURY and CENTURY II trials, Ultimaster IFU and data on file at Terumo Corporation; 2. Saito S et al. Eur Heart J 2014;35:2021–31; 3. Orvin K et al. Catheterization cardiovascular interventions. DOI: 10.1002/ccd.26150; 4. Merkely B. Presented at EuroPCR 2015, abstract OP135; 5. Valdés M. Presented at EuroPCR 2015, abstract OP043; 6. Wöhrle J et al. Presented at EuroPCR 2015, abstract OP066; 7. Iniguez R. Presented at EuroPCR 2015, abstract OP071; 8. Fabbiocchi F et al. Presented at EuroPCR 2015, abstract POS155; 9. Lesiak M. Presented at EuroPCR 2015, abstract OP016.

Safety & efficacy confirmed in high-risk patients

Proven clinical efficacy

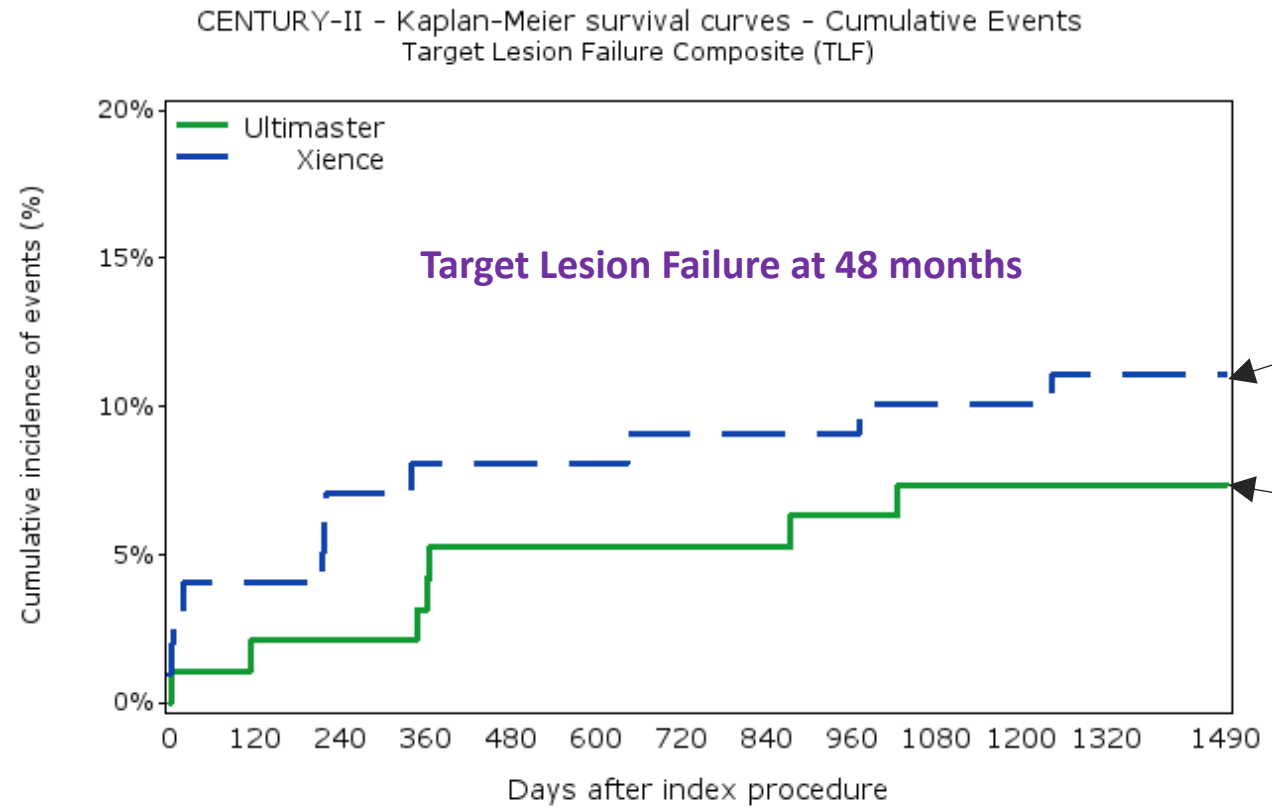
Clinically driven TLR at 2 years remained low and comparable to Xience:[1]



1. Saito S et al. Eur Heart J 2014;35:2021–31; 2. Orvin K et al. Catheterization cardiovascular interventions. DOI: 10.1002/ccd.26150; 3. Merkely B. Presented at Euro PCR 2015, abstract OP135; 4. Valdés M. Presented at EuroPCR 2015, abstract OP043; 5. Wöhrle J et al. Presented at EuroPCR 2015, abstract OP066; 6. Iniguez R. Pres ented at EuroPCR 2015, abstract OP071; 7. Fabbiocchi F et al. Presented at EuroPCR 2015, abstract POS155; 8. Lesiak M. Presented at EuroPCR 2015, abstract OP016.

CENTURY II

- Bifurcation lesions

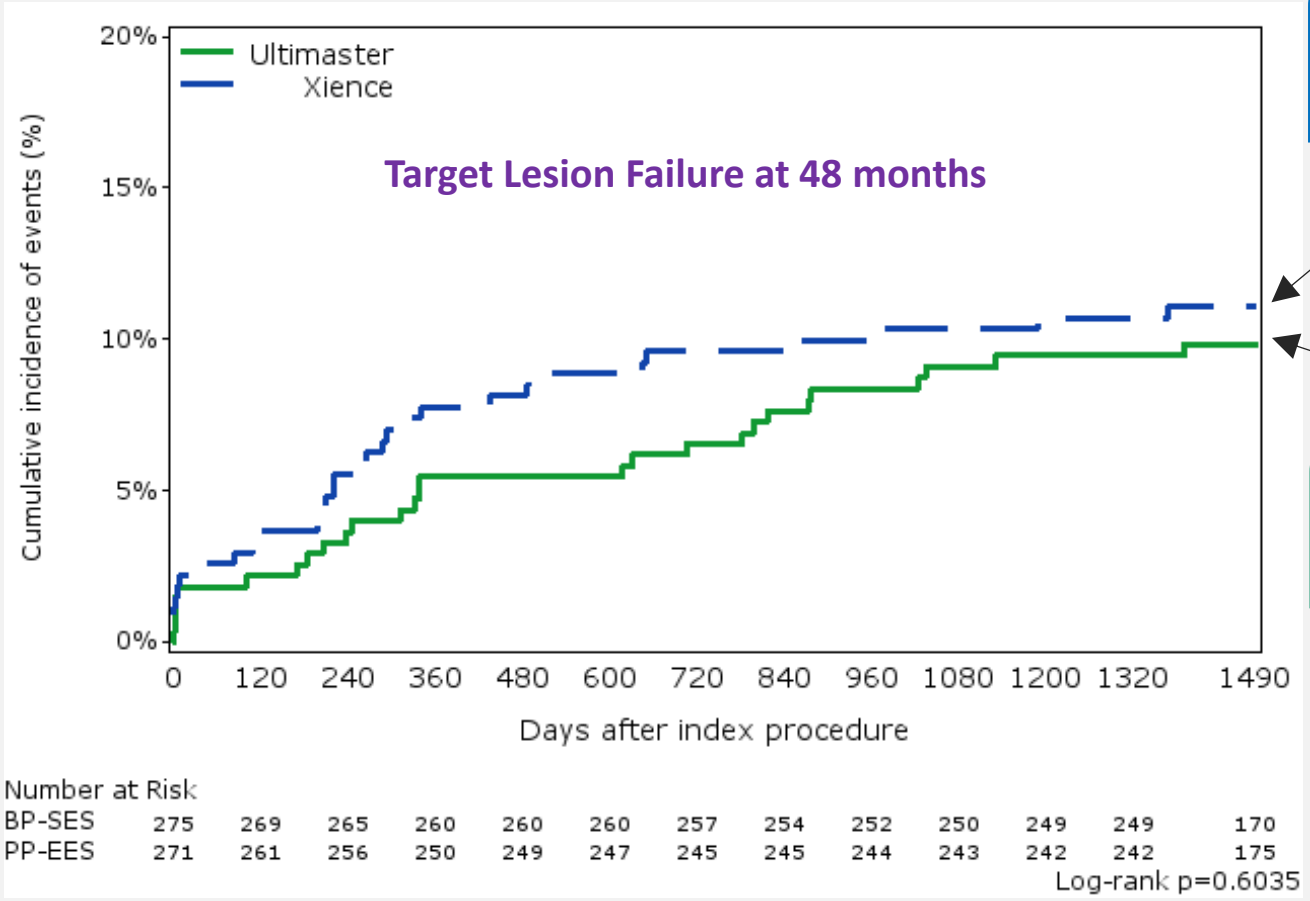


Xience
11.11%
[5.68% ; 19.01%]

Ultimaster
7.37%
[3.01%; 14.59%]

CENTURY II
- Multivessel disease

TLF Kaplan-Meier curves – 4 years

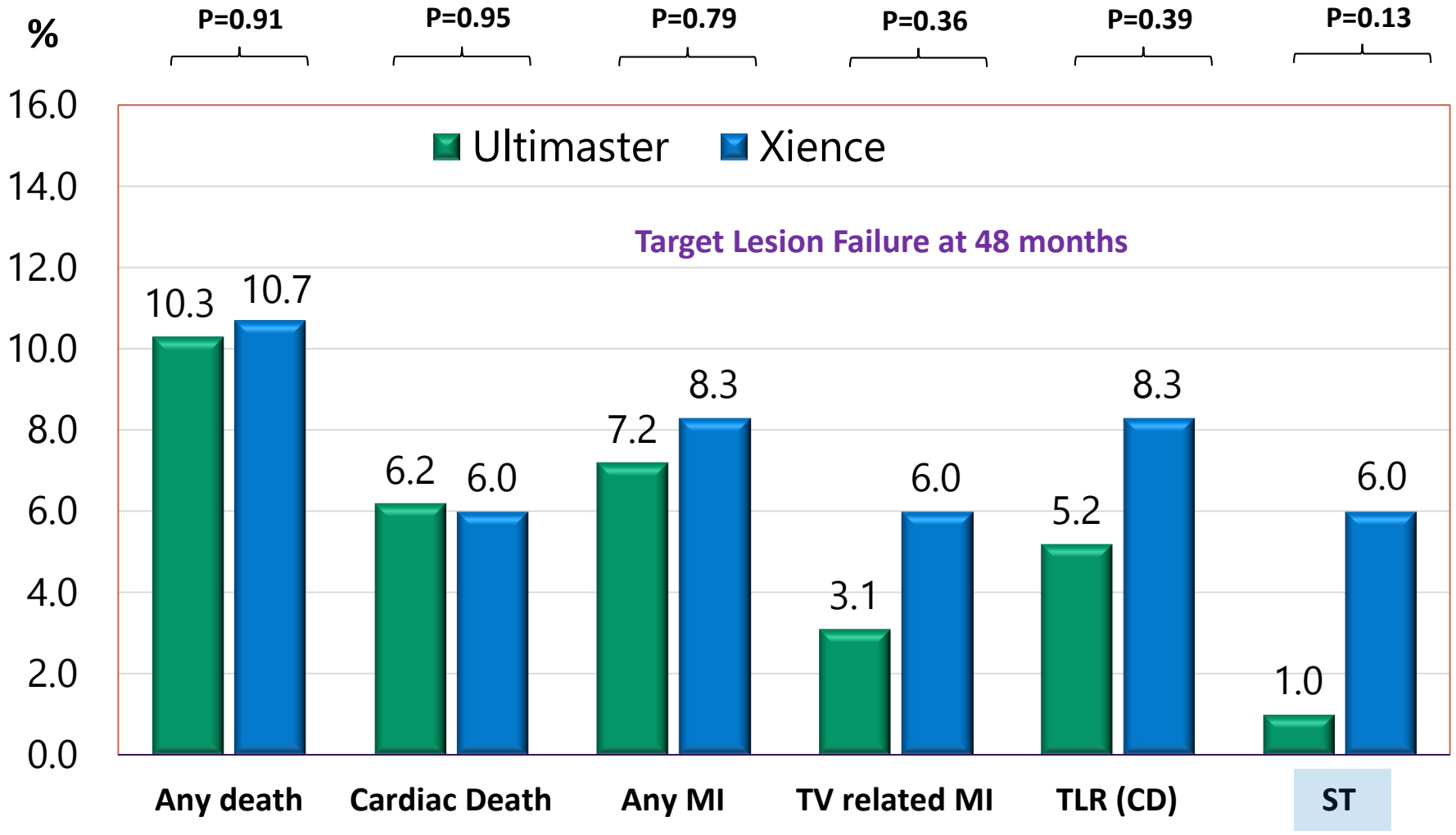


Xience
11.07%
[7.87% ; 15.45%]

Ultimaster
9.82%
[6.84% ; 13.99%]

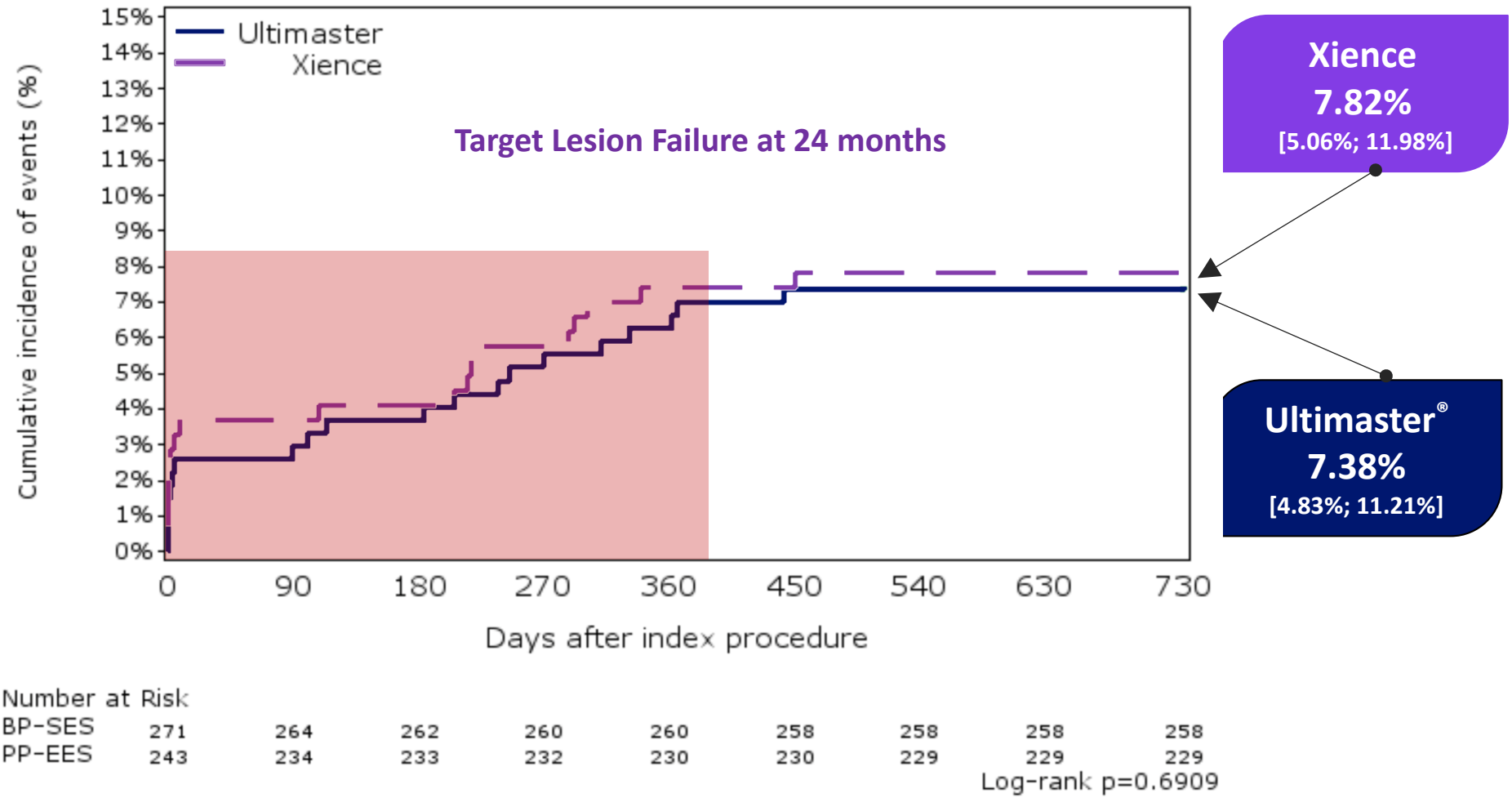
CENTURY II

- MVD & DM



CENTURY II

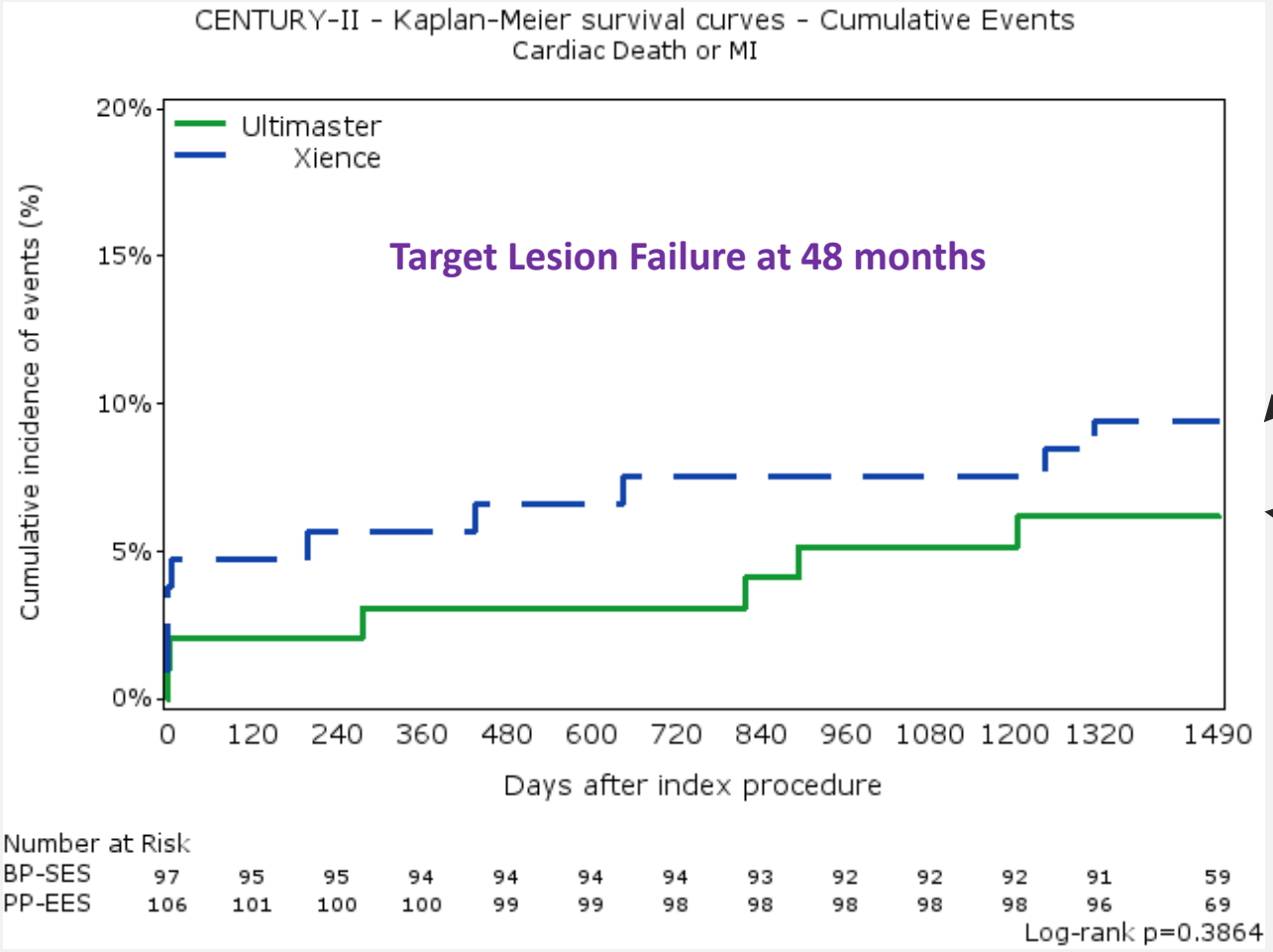
- Small vessel disease



CENTURY II

- NSTEMI subgroup/MASTER

Cardiac death or MI Kaplan-Meier curves – 4 years



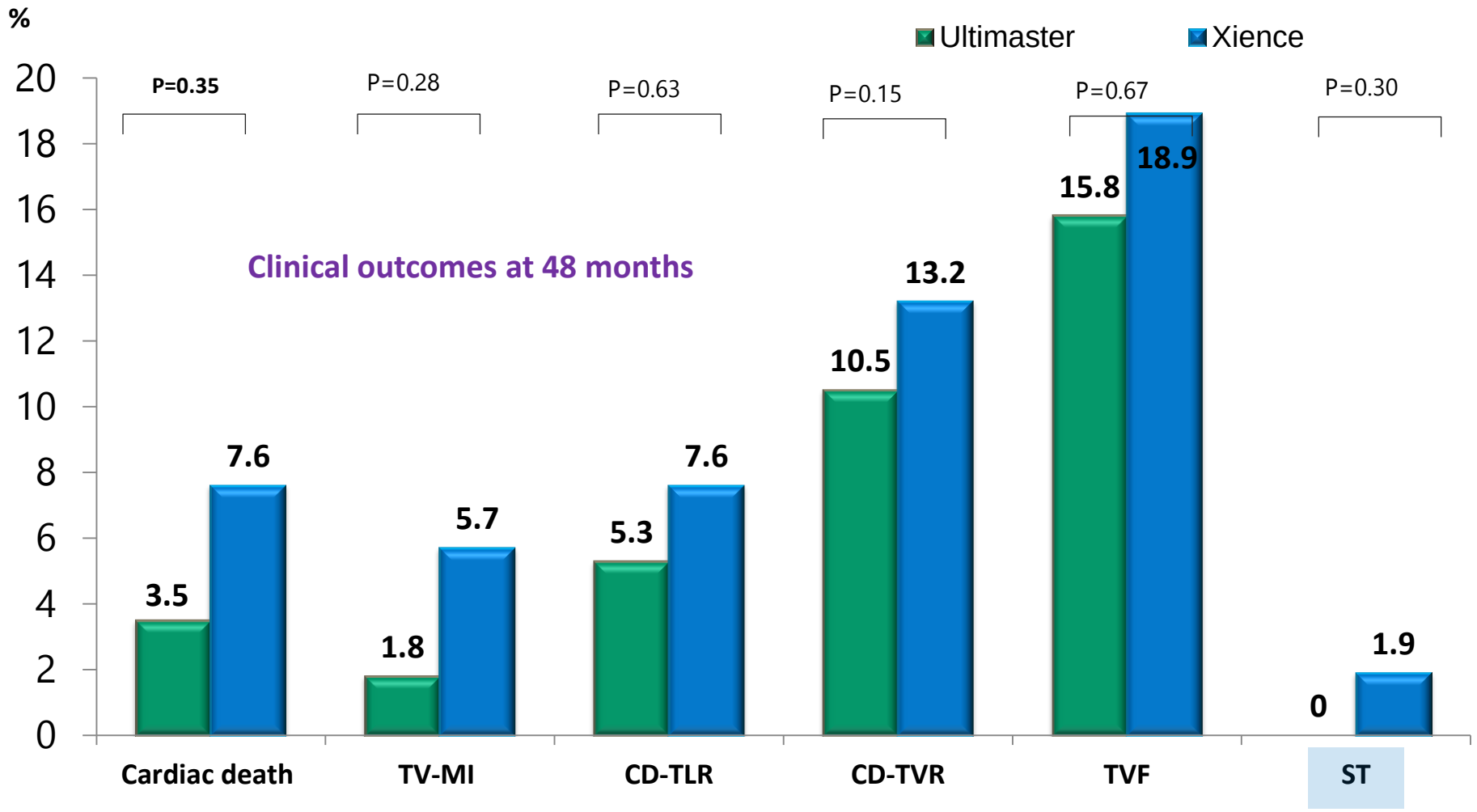
Xience
9.43%
[5.19% ; 16.82%]

Ultimaster
6.19%
[2.83% ; 13.25%]

CENTURY II

- Long lesion

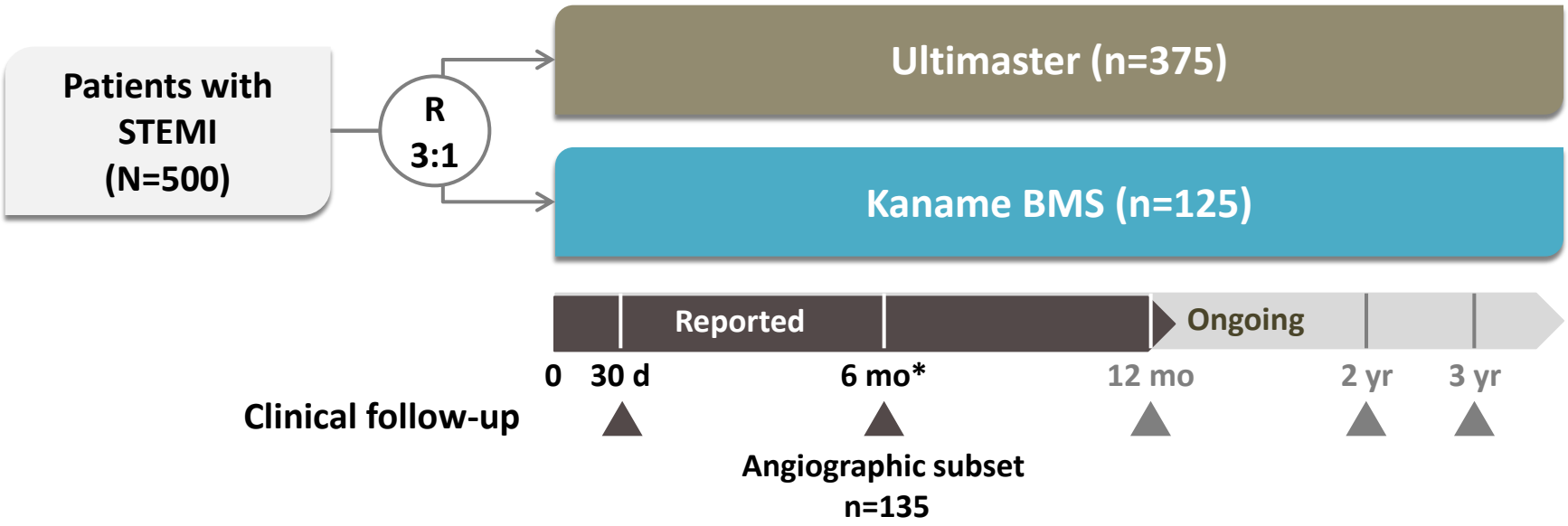
Long lesion treated with overlapping stents (n=110)



Safety and efficacy of Ultimaster in STEMI patients

MASTER: 500 STEMI patients, randomised 3:1 vs Kaname BMS

Generate further evidence for benefits of primary PCI with BP- DES in patients with STEMI

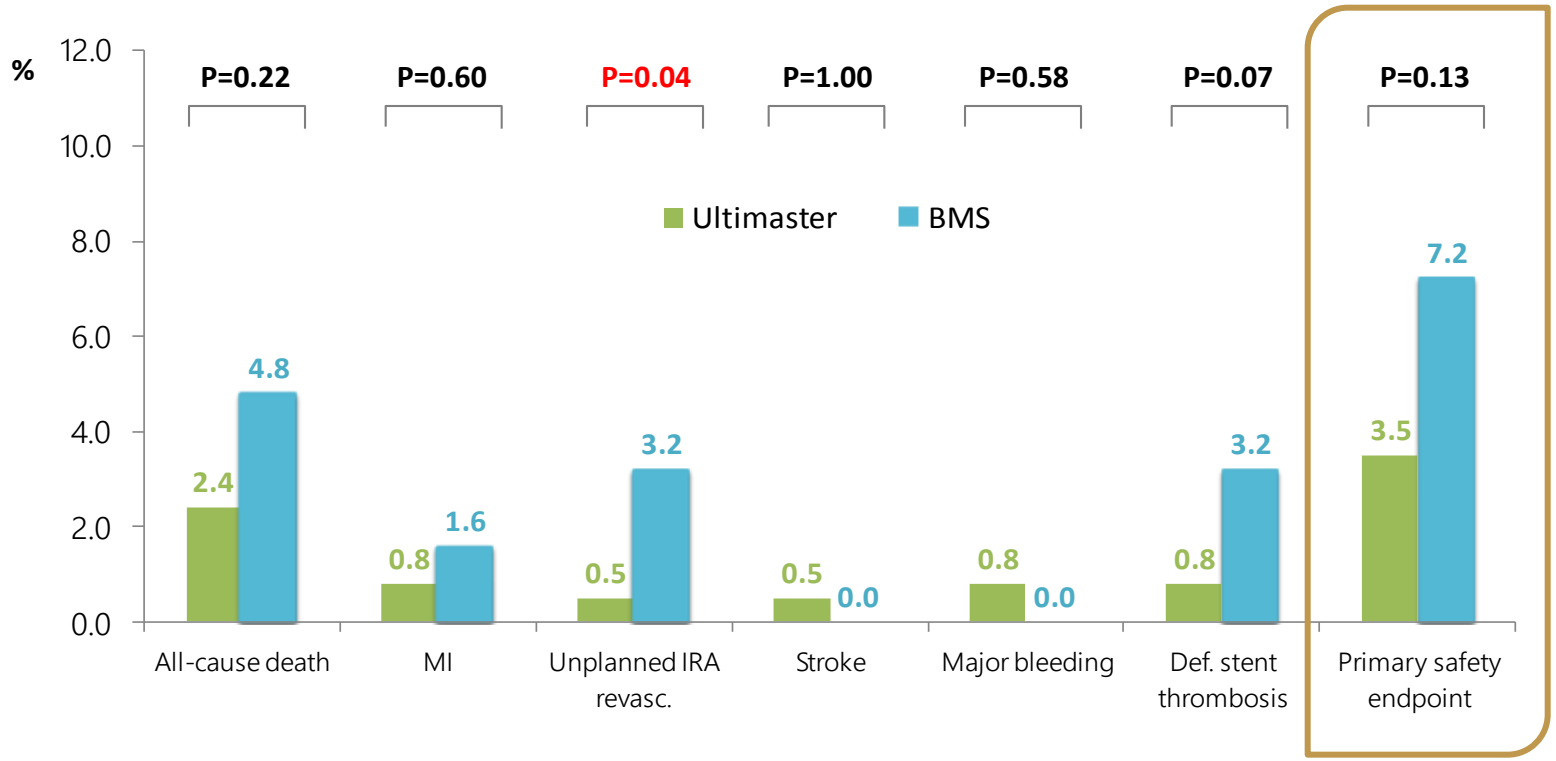


Triple primary endpoint at 1 (safety), 6 (efficacy) and 12 months (safety/efficacy)

M. VALDES-CHAVARRI. Presented at EuroPCR 2016

Safety and efficacy of Ultimaster in STEMI patients

Primary safety endpoint at 1 month was met.

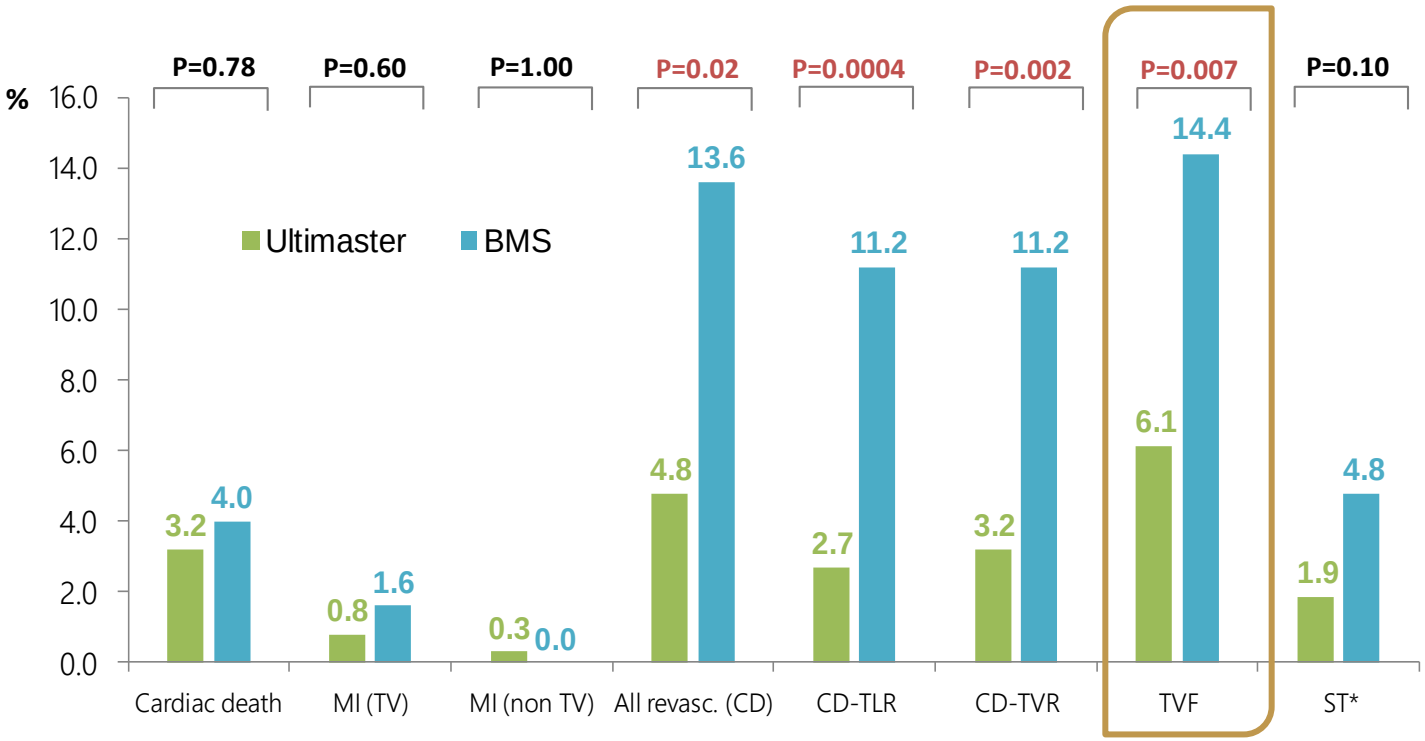


Primary safety endpoint:
Composite of all-cause death, recurrent MI, unplanned infarct-related artery (IRA) revascularization, stroke, definite stent thrombosis or major bleeding at 1 month

M. VALDES-CHAVARRI. Presented at EuroPCR 2016

Safety and efficacy of Ultimaster in STEMI patients

Ultimaster showed significant diffference with BMS in TVF at 12 month



Primary endpoint: TVF at 12 M.

TVF : Target Vessel Failure (composite endpoint of cardiac death and MI not clearly attributable to a non-target vessel , and clinically driven TVR)

*** Definite or probable ST according to ARC definitions**

M. VALDES-CHAVARRI. Presented at EuroPCR 2016

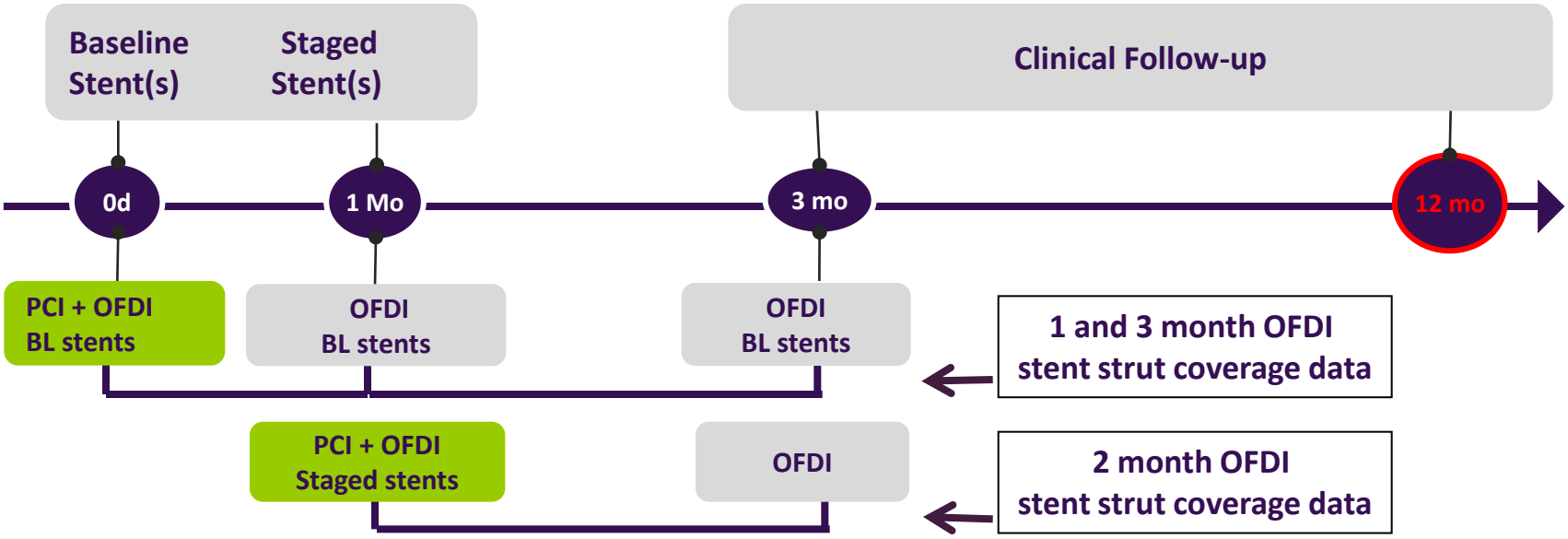
DISCOVERY 1TO3

- Assess endothelial coverage at 1, 2 and 3 months by OFDI

DISCOVERY 1TO3

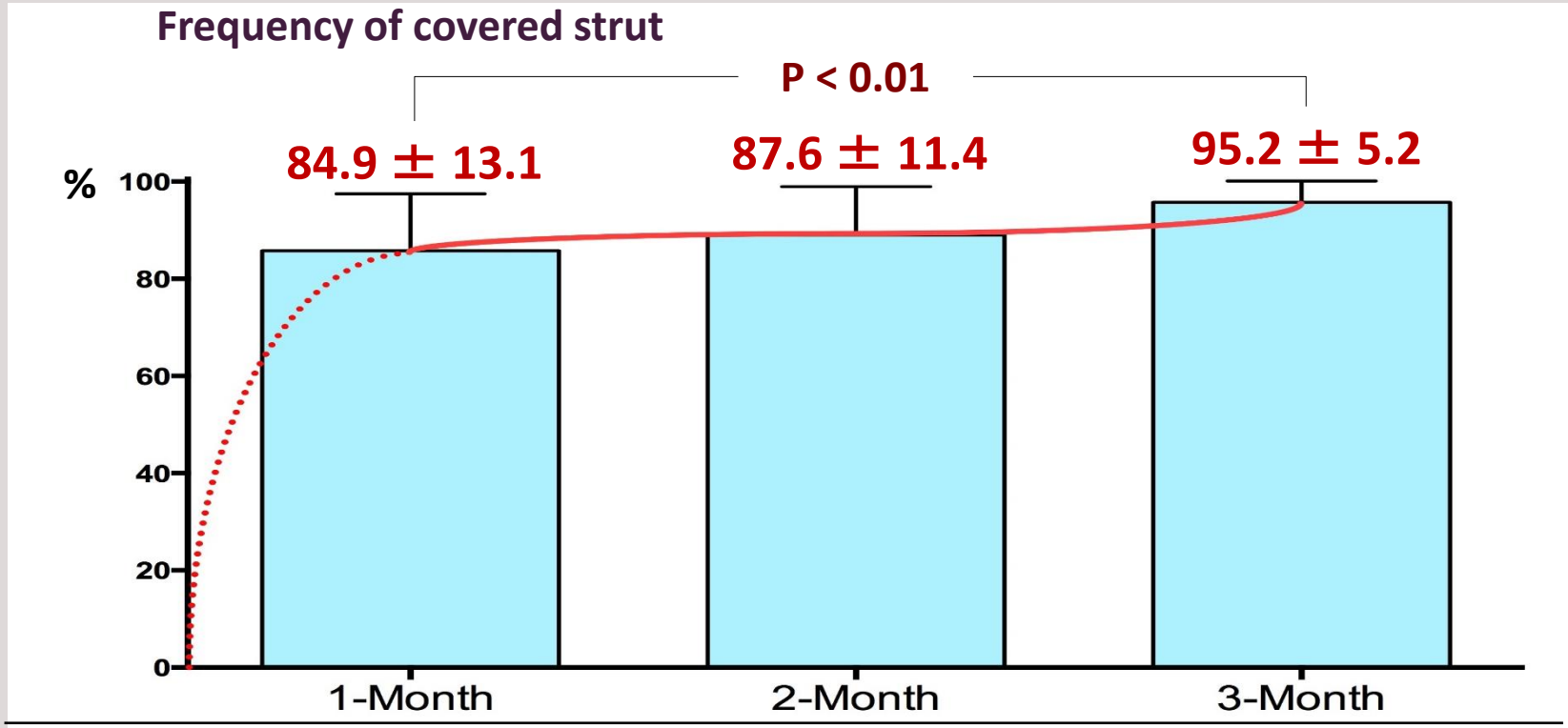
Investigate possibility for shorter DAPT by generating relevant clinical scientific data

60 MVD patients with OFDI, single arm, primary endpoint TLF @ 12M.

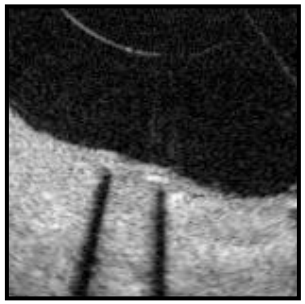


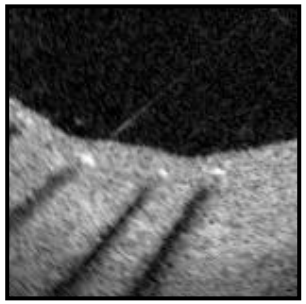
Bernard Chevalier. Presented at EuroPCR 2016;

85% strut coverage as early as 1 month



Stent Length: 19.9 ± 5.6 | 18.6 ± 6.7 | 19.9 ± 5.6





Presented at EuroPCR 2016

MECHANISM-ULTIMASTER trial

Objective:

- To assess the early and late vascular healing to ULTIMASTER DES for treatment of patients with STEMI and SAP.

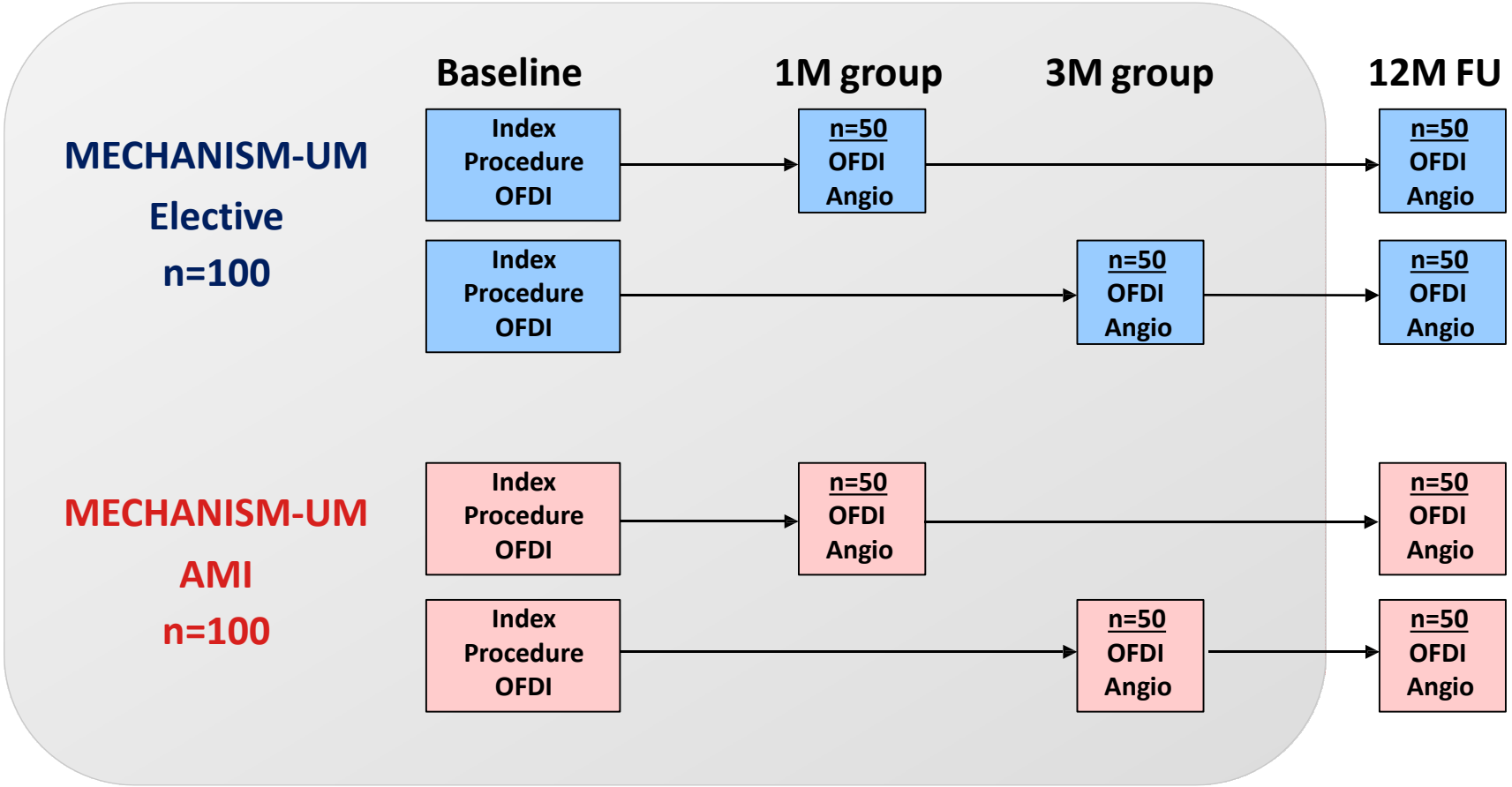
Design:

- Prospective multicenter registry, Investigators initiated study with 21 investigators conducted in Japan

Primary Endpoint:

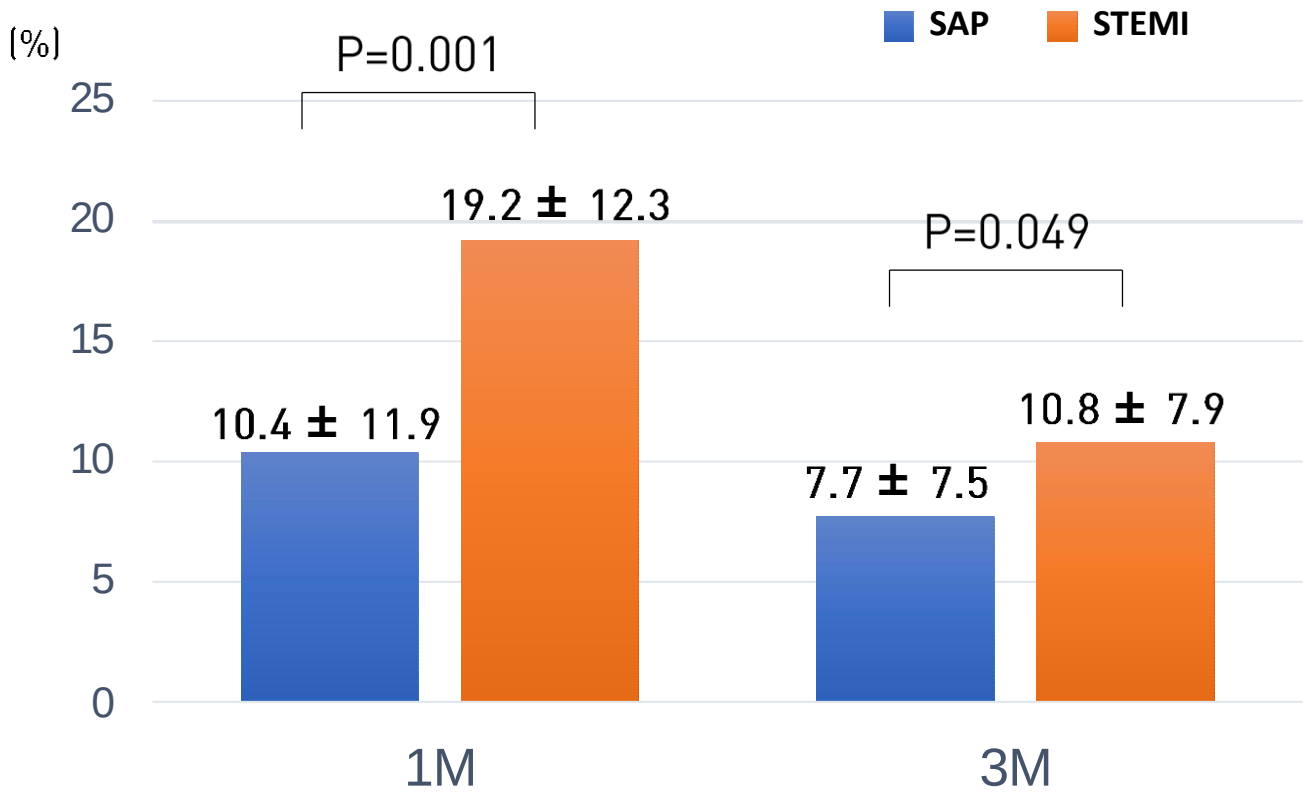
- Percentage of stent strut coverage by OFDI at 1 month (STEMI) and 3 month (Elective) evaluated by independent imaging core laboratories

MECHANISM-ULTIMASTER trial



MECHANISM-ULTIMASTER trial

PEP : % uncovered struts



Conclusion

- ✓ Advantage of BP-DES
- ✓ Superiority of BP-DES to BMS and 1st G. DP-DES
- ✓ Similar efficacy and safety of BP-DES to 2nd G. DP-DES
  - ✓ Limited data on the superiority of EES to BP-DES
- ✓ Higher rates of inflammation during active bioresorption of polymer
- ✓ Ultimaster put up a good fight against EES.
- ✓ Biodegradability of polymer & the optimal combination of stent alloy, design, strut thickness, polymer, and drug all combined determine the safety of DES.

Thank you for your attention^^.