

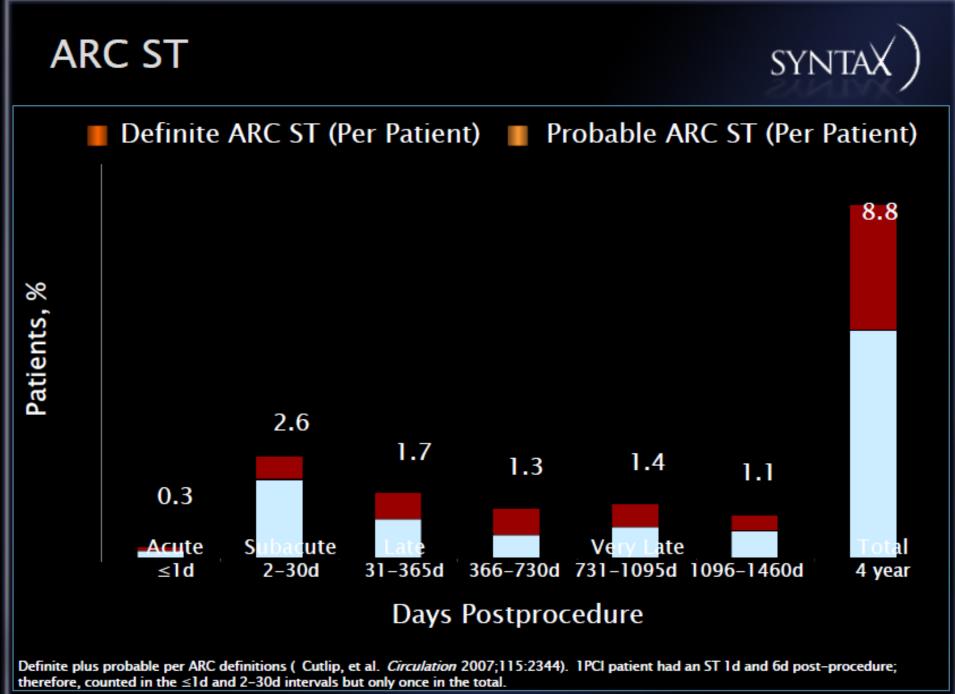
Metallic DES: Is there a room for further progress? Yes!

Bernard Chevalier MD, FESC, FACC, FSCAI ICPS Massy, France

 In the last five years, I received research grants or speaker fees or I am/was consultant for: Abbott Vascular, Asahi, Astra Zeneca, AVI, Boston Scientific, Biotronik, Colibri, Cook, Cordis, Daichi-Sankyo, Eli-Lilly, Iroko, Medtronic, Terumo. I am currently minor shareholder & general director of CERC

My wish list

 More efficient DES in complex CAD including diabetic patient



SYNTAX Overall RCT 4-year Outcomes • November 8th, 2011 • TCT • San Francisco, CA • Slide 10

Would SYNTAX have been a positive trial if XIENCE V had been used instead of TAXUS?: A meta-analysis of a first-generation vs. a second-generation drug-eluting stent system.

Claessen BE, Stone GW, Smits PC, Kedhi E, Kikkert WJ, Piek JJ, Henriques JP.

Department of Cardiology, Academic Medical Center, Amsterdam, the Netherlands.

Abstract

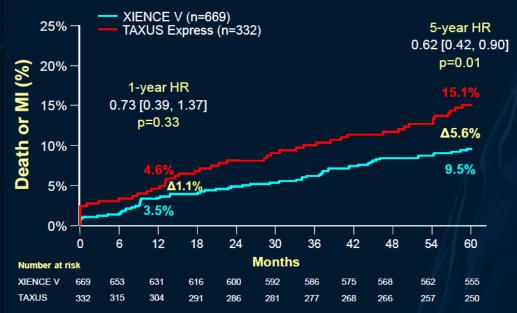
All-case dealth <u>thy or X-black or Ventor V</u>	Treatment on	tione for coror		accularica	tion inclu	ido n	arcutanaaue.cor	on any intervention (PCI) on	coronary artery bypass grafting (CABG). In the 'synergy between PCI with TAXUS and
Development building studie Pack Nation Pack Nation<									
NPTIT 0 220 1 70 1.98 0.12 [00, 20, 20] 0.12 [00, 20, 20] NPTIT 0 220 1 10 10 0 10.2 [00, 20, 20] 0.12 [00, 20, 20] 0.12 [00, 20, 20] 0.12 [00, 20, 20] 0.12 [00, 20, 20] 0.12 [00, 20, 20] 0.12 [00, 20, 20] 0.12 [00, 20, 20] 0.12 [00, 20, 20] 0.12 [00, 20, 20] 0.12 [00, 20] <t< td=""><td></td><td>Everolimus Elutin</td><td>g Stent</td><td>Paclitaxel Eluti</td><td>ing Stent</td><td></td><td>Risk Ratio</td><td></td><td></td></t<>		Everolimus Elutin	g Stent	Paclitaxel Eluti	ing Stent		Risk Ratio		
$\frac{1}{100} \frac{1}{100} \frac{1}$	Study or Subgroup	Events		Events					leat intervention rate. We hypothesised that the use of a superior drug-eluting stent
PHET M $\frac{2}{10}$ $\frac{2}{100}$ $\frac{1}{100}$ $\frac{1}{100$	SPIRIT II	•		1				4	
Dyper APRE 10 003 1 00	SPIRIT III								
ref (9% c) the over multiple (2, 2, 2, 3, 4) (7, 2, 2, 3, 4) (7, 2, 2, 4) (7, 2, 3, 4) (7, 2, 4) (7, 2, 3, 4) (7, 2, 4) (7, 2, 3, 4) (7, 2, 4) (7, 2, 3, 4) (7, 2, 4) (7, 2, 3, 4) (7, 2, 4) (7, 2, 4) (7, 4	SPIRIT IV	25	2416	15	1195	45.4%	0.82 [0.44, 1.56]		
tal events terrorents Turing of the contract Link Sterr Print i divents terrorents Link Sterr Print i divents 107 Print i divents 107 20 20 20 20 20 20 20 20 20 20	COMPARE	18	903	15	897	39.9%	1.19 [0.60, 2.35]		
herrogenetic Turit = 0.00; Chr = 2.29; dr = 1 or = 0.51; P = 0:% b 1 b 2 o b 1 b 0 b 0	Total (95% CI)		4194		2489	100.0%	0.94 [0.61, 1.45]	-	
herrogenetic Turit = 0.00; Chr = 2.29; dr = 1 or = 0.51; P = 0:% b 1 b 2 o b 1 b 0 b 0	Total events	51		35					
La Li 2 d 2 d 3 d 4 d 3 d 2 d 3 d 4 d 3 d 3 d 2 d 3 d 4 d 3 d 3 d 3 d 3 d 3 d 3 d 3 d 3			if = 3 (P = 0						
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uby or Subgroup Pirt II 2 Pirt II 1 Pirt	B Myocardial i	infarction							
UPRT II 1 2 200 2 76 22% 0.35 (0.5, 2.41) UPRT II 18 655 13 221 167% 0.68 (0.3, 4, 0.7) VMFARE 25 903 46 907 1105 44.6% 0.00 (0.3, 0, 0.2) 0.57 (0.43, 0.76) VMFARE 25 903 46 907 100 100 100 Stor overaliset 2 = 3.80 (P = 0.807) 100 0.57 (0.43, 0.76) 0.57 (0.43, 0.76) 0.57 (0.43, 0.76) 0.57 (0.43, 0.76) Using Store prevacularization Everaliset filter 2 = 3.80 (P = 0.807) 100 MH, Random, 95% Cl MH, Random,									
Definition 10 665 13 21 16.7% 0.68 0.24 13.7 14.7% 0.68 0.23 0.3.7 0.33 0.43 0.97 0.55 0.52 0.33 0.57 0.43 0.67 0.44 0.57 0.43 0.76 0.57 0.43 0.76 0.57 0.43 0.76 0.57 0.43 0.57									
$\frac{P_{\text{PTT}} \text{ W}}{\text{tal} \text{ (events}}} \underbrace{\frac{45}{25} & \frac{2416}{933} & \frac{37}{48} & \frac{1195}{987} & \frac{44.95}{96.5\%} & 0.52[0.32, 0.82] \\ \frac{1}{0.1} & \frac{1}{0.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{0.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{6} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{2} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{2} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{2} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{10} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{0} & \frac{1}{10} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{2} & \frac{1}{0.5} & \frac{1}{10.5} \\ \frac{1}{10.2} & \frac{1}{0.5} & \frac{1}{10.5} & \frac{1}{10.5} & \frac{1}{10.5} & \frac{1}{10.5} & \frac{1}{10.2} & \frac{1}{10.5} & \frac{1}{10.2} & \frac{1}{10.5} & 1$	SPIRIT II							· · · · · · · · · · · · · · · · · · ·	
$\begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} $	SPIRIT III								
$\frac{1}{10} \frac{1}{2} 1$	SPIRIT IV	45	2416	37	1195	44.6%	0.60 [0.39, 0.92]		
that events 90 100 testeropenety Target 200, Chie 2 nd, Tif 43 0F 0.87), If 43 0F 0.87 , If 136 0S 0.30 , 0.10, 0.85 Favours EES Favours PES UNCENT Nerthin 2 20 655 1195 524% 0.55 0138, 0.78] HT II 10 2 0.5 1 2 0.5 1 2 5 10 NHARAGON 95% CI M-H.Randon, 95% CI M	COMPARE	25	903	48	897	36.5%	0.52 [0.32, 0.83]		
Terrogenelity: Tau ² = 0.00; Ch ² = 0.71, df = 3 (P = 0.87); P = 0.87 test for overall effect Z = 3.80 (P = 0.001) CTarget lesion revascularization <u>twor of subgroup</u> <u>Events</u> <u>Total</u> <u>Weight MH, Random, 95% CI</u> <u>MH, Random, 95% CI</u> <u>HH, Random, 95% CI</u>	Total (95% CI)		4194		2489	100.0%	0.57 [0.43, 0.76]	•	
LT 10 20 30 1 2 3 10 Part II 1 2 20 37 1 2 3 10 Part II 1 2 20 37 1 7 6 6.0% 0.30 [0 10, 0.85] Part II 1 2 20 57 1 7 7 6 6.0% 0.30 [0 10, 0.85] Part II 1 2 2 655 1 8 32.1 18.1% 0.60 [0.33, 1.78] Part II 1 2 2 655 1 8 32.35% 0.37 [0.22, 0.64] Part II 1 2 2 655 1 8 32.35% 0.37 [0.22, 0.64] Part II 1 2 2 655 1 8 32.35% 0.37 [0.22, 0.64] Part II 1 2 2 655 1 8 32.35% 0.37 [0.22, 0.64] Part II 1 2 2 655 1 8 32.35% 0.37 [0.22, 0.64] Part II 1 2 2 655 1 8 32.35% 0.37 [0.22, 0.64] Part II 1 2 2 655 1 10 5 2.4% 0.49 [0.38, 0.64] Part II 1 2 2 655 1 19 5 52.4% 0.49 [0.20, 0.64] Part II 1 2 2 655 1 19 5 52.4% 0.49 [0.20, 0.64] Part II 1 2 2 65 1 19 5 52.4% 0.49 [0.20, 0.64] Part II 1 2 0 0.00 (Chir = 2.69, off = 3 (P = 0.14); P = 0\% Part II 1 7 2 128 Part II 1 7 2 655 2 1 30 1 20 10, 0.28 21 Part II 1 7 2 655 2 1 30 1 20 10, 0.49 [0.28, 0.64] Part II 1 7 0 220 1 7 6 6.4% 0.12 [0.00, 28 2] Part II 1 7 2 655 2 2 31 20 10, 10, 0.7 2] Part II 1 7 2 655 2 2 31 20 10, 10, 0.7 2] Part II 1 7 2 655 2 2 31 20 10, 0.7 12 20, 0.64 1 7 2 [0.38, 0.21] Part II 1 7 2 655 2 2 31 20 10, 0.7 2 20 1 7 6 6.4% 0.12 [0.00, 28 2] Part II 1 7 2 655 2 2 31 20 10, 0.7 2 20 1 7 6 6.4% 0.27 [0.11, 0.67] Part II 1 7 2 655 2 2 31 20 10, 0.7 2 20 1 7 6 6.4% 0.27 [0.11, 0.67] Part II 1 7 2 655 2 2 31 2 0.15, P = 3.0 20 [0.00, 0.89] Part II 1 7 2 0.33 2 2 897 37.2% 0.20 [0.11, 0.67] Part II 1 7 2 655 2 2 31 2 0.15, P = 3.0 20 [0.00, 0.89] Part II 1 7 2 0.33 2 2 897 37.2% 0.20 [0.11, 0.67] Part II 1 7 2 0.33 2 2 897 37.2% 0.20 [0.11, 0.67] Part II 1 7 2 0.33 2 2 897 37.2% 0.20 [0.11, 0.67] Part II 1 7 2 0.33 2 2 897 37.2% 0.20 [0.11, 0.67] Part II 1 7 2 0.33 2 2 897 37.2% 0.20 [0.11, 0.67] Part II 1 7 2 0.33 2 2 897 37.2% 0.20 [0.11, 0.67] Part II 1 7 2 0.30 (0.7) 2 9 0 10 0.0% 0.36 [0.16, 0.85] Part Part Part Part Part Part Part Part	Total events	90		100					
Li 10 2 0 3 1 2 3 10 F Pavours EES Favours PES Toraget lesion revascularization <u>two or subgroup</u> <u>Verits</u> <u>Total Weight MH, Random, 95% CI</u> <u>HRT III 2 2 655 18 325 % 0.37 [0.2, 0.64]</u> <u>HRT III 2 2 655 18 325 % 0.37 [0.2, 0.64]</u> <u>HRT III 2 2 655 18 325 % 0.37 [0.2, 0.64]</u> <u>HRT III 2 2 655 18 325 % 0.37 [0.2, 0.64]</u> <u>HRT III 2 2 655 18 325 % 0.37 [0.2, 0.64]</u> <u>HIT III 2 0 0.5 1 2 5 1 5 15 5 135 5 2.4% 0.55 [0.38, 0.78]</u> <u>HRT III 2 2 655 18 325 % 0.37 [0.2, 0.64]</u> <u>HIT III 2 0 5 1 2 416 5 5 135 5 135 5 2.4% 0.55 [0.38, 0.78]</u> <u>HIT III 2 0 0.5 (Ch² 2 5 0 0.44), P = 0.%</u> <u>HIT III 0 2 0 5 1 2 5 1 5 1 5 5 1 2 5 1 5 5 5 1 5 5 1 5 5 1 5 5 1 5 5 1 5 5 1 5 5 1 5 5 5 1 5 5 1 5 5 5 1 5 5 5 1 5 5 1 5 5 5 1 5 5 1 5 5 5 1 5 5 5 1 5 5 5 1 5 5 5 1 5 5 1 5 5 5 1 5 5 5 1 5 5 5 1 5 5 5 1 5 5 5 1 5 5 5 1 5 5 5 1 5 5 5 1 5 5 5 1 5 5 5 1 5 5 5 5 5 1 5 5 5 5 5 1 5</u>	Heterogeneity: Tau ² =	= 0.00; Chi ² = 0.71, d	if = 3 (P = 0	0.87); I ² = 0%					
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Everofinus Eluting Stent Pacifitaxe Eluting Stent Risk Ratio Market in 2 Subgroup Events Total Vents								Favours EES Favours PES	I ISA MODARN I DES
Udy or Subgroup Events Total Events Total Weight M+H, Random, 95% CI VIRTI II 6 220 7 76 6.0% 0.30 [0.10, 0.85] M+H, Random, 95% CI VIRTI II 22 655 18 321 18.1% 0.00 [0.33, 1.10] VIRTI IV 61 2416 55 1195 52.4% 0.55 [0.38, 0.78] VIRTI II 20 303 48 997 23.5% 0.37 [0.22, 0.64] VIRTI II 21 24.0% 0.49 [0.38, 0.49]	C Target lesior								
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$\frac{22 \text{ (RT III)}}{21 \text{ (RT IV)}} = \frac{22}{665} \frac{655}{18} \frac{321}{321} \frac{18.1\%}{185} \frac{0.60[0.33]}{0.50[0.38]} \frac{1.0]}{0.50[0.38]} + \frac{1.0}{1022,0.64} + \frac{1.0}{1022,0.64} + \frac{1.0}{1022,0.65} + \frac{1.0}{2.5} + \frac{1.0}{2.5} + \frac{1.0}{102} + \frac{1.0}{1022,0.64} + \frac{1.0}{1022,0.65} + \frac{1.0}{2.5} + \frac{1.0}{2.5} + \frac{1.0}{1022,0.65} + \frac{1.0}{2.5} + \frac{1.0}{1022,0.5} + \frac{1.0}{2.5} + \frac{1.0}{102,0.5} + \frac{1.0}{2.5} + \frac{1.0}{102,0.5} + \frac{1.0}{2.5} + \frac{1.0}{102,0.5} + \frac{1.0}{2.5} + \frac{1.0}{102,0.5} + \frac{1.0}{2.5} + \frac{1.0}{2.5} + \frac{1.0}{1002,0.5} + \frac{1.0}{2.5} + \frac{1.0}{2.$								M-H, Random, 95% Cl	
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DMPARE 18 903 48 897 23.5% 0.37 0.22, 0.64 tat (95% Cl) 4194 2489 100.0% 0.49 0.38, 0.64 •• tat (92% Cl) 4194 2489 100.0% 0.49 0.38, 0.64 •• tat (92% Cl) 4194 2489 100.0% 0.49 0.38, 0.64 •• tat (92% Cl) (90.44); P = 0% 0.10, 2 0.5 1 2 5 10 Definite/probable stent thrombosis Eventimus Eluting Stent Pacifitaxel Eluting Stent Risk Ratio MH, Random, 95% Cl VERT III 0 220 1 76 6.4% 0.12 (0.00, 2.82) •• <th< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></th<>									
tal (95% CI) 4194 2489 100.0% 0.49 [0.38, 0.64] tal events 107 128 eterogeneity. Tau ² = 0.00; Chi ² = 2.69, df = 3 ($P = 0.44$); $P = 0\%$ tstfor overall effect $Z = 5.39$ ($P < 0.00001$) D Definite/probable stent thrombosis Everofimus Eluting Stent Pacificaxel Eluting Stent Verofit M-H, Random, 95% CI PIRT II 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.38, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.38, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.38, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.38, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.38, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.38, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.38, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.38, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.38, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 7 665 2 321 20.1% 1.72 [0.36, 8.21] PIRT II 7 7 2391 13 1195 36.4% 0.27 [0.11, 0.63] PIRT II 7 7 2391 13 1195 36.4% 0.27 [0.11, 0.63] PIRT II 7 7 2391 13 1195 36.4% 0.27 [0.11, 0.63] PIRT II 7 7 2391 13 1195 36.4% 0.27 [0.11, 0.63] PIRT II 7 7 7 2391 13 1195 36.4% 0.27 [0.11, 0.63] PIRT II 7 7 7 2391 13 1195 36.4% 0.27 [0.11, 0.63] PIRT II 7 7 7 2391 13 1195 36.4% 0.27 [0.11, 0.63] PIRT II 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7 7	SPIRIT IV								
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eterogeneily: Tau ² = 0.00; Chi ² = 2.69, df = 3 (P = 0.44); I ² = 0% 0.1 0.2 0.5 1 2 5 10 tist for overall effect: Z = 5.39 (P < 0.00001)	Total (95% CI)		4194		2489	100.0%	0.49 [0.38, 0.64]	•	
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eterogeneity: Tau ² = 0.30; Chi ² = 5.15, df = 3 (P = 0.16); i ² = 42% 0.1 0.2 0.5 1 2 5 10	Total (95% CI) Total events	20	4169	30	2489	100.0%	0.36 [0.16, 0.85]		
			f= 3 (P = 0						
favours EES favours PES				0.10/11 - 42.70				0.1 0.2 0.5 1 2 5 10	
	reactor overall effect	. <u>2</u> = 2.35 (F = 0.02)						favours EES favours PES	

Major Adverse Cardiac Events Through 5 Years

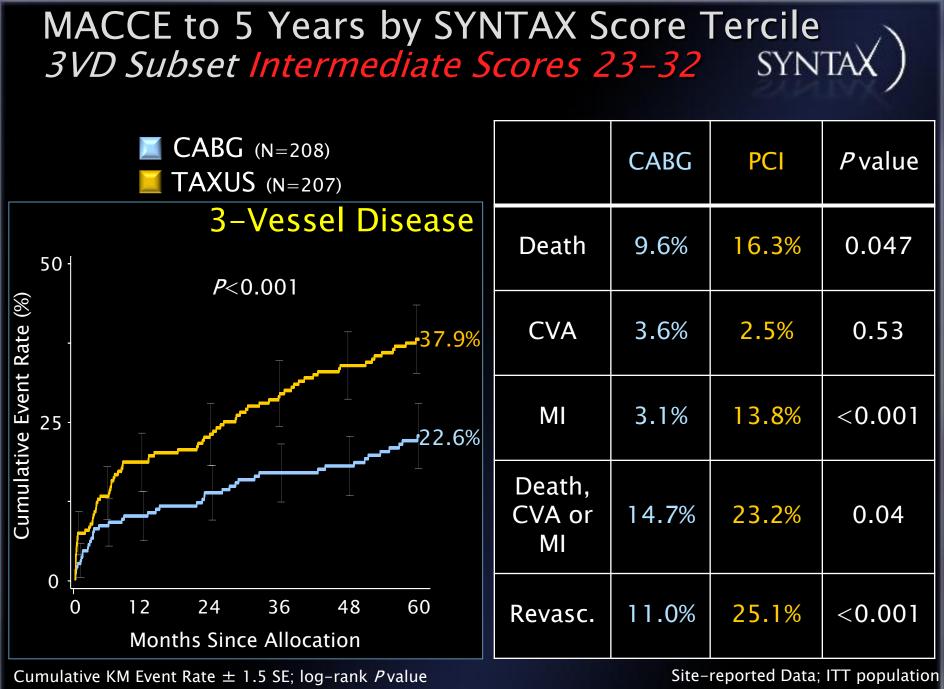


MACE = cardiac death, MI, or ischemic-driven TLR

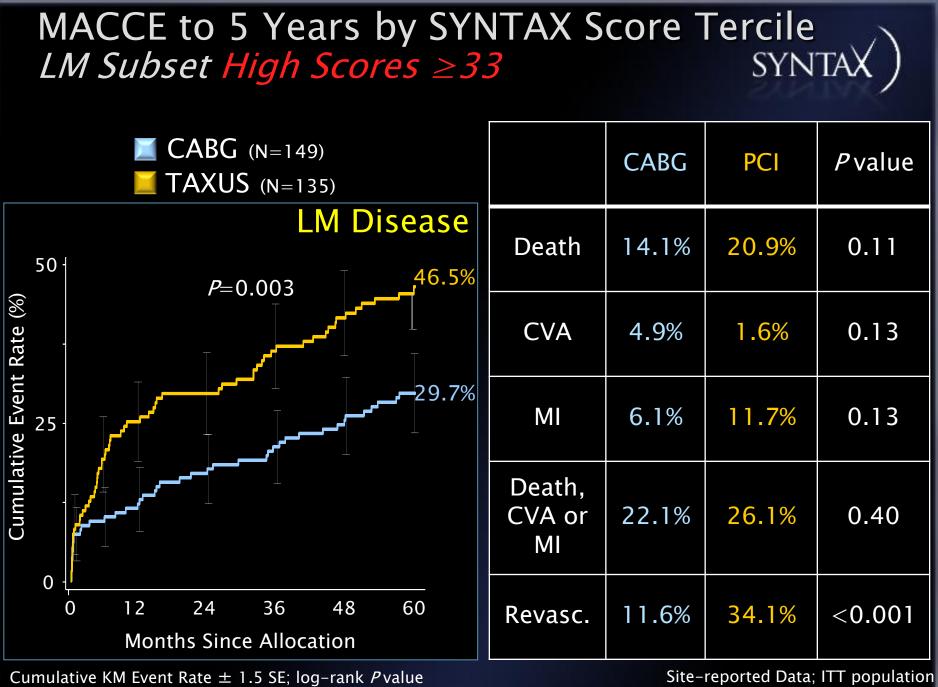
All-Cause Death or MI Through 5 Years

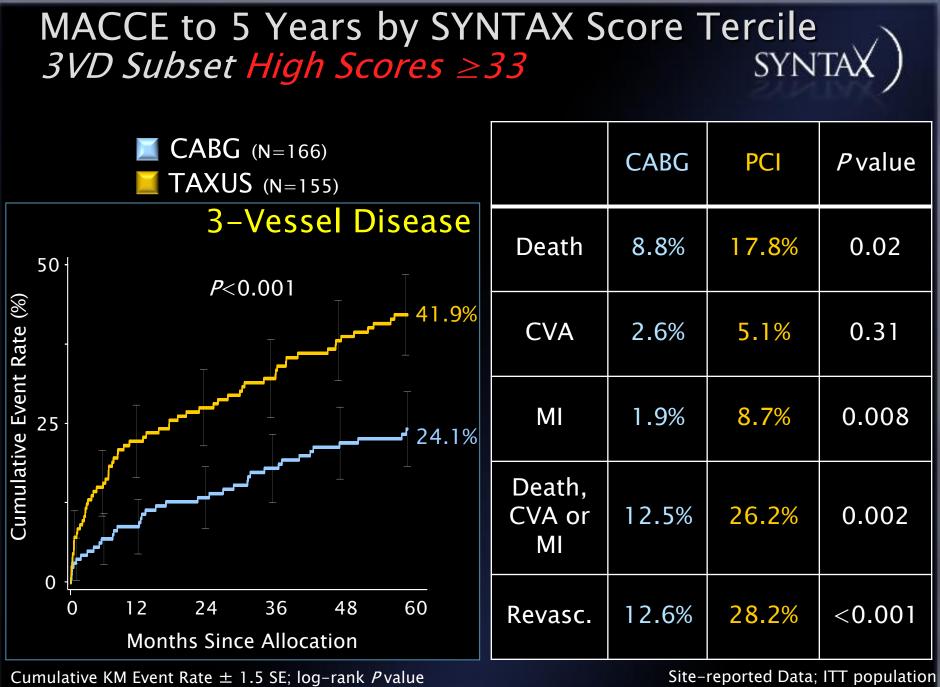


Spirit



SYNTAX 3VD 5-year Outcomes • TCT 2012 • Mohr • 23 October 2012 • Slide





My wish list

More efficient DES in complex CAD including diabetic patient

• DES with less late catch-up

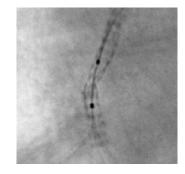
Ischemia-driven TLR Through 5 Years



Spirit III

INSTITUT CARDIOVASCULAIRE PARIS SUD

- Conformability ?
- Fracture ?
- Drug resistance ?



Polymer compatibility ?

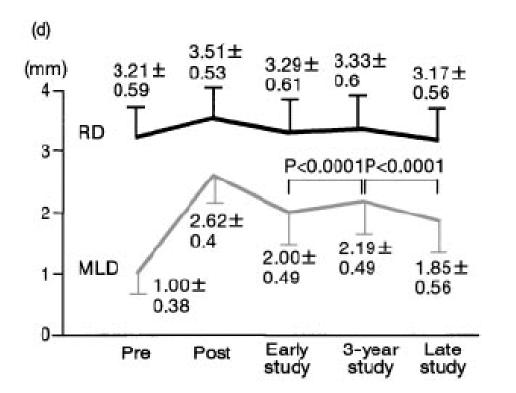
Biological effect: Brenner hypothesis

- Vessel 3 mm lesion
 <15 mm
- 1 million of SMC
- Doubling time : 1.7 m.
- 5 millions=severe restenosis
- Delay 4 m. + for BMS

- Proliferation inhibition in 99,9% of SMC
- 1 000 SMC
- 5 000 SMC @ 4 m.
- 5 millions @ 23 m. + for DES

Brenner et al. Int J Radiat Oncol Biol Phy 1996; 36: 805-810 www.icps.com.fr INSTITUT CARDIOVASCULAIRE PARIS SUD

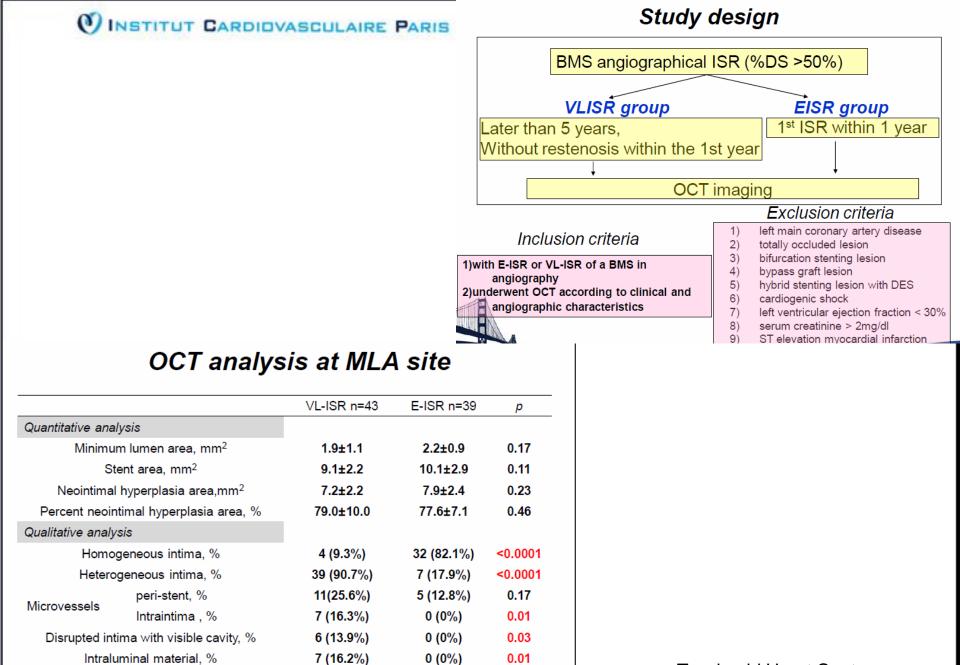
Very late restenosis exists for BMS: 173 patients/179 lesions @ 6.6 years



VERY late restenosis : 28%

VERY late TLR : 11%

Kimura et al. Circulation 2002



With shadowing

Without shadowing

6 (14.0%)

1 (2.3%)

0 (0%)

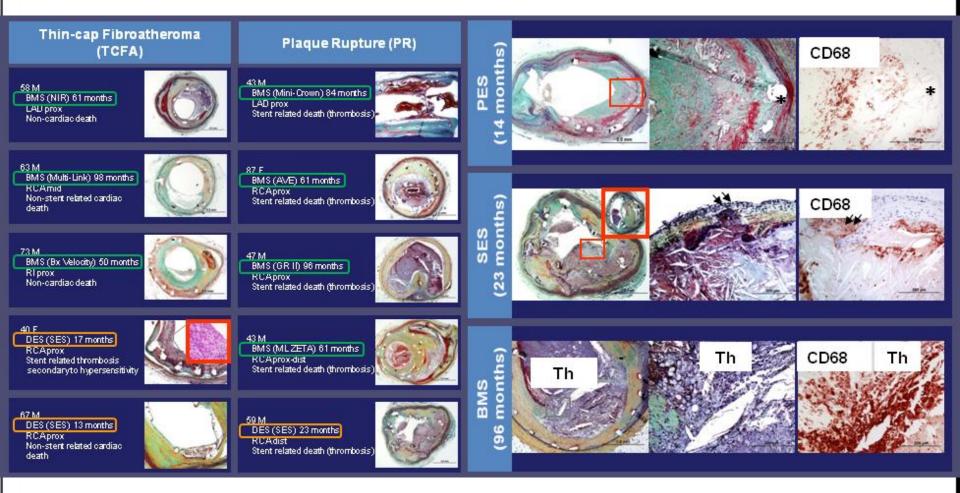
0 (0%)

0.03

>0.99

Toyohashi Heart Centre

Late atheroma for DES



My wish list

More efficient DES in complex CAD including diabetic patient

• DES with less late catch-up

• No need for prolonged DAPT

ESC guidelines 2010

(b) Recommended duration of dual antiplatelet therapy

After percutaneous coronary intervention

- 1 month after BMS implantation in stable angina;^{55,60,94}
- 6–12 months after DES implantation in all patients;^{60,94}
- 1 year in all patients after ACS, irrespective of revascularization strategy.

Eur Heart J 2010; 31: 2501-2555

Selected trials of DAPT duration

Trial	Candidates for prolonged DAPT	ENDPOINTS HAZARD RATIO (95% CI) D/MI/CVA	P-VALUES P=0.91	eeding events	Status
Park et al	Yes	D/MI D/CVA	P=0.62 P=0.57	No ference (TIMI major)	Published (NEJM 2010)
PRODIGY	Yes	Def ST Key safety EP TIMI Major Bleed	P=0.80	months better BARC)	Published (Circ 2012)
RESET	Yes	RBC Transfusion Net Adverse Clinical Events	P=0.041 P=0.041 P=0.025	No ference	Presented (ACC 2012)
DAPT	Yes	1.5 1 0.5 24-month DAPT better 6-month DAPT		NYK	Ongoing
www.icp	os.com.fr		FRODIGY	*	ueatri, ivii, CVA

Non DES candidate whatever risk of restenosis ??

Table 35Relative clinical contraindications to the useof drug-eluting stents

- Clinical history difficult to obtain, especially in the setting of acute severe clinical conditions (STEMI or cardiogenic shock).
- Expected poor compliance with DAPT, including patients with multiple comorbidities and polypharmacy.
- Non-elective surgery required in the short term that would require interruption of DAPT.
- · Increased risk of bleeding.
- · Known allergy to ASA or clopidogrel/prasugrel/ticagrelor.
- Absolute indication for long-term anticoagulation.

ASA = acetylsalicylic acid; DAPT = dual antiplatelet therapy; DES = drug-eluting stent; STEMI = ST-segment elevation myocardial infarction.

2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention

A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions

DES Generally Preferred Over	BMS Preferred Over DES
BMS (Efficacy Considerations)	(Safety Considerations)
 Left main disease Small vessels In-stent restenosis Bifurcations Diabetes Long lesions Multiple lesions Saphenous vein grafts 	 Unable to tolerate or comply with DAPT Anticipated surgery requiring discontinuation of DAPT within 12 mo High risk of bleeding

My wish list

More efficient DES in complex CAD including diabetic patient

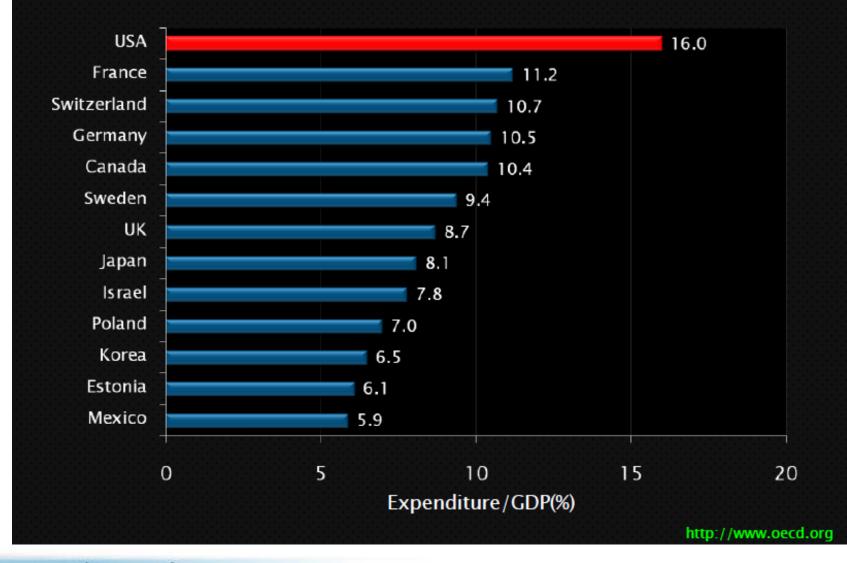
• DES with less late catch-up

No need for prolonged DAPT

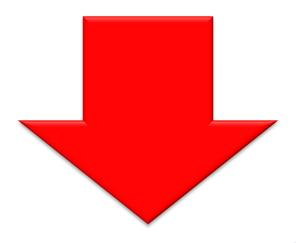
• Less costly DES

INSTITUT CARDIOVASCULAIRE PARIS SUD

Comparative Health Expenditure (2010)



A turning point for stent manufacturers?



Flat market New indications? Market expansion ??

Development cost Clinical program Regulatory burden Low cost competition Shareholder pressure

Superiority validation? A challenge

Trial Requirements for New DES Superiority RCT (vs. SPIRIT IV – 12 months)

Event	PROMUS (n=2416) (%)	NEW DES RCT 50% Reduction [#]	NEW DES RCT 30% Reduction [#]	
Death (all)	25 (1.0)	10,000	31,000	
Death (cardiac)	10 (0.1)	102,000	310,000	
AMI (all)	45 (1.9)	5,300	16,000	
Stent Thrombosis*	7 (0.3)	34,000	104,000	
TLR	61 (2.5)	4,010	12,000	
TVR	94 (3.9)	2,544	7,700	
TLF [†]	101 (4.2)	2,358	7,120	
MACE	102 (4.2)	2,358	7,120	

[#]Total sample size is based on equal allocation of New DES and PROMUS with 80% power and 2-sided alpha of 5% *Stent Thrombosis = ARC Definite/Probable

[†]Primary Endpoint (TLF = Cardiac Death, Target Vessel MI, or ischemia driven TLR)

Should we believe in the miracle?



Is my dream becoming real?

- Reduced/absorbable polymer or no polymer
 - No efficacy compromise ?
- Low dose drug combination
 No safety compromise ?

Fully absorbable DES

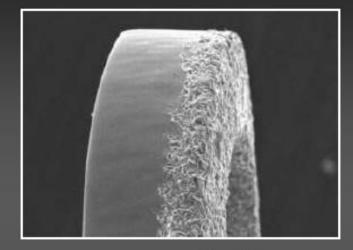
BioFreedom Drug Coated Stent (DCS)

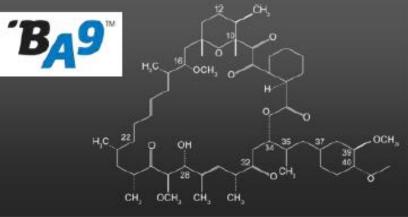
<u>Hypothesis</u>: Polymer-free drug release via porous-eluting stents may reduce late events caused by polymer stent coatings

Potential advantage

- Avoid long-term late adverse effects that might be attributable to the polymer
- Improved surface integrity since there is no polymer to be sheared or pealed away from the stent struts
- Possible shorter need of dual antiplatelet therapy

Selectively micro-structured surface holds drug in abluminal surface structures







LEADERS FREE TRIAL

- Age \geq 75 years old
- Adjunctive oral anticoagulation treatment planned to continue after PCI
- Baseline Hb <11 g/dl (or anemia requiring TF during the prior 4 weeks)</p>
- Any prior intra-cerebral bleed at any time
- Any stroke during the past year
- > Hospital admission for bleeding during the prior 12 months
- ➢ Non-skin cancer diagnosed or treated ≤ 3 years
- > Planned daily NSAID (other than aspirin) or steroids for \geq 30 days after PCI
- Planned major surgery (within 1 year)
- Expected non-compliance to prolonged DAPT for other non-financial reasons

• There is room for improvement

 There are some technical solutions (even for late catch-up??)

- Validation of benefit is only possible in high risk groups of patients
- And absorbable DES are on their way...