

Supporting Information

Acute Myocardial Infarction Treated with Novel Resolute Onyx and Orsiro Stents in the Randomized BIONYX Trial

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Table S1. Baseline patient, lesion, and procedural characteristics of acute MI patients treated with Resolute Onyx versus Orsiro

	Resolute Onyx n=626	Orsiro n=649	p-value
General characteristics			
Age, years	63.4(11.1)	61.9(11.8)	0.019
Women	151(50.2)	150(49.8)	0.67
Body-mass index, kg/m²	27.7(4.5)	27.9(4.6)	0.51
Current smoker	222/611(36.3)	247/634(39.0)	0.34
Medical history			
Diabetes, medically treated	109(17.4)	110(16.9)	0.83
Hypertension	282/614(45.9)	287/643(44.6)	0.65
Hypercholesterolemia	220/607(36.2)	242/633(38.2)	0.47
Prior myocardial infarction	72(11.5)	80(12.3)	0.65
Prior percutaneous coronary intervention	92(14.7)	93(14.3)	0.85
Prior coronary artery bypass surgery	23(3.7)	25(3.9)	0.87
Lesion and procedural characteristics			
At least 1 bifurcation	243(38.8)	261(40.2)	0.61
At least 1 severely calcified lesion	93(14.9)	111(17.1)	0.27
At least 1 complex lesion	504(80.5)	536(82.6)	0.34
Total stent length	30[18-48]	30[18-44]	0.65
Multi-vessel treatment	118(18.8)	101(15.6)	0.12
Direct stenting	142(22.7)	170(26.2)	0.15
Post dilation	444(70.9)	443(68.3)	0.30

Values are mean(SD), median[interquartile range], n(%) or n/N(%).

Table S2. Details of stent thrombosis in acute MI patients

				Index intervention			Event			
	Sex (age)	Clinical presentation	Diabetes	Randomized stent	Lesion details	Stent details	Timing stent thrombosis (days)	Clinical presentation	Patient on DAPT?	Treatment
Definite stent thrombosis	Male (63)	STEMI	No	Orsiro	LAD, complex, severely calcified	Number of stents:1 Orsiro: 3.5x18mm	Early; Acute (0)	Persistent angina after primary PCI, angiographic thrombus	Yes, Ticagrelor	TLR; Balloon angioplasty. DAPT with Ticagrelor for 1 year
	Male (72)	STEMI	No	Orsiro	CX, complex	Number of stents: 1 Orsiro: 2.5x18mm	Early; Subacute (3)	STEMI	Yes, Ticagrelor	TLR; PCI. Switch from ticagrelor to prasugrel for 1 year
	Female* (64)	NSTEMI	Yes	Orsiro	RCA, complex, severely calcified, bifurcation, CTO (collateral flow from left coronary)	Number of stents: 6 5 Orsiro: 2.25x18mm; 2.5x22mm; 3.0x35mm; 3.5x40mm; 2.5x9mm; 1 Resolute Onyx: 2.0x12mm	Early; Subacute (22)	NSTEMI; stent thrombosis in segment 2	Yes, Ticagrelor	TLR; CABG. subsequent antiplatelet treatment: aspirin
	Male (75)	NSTEMI	No	Orsiro	RCA, complex	Number of stents: 2 Orsiro: 3.0x30mm; 3.0x30mm	Very Late (405)	STEMI	No, Ticagrelor had been stopped 1 month prior	TLR; PCI. DAPT with Ticagrelor 90mg twice daily for 1 year, followed by 60mg twice daily
	Male (62)	NSTEMI	No	Orsiro	CX, complex, in-stent restenosis	Number of Stents: 3 Orsiro: 2.25x13mm; 3.0x13mm; 2.25x9mm	Very Late (423)	STEMI	No, clopidogrel had been	TLR; Balloon angioplasty. DAPT with Ticagrelor 90mg twice

									stopped 2 months prior	daily for 1 year, followed by 60mg twice daily
	Male (63)	NSTEMI	Yes	Resolute Onyx	Index PCI CX, bifurcation lesion. Staged PCI LAD/D, bifurcation lesion (stent thrombosis in LAD/D).	Number of stents CX: 1 Resolute Onyx: 3.5x18mm Number of stents LAD: 3 Resolute Onyx: 3.0x8mm; 2.0x18mm; 3.0x15mm	Very Late (516)	STEMI	Yes	TLR; PCI. DAPT with Ticagrelor for 1 year
	Male (76)	STEMI	No	Orsiro	venous graft, complex	Number of stents: 1 Orsiro 4.0x18mm	Very Late (599)	NSTEMI	No	Recanalization of the venous graft was unsuccessful; long-acting nitrate was prescribed
Probable stent thrombosis	Male (67)	NSTEMI	No	Orsiro	Graft, ostial, complex	Number of stents: 1 Orsiro 3.5x9mm	Early; Subacute (7)	Sudden death of unknown cause (adjudicated as cardiac death)	Yes	-
	Male (64)	STEMI	No	Orsiro	LAD, bifurcation, complex	Number of stents: 2 Orsiro 3.0x30mm; 3.5x13mm	Early; Subacute (7)	Sudden death of unknown cause (adjudicated as cardiac death)	Yes	-

* This patient received one unassigned stent which, according to independent CEC adjudication, bore no relation to the stent thrombosis event.

Abbreviations: CABG = coronary artery bypass grafting; CX = circumflex artery; CTO = chronic total occlusion; DAPT = dual antiplatelet therapy; LAD = left anterior descending; NSTEMI = non-ST-segment-elevation myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery; STEMI = ST-segment-elevation myocardial infarction; TLR = target lesion revascularization.

Table S3. Subgroup analyses for the 2-year rates of target vessel failure in patients presenting with acute myocardial infarction

	RO-ZES	O-SES	Forest plot	Hazard ratio (95% CI)	P value	P interaction
All patients	38/626 (6.1)	39/649 (6.0)		1.01 (0.65-1.57)	0.96	
Men	29/475 (6.1)	31/499 (6.2)		0.98 (0.59-1.62)	0.95	0.80
Women	9/151 (6.0)	8/150 (5.3)		1.13 (0.44-2.92)	0.81	
Diabetes	12/109 (11.0)	11/110 (10.0)		1.09 (0.48-2.48)	0.81	0.81
No diabetes	26/517 (5.0)	28/539 (5.2)		0.97 (0.57-1.65)	0.90	
Renal insufficiency	2/35 (5.7)	6/38 (15.8)		0.33 (0.06-1.63)	0.26*	0.15
No renal insufficiency	36/591 (6.1)	33/611 (5.4)		1.13 (0.71-1.81)	0.61	
Multivessel treatment	12/118 (10.2)	12/101 (11.9)		0.85 (0.38-1.90)	0.69	0.69
Single vessel treatment	26/508 (5.1)	27/548 (4.9)		1.04 (0.61-1.78)	0.89	
Small vessel <2.75 mm	25/325 (7.7)	22/308 (7.1)		1.08 (0.61-1.91)	0.79	0.63
No small vessel	13/301 (4.3)	17/341 (5.0)		0.86 (0.42-1.77)	0.69	
Bifurcation	16/243 (6.6)	21/261 (8.0)		0.80 (0.42-1.53)	0.53	0.32
No bifurcation	22/383 (5.7)	18/388 (4.6)		1.25 (0.67-2.34)	0.49	
Lesion length >27 mm	7/123 (5.7)	16/143 (11.2)		0.49 (0.20-1.19)	0.11	0.052
Lesion length ≤ 27 mm	31/503 (6.2)	23/506 (4.5)		1.47 (0.80-2.35)	0.25	
In-stent restenosis	5/14 (35.7)	1/10 (10.0)		4.25 (0.50-36.45)	0.34*	0.17
No in-stent restenosis	33/612 (5.4)	38/639 (5.9)		0.90 (0.57-1.44)	0.67	
Bypass graft	2/7 (28.6)	2/12 (16.7)		1.82 (0.26-12.94)	0.60*	0.51
No bypass graft	36/619 (5.8)	37/637 (5.8)	1.00 (0.63-1.58)	>0.99		
Only stents ≤3.00 mm	22/314 (7.0)	22/312 (7.1)	0.99 (0.55-1.79)	0.98	0.93	
Only stents >3.00 mm	15/311 (4.8)	17/337 (5.0)	0.95 (0.48-1.91)	0.90		
Age ≥75 years	7/105 (6.7)	14/110 (12.7)	0.51 (0.21-1.26)	0.14	0.09	
Age <75 years	25/539 (4.6)	31/521 (6.0)	1.28 (0.76-2.17)	0.34		

*Fisher’s exact test used

Abbreviations: O-SES, Orsiro sirolimus-eluting stent; RO-ZES, Resolute Onyx zotarolimus-eluting stent.

Table S4. Two-year clinical outcome of Resolute Onyx versus Orsiro in each clinical syndrome

STEMI						
	RO-ZES n = 282	O-SES n = 339	Hazard ratio (95% CI)	P _{log-rank}	Adjusted HR (95%-CI)†	p-value
Target vessel failure	11 (4.0)	19 (5.6)	0.69 (0.33-1.45)	0.33	0.69 (0.33-1.46)	0.33
Cardiac death	0	6 (1.8)	0.02 (0.00-13.37)	0.23*	-	-
Target vessel MI	2 (0.7)	7 (2.1)	0.34 (0.07-1.64)	0.16	0.34 (0.07-1.64)	0.18
Clinically indicated TVR	11 (4.0)	12 (3.6)	1.01 (0.48-2.49)	0.82	1.10 (0.49-2.50)	0.82
Target lesion failure	9 (3.3)	14 (4.1)	0.77 (0.33-1.78)	0.54	0.78 (0.34-1.80)	0.56
Clinically indicated TLR	9 (3.3)	7 (2.1)	1.55 (0.58-4.17)	0.38	1.57 (0.58-4.21)	0.37
Definite-or-probable stent thrombosis	0	4 (1.2)	0.02 (0.00-59.04)	0.07	-	-
Definite stent thrombosis	0	3 (0.9)	0.02 (0.00-207.22)	0.11	-	-
NSTEMI						
	RO-ZES n = 344	O-SES n = 310	Hazard ratio (95% CI)	P _{log-rank}	Adjusted HR (95%-CI)	p-value
Target vessel failure	27 (7.9)	20 (6.5)	1.22 (0.68-2.17)	0.50	1.17 (0.66-2.10)	0.59
Cardiac death	5 (1.5)	6 (2.0)	0.74 (0.23-2.44)	0.63	0.74 (0.22-2.42)	0.61
Target vessel MI	10 (3.0)	9 (3.0)	1.00 (0.41-2.45)	0.995	0.98 (0.40-2.41)	0.96
Clinically indicated TVR	18 (5.3)	10 (3.3)	1.62 (0.75-3.51)	0.22	1.55 (0.72-3.37)	0.26
Target lesion failure	23 (6.8)	17 (5.6)	1.22 (0.65-2.29)	0.53	1.21 (0.65-2.27)	0.55
Clinically indicated TLR	14 (4.1)	7 (2.3)	1.80 (0.73-4.47)	0.20	1.79 (0.72-4.45)	0.21
Definite-or-probable stent thrombosis	1 (0.3)	4 (1.3)	0.22 (0.03-2.00)	0.14	0.21 (0.02-1.89)	0.17
Definite stent thrombosis	1 (0.3)	3 (1.0)	0.30 (0.03-2.85)	0.26	0.28 (0.03-2.72)	0.28
Unstable angina						
	RO-ZES n = 254	O-SES n = 236	Hazard ratio (95% CI)	P _{log-rank}	Adjusted HR (95%-CI)	p-value
Target vessel failure	28 (11.1)	20 (8.7)	1.29 (0.73-2.29)	0.38	1.26 (0.71-2.24)	0.43
Cardiac death	2 (0.8)	0	59.40 (0.00-5259873.18)	0.18	-	-
Target vessel MI	12 (4.8)	6 (2.6)	1.83 (0.69-4.89)	0.22	1.78 (0.67-4.75)	0.25
Clinically indicated TVR	21 (8.3)	16 (6.9)	1.21 (0.63-2.32)	0.56	1.19 (0.62-2.29)	0.59
Target lesion failure	24 (9.5)	14 (6.1)	1.59 (0.82-3.07)	0.17	1.56 (0.80-3.01)	0.19
Clinically indicated TLR	16 (6.3)	10 (4.4)	1.48 (0.67-3.27)	0.33	1.46 (0.66-3.23)	0.35
Definite-or-probable stent thrombosis	1 (0.4)	2 (0.9)	0.46 (0.04-5.06)	0.51	0.44 (0.04-4.84)	0.50
Definite stent thrombosis	1 (0.4)	2 (0.9)	0.46 (0.04-5.06)	0.51	0.44 (0.04-4.84)	0.50
Stable angina						
	RO-ZES n = 363	O-SES n = 360	Hazard ratio (95% CI)	P _{log-rank}	Adjusted HR (95%-CI)	p-value
Target vessel failure	27 (7.5)	28 (7.9)	0.96 (0.56-1.62)	0.87	0.95 (0.56-1.62)	0.86
Cardiac death	5 (1.4)	8 (2.3)	0.62 (0.20-1.89)	0.40	0.62 (0.20-1.90)	0.40
Target vessel MI	10 (2.8)	6 (1.7)	1.66 (0.60-4.56)	0.32	1.65 (0.60-4.54)	0.33
Clinically indicated TVR	16 (4.5)	19 (5.4)	0.83 (0.43-1.61)	0.57	0.82 (0.42-1.60)	0.57

Target lesion failure	20 (5.6)	26 (7.4)	0.76 (0.42-1.36)	0.36	0.76 (0.42-1.36)	0.36
Clinically indicated TLR	9 (2.5)	17 (4.9)	0.52 (0.23-1.16)	0.11	0.52 (0.23-1.16)	0.11
Definite-or-probable stent thrombosis	3 (0.8)	3 (0.9)	0.99 (0.20-4.90)	0.99	0.98 (0.20-4.88)	0.98
Definite stent thrombosis	3 (0.8)	3 (0.9)	0.99 (0.20-4.90)	0.99	0.98 (0.20-4.88)	0.98

*Wald-test used because $p_{\log\text{-rank}}$ (based on chi-square) did not correspond with 95%-CI due to 0 events in RO-ZES ($P_{\log\text{-rank}}=0.03$).

† Multivariate models included variables that significantly differed between groups at baseline and had a significant association with target vessel failure. In addition, sex and diabetes were included in the models because randomization was stratified for these variables. The final model for STEMI, unstable angina, and stable angina included sex and diabetes. The final model for NSTEMI included sex, diabetes, and total stent length.

Abbreviations: CI, confidence interval; MI, myocardial infarction; NSTEMI, non-ST-segment elevation MI; O-SES, Orsiro sirolimus-eluting stent; RO-ZES, Resolute Onyx zotarolimus-eluting stent; STEMI, ST-segment elevation MI; TLR, target lesion revascularization; TVR, target vessel revascularization.

Table S5. Two-year clinical outcome of RO-ZES versus O-SES in patients presenting with acute and chronic coronary syndrome

Acute Coronary Syndrome				
	RO-ZES n = 880	O-SES n = 885	Hazard ratio (95% CI)	P_{log-rank}
Target vessel failure	66 (7.6)	59 (6.7)	1.12 (0.79-1.59)	0.53
Cardiac death	7 (0.8)	12 (1.4)	0.58 (0.23-1.48)	0.25
Target vessel MI	24 (2.8)	22 (2.5)	1.09 (0.61-1.94)	0.77
Clinically indicated TVR	50 (5.8)	38 (4.4)	1.32 (0.87-2.01)	0.20
Target lesion failure	56 (6.4)	45 (5.1)	1.25 (0.85-1.85)	0.26
Clinically indicated TLR	39 (4.5)	24 (2.8)	1.64 (0.98-2.72)	0.056
Definite-or-probable stent thrombosis	2 (0.2)	10 (1.1)	0.20 (0.04-0.91)	0.02
Definite stent thrombosis	2 (0.2)	8 (0.9)	0.25 (0.05-1.17)	0.057
Chronic Coronary Syndrome				
	RO-ZES n = 363	O-SES n = 360	Hazard ratio (95% CI)	P_{log-rank}
Target vessel failure	27 (7.5)	28 (7.9)	0.96 (0.56-1.62)	0.87
Cardiac death	5 (1.4)	8 (2.3)	0.62 (0.20-1.89)	0.40
Target vessel MI	10 (2.8)	6 (1.7)	1.66 (0.60-4.56)	0.32
Clinically indicated TVR	16 (4.5)	19 (5.4)	0.83 (0.43-1.61)	0.57
Target lesion failure	20 (5.6)	26 (7.4)	0.76 (0.42-1.36)	0.36
Clinically indicated TLR	9 (2.5)	17 (4.9)	0.52 (0.23-1.16)	0.11
Definite-or-probable stent thrombosis	3 (0.8)	3 (0.9)	0.99 (0.20-4.90)	0.99
Definite stent thrombosis	3 (0.8)	3 (0.9)	0.99 (0.20-4.90)	0.99

Numbers are n (%).

Abbreviations: CI = confidence interval; O-SES = Orsiro sirolimus-eluting stent; MI = myocardial infarction; RO-ZES = Resolute Onyx zotarolimus-eluting stent; TLR = Target lesion revascularization; TVR = Target vessel revascularization.