

Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Stone GW, Moses JW, Ellis SG, et al. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. *N Engl J Med* 2007;356:998-1008.

Electronic (Online) Supplemental Appendix

I. Stent Thrombosis Definitions

Sirolimus-eluting stent trials

RAVEL, SIRIUS, E-SIRIUS, C-SIRIUS:

Within 30 days: Angiographic documentation of stent thrombosis with associated ischemia; OR

Q-wave myocardial infarction in the in the distribution of the treated vessel without angiography; OR

Death without other obvious cause

After 30 days: Angiographic documentation of stent thrombosis with associated ischemia

SIRIUS, E-SIRIUS, C-SIRIUS also required the absence of intervening target lesion revascularization in all definitions of stent thrombosis

The clinical events committee for each trial (blinded to treatment assignment) could apply clinical judgment when adjudicating borderline or otherwise difficult to define cases

Paclitaxel-eluting stent trials

TAXUS-II:

Within 30 days: Angiographic documentation of a complete occlusion (TIMI flow 0 or 1) of a previously successfully treated artery (TIMI

flow 3 and residual diameter stenosis $\leq 30\%$); OR

Angiographic documentation of a flow limiting thrombus (TIMI flow 1 or 2) of a previously successfully treated artery; OR

Death without other obvious cause

After 30 days: Angiographic documentation of a complete occlusion or a flow limiting thrombus of a previously successfully treated artery

TAXUS-I, -IV, -V, and –VI:

Within 30 days: Clinical presentation of an acute coronary syndrome with angiographic evidence of stent thrombosis, defined as either complete occlusion (TIMI flow 0 or 1) of a previously successfully treated artery (TIMI flow 2 to 3 and diameter stenosis $\leq 30\%$) and/or a flow limiting thrombus within or adjacent to a previously successfully treated lesion; OR
Acute myocardial infarction (Q-wave or non-Q-wave) in the distribution of the treated vessel; OR
Death without other obvious cause

After 30 days: Clinical presentation of an acute coronary syndrome with angiographic evidence of stent thrombosis as defined above,
OR
Acute myocardial infarction (Q-wave or non-Q-wave) in the distribution of the treated vessel

TAXUS-IV, -V and –VI also required the absence of intervening target lesion revascularization in all definitions of stent thrombosis

The clinical events committee for each trial (blinded to treatment assignment) could apply clinical judgment when adjudicating borderline or otherwise difficult to define cases

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II. Clinical Outcomes at 4 Years (complete results, all pre-specified intervals)

	Sirolimus-eluting stent (N=878)	Bare metal stent (N=870)	Hazard ratio [95% CI]*	P value†	Paclitaxel-eluting stent (N=1,755)	Bare metal stent (N=1,758)	Hazard ratio [95% CI]*	P value†
Stent thrombosis	1.2% (10)	0.6% (5)	2.00 [0.68, 5.85]	0.20	1.3% (20)‡	0.9% (14)	1.44 [0.73, 2.84]	0.30
0 - 30 days	0.5% (4)	0.1% (1)	3.98 [0.45, 35.62]	0.23	0.5% (8)	0.6% (10)	0.80 [0.32, 2.03]	0.79
30 days – 4 years	0.7% (6)	0.5% (4)	1.50 [0.42, 5.30]	0.57	0.8% (12)	0.3% (4)	3.03 [0.98, 9.38]	0.036
30 days – 1 year	0.1% (1)	0.5% (4)	0.25 [0.03, 2.22]	0.18	0.2% (4)	0.1% (2)	2.01 [0.37, 10.97]	0.28
1 year – 4 years	0.6% (5)	0.0% (0)	-	0.025	0.7% (9)	0.2% (2)	4.54 [0.98, 21.03]	0.028
Death, all cause	6.7% (57)	5.3% (45)	1.27 [0.86, 1.88]	0.23	6.1% (86)	6.6% (92)	0.94 [0.70, 1.26]	0.68
0 - 30 days	0.1% (1)	0.1% (1)	0.99 [0.06, 15.86]	1.0	0.1% (2)	0.3% (5)	0.40 [0.08, 2.07]	0.43
30 days – 4 years	6.6% (56)	5.2% (44)	1.27 [0.86, 1.89]	0.23	6.0% (84)	6.3% (87)	0.97 [0.72, 1.31]	0.85
30 days – 1 year	1.1% (10)	0.7% (6)	1.66 [0.60, 4.56]	0.32	1.5% (26)	1.5% (26)	1.00 [0.58, 1.73]	0.99
1 year – 4 years	5.5% (46)	4.6% (38)	1.21 [0.79, 1.87]	0.37	4.6% (58)	4.9% (61)	0.96 [0.67, 1.37]	0.81
Death, cardiac	3.5% (29)	2.7% (23)	1.26 [0.73, 2.18]	0.40	2.4% (36)	3.0% (42)	0.86 [0.55, 1.35]	0.51
0 - 30 days	0.1% (1)	0.1% (1)	0.99 [0.06, 15.86]	1.0	0.1% (2)	0.3% (5)	0.40 [0.08, 2.07]	0.43
30 days – 4 years	3.4% (28)	2.6% (22)	1.28 [0.73, 2.23]	0.39	2.3% (34)	2.7% (37)	0.92 [0.58, 1.47]	0.74
30 days – 1 year	0.3% (3)	0.3% (3)	0.99 [0.20, 4.93]	0.96	0.8% (13)	0.9% (15)	0.87 [0.41, 1.83]	0.71
1 year – 4 years	3.0% (25)	2.3% (19)	1.32 [0.73, 2.40]	0.36	1.5% (21)	1.8% (22)	0.96 [0.53, 1.75]	0.90
Death, non-cardiac	3.3% (28)	2.7% (22)	1.27 [0.73, 2.23]	0.40	3.8% (50)	3.7% (50)	1.01 [0.68, 1.49]	0.98
0 - 30 days	0.0% (0)	0.0% (0)	-	-	0.0% (0)	0.0% (0)	-	-
30 days – 4 years	3.3% (28)	2.7% (22)	1.27 [0.73, 2.23]	0.40	3.8% (50)	3.7% (50)	1.01 [0.68, 1.49]	0.97
30 days – 1 year	0.8% (7)	0.3% (3)	2.32 [0.60, 8.96]	0.27	0.8% (13)	0.6% (11)	1.19 [0.53, 2.65]	0.68
1 year – 4 years	2.5% (21)	2.3% (19)	1.11 [0.60, 2.06]	0.75	3.1% (37)	3.1% (39)	0.96 [0.61, 1.50]	0.84
Myocardial infarction, all	6.4% (55)	6.2% (53)	1.03 [0.71, 1.51]	0.86	7.0% (111)	6.3% (105)	1.06 [0.81, 1.39]	0.66
0 - 30 days	2.5% (22)	2.0% (17)	1.29 [0.68, 2.42]	0.43	3.8% (66)	3.1% (55)	1.20 [0.84, 1.72]	0.31
30 days – 4 years	4.1% (34)	4.4% (37)	0.91 [0.57, 1.45]	0.69	3.6% (49)	3.5% (54)	0.91 [0.62, 1.34]	0.62
30 days – 1 year	1.3% (11)	2.2% (19)	0.57 [0.27, 1.20]	0.13	0.8% (14)	1.8% (31)	0.45 [0.24, 0.85]	0.01

1 year – 4 years	2.8% (23)	2.2% (18)	1.28 [0.69, 2.37]	0.43	2.8% (36)	1.8% (25)	1.45 [0.87, 2.42]	0.15
Myocardial infarction, Q-wave	2.1% (18)	1.3% (11)	1.64 [0.77, 3.47]	0.19	1.4% (22)	1.1% (17)	1.30 [0.69, 2.45]	0.42
0 - 30 days	0.7% (6)	0.1% (1)	5.96 [0.72, 49.46]	0.09	0.4% (7)	0.4% (7)	1.00 [0.35, 2.86]	1.0
30 days – 4 years	1.4% (12)	1.2% (10)	1.20 [0.52, 2.77]	0.67	1.1% (17)	0.8 (11)	1.55 [0.73, 3.32]	0.25
30 days – 1 year	0.6% (5)	0.6% (5)	0.99 [0.29, 3.42]	0.99	0.4% (7)	0.2% (3)	2.34 [0.61, 9.06]	0.17
1 year – 4 years	0.8% (7)	0.6% (5)	1.41 [0.45, 4.43]	0.56	0.7% (11)	0.6% (8)	1.38 [0.56, 3.44]	0.48
Myocardial infarction, non-Q-wave	4.5% (38)	5.0% (43)	0.88 [0.57, 1.36]	0.55	5.8% (91)	5.3% (90)	1.02 [0.76, 1.36]	0.92
0 - 30 days	1.8% (16)	1.8% (16)	0.99 [0.50, 1.99]	0.99	3.4% (59)	2.7% (48)	1.23 [0.84, 1.80]	0.28
30 days – 4 years	2.8% (23)	3.3% (28)	0.81 [0.47, 1.41]	0.46	2.6% (33)	2.8% (45)	0.73 [0.47, 1.15]	0.17
30 days – 1 year	0.7% (6)	1.6% (14)	0.42 [0.16, 1.10]	0.07	0.4% (7)	1.6% (28)	0.25 [0.11, 0.57]	<0.001
1 year – 4 years	2.1% (17)	1.7% (14)	1.22 [0.60, 2.46]	0.59	2.1% (26)	1.3% (19)	1.38 [0.76, 2.49]	0.28
Death or myocardial infarction	11.6% (100)	10.4% (89)	1.12 [0.84, 1.49]	0.44	12.4% (187)	11.8% (183)	1.03 [0.84, 1.26]	0.79
0 - 30 days	2.6% (23)	2.1% (18)	1.27 [0.69, 2.35]	0.44	3.9% (68)	3.3% (58)	1.18 [0.83, 1.67]	0.36
30 days – 4 years	9.2% (78)	8.8% (75)	1.03 [0.75, 1.41]	0.86	9.1% (127)	9.2% (134)	0.95 [0.74, 1.21]	0.67
30 days – 1 year	2.3% (20)	2.8% (24)	0.82 [0.45, 1.49]	0.51	2.2% (38)	3.1% (54)	0.70 [0.46, 1.06]	0.09
1 year – 4 years	7.4% (62)	6.3% (53)	1.17 [0.81, 1.69]	0.39	7.1% (90)	6.5% (84)	1.08 [0.80, 1.46]	0.60
Death or Q-wave myocardial infarction	8.2% (70)	6.4% (54)	1.30 [0.91, 1.86]	0.14	7.3% (105)	7.5% (107)	0.99 [0.76, 1.29]	0.93
0 - 30 days	0.8% (7)	0.2% (2)	3.48 [0.72, 16.74]	0.13	0.5% (9)	0.6% (11)	0.82 [0.34, 1.98]	0.66
30 days – 4 years	7.4% (63)	6.3% (53)	1.19 [0.83, 1.71]	0.35	6.9% (98)	7.0% (97)	1.02 [0.77, 1.35]	0.90
30 days – 1 year	1.6% (14)	1.3% (11)	1.26 [0.57, 2.78]	0.56	1.8% (32)	1.7% (29)	1.11 [0.67, 1.83]	0.69
1 year – 4 years	6.1% (51)	5.0% (42)	1.22 [0.81, 1.83]	0.34	5.2% (67)	5.4% (68)	0.99 [0.71, 1.39]	0.97
Cardiac death or myocardial infarction	8.8% (75)	8.2% (70)	1.07 [0.77, 1.48]	0.69	8.9% (139)	8.5% (136)	1.03 [0.81, 1.30]	0.82
0 - 30 days	2.6% (23)	2.1% (18)	1.27 [0.69, 2.35]	0.44	3.9% (68)	3.3% (58)	1.18 [0.83, 1.67]	0.36
30 days – 4 years	6.3% (53)	6.5% (55)	0.95 [0.65, 1.39]	0.81	5.4% (77)	5.6% (84)	0.92 [0.67, 1.25]	0.58
30 days – 1 year	1.5% (13)	2.5% (22)	0.58 [0.29, 1.16]	0.12	1.4% (25)	2.5% (43)	0.58 [0.35, 0.95]	0.03
1 year – 4 years	5.2% (43)	4.1% (34)	1.27 [0.81, 1.99]	0.30	4.1% (53)	3.5% (45)	1.19 [0.80, 1.77]	0.39

Values are x% (y), where x is the Kaplan-Meier estimate and y is the actual number of patients with events. Only the first event is counted within any interval. CI = confidence interval. *Estimate calculated from a Cox proportional hazards model; † 2-sided log-rank or exact log-rank. ‡One patient had two stent thrombosis events, one before 1 year and one after 1 year.

Electronic (Online) Supplemental Appendix

III. Procedural and Follow-up Angiographic Results

	Sirolimus-eluting stent	Bare metal stent	P value	Paclitaxel-eluting stent	Bare metal stent	P value
<u>Post procedure</u>	N=874	N=869		N=1739	N=1748	
Reference vessel diameter (mm)	2.76 ± 0.42	2.76 ± 0.46	0.98	2.80 ± 0.50	2.80 ± 0.50	1.0
Minimal luminal diameter (mm)						
- In-stent	2.58 ± 0.40	2.57 ± 0.41	0.48	2.61 ± 0.46	2.60 ± 0.45	0.57
- In-segment	2.28 ± 0.45	2.27 ± 0.46	0.86	2.18 ± 0.51	2.19 ± 0.51	0.91
Diameter stenosis						
- In-stent (%)	6.8 ± 8.3	7.2 ± 8.6	0.40	6.2 ± 10.3	6.4 ± 10.7	0.53
- In-segment (%)	17.7 ± 9.8	17.8 ± 9.4	0.84	21.4 ± 10.3	21.3 ± 10.5	0.84
Acute gain (mm)						
- In-stent	1.64 ± 0.43	1.64 ± 0.43	0.93	1.70 ± 0.45	1.69 ± 0.44	0.27
- In-segment	1.33 ± 0.47	1.34 ± 0.47	0.74	1.28 ± 0.48	1.28 ± 0.49	0.76
<u>Follow-up*</u>	N=658	N=670		N=1352	N=1342	
Reference vessel diameter (mm)	2.73 ± 0.43	2.67 ± 0.44	0.01	2.75 ± 0.49	2.70 ± 0.50	0.005
Minimal luminal diameter (mm)						
- In-stent	2.42 ± 0.54	1.57 ± 0.74	<0.001	2.19 ± 0.66	1.69 ± 0.70	<0.001
- In-segment	2.09 ± 0.55	1.50 ± 0.67	<0.001	1.95 ± 0.63	1.61 ± 0.65	<0.001
Diameter stenosis						
- In-stent (%)	12.0 ± 15.0	41.6 ± 24.4	<0.001	20.3 ± 20.1	37.9 ± 22.2	<0.001
- In-segment (%)	23.9 ± 14.7	44.2 ± 22.2	<0.001	29.6 ± 18.2	41.0 ± 20.3	<0.001
Late loss (mm)						
- In-stent	0.14 ± 0.42	0.99 ± 0.66	<0.001	0.41 ± 0.54	0.90 ± 0.59	<0.001
- In-segment	0.17 ± 0.44	0.75 ± 0.64	<0.001	0.31 ± 0.50	0.67 ± 0.58	<0.001
Binary restenosis						
- In-stent	17/657 (2.6%)	245 (36.6%)	<0.001	137/1350 (10.1%)	394/1340 (29.4%)	<0.001

- In-segment	42 (6.4%)	253 (37.8%)	<0.001	189 (14.0%)	425 (31.7%)	<0.001
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* 6 months for RAVEL, TAXUS-I and TAXUS-II; 8 months for SIRIUS, E-SIRIUS and C-SIRIUS; 9 months for TAXUS-IV, TAXUS-V and TAXUS-VI