Supplementary Online Content

Lopes RD, de Barros e Silva PGM, de Andrade Jesuíno I, et al. Timing of loading dose of atorvastatin in patients undergoing percutaneous coronary intervention for acute coronary syndromes: insights from the SECURE-PCI randomized trial. *JAMA Cardiol*. Published online September 24, 2018. doi:10.1001/jamacardio.2018.3408

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

eAppendix – Statistical Analysis

Continuous variables are reported as mean and standard deviation (SD), or medians and interquartile ranges as appropriate. Categorical variables are summarized as frequencies.

Times to events are presented using Kaplan-Meier survival curves.

Both primary and secondary outcomes were analyzed according to percutaneous coronary intervention (PCI) and type of acute coronary syndrome (ACS).

The treatment effect of 80mg of atorvastatin versus placebo was assessed using Cox regression analysis adjusted for Age, Sex, ACS type, Previous use of chronic statin therapy, Hypertension, Hypercholesterolemia, Diabetes mellitus, Tobacco use, Previous MI, Previous PCI, Previous CABG, Previous Stroke, Previous Heart Failure, Renal Impairment, Obesity, Aspirin, and Clopidogrel/Ticagrelor/Prasugrel and expressed by hazard ratio (HR) and 95% confidence intervals (CI).

Analyses according to the type of ACS and to the timing of study drug administration before PCI were analyzed by interaction parameter testing in the unadjusted Cox regression.

All analyses considered a two-tailed alpha of 5% as statistically significant and were performed using R software, version 3.3.3. (R Foundation for Statistical Computing).

eTable 1: Baseline Participant Characteristics of Patients Not Undergoing PCI

Characteristic	Atorvastatin (n = 734)	Placebo (n = 743)
Age (years) – mean ± sd	61.7 ± 11.7 (n=734)	61.1 ± 12.1 (n=743)
Female sex n (%)	206/734 (28.1%)	228/743 (30.7%)
Diagnosis		
STEMI (%)	78/699 (11.2%)	69/710 (9.7%)
NSTEMI (%)	432/699 (61.8%)	448/710 (63.1%)
Unstable angina	189/699 (27%)	193/710 (27.2%)
Previous use of chronic statin therapy (6 months before randomization) n (%)	243/734 (33.1%)	236/743 (31.8%)
Medical history (%)		
Hypertension	550/734 (74.9%)	548/743 (73.8%)
Hypercholesterolemia	276/734 (37.6%)	281/743 (37.8%)
Diabetes mellitus	238/734 (32.4%)	247/743 (33.2%)
Tobacco use	156/734 (21.3%)	191/743 (25.7%)
Previous MI	152/734 (20.7%)	135/743 (18.2%)
Previous PCI	106/734 (14.4%)	96/743 (12.9%)
Previous CABG	41/734 (5.6%)	37/743 (5%)
Previous Stroke	36/734 (4.9%)	31/743 (4.2%)
Renal Impairment	26/734 (3.5%)	24/743 (3.2%)
Obesity	121/734 (16.5%)	123/743 (16.6%)
Treatment strategy		
CABG	162/734 (22.1%)	171/743 (23%)
Medical Management	572/734 (77.9%)	572/743 (77%)
Reason why PCI was not performed		
Clinical treatment	450/734 (61.3%)	472/743 (63.5%)
CABG	162/734 (22.1%)	171/743 (23.0%)
Not a final diagnosis ofACS	109/734 (14.9%)	88/743 (11.8%)
Unknown	13/734 (1.8%)	12/743 (1.6%)
Other medical therapy (%)		
Aspirin	567/734 (77.2%)	552/743 (74.3%)
Clopidogrel/Ticagrelor/Prasugrel	465/734 (63.4%)	443/743 (59.6%)
Beta-blockers	485/734 (66.1%)	480/743 (64.6%)

ACE inhibitors or ARA	409/734 (55.7%)	410/743 (55.2%)
Enoxaparin	246/734 (33.5%)	225/743 (30.3%)
Non-fractioned heparin	49/734 (6.7%)	40/743 (5.4%)
Fondaparinux	138/734 (18.8%)	137/743 (18.4%)

eTable 2. Timing of study drug administration according to study group and type of acute coronary syndrome

Timing of drug administration before PCI	**Atorvastatin**	**Placebo**
Overall	(n=1351)	(n=1359)
Didn't received study drug before PCI	25/1351 (1.9%)	27/1359 (2%)
Up to 2 hours before PCI	577/1326 (43.5%)	571/1332 (42.9%)
Between 2 and 4 hours before PCI	463/1326 (34.9%)	484/1332 (36.3%)
Between 4 and 12 hours before PCI	236/1326 (17.8%)	201/1332 (15.1%)
More than 12 hours before PCI	50/1326 (3.8%)	76/1332 (5.7%)
STEMI	(n=417)	(n=448)
Didn't received study drug before PCI	10/417 (2.4%)	12/448 (2.7%)
Up to 30 minutes before PCI	164/407 (40.3%)	174/436 (39.9%)
Between 30 minutes and 2 hours before PCI	147/407 (36.1%)	148/436 (33.9%)
More than 2 hours before PCI	96/407 (23.6%)	114/436 (26.1%)
Non-STE ACS	(n=915)	(n=891)
Didn't received study drug before PCI	14/915 (1.5%)	14/891 (1.6%)
Up to 2 hours before PCI	252/901 (28%)	243/877 (27.7%)
Between 2 to 4 hours before PCI	416/901 (46.2%)	413/877 (47.1%)
Between 4 to 12 hours before PCI	192/901 (21.3%)	157/877 (17.9%)
More than 12 hours before PCI	41/901 (4.6%)	64/877 (7.3%)

eTable 3: Treatment effect according to the type of treatment in the Non-PCI group

	Atorvastatin	Placebo	Absolute difference (%) (95% CI) [a]	Hazard ratio (95% CI)	P Value
CABG group	20/162 (12.3%)	12/171 (7%)	-5.33 (-12.28; 1.62)	1.83 [0.90; 3.75]	0.10
Medical management	29/572 (5.1%)	25/572 (4.4%)	-0.70 (-3.33; 1.93)	1.17 [0.69; 2.00]	0.56

Abbreviatons: CI denotes confidence interval.
Data presented as No. /total No. (%)
[a]Positive values favors Atorvastatin

eTable 4. Exploratory Analysis in STEMI Patients Subgroup

Outcomes	Atorvastatin	Placebo	Absolute difference (%) (95% CI) [b]	Unadjusted Hazard ratio (95% CI)	P value
Exploratory analysis in STEMI patients subgroup at 30 days					
MACE	30/417 (7.2%)	58/448 (12.9%)	5.75 (1.54 to 9.96)	0.54 (0.35 to 0.84)	0.01
Death	19/417 (4.6%)	34/448 (7.6%)	3.03 (-0.36 to 6.43)	0.59 (0.34 to 1.04)	0.07
Cardiovascular Death	19/417 (4.6%)	32/448 (7.1%)	2.59 (-0.76 to 5.93)	0.63 (0.36 to 1.11)	0.11
Myocardial Infarction	11/417 (2.6%)	30/448 (6.7%)	4.06 (1.05 to 7.07)	0.39 (0.19 to 0.77)	0.01
Peri-PCI MI	9/417 (2.2%)	19/448 (4.2%)	2.08 (-0.48 to 4.64)	0.51 (0.23 to 1.12)	0.09
Non-PCI related MI	3/417 (0.7%)	13/448 (2.9%)	2.18 (0.20 to 4.17)	0.24 (0.07 to 0.85)	0.03
Revascularization	2/417 (0.5%)	4/448 (0.9%)	0.41 (-0.91 to 1.74)	0.53 (0.10 to 2.89)	0.46
Urgent/Target Vessel	1/417 (0.2%)	3/448 (0.7%)	0.43 (-0.69 to 1.55)	0.35 (0.04 to 3.38)	0.37
Stroke	1/417 (0.2%)	4/448 (0.9%)	0.65 (-0.57 to 1.87)	0.26 (0.03 to 2.33)	0.23
Stent Thrombosis	4/417 (1%)	10/448 (2.2%)	1.27 (-0.62 to 3.16)	0.42 (0.13 to 1.33)	0.14
Exploratory analysis at 7 days or hospital discharge					
Bleeding[a]	1/417 (0.2%)	2/448 (0.4%)	0.21 (-0.78; 1.19)	0.69 (0.14; 3.43)[a]	1.00
Rhabdomyolysis[a]	0/417 (0%)	1/448 (0.2%)	-	-	-

Abbreviatons: CI denotes confidence interval.
Data presented as No. /total No. (%)
[a]Effect estimates are risk ratios instead of hazard ratios.
[b]Positive values favors Atorvastatin

eTable 5. Exploratory analysis in Non-STE ACS patients subgroup.

Outcomes	Atorvastatin	Placebo	Absolute difference (%) (95% CI) [b]	Unadjusted Hazard ratio (95% CI)	P value
Clinical Outcomes at 30 days					
MACE	47/915 (5.1%)	54/891 (6.1%)	0.92 (-1.31 to 3.16)	0.84 (0.57 to 1.24)	0.39
Death	10/915 (1.1%)	9/891 (1%)	-0.08 (-1.11 to 0.94)	1.09 (0.44 to 2.68)	0.86
Cardiovascular Death	8/915 (0.9%)	5/891 (0.6%)	-0.31 (-1.20 to 0.58)	1.56 (0.51 to 4.78)	0.43
Myocardial Infarction	35/915 (3.8%)	40/891 (4.5%)	0.66 (-1.29 to 2.62)	0.84 (0.54 to 1.33)	0.47
Peri-PCI MI	30/915 (3.3%)	35/891 (3.9%)	0.65 (-1.18 to 2.48)	0.83 (0.51 to 1.35)	0.45
Non-PCI related MI	5/915 (0.5%)	6/891 (0.7%)	0.13 (-0.70 to 0.96)	0.81 (0.25 to 2.66)	0.73
Coronary Revascularization	6/915 (0.7%)	8/891 (0.9%)	0.24 (-0.68 to 1.16)	0.73 (0.25 to 2.11)	0.57
Urgent/Target Vessel	2/915 (0.2%)	4/891 (0.4%)	0.23 (-0.41 to 0.87)	0.49 (0.09 to 2.67)	0.41
Stroke	3/915 (0.3%)	4/891 (0.4%)	0.12 (-0.56 to 0.81)	0.73 (0.16 to 3.27)	0.68
Stent Thrombosis	3/915 (0.3%)	5/891 (0.6%)	0.23 (-0.49 to 0.96)	0.59 (0.14 to 2.46)	0.47
Clinical Outcomes at 7 days or hospital discharge					
Bleeding[a]	4/915 (0.4%)	6/891 (0.7%)	0.24 (-0.56 to 1.03)	0.79 (0.37 to 1.69)[a]	0.54
Rhabdomyolysis[a]	0	0	-	-	-

Abbreviatons: CI denotes confidence interval.
Data presented as No. /total No. (%)
[a]Effect estimates are risk ratios instead of hazard ratios.
[b]Positive values favors Atorvastatin