



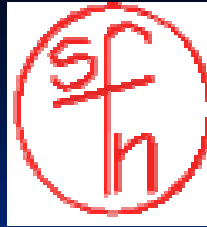
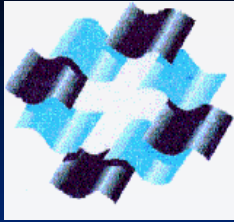
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The Pulse  of Cardiology

Dr. Germano Di Sciascio

ARMYDA-ACS: Atorvastatin Pretreatment Improves Outcome in Patients With Acute Coronary Syndromes Undergoing Percutaneous Coronary Intervention





ARMYDA-ACS (Atorvastatin for Reduction of MYocardial Damage during Angioplasty- Acute Coronary Syndromes) trial

Multicenter, randomized, double blind, prospective study evaluating effects on outcome of atorvastatin pre-treatment in patients with Acute Coronary Syndromes undergoing early PCI

***Chairman of the Study:* Germano Di Sciascio**

***Principal Investigators:* Giuseppe Patti, Vincenzo Pasceri, Rino Sardella, Giuseppe Colonna**

***Investigators:* Antonio Montinaro, Marco Miglionico, Luigi Fischetti, Andrea D'Ambrosio, Annunziata Nusca, Giordano Dicuonzo, Bibi NGuyen, Laura Gatto, Fabio Mangiacapra**

Randomized Trial of Atorvastatin for Reduction of Myocardial Damage During Coronary Intervention

Results From the ARMYDA (Atorvastatin for Reduction of MYocardial Damage during Angioplasty) Study

Vincenzo Pasceri, MD, PhD; Giuseppe Patti, MD; Annunziata Nusca, MD; Christian Pristipino, MD; Giuseppe Richichi, MD; Germano Di Sciascio, MD; on behalf of the ARMYDA Investigators

Background—Small myocardial infarctions after percutaneous coronary intervention have been associated with higher risk of cardiac events during follow-up. Observational studies have suggested that statins may lower the risk of procedural myocardial injury. The aim of our study was to confirm this hypothesis in a randomized study.

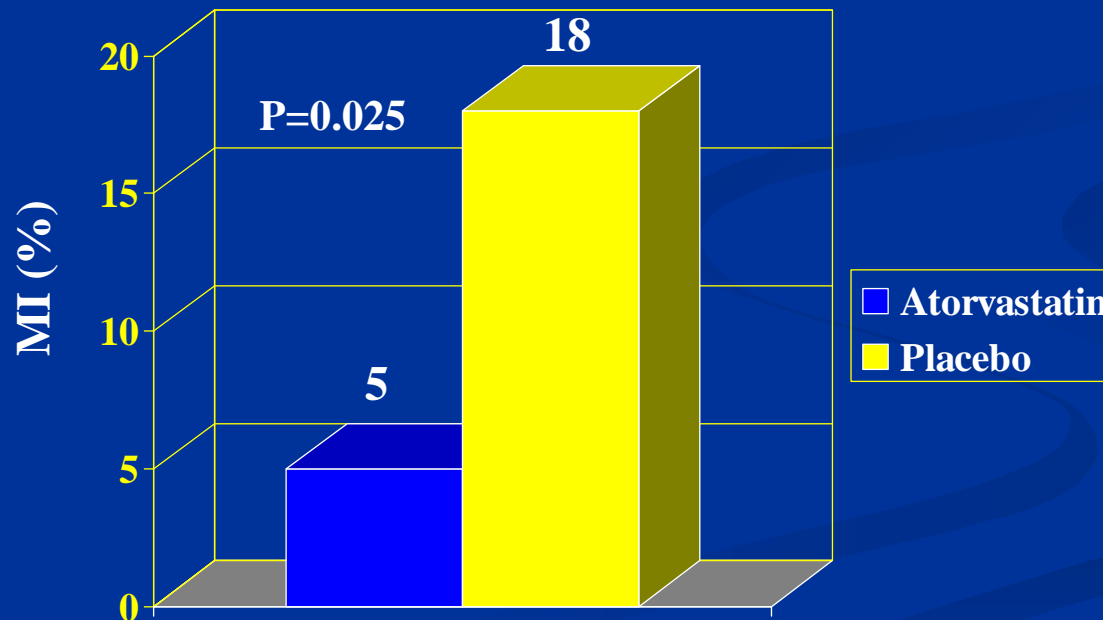
Methods and Results—One hundred fifty-three patients with chronic stable angina without previous statin treatment were enrolled in the study. Patients scheduled for elective coronary intervention were randomized to atorvastatin (40 mg/d, n=76) or placebo (n=77) 7 days before the procedure. Creatine kinase-MB, troponin I, and myoglobin levels were measured at baseline and at 8 and 24 hours after the procedure. Detection of markers of myocardial injury above the upper normal limit was significantly lower in the statin group versus the placebo group: 12% versus 35% for creatine kinase-MB ($P=0.001$), 20% versus 48% for troponin I ($P=0.0004$), and 22% versus 51% for myoglobin ($P=0.0005$). Myocardial infarction by creatine kinase-MB determination was detected after coronary intervention in 5% of patients in the statin group and in 18% of those in the placebo group ($P=0.025$). Postprocedural peak levels of creatine kinase-MB (2.9 ± 3 versus 7.5 ± 18 ng/mL, $P=0.007$), troponin I (0.09 ± 0.2 versus 0.47 ± 1.3 ng/mL, $P=0.0008$), and myoglobin (58 ± 36 versus 81 ± 49 ng/mL, $P=0.0002$) were also significantly lower in the statin than in the placebo group.

Conclusions—Pretreatment with atorvastatin 40 mg/d for 7 days significantly reduces procedural myocardial injury in elective coronary intervention. These results may influence practice patterns with regard to adjuvant pharmacological therapy before percutaneous revascularization. (*Circulation*. 2004;110:674-678.)

BACKGROUND

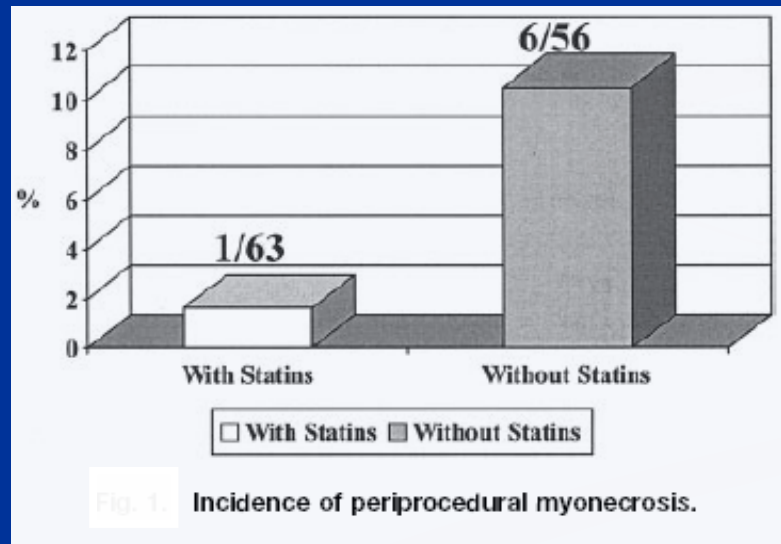
❖ The original ARMYDA trial demonstrated that 7-day pretreatment with atorvastatin (40 mg/day) confers 81% risk reduction of peri-procedural MI in patients with Stable Angina undergoing elective PCI

Primary end point: Incidence of MI



BACKGROUND

- ❖ Efficacy of statin pretreatment in patients with ACS undergoing early PCI has not characterized
- ❖ An observational study on 119 pts has suggested that patients with ACS who were already receiving statins at the time of intervention have a lower incidence of peri-procedural myonecrosis; however, patients were treated with different types of statins, variable doses and unknown duration of previous treatment, and those findings have not been validated in a randomized trial.



ARMYDA-ACS trial

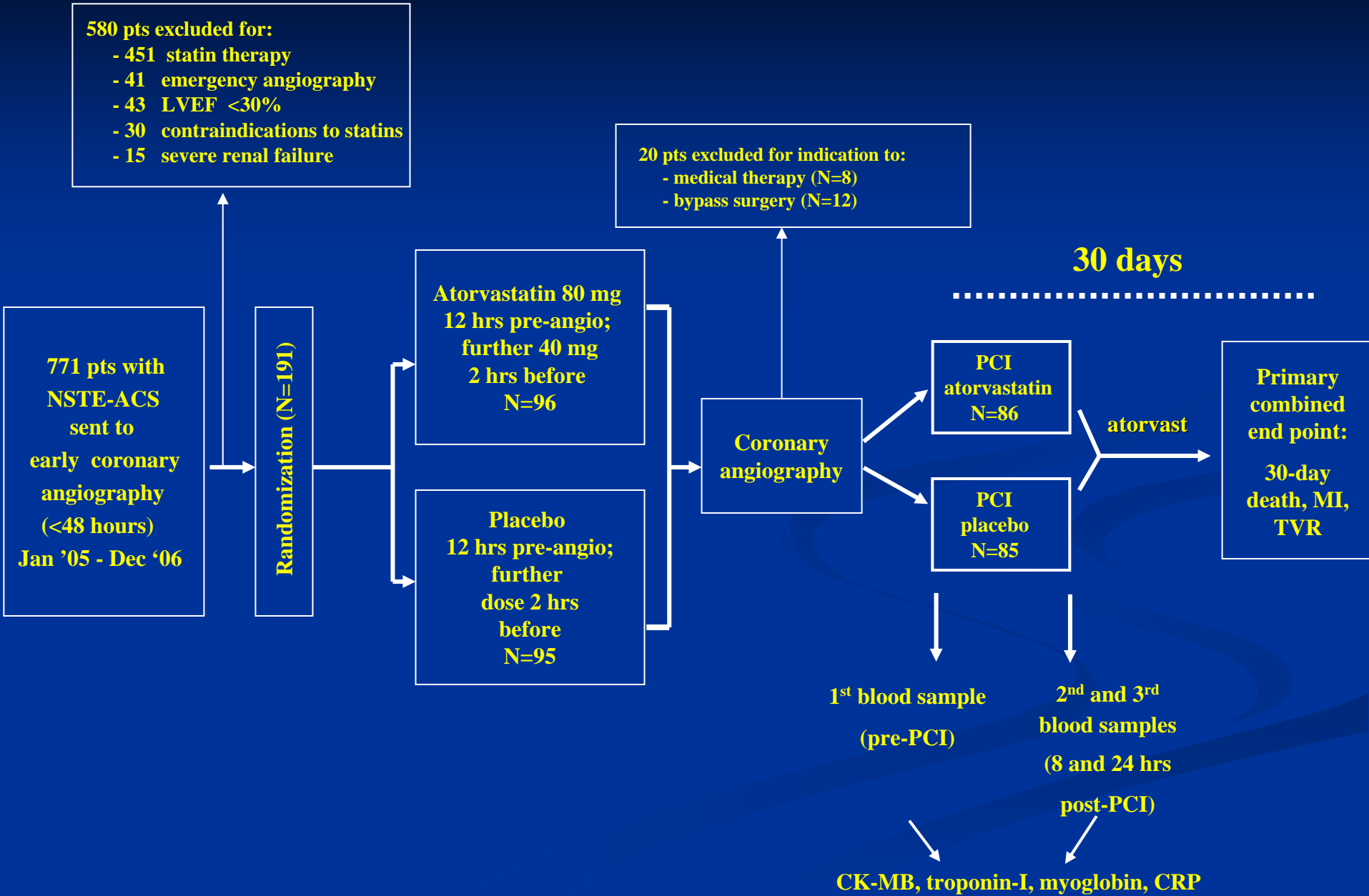
Inclusion criteria:

- ✓ NSTEMI-ACS undergoing early angiography (<48 hrs)

Exclusion criteria:

- ✓ STEMI
- ✓ ACS with high risk features warranting emergency angiography
- ✓ Previous or current statin therapy
- ✓ LVEF <30%
- ✓ Contraindications to statins (liver or muscle disease)
- ✓ Severe renal failure (creatinine >3 mg/dl)

ARMYDA-ACS trial: Study design



ARMYDA-ACS trial: Study end points

Primary end point:

Incidence of major adverse cardiac events (MACE: death, MI, TVR) from the procedure up to 30 days

MI definition:

- If normal baseline levels of CK-MB: post-procedural increase of CK-MB >2 times above UNL, according to the consensus statement of the Joint ESC/ACC Committee for the Redefinition of Myocardial Infarction for clinical trials on coronary intervention.
- If elevated baseline levels of CK-MB: subsequent rise of >2 times in CK-MB from baseline value

Secondary end points:

- ✓ Any post-procedural increase of markers of myocardial injury above UNL (CK-MB, troponin-I, myoglobin)
- ✓ Post-PCI variations from baseline of CRP levels in the 2 arms

ARMYDA-ACS: Main Clinical Features in the Atorvastatin and Placebo Groups

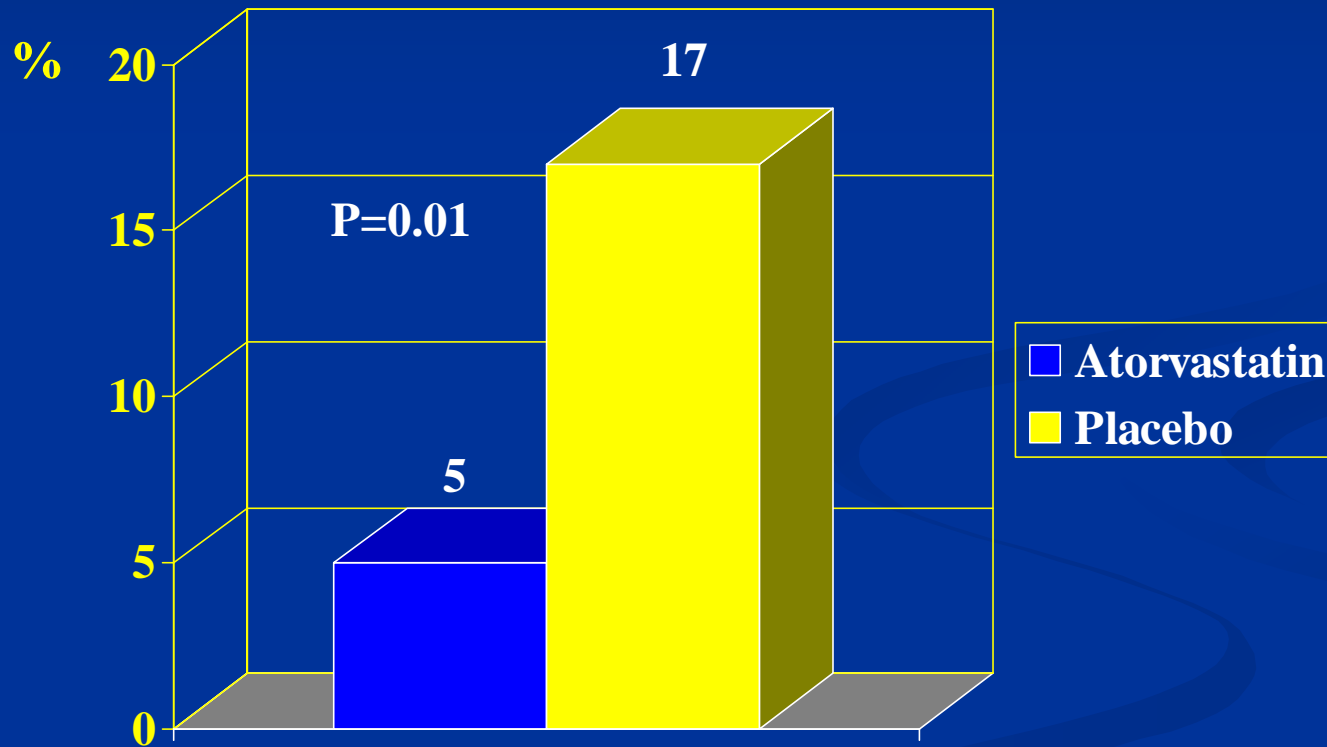
Variable	Atorvastatin (n=86)	Placebo (n = 85)	p
Male sex	68 (79)	67 (79)	0.88
<u>Age (years)</u>	<u>64±11</u>	<u>67±10</u>	<u>0.06</u>
<u>Diabetes mellitus</u>	<u>25 (29)</u>	<u>28 (33)</u>	<u>0.70</u>
Systemic hypertension	63 (73)	63 (74)	0.96
Hypercholesterolemia	27 (31)	28 (33)	0.96
<u>Chronic Renal Failure</u>	<u>12 (14)</u>	<u>13 (15)</u>	<u>0.81</u>
Current smokers	27 (31)	18 (21)	0.18
Previous coronary intervention	9 (10)	9 (11)	0.82
Previous by-pass surgery	2 (2)	3 (4)	0.99
Left ventricular ejection fraction (%)	55±7	54±8	0.38
Multivessel coronary artery disease	29 (34)	39 (46)	0.14
<u>CLINICAL PATTERN</u>			
NSTEMI	34 (40)	27 (32)	0.37
<u>Mean time to angiography (hrs)</u>	<u>23±12</u>	<u>22±10</u>	<u>0.56</u>
<u>PHARMACOLOGICAL Rx:</u>			
Aspirin	86 (100)	85 (100)	1
<u>Clopidogrel - 600 mg load</u>	<u>86 (100)</u>	<u>85 (100)</u>	<u>1</u>
Beta-Blockers	26 (30)	23 (27)	0.77
Ace-Inhibitors	67 (78)	65 (76)	0.97
<u>IIb/IIIa Inhibitors</u>	<u>23 (27)</u>	<u>18 (21)</u>	<u>0.50</u>

ARMYDA-ACS: Procedural Features in the Atorvastatin and Placebo Groups

Variable	Atorvastatina (N=86)	Placebo (N=85)	P
Vessel treated:			
Left main	-	1 (1)	0.97
Left anterior descending	51 (50)	54 (59)	0.94
Left circumflex	31 (30)	28 (25)	0.56
Right coronary artery	20 (19)	26 (24)	0.56
Saphenous vein graft	1 (1)	1 (1)	0.51
<u>Lesion type B2/C</u>	<u>73 (85)</u>	<u>71 (84)</u>	<u>0.97</u>
<u>Multivessel intervention</u>	<u>17 (20)</u>	<u>25 (29)</u>	<u>0.20</u>
Type of intervention:			
Balloon only	1 (1)	1 (1)	0.48
Stent	85 (99)	84 (99)	0.48
Bifurcations with kissing balloon	8 (9)	8 (9)	0.81
No.of stents per patient	1.4±0.6	1.5±0.9	0.40
Stent diameter (mm)	3.1±0.4	3.1±0.3	0.90
Total stent length (mm)	16.7±5.7	16.9±5.5	0.82
<u>Use of DES</u>	<u>55 (64)</u>	<u>47 (55)</u>	<u>0.32</u>
Direct stenting	41 (48)	36 (42)	0.59
No. of pre-dilatation	2.1±1.4	2.2±1.7	0.68
Stent-deployment pressure (atm)	11.2±4.1	11.6±2.7	0.44
Duration of stent deployment (sec)	16±7	16±5	1

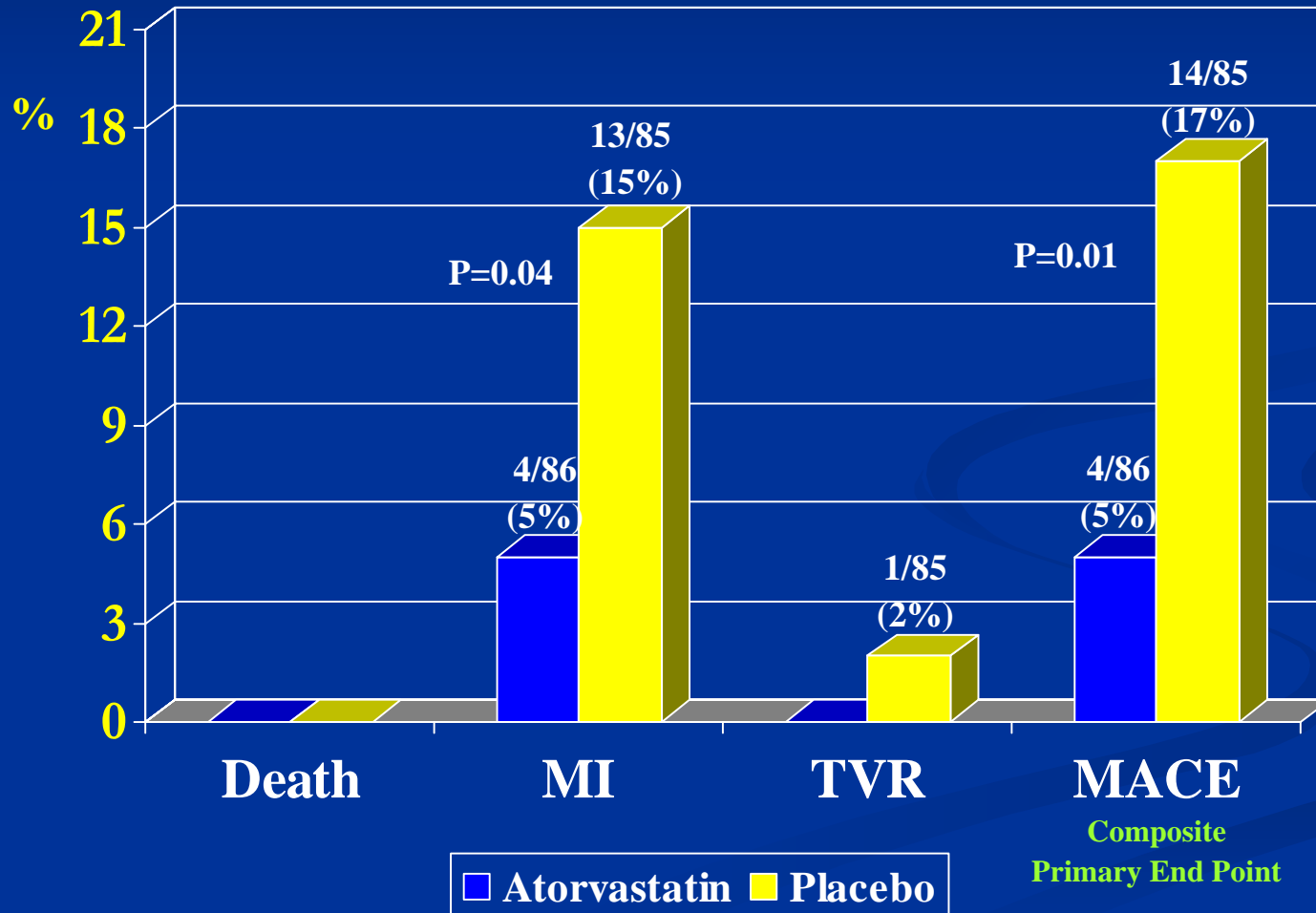
ARMYDA-ACS trial

Composite primary end-point (30-day death, MI, TVR)



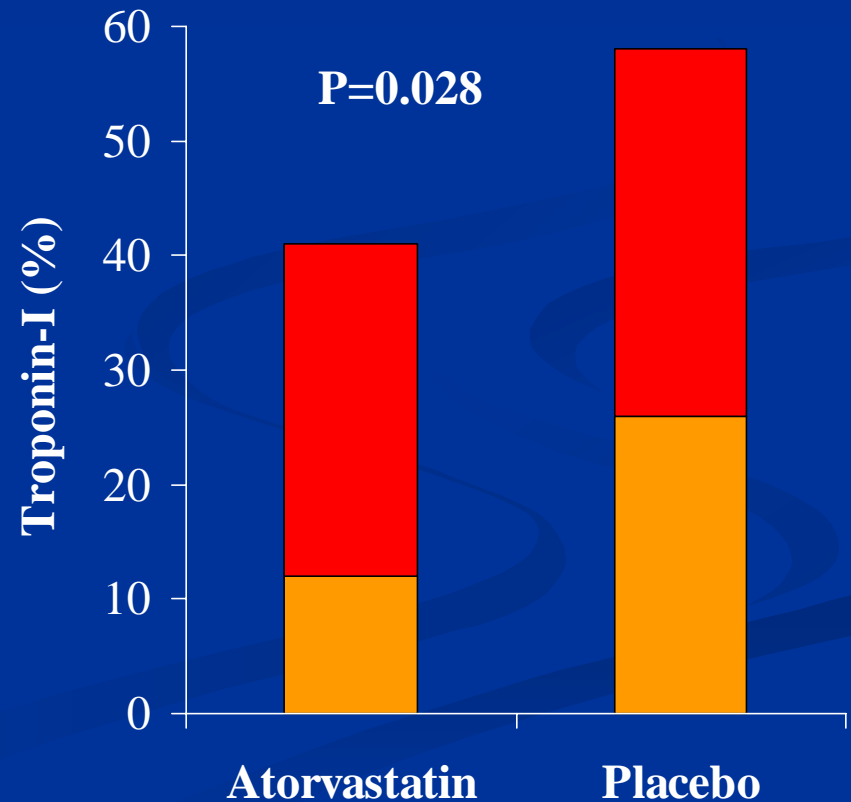
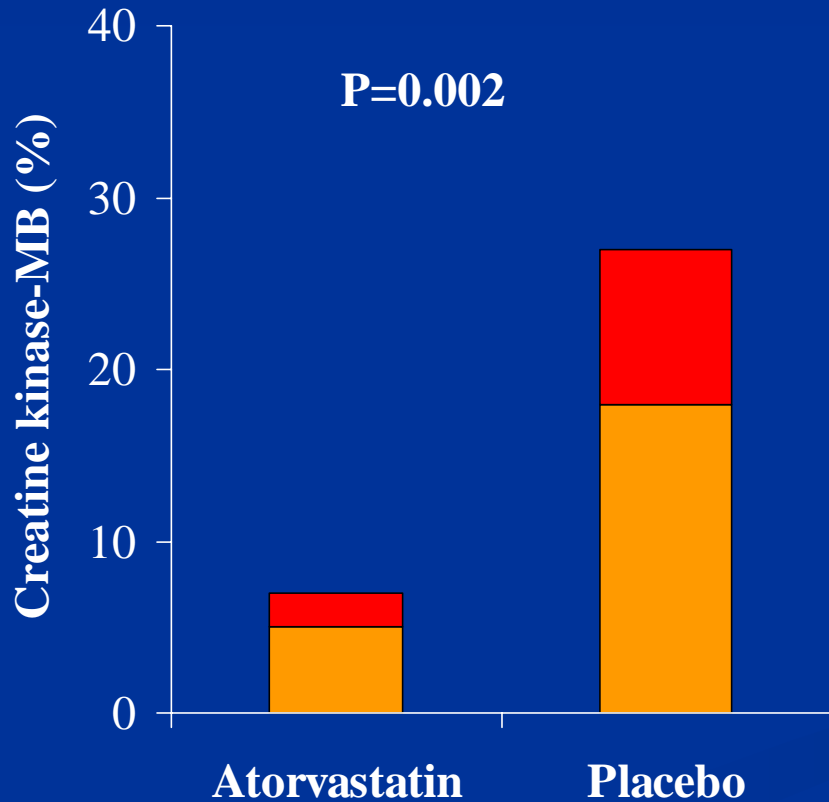
ARMYDA-ACS

Individual and Combined Outcome Measures of the Primary End Point at 30 days



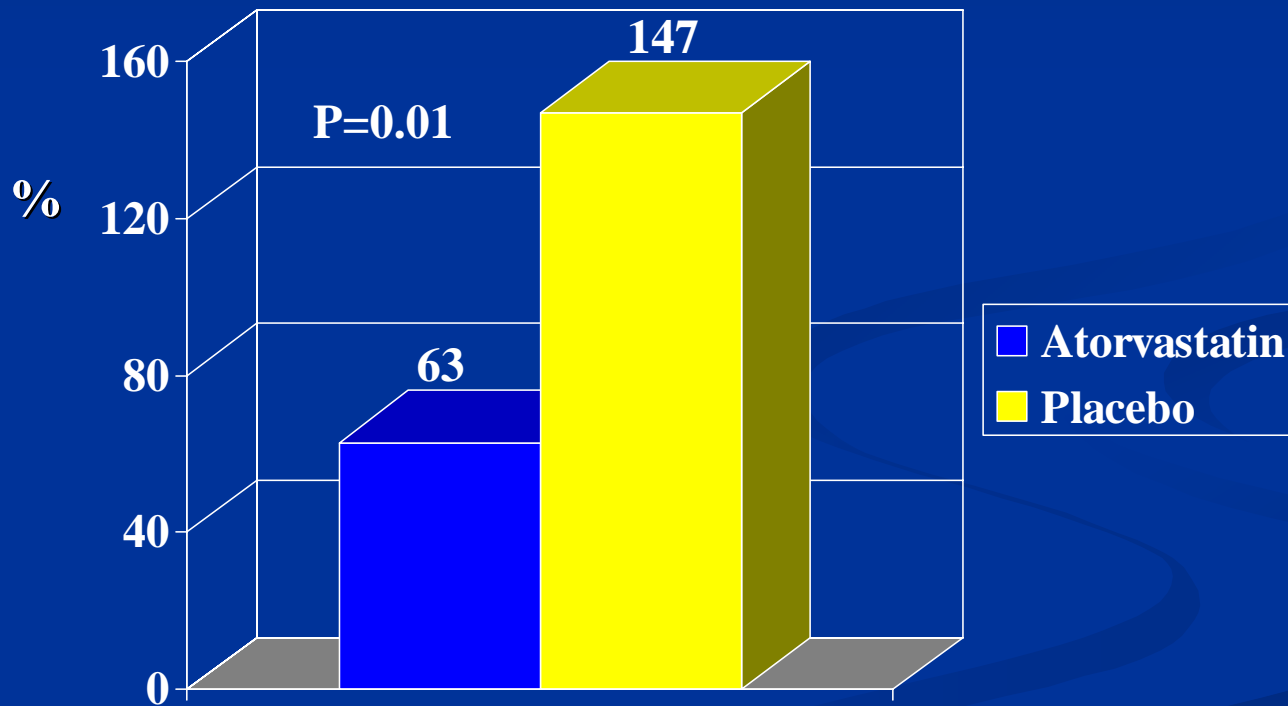
ARMYDA-ACS: Secondary end point Cardiac markers elevations

1-3 times >3 times

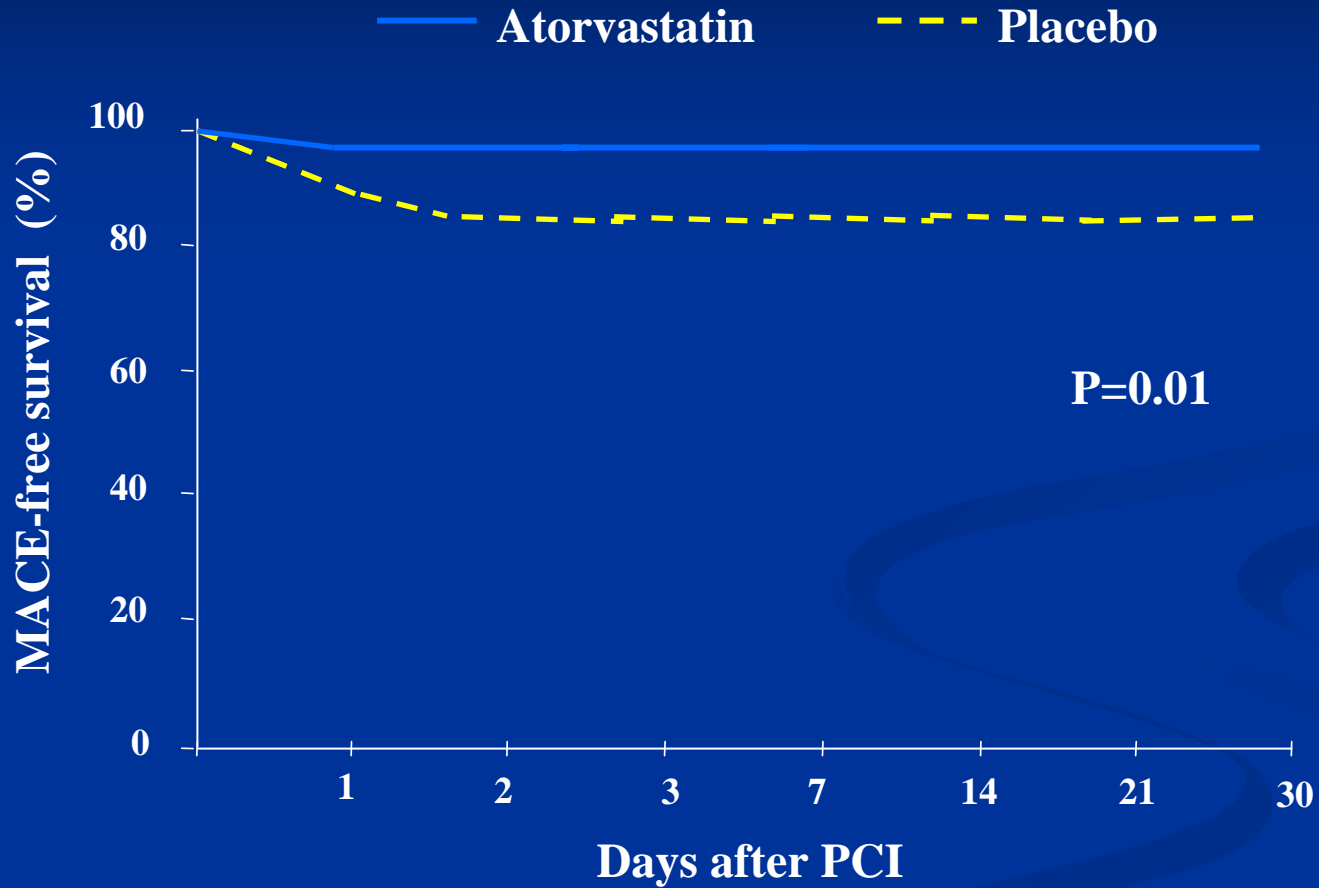


ARMYDA-ACS: Secondary end point

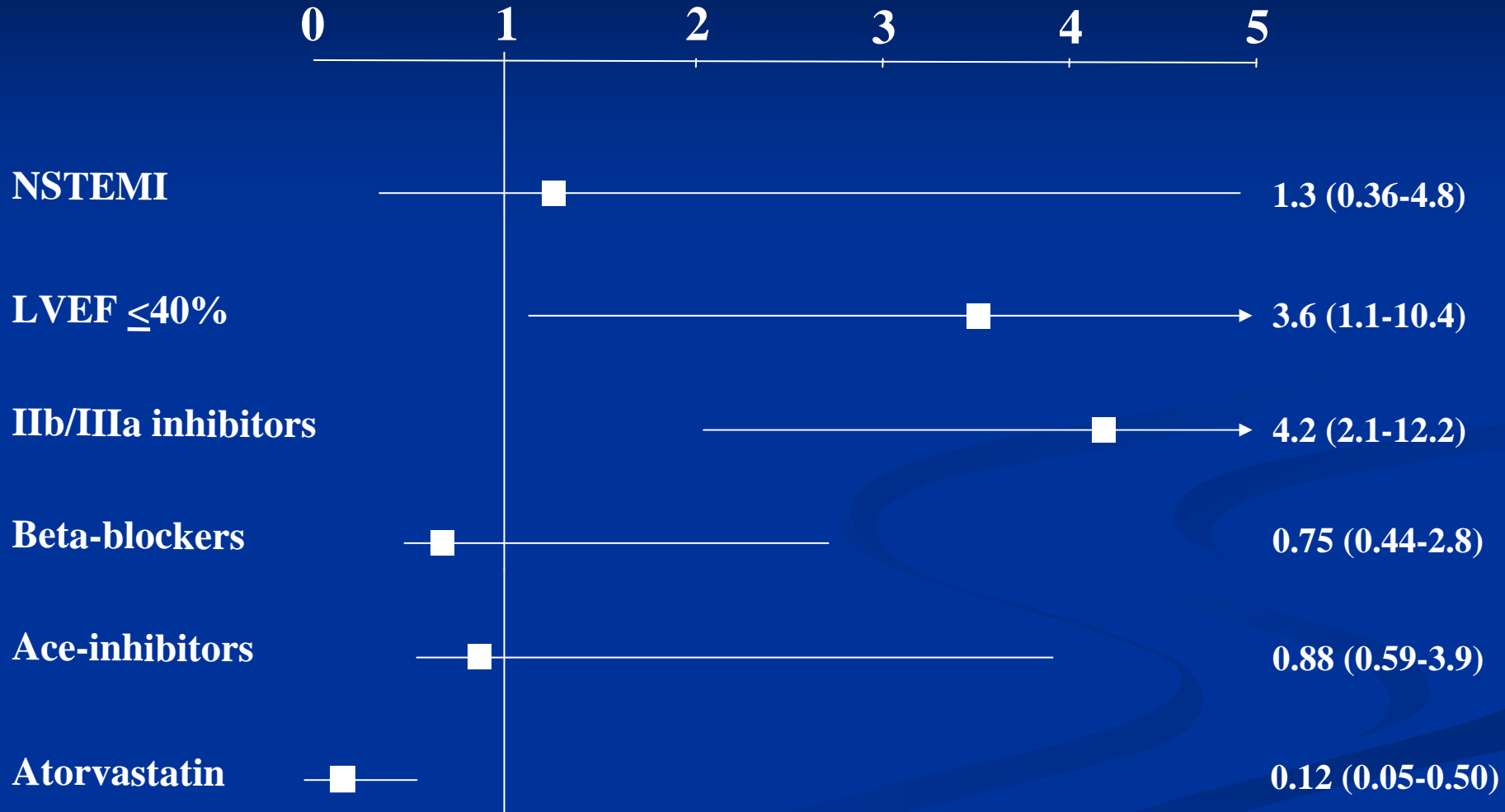
Post-PCI percent increase of CRP levels from baseline



ARMYDA-ACS: Actuarial Survival curves



ARMYDA-ACS: Odds Ratio for 30-day MACE



ARMYDA-ACS: CONCLUSIONS

- ❖ The ARMYDA-ACS trial indicates that even a short-term atorvastatin pretreatment prior to PCI may improve outcome in patients with Unstable Angina and NSTEMI.
- ❖ This benefit is mostly driven by a reduction of peri-procedural MI (70% risk reduction)
- ❖ Lipid-independent pleiotropic actions of atorvastatin may explain such effect
- ❖ These findings may support the indication of “upstream” administration of high dose statins in patients with Acute Coronary Syndromes treated with early invasive strategy

Final results of the ARMYDA-ACS (Atorvastatin for Reduction of MYocardial Damage during Angioplasty-Acute Coronary Syndromes) trial

