

La facilitazione alla PCI con statine

Bertinoro, 16 aprile 2010



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The background of the slide is a dark teal color with a faint, light teal ECG (heart rate) line running diagonally across it. The text is centered in a bright yellow-green color.

**Are statins beneficial in
patients undergoing PCI?**

CLINICAL STUDIES

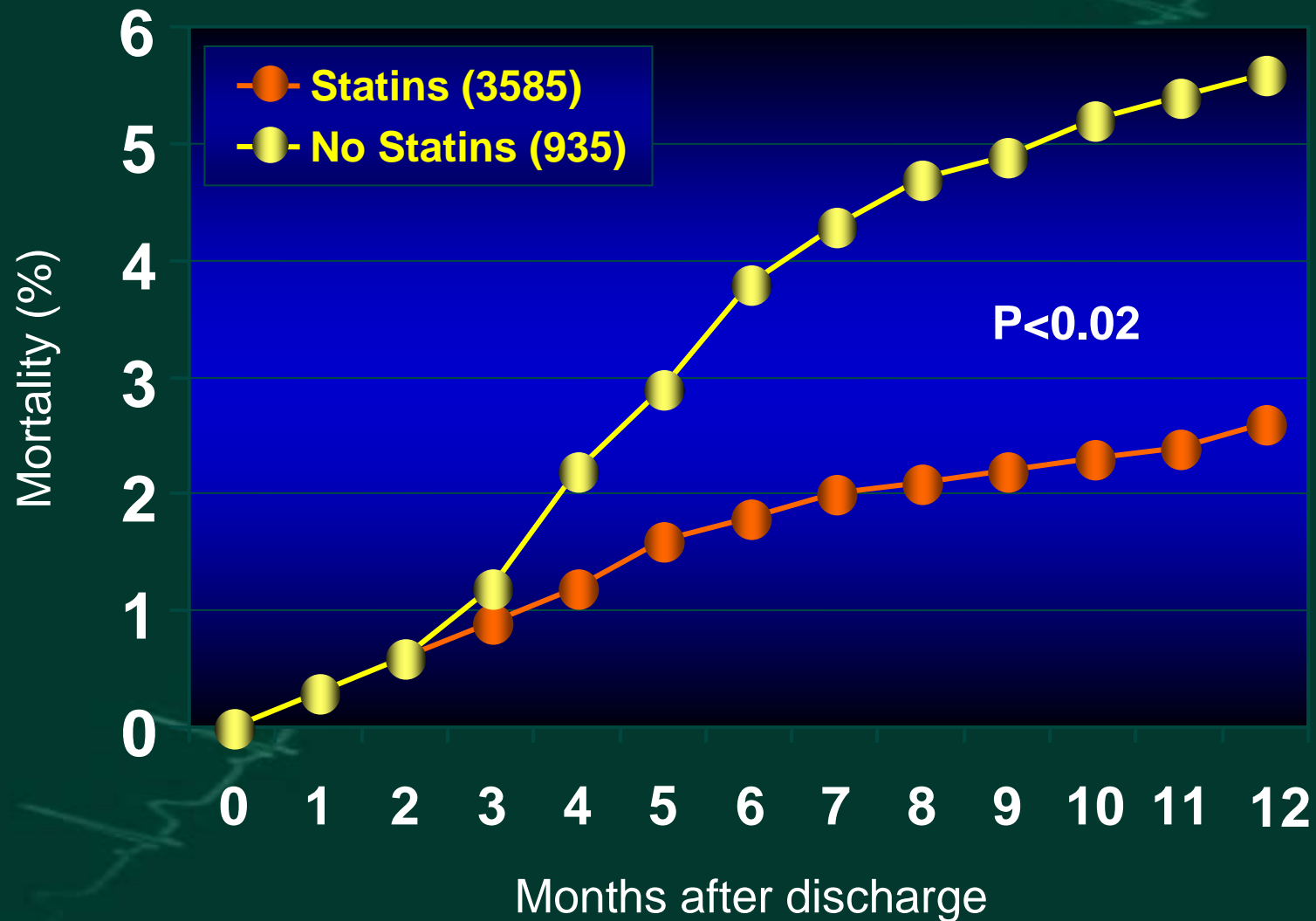
Percutaneous Coronary Intervention

Statin Treatment Following Coronary Artery Stenting and One-Year Survival

Albert Schömig, MD,*† Julinda Mehilli, MD,* Heidrun Holle, RN,* Karin Hösl, RN,* Dorejd Kastrati,*
Jürgen Pache, MD,† Melchior Seyfarth, MD,† Franz-Josef Neumann, MD,† Josef Dirschinger, MD,†
Adnan Kastrati, MD*

Munich, Germany

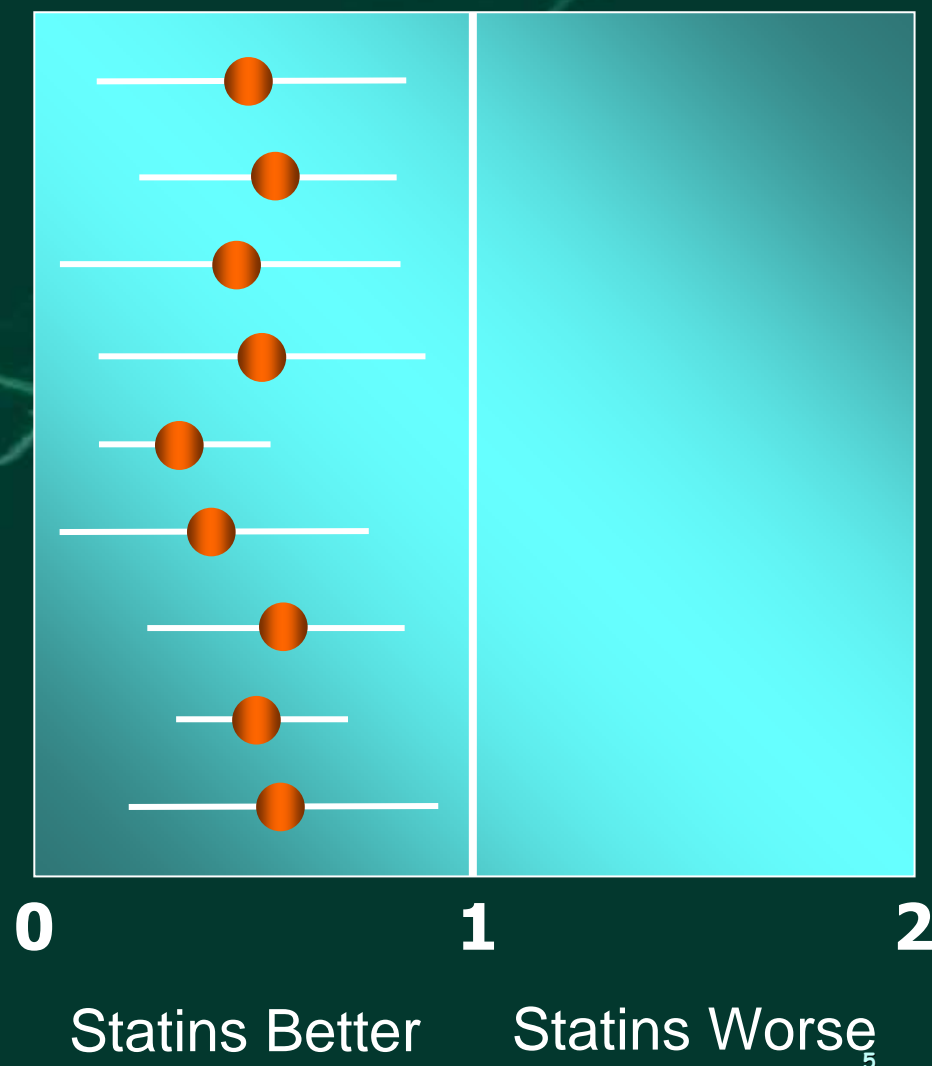
Statin therapy after coronary artery stent implantation



(Schomig et al., JACC 2002)

Risk ratios for various variables comparing statins vs no statins therapy after coronary artery stenting

- Cholesterol > 200 mg%
- Cholesterol < 200 mg%
- Acute Myocardial Infarction
- Unstable Angina
- Stable Angina
- Diabetes
- No Diabetes
- Men
- Women

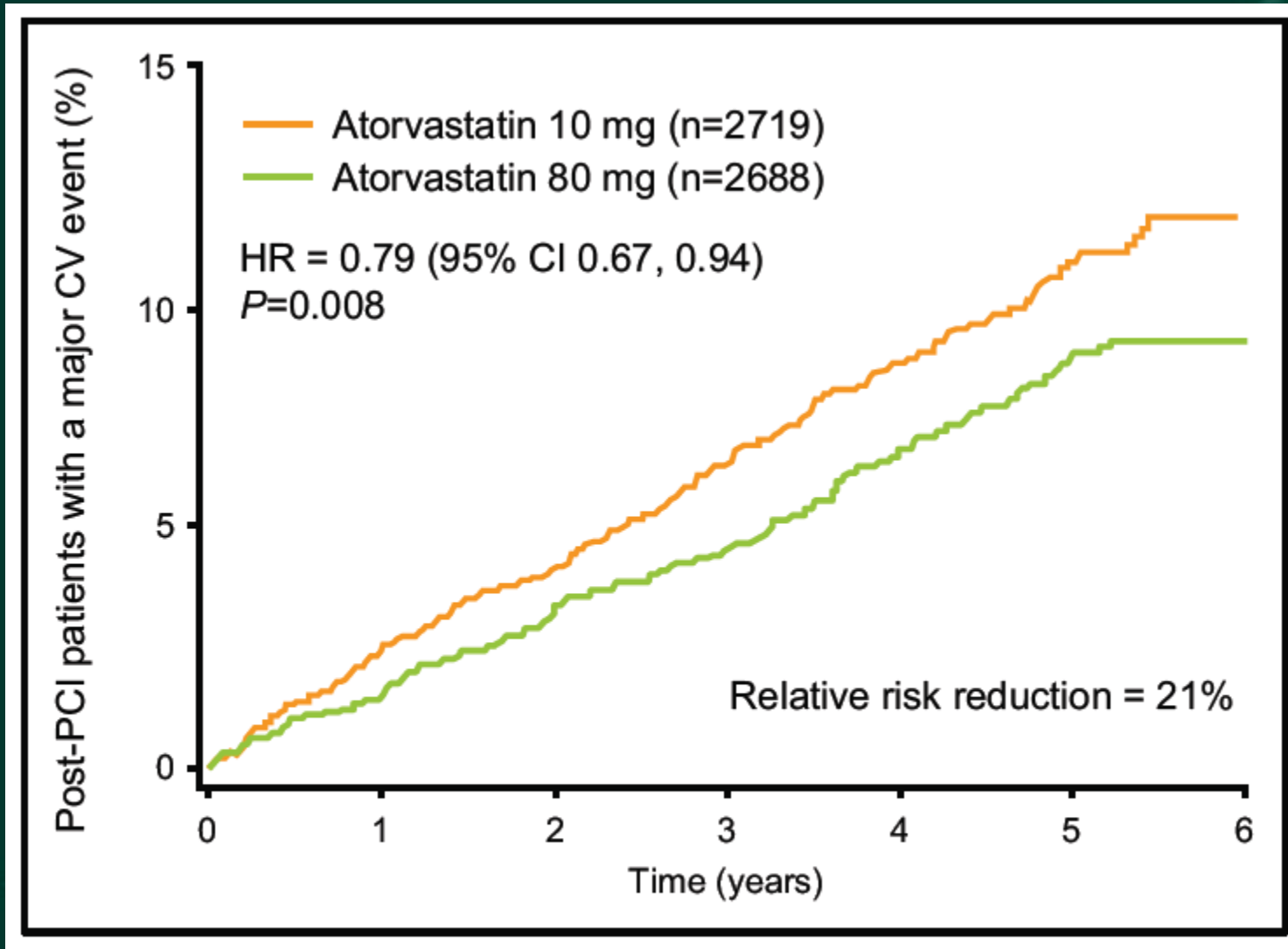


Comparison of Effectiveness of *Atorvastatin* 10 mg Versus 80 mg in Reducing Major Cardiovascular Events and Repeat Revascularization in Patients With Previous Percutaneous Coronary Intervention (Post Hoc Analysis of the Treating to New Targets [TNT] Study)

Colleen Johnson, MD^a, David D. Waters, MD^{a,*}, David A. DeMicco, PharmD^b, Andrei Breazna, PhD^b, Vera Bittner, MD^d, Heiner Greten, MD^e, Scott M. Grundy, MD, PhD^f, and John C. LaRosa, MD^c, for the Treating to New Targets Steering Committee and Investigators

The Treating to New Targets (TNT) study demonstrated that intensive atorvastatin therapy to achieve low-density lipoprotein cholesterol concentrations well below recommended target levels provides an incremental clinical benefit in patients with stable coronary artery disease. This post hoc analysis of the TNT study was conducted to investigate whether this benefit extends to patients with previous percutaneous coronary intervention (PCI). A total of 10,001 patients with clinically evident coronary artery disease, including 5,407 patients with previous PCI, were randomized to atorvastatin 10 or 80 mg/day and followed for a median of 4.9 years. The primary end point was the occurrence of a first major cardiovascular event. Revascularization, a component of a secondary end point, was also examined. In patients with previous PCI, mean low-density lipoprotein cholesterol levels at study end were 79.5 mg/dl in the 80-mg arm and 100.8 mg/dl in the 10-mg arm. First major cardiovascular events occurred in 230 patients (8.6%) receiving high-dose atorvastatin and 289 patients (10.6%) receiving low-dose atorvastatin (hazard ratio 0.79, 95% confidence interval 0.67 to 0.94, $p = 0.008$). Repeat revascularization during follow-up (PCI or coronary artery bypass grafting) was performed in 466 patients (17.3%) in the 80-mg arm and 624 patients (22.9%) in the 10-mg arm (hazard ratio 0.73, 95% confidence interval 0.65 to 0.82, $p < 0.0001$). In conclusion, intensive lipid lowering to a mean low-density lipoprotein cholesterol level of 79.5 mg/dl (2.1 mmol/L) with atorvastatin 80 mg/day in patients with previous PCI reduces major cardiovascular events by 21% and repeat revascularizations by 27% compared with a less intensive lipid-lowering regimen. © 2008 Elsevier Inc. All rights reserved. (Am J Cardiol 2008;102:1312–1317)

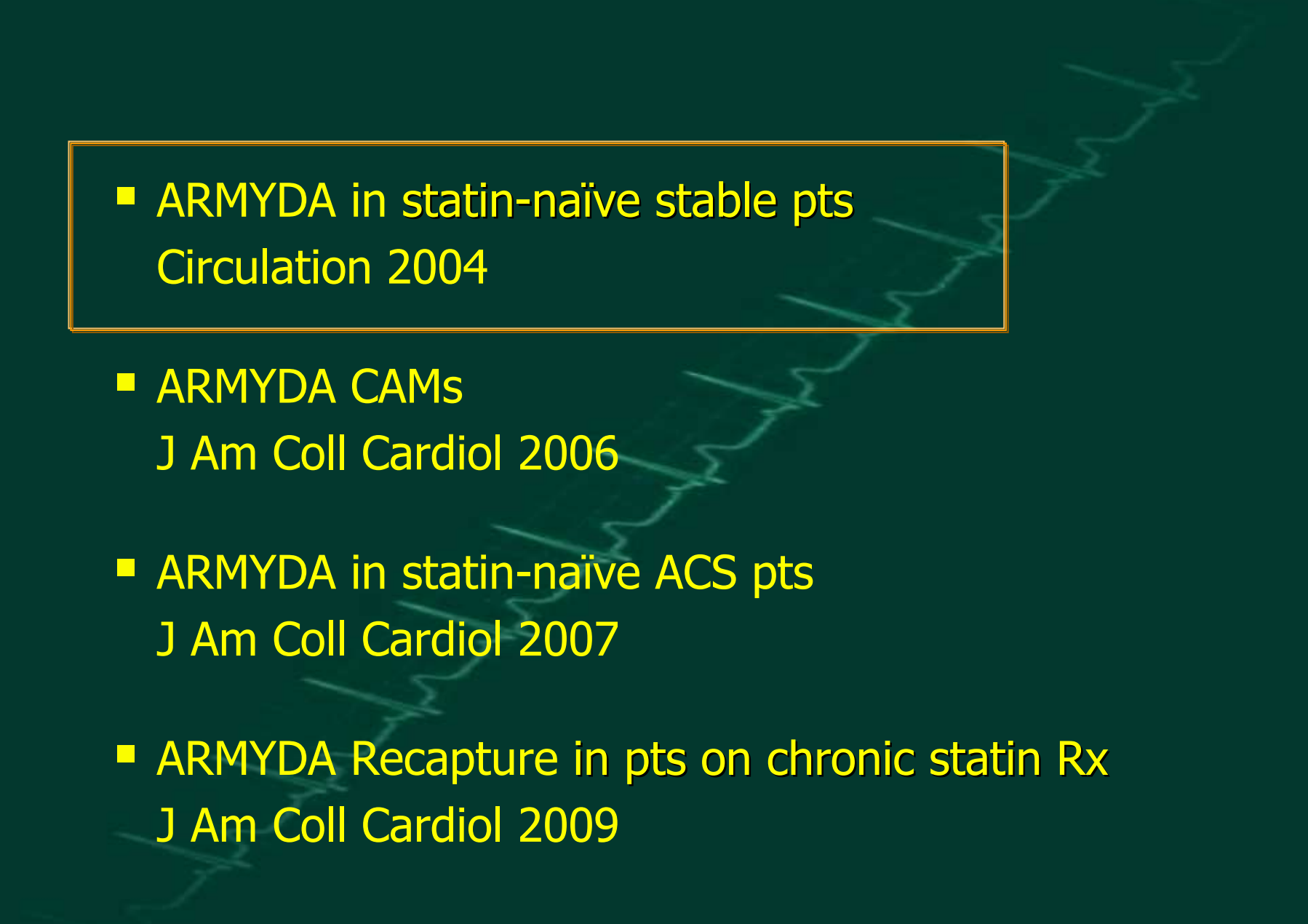
Cumulative incidence of Major Cardiovascular Events in patients with previous PCI



**Intensive statin therapy in patients
undergoing
Percutaneous Coronary Intervention and
Cardiac Surgery:**

Evidence from the ARMYDA Trials

**Atorvastatin for Reduction of
MYocardial Damage during Angioplasty**

- 
- ARMYDA in statin-naïve stable pts
Circulation 2004
 - ARMYDA CAMs
J Am Coll Cardiol 2006
 - ARMYDA in statin-naïve ACS pts
J Am Coll Cardiol 2007
 - ARMYDA Recapture in pts on chronic statin Rx
J Am Coll Cardiol 2009

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

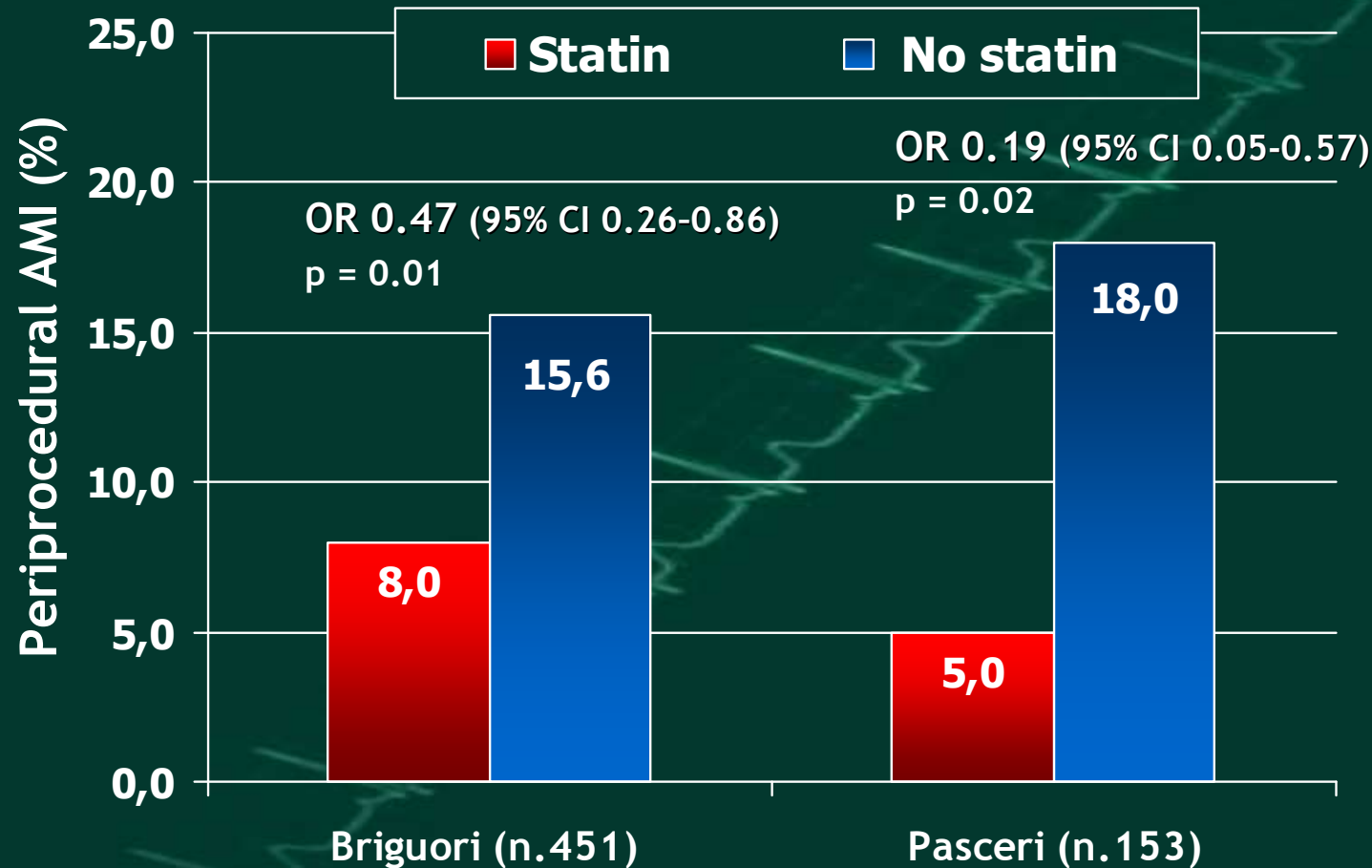
Vincenzo Pasceri, MD, PhD; Giuseppe Patti, MD; Annunziata Nusca, MD; Christian Pristipino, MD; Giuseppe Richichi, MD; Germano Di Sciascio, MD; on behalf of the ARMYDA Investigators

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.)

Pre-PCI statin Rx reduces the incidence of large peri-procedural nonQ-AMI – *elective* PCI



Il pre-trattamento con atorvastatina andrebbe effettuato come terapia adiuvante prima di una PCI

Briguori et al, Eur Heart J 2004; 25: 1822-1828 - *statin administration 3 days before*
Pasceri et al, Circulation 2004;110:674 (ARMYDA) - *atorvastatin 40 mg 7 day before*

***Atorvastatin* given before PCI: ARMYDA trials findings**



- 40 mg 7-day Rx associated with **81%** risk reduction of cardiac events at 1 month in statin-naïve **stable** pts (ARMIDA)

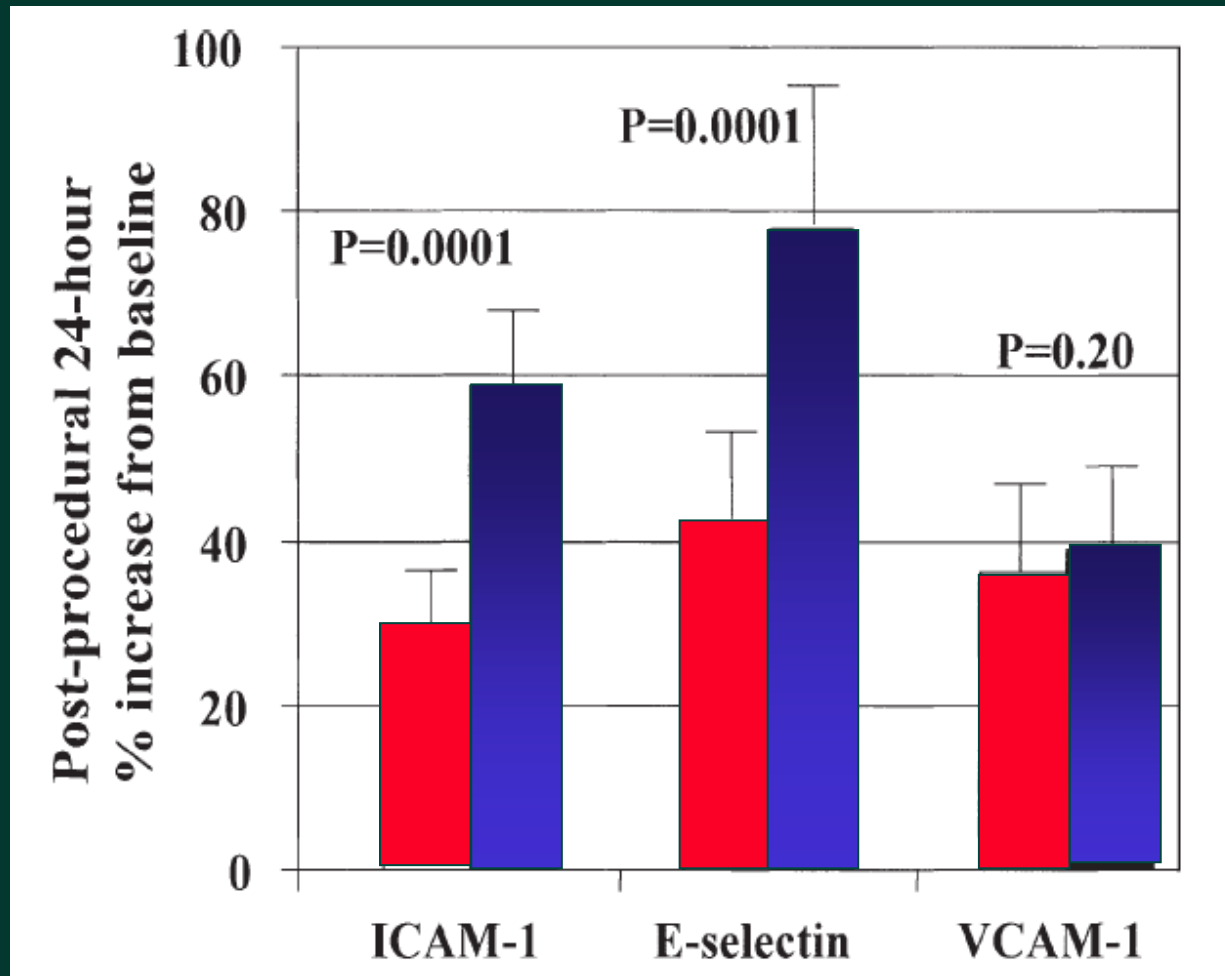
- ARMYDA in statin-naïve stable pts
Circulation 2004

- ARMYDA CAMs
J Am Coll Cardiol 2006

- ARMYDA in statin-naïve ACS pts
J Am Coll Cardiol 2007

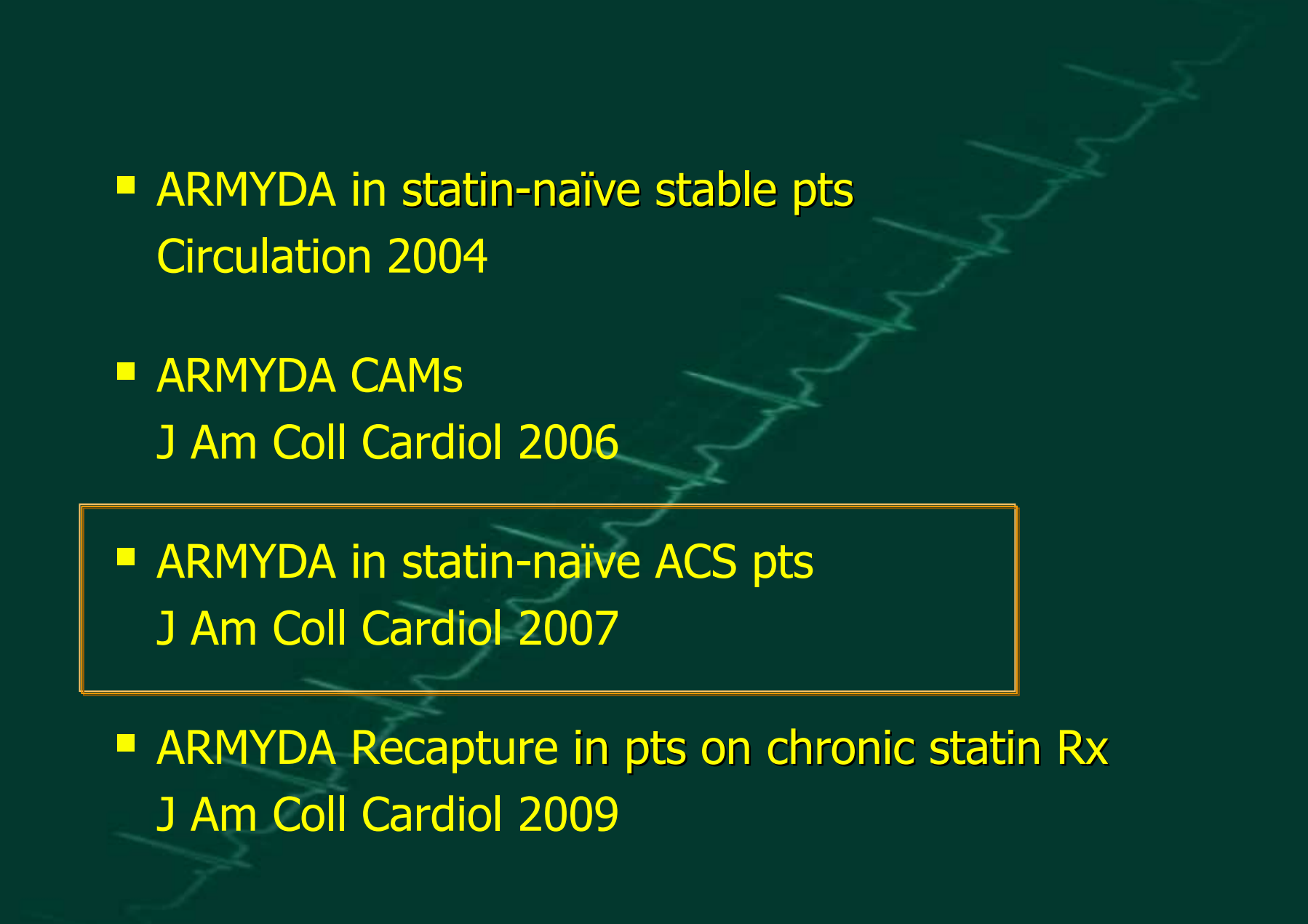
- ARMYDA Recapture in pts on chronic statin Rx
J Am Coll Cardiol 2009

7-day atorvastatin pretreatment decreases adhesion molecules after PCI



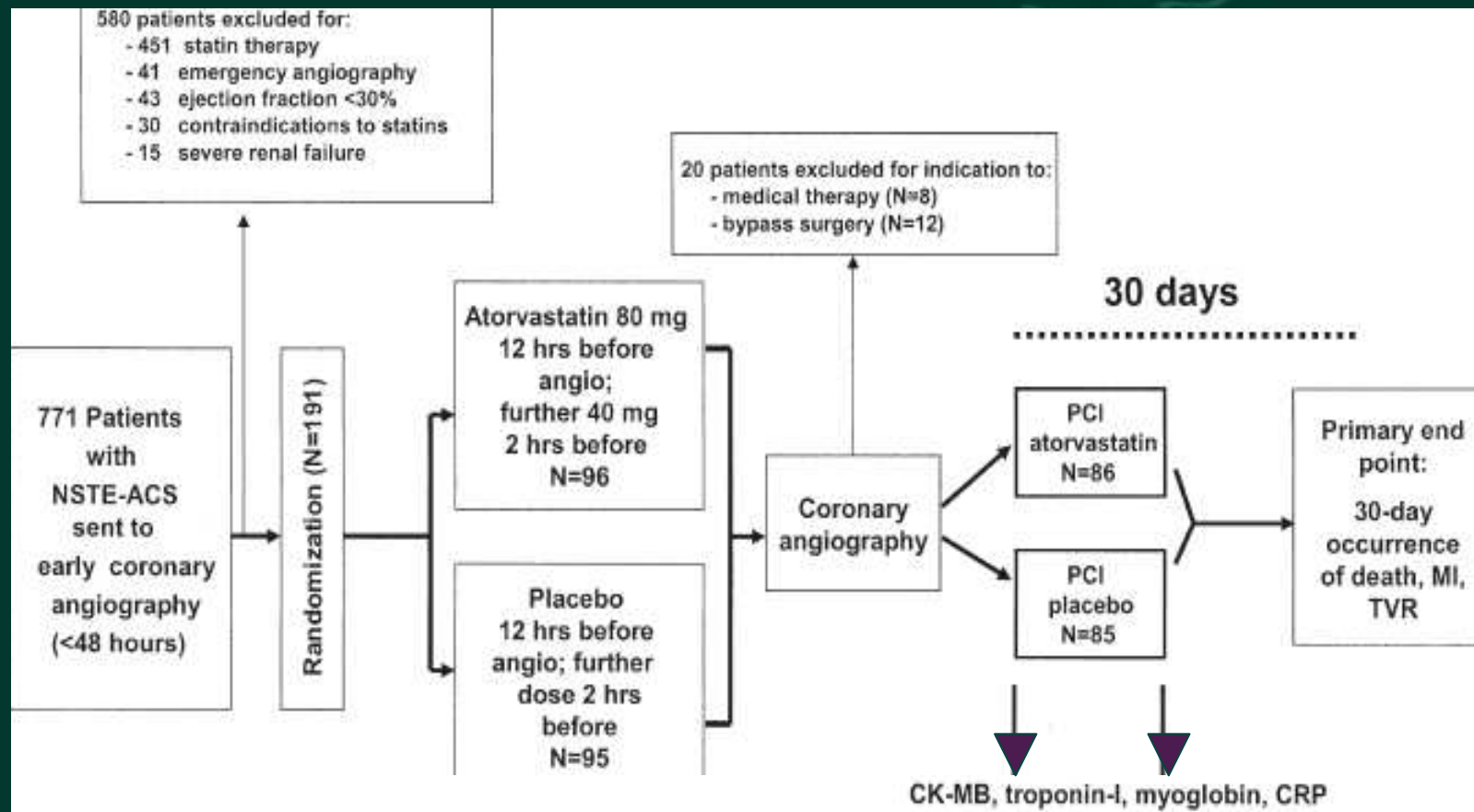
■ atorvastatin
■ placebo

Il pretrattamento per 7 giorni con atorvastatina 40 mg in pazienti con angina stabile sottoposti a PCI è associato sia a una riduzione del danno miocardico procedurale sia a una riduzione dell'aumento dei livelli di ICAM-1 ed E-selectina, molecole di adesione dei leucociti la cui riduzione dell'espressività, ha contribuito al raggiungimento dell'endpoint primario

- 
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Atorvastatin Pretreatment Improves Outcomes in Patients With Acute Coronary Syndromes Undergoing Early Percutaneous Coronary Intervention

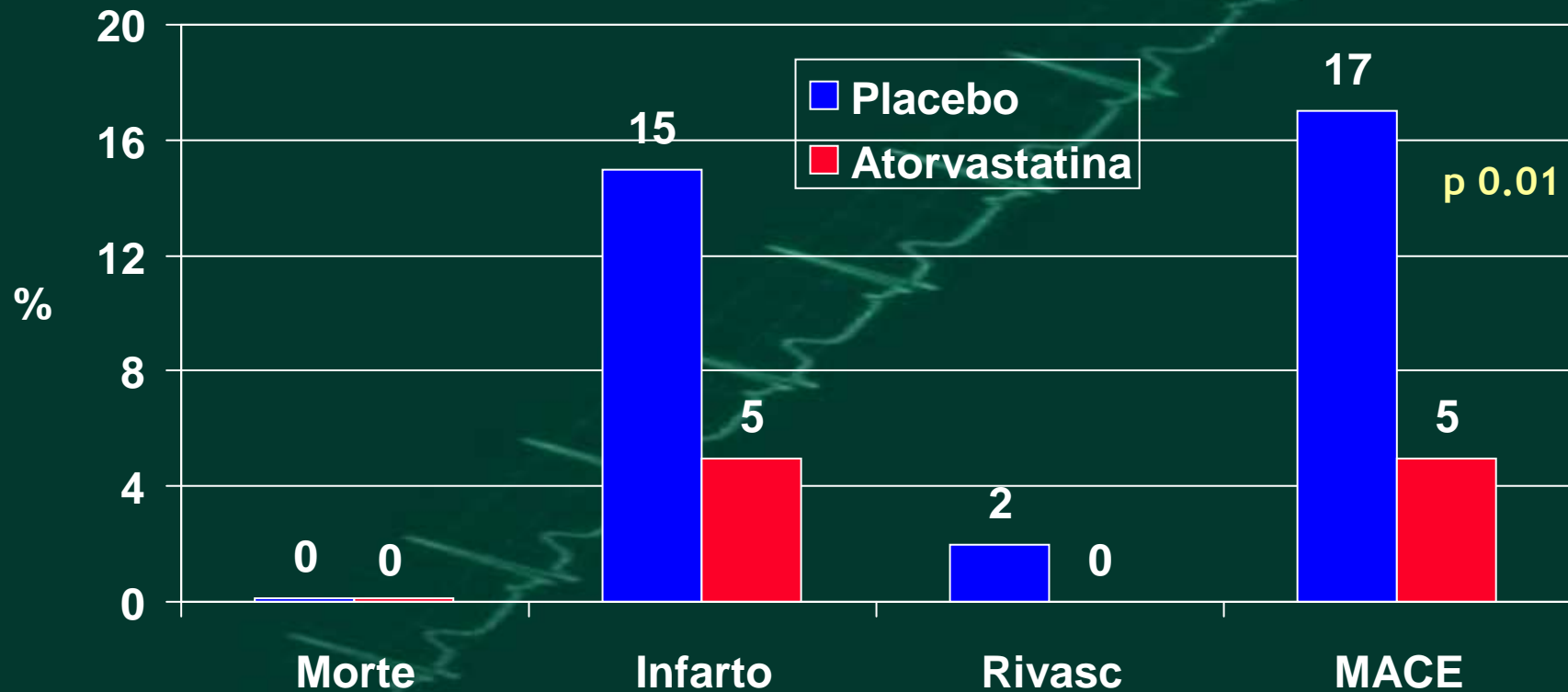
Results of the ARMYDA-ACS Randomized Trial



Patti et al, J Am Coll Cardiol 2007; 49:1272

Nel gruppo pretrattato con atorva riduzione degli indici di necrosi miocardica dal 17 al 5%, nelle prime 24 ore.

Studio ARMYDA-ACS: pretrattamento con atorvastatina ed eventi cardiaci post-procedurali



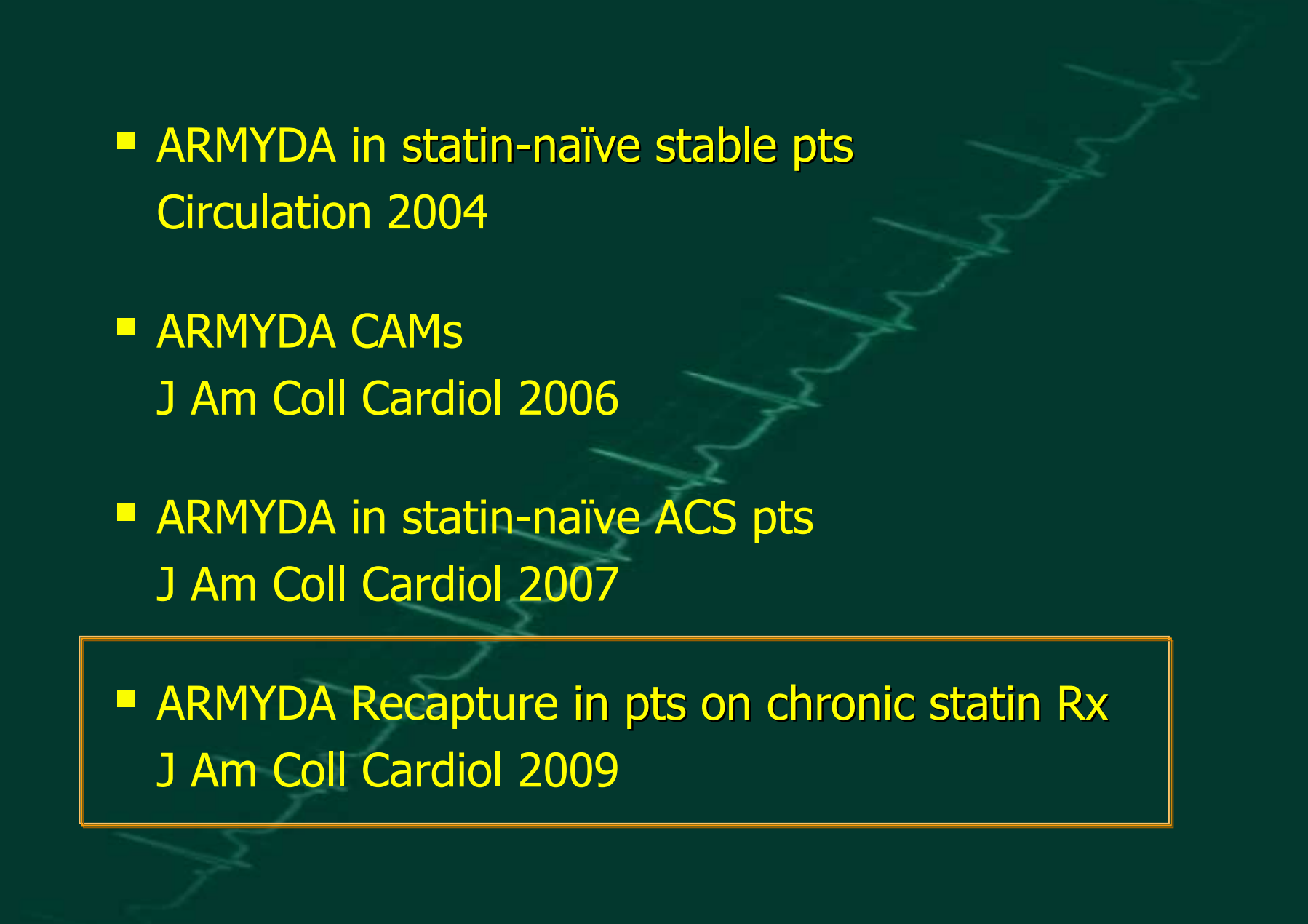
Significativa riduzione dell'end-point primario composto nel follow-up a 30 giorni post-PCI

Patti et al. J Am Coll Cardiol 2007; 49: 1272

***Atorvastatin* given before PCI: ARMYDA trials findings**



- 40 mg 7-day Rx associated with 81% risk reduction of cardiac events at 1 month in statin-naïve stable pts (ARMYDA)
- 80 mg load associated with **88%** risk reduction of cardiac events at 1 month in statin-naïve **ACS** pts (ARMYDA-ACS)



- ARMYDA in statin-naïve stable pts
Circulation 2004

- ARMYDA CAMs
J Am Coll Cardiol 2006

- ARMYDA in statin-naïve ACS pts
J Am Coll Cardiol 2007

- ARMYDA Recapture in pts on chronic statin Rx
J Am Coll Cardiol 2009

EXPEDITED PUBLICATIONS

Efficacy of Atorvastatin Reload in Patients on Chronic Statin Therapy Undergoing Percutaneous Coronary Intervention

Results of the ARMYDA-RECAPTURE (Atorvastatin for
Reduction of Myocardial Damage During Angioplasty) Randomized Trial

Germano Di Sciascio, MD,* Giuseppe Patti, MD,* Vincenzo Pasceri, MD,†
Achille Gaspardone, MD,‡ Giuseppe Colonna, MD,§ Antonio Montinaro, MD§

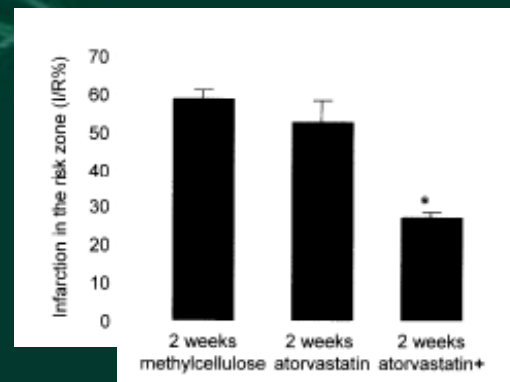
Rome and Lecce, Italy

ARMYDA Recapture trial

Do patients on chronic statin treatment have a clinical benefit similar to that observed with acute administration?

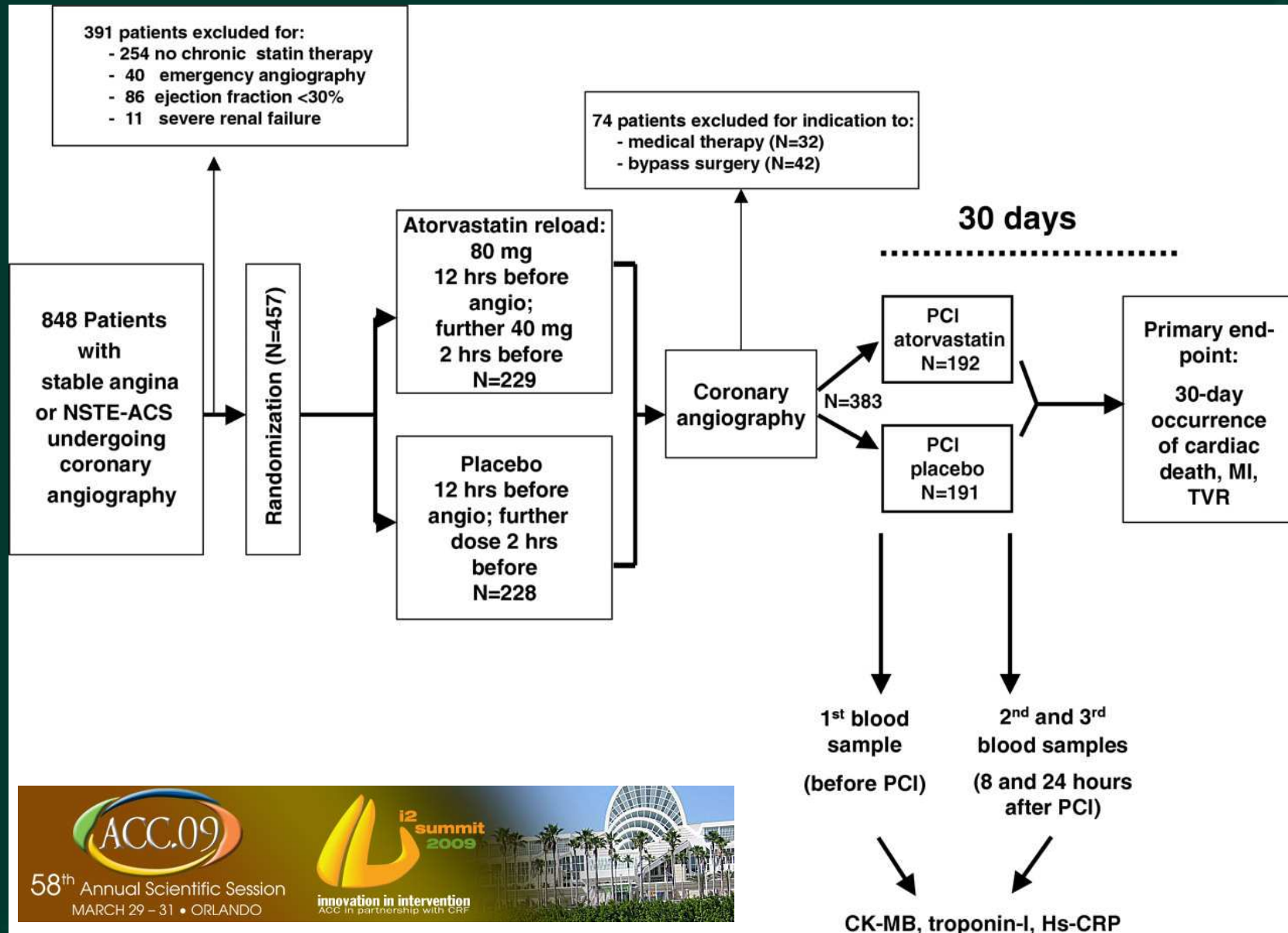
ARMYDA Recapture trial

In a rat model (Langerdoff rats) of ischemia/reperfusion, the acute protective effect of atorvastatin on myocardial injury wanes with a longer treatment, but this effect can be recaptured by a “reloading” given immediately before ischemia/reperfusion



+ Supplementary dose given a few hours before ischemia/reperfusion

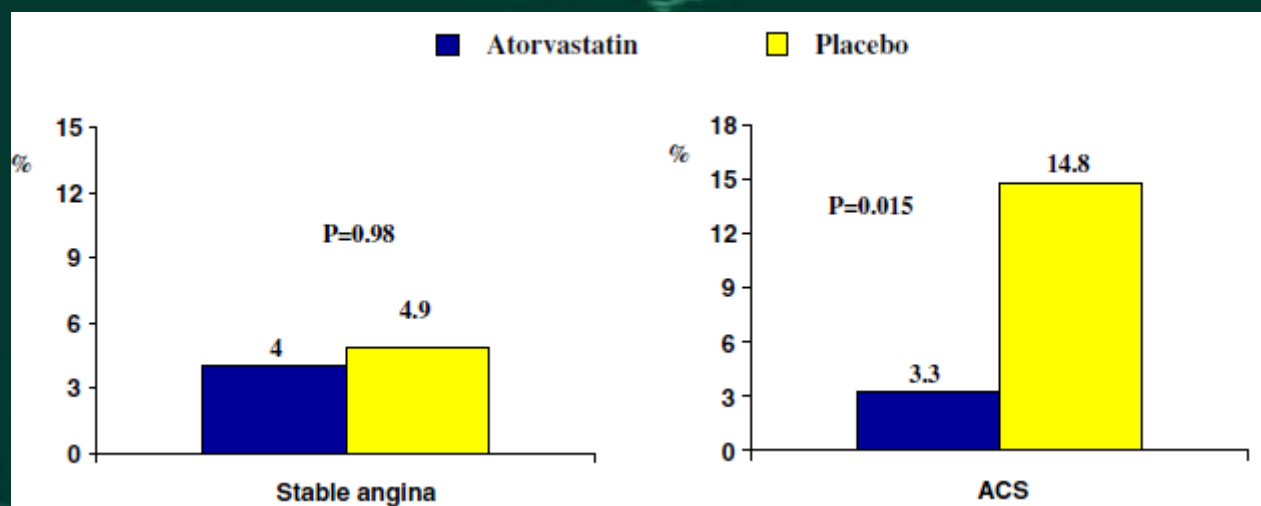
ARMYDA Recapture trial



ARMYDA Recapture Primary End Point

Individual and combined outcome measures at 30 days

	Atorvastatin Reload (n = 192)	Placebo (n = 191)	p Value
Cardiac death	0	1 (0.5)	NS
Myocardial infarction	7 (3.7)	17 (8.9)	0.056
Stent thrombosis	0	1 (0.5)	NS
Target vessel revascularization	0	1 (0.5)	NS
Total MACE	7 (3.7)	18 (9.4)	0.037



Incidence of major adverse cardiac events at 30 days according to clinical presentation

Di Sciascio G et al, J Am Coll Cardiol 2009; 54:558-65

ARMYDA Recapture: conclusions

- **Reloading with high dose atorvastatin is associated with improved clinical outcome in patients on chronic statin therapy undergoing PCI**
- **Acute atorvastatin bolus 80 mg 12 hrs + 40 mg 2 hrs pre-PCI gives a 48% Relative Risk Reduction of 30-day MACE at MV analysis (NNT=17)**
- **The benefit is largely localized to patients who presented with ACS (87% Risk Reduction, NNT=9)**

ARMYDA Recapture: conclusions

- **Rapid LDL-independent cardioprotective effects may be responsible of this phenomenon**
- **These findings may support a strategy of routine reload with high dose atorvastatin early before intervention even in the background of chronic therapy**
- **If confirmed by future studies, results of ARMYDA-RECAPTURE may influence practice patterns for the acute care of non ST-segment elevation ACS**

***Atorvastatin* given before PCI: major ARMYDA trials findings**

- 40 mg 7-day Rx associated with 81% risk reduction of cardiac events at 1 month in statin-naïve stable pts (ARMYDA)
- 80 mg load associated with 88% risk reduction of cardiac events at 1 month in statin-naïve ACS pts (ARMYDA-ACS)
- 80 mg re-load associated with **48%** relative risk reduction of MACE at 30 days in pts on chronic statin Rx (ARMYDA-RECAPTURE)



ARMIDA Recapture

I risultati supportano una strategia di routine finalizzata ad instaurare un trattamento di carico con atorvastatina 80 mg in tutti i pazienti sottoposti a PCI indipendentemente da una precedente terapia con statine

High-dose atorvastatin in ACS: an intriguing hypothesis

- **Early benefits** derived largely from the **anti-inflammatory effects** of the drug.
- The **delayed benefits** are **lipid-modulated**.

