Driving Optimal CV Outcome for ACS Patients

Time Matters

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- Disclosure of Conflicts

Company sponsored symposium

Probably receives honorarium from Pfizer Inc. Korea

1. High recurrence in early after ACS event

2. Evidences for early intensive statin in ACS

- **MIRACL**
- **PROVE-IT**
- **ARMYDA**

Why are Early Benefits important?

Background

- Atherosclerotic cardiovascular disease remains the most common cause of death in the world, despite significant advances in preventive and treatment modalities
- The NCEP ATP III recommends intensive statin treatment (below 100 mg/dL) as the cornerstone of therapy for primary and secondary prevention of coronary artery disease (CAD)
- Recently, in addition to intensive lipid management for high risk patients, many landmark trials emphasize an urgent need for more aggressive intervention and early benefits for primary and secondary CVD events prevention.

Braunwald and Gotto. *Am J Cardiol*. 2005;96(suppl):1F.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486.

Clinical Trials Of Statins In Primary And Secondary Prevention

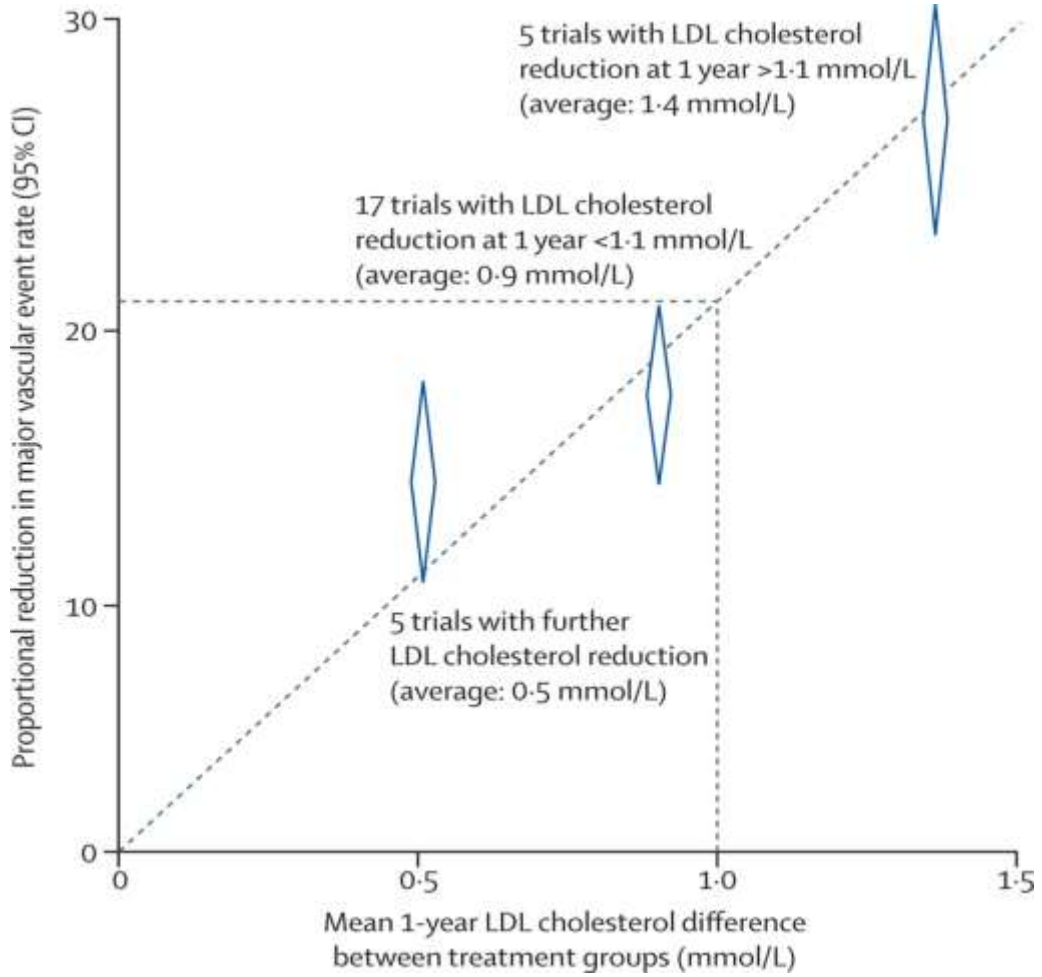
Trial	Baseline LDL-C (mg/dL)	On-Treatment LDL-C (% reduction)	Statin Event* Rate (%)	Placebo Event* Rate (%)	RRR (%)	ARR (%)	NNT
4S	188	122 (35)	19.4	28.0	34	8.6	12
LIPID	150	112 (25**)	12.3	15.9	24	3.6	28
CARE	139	98 (32)	10.2	13.2	24	3.0	34
HPS	~126	~89 (29**)	19.9	25.4	24	5.5	18
WOSCOPS	192	159 (26)	5.3	7.5	29	2.2	46
AFCAPS	150	115 (25)	3.5	5.5	37	2.0	50

*Nonfatal MI or CHD death in WOSCOPS, CARE, LIPID; nonfatal or fatal MI, unstable angina, or sudden cardiac death in AFCAPS; nonfatal MI, coronary death, or resuscitated cardiac arrest in 4S; major vascular events (total CHD, total stroke, revascularizations) in HPS; **Versus placebo.

ARR = absolute risk reduction; NNT = number needed to treat; RRR = relative risk reduction.

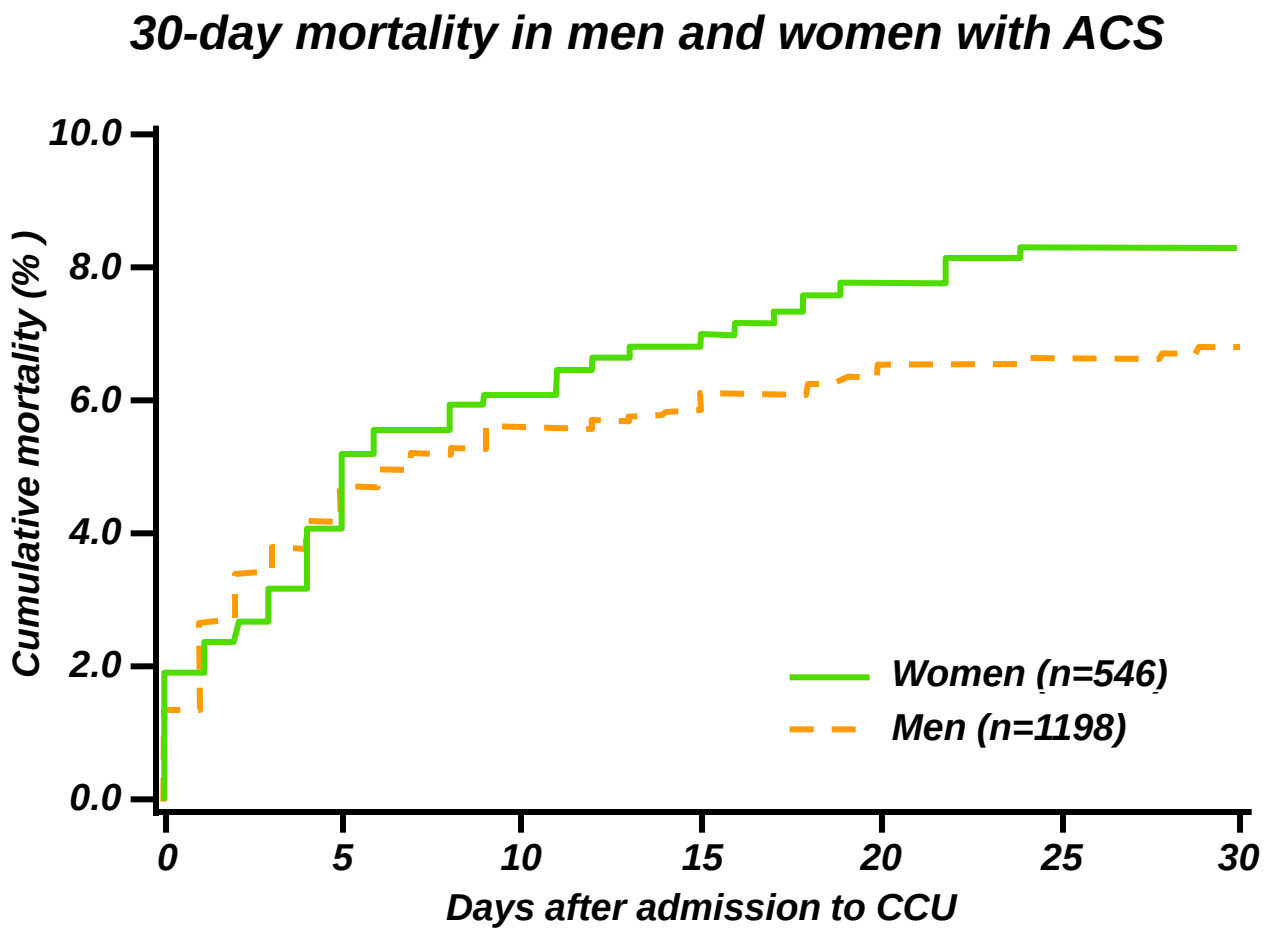
Reproduced from Gotto. *Am J Cardiol.* 2005;96(suppl):34F, with permission.

LDL-C Reduction with Statins and CV Event Reduction



Collins R et al, Lancet epub Sept 9, 2016

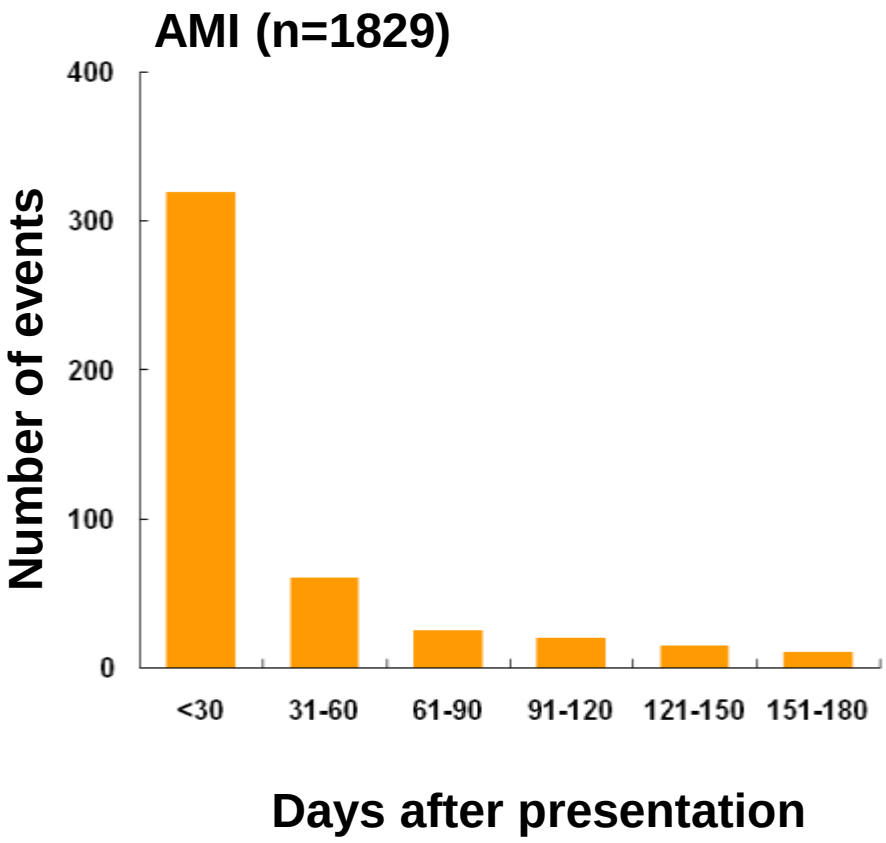
ACS Are at High Risk of Early Mortality

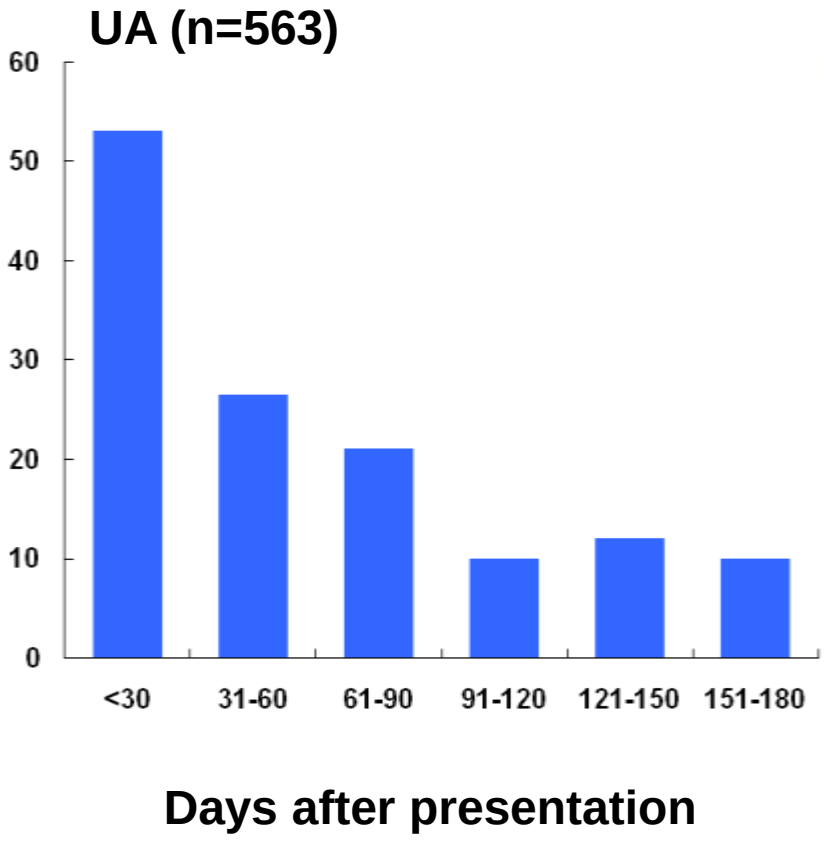


CCU=coronary care unit.

Adapted from Perers E et al. Int J Cardiol. 2005;103:120-127.

High risk of recurrence in 30 d after index event

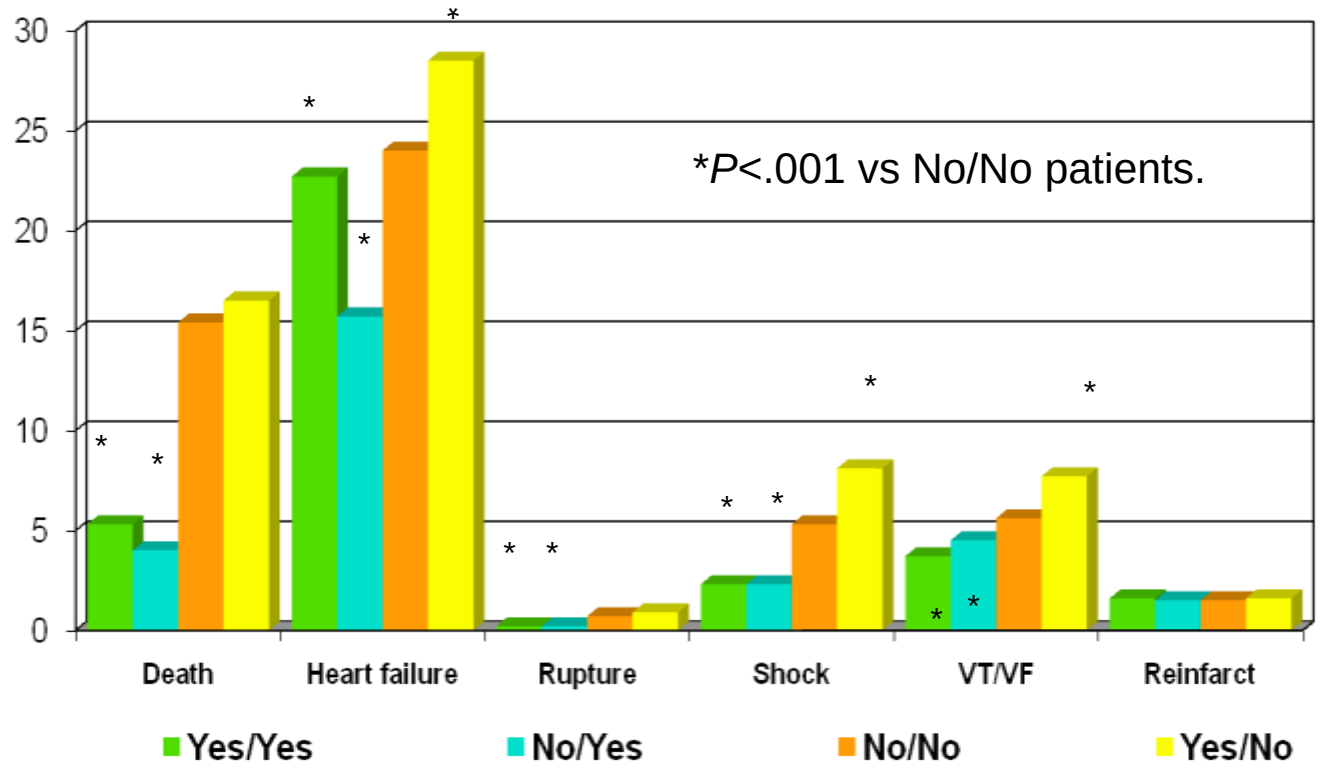




Heart 2003;89:1268

NRMI: Statin Use Within 24 Hours of AMI Is Associated With Reduced Early Morbidity and Mortality

Clinical events (%)



Yes/yes =patients continued on statin therapy;

no/yes =patients newly started on statin therapy;

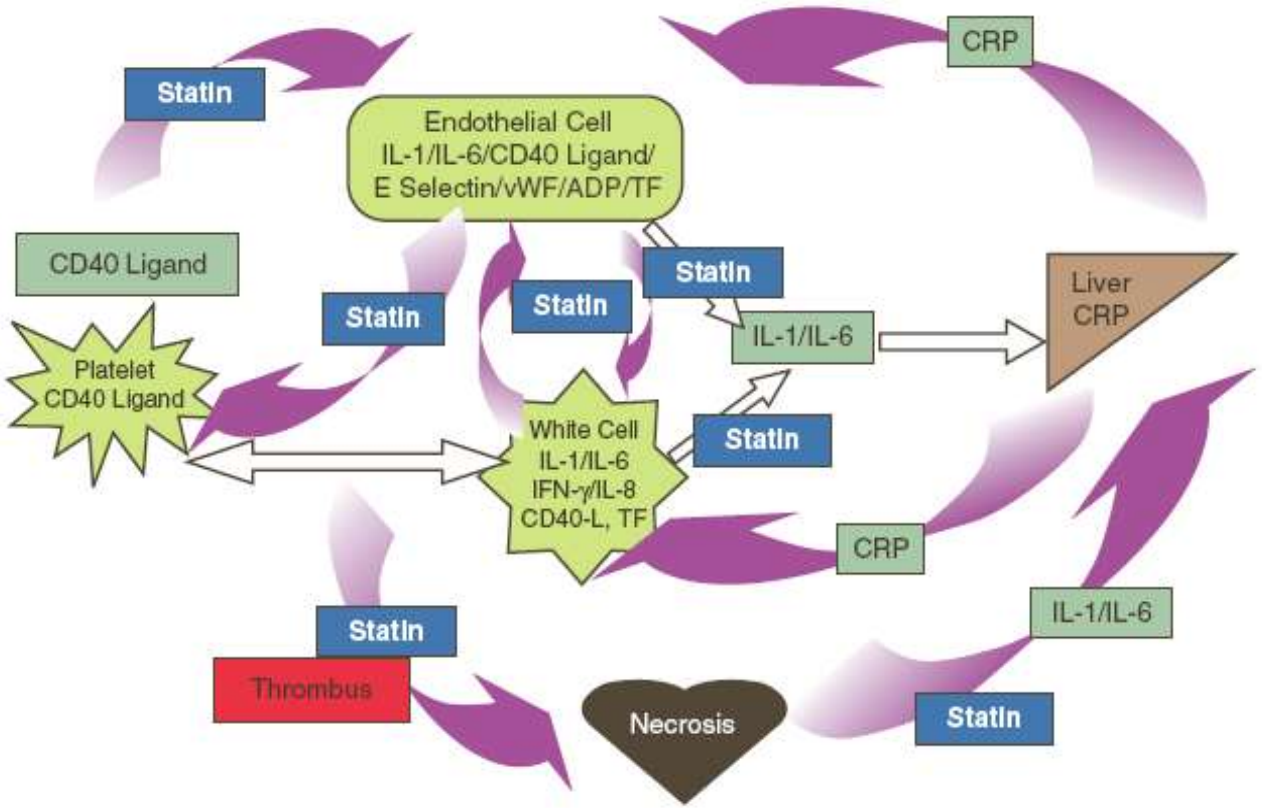
no/no =patients who did not receive statin before or within the first 24 h of hospitalization;

yes/no =patients in whom statin therapy was discontinued.

Adapted from Fonarow GC et al. *Am J Cardiol*. 2005;96:611-616.

Early benefits of statin in Landmark trials

Role Of Statins In ACS: Non-Lipid Effects



ADP = adenosine diphosphate; CD40-L = CD40 ligand; IFN = interferon; IL = interleukin; vWF = von Willebrand factor.

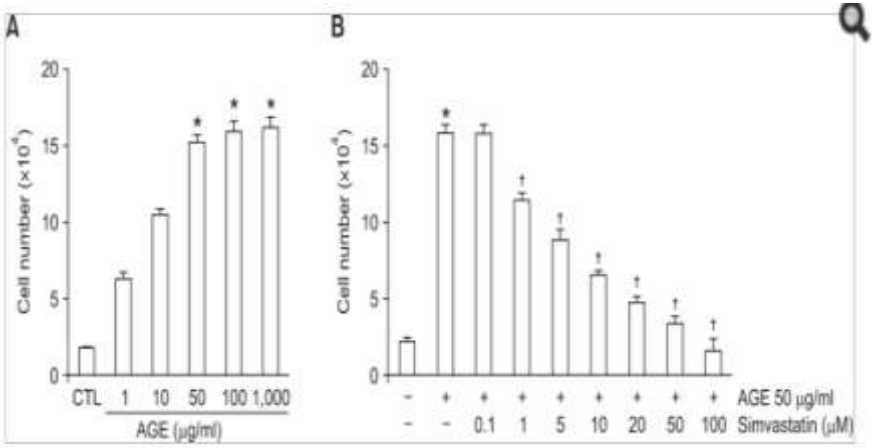
Reproduced from Ray and Cannon. *J Thromb Thrombolysis*. 2004;18:89, with permission.

Cannon and Ray. *Am J Cardiol*. 2005;96:54F.

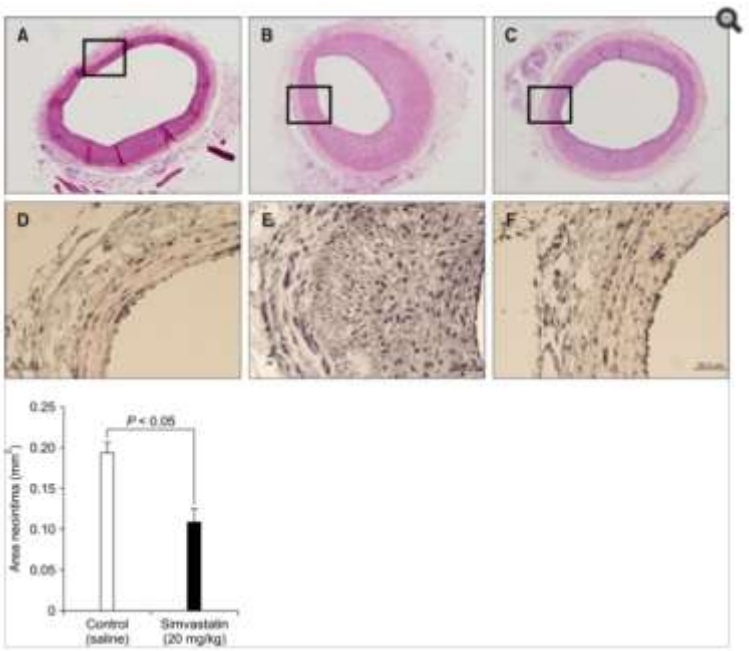
Statin may induce anti-inflammatory and endothelial cell protective actions

the beneficial effects of statin in patients at risk for cardiovascular events

Effect of AGEs and statin on VSMC proliferation



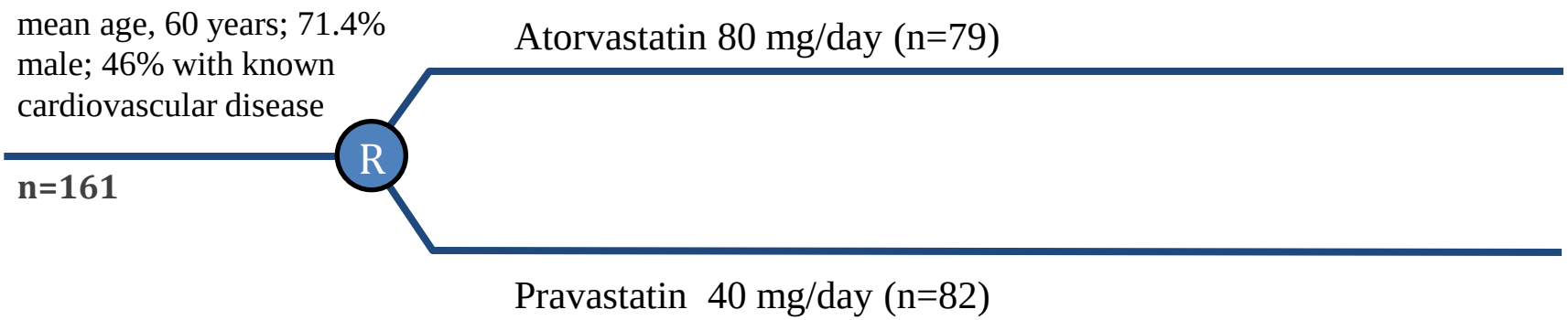
Impact of statin on neo intimal hyperplasia and expression of of COX-2 in carotid artery of diabetic ratCOX-2



Yoon S-J, Yoon YW, Lee BK, et al. Potential role of HMG CoA reductase inhibitor on oxidative stress induced by advanced glycation endproducts in vascular smooth muscle cells of diabetic vasculopathy. Experimental & Molecular Medicine. 2009;41(11):802-811. doi:10.3858/emm.2009.41.11.086

ARBITER: Arterial Biology for the Investigation of the Treatment Effects of Reducing Cholesterol

- Objectives : Comparison of intensive lipid lowering effect of atorvastatin 80 mg with pravastatin 40 mg
- Methods: Prospective, randomized, double-blind, single-center



- Primary end point :

LDL reduction, Carotid intima-media thickness (CIMT)

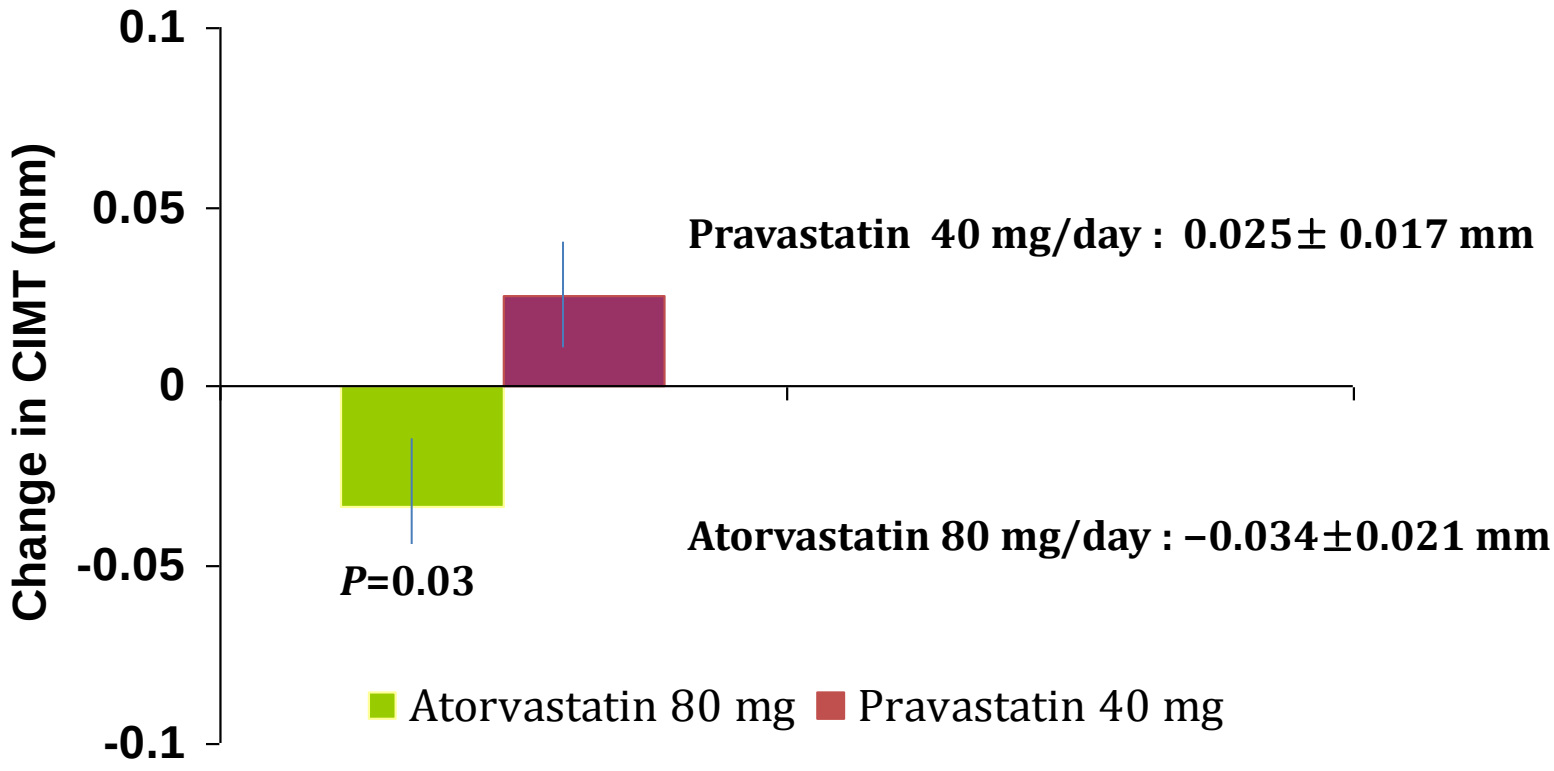
- Follow-up duration : 12 months

Circulation. 2002; 106: 2055-2060

Reduced progression of atherosclerotic plaque

ARBITER study : N=161 pts with CVD
randomized to pravastatin 40 or atorvastatin 80 mg.

[Change in Carotid intima-media thickness (CIMT) at 18 months]



Taylor AJ, et al. Circulation. 2002;106:2055-2060

High-dose atorvastatin pretreatment could diminishes microvascular impairment in patients undergoing elective PCI

43 patients were randomly assigned to high dose atorvastatin (40 mg/d) for 7 days before PCI (high dose group),

41 patients were assigned to low-dose atorvastatin (20 mg/d) for 7 days before PCI (low-dose group).

All patients received atorvastatin 20 mg/d for 6months after PCI.

Results of PCI.

Variable	High-dose group ($n = 43$)	Low-dose group ($n = 41$)	*P* value
Procedure time, min	75 ± 38	79 ± 42	0.65
Post-dilation, *n*	35	39	0.26
Maximum inflation pressure, atm	21.2 ± 3.1	22.1 ± 1.5	0.09
FFR			
pre-PCI	0.61 ± 0.13	0.55 ± 0.16	0.06
post-PCI	0.93 ± 0.07	0.95 ± 0.04	0.11
IMR post-PCI	16.5 ± 6.1	31.2 ± 16.0	< 0.001
cTnI, ng/mL			
pre-PCI	0.028 ± 0.05	0.022 ± 0.04	0.55
post-PCI	0.11 ± 0.02	0.16 ± 0.09	< 0.001

Data are expressed as mean ± SD or as *n* (%), unless other indicated. cTnI: cardiac troponin I; FFR: fractional flow reserve; IMR: microcirculatory resistance; LAD: left anterior decending coronary artery; LCX: left circumflex coronary artery; RCA: right coronary artery; PCI: percutaneous coronary intervention.

"Routin daily use of high-dose statins pre-teatment is reasonable in patients undergoing elective PCI for stable angina pectoris."

Gui-Xin He et al. J Geriatr Cardiol. 2013;10:355-360.

Time to Separation of 1° Endpoint Curve

FLORIDA	Fluva 80 mg vs placebo	8 days	540	1 year	8	NS
PACT	Prava 20/40 mg vs placebo	24 hours	3408	30 days	6.4	NS
A to Z	Simva 40/80 mg vs placebo/simva 20 mg	5 days to 4 months	4497	2 years	11	NS
MIRACL	Atorva 80 mg vs placebo	24–96 hours	3086	16 weeks	16	.048
PROVE IT	Atorva 80 mg vs prava 40 mg	10 days	4162	4 months 2 years	19 16	.03 .005
ARMYDA - ACS	Atorva 80mg(12Hr) /40mg(2Hr) vs placebo	12 hours	171	30 days	14	.01

Liem AH et al. *Eur Heart J*. 2002;23:1931-1937; Thompson PL et al. *Am Heart J.* 2004;148:e2; de Lemos JA et al. *JAMA.* 2004;292:1307-1316; Schwartz GG et al. *JAMA.* 2001;285:1711-1718; Cannon CP et al. *N Engl J Med.* 2004;350:1495-1504; Ray KK et al. *Am J Cardiol*. 2005;46:1405-1410.

Urgent Intensive Statin Therapy After ACS

: Insights from clinical trial

- MIRACL
- PROVE IT-TIMI 22
- A to Z

Randomized Controlled Studies of Lipid-Lowering Therapy in Patients with ACS

	Patients	Comparator	Study Period	N=
MIRACL Atorvastatin 80mg	UA or AMI	Placebo	16 weeks	3,086
PROVE-IT* Atorvastatin 80mg	Post ACS (within 10 days)	Pravastatin 40mg	24 months	4,162
Phase Z of A to Z Simvastatin 40-80mg	ACS, MI	Placebo+ Simvastatin 20mg	24 months	4,497

* PROVE-IT was sponsored by Bristol Myers Squibb and Sankyo

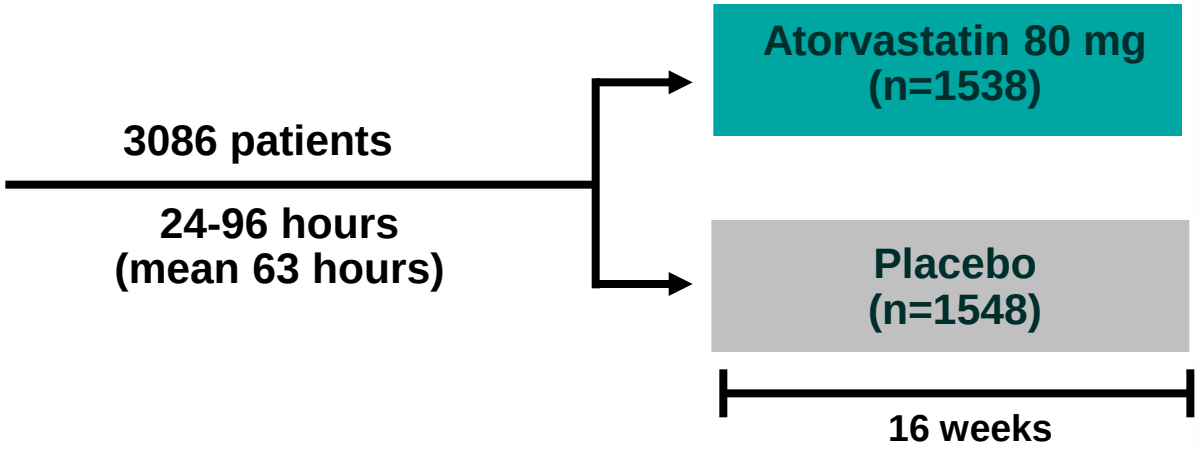
1. Schwartz GG et al. *JAMA.* 2001;285:1711-1718. 2. Cannon CP, et al. *N Engl J Med*. 2004;350:1495-1504. 3. de Lemos JA et al. *JAMA*. 2004;292:1307-1316.

MIRACL: Study Design

The First Randomized Controlled Trial to Examine the Benefit of Statin Therapy in Patients With ACS

Patient population

- Men and women aged ≥18 years
- UA or AMI
- TC ≤270 mg/dL
- Excluded if planned/anticipated coronary revascularization



Primary efficacy end point

- Composite of death, nonfatal AMI, cardiac arrest with resuscitation, or recurrent symptomatic myocardial ischemia requiring rehospitalization

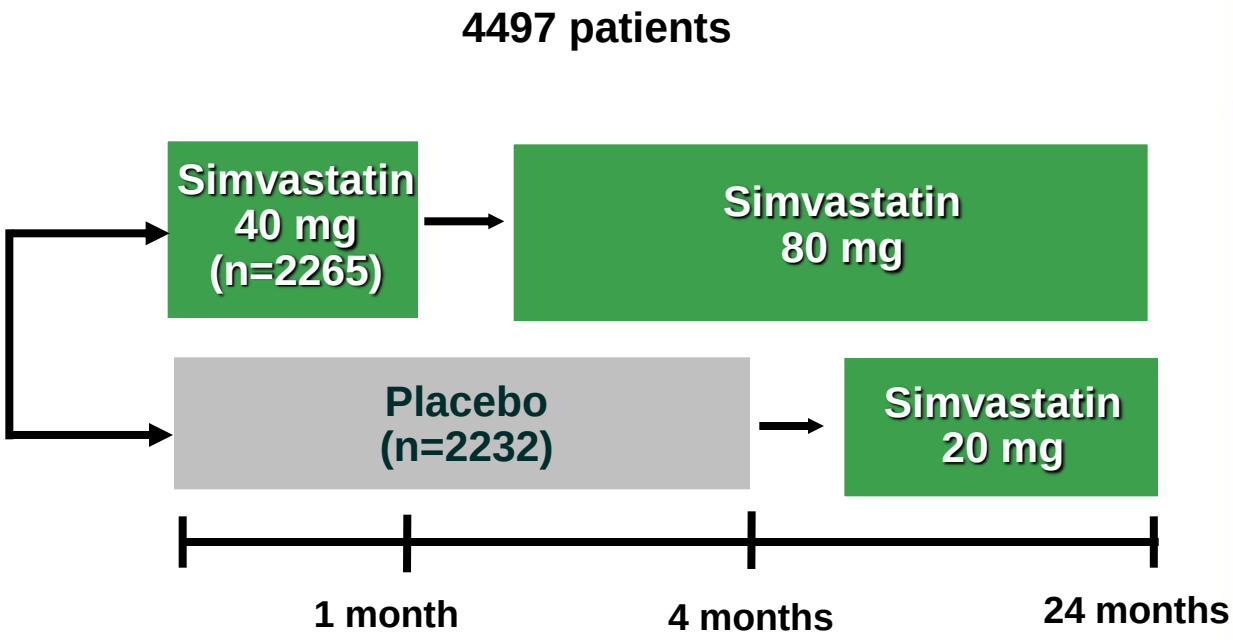
TC=total cholesterol.

Schwartz GG et al. *JAMA.* 2001;285:1711-1718.

Phase Z of the A to Z Trial: Study Design

Patient population

- Men and women aged 21-80 years
- ACS, MI
- TC ≤250 mg/dL
- Met stability criteria
- At least 1 high-risk factor for CVD in addition to cardiac biomarker elevation

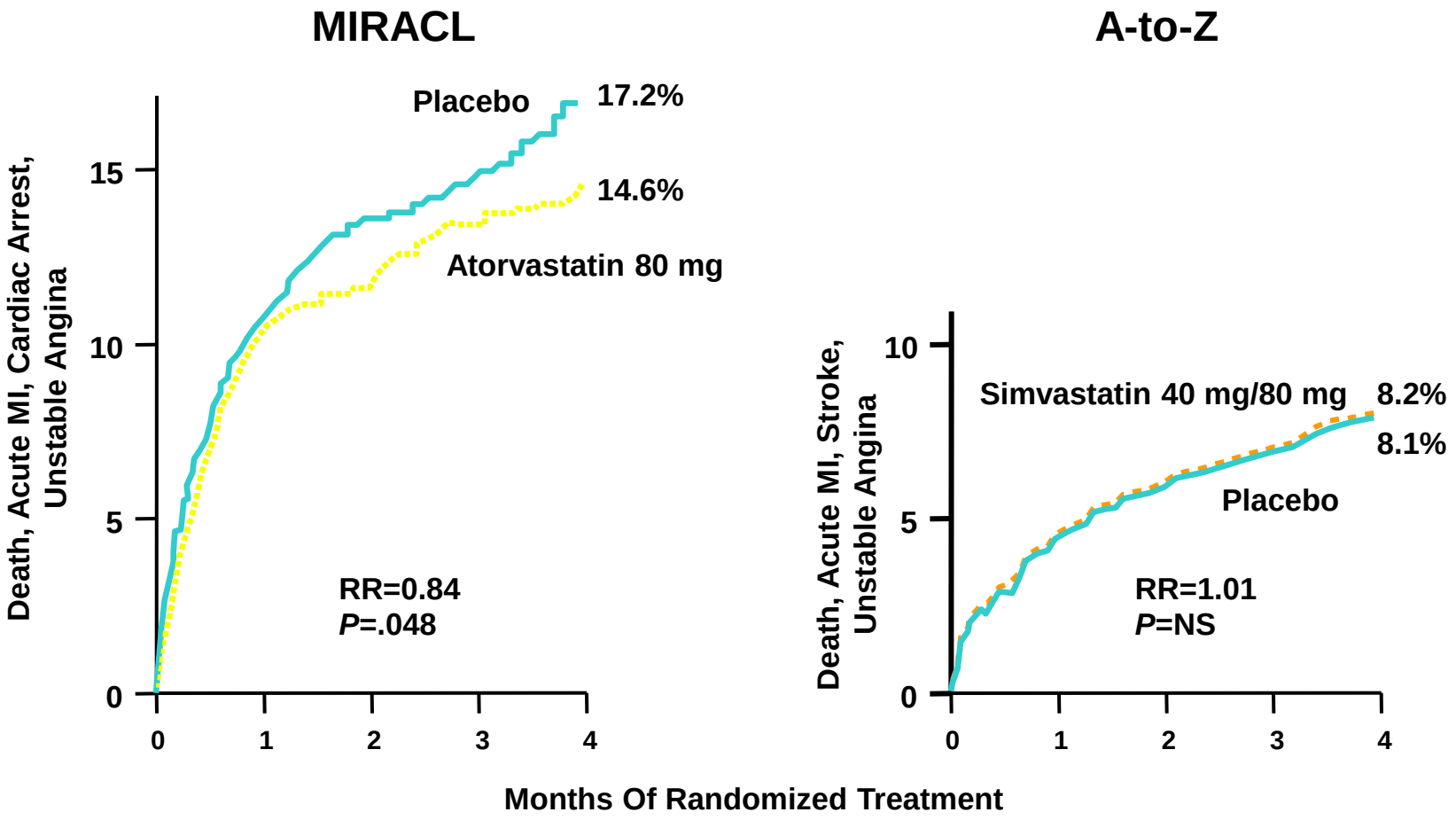


Primary efficacy end point

- Composite of CV death, nonfatal MI, readmission for ACS, and stroke

de Lemos JA et al. *JAMA*. 2004;292:1307-1316.

MIRACL: Intensive Atorvastatin Therapy Reduces Early Events within 16 weeks After ACS



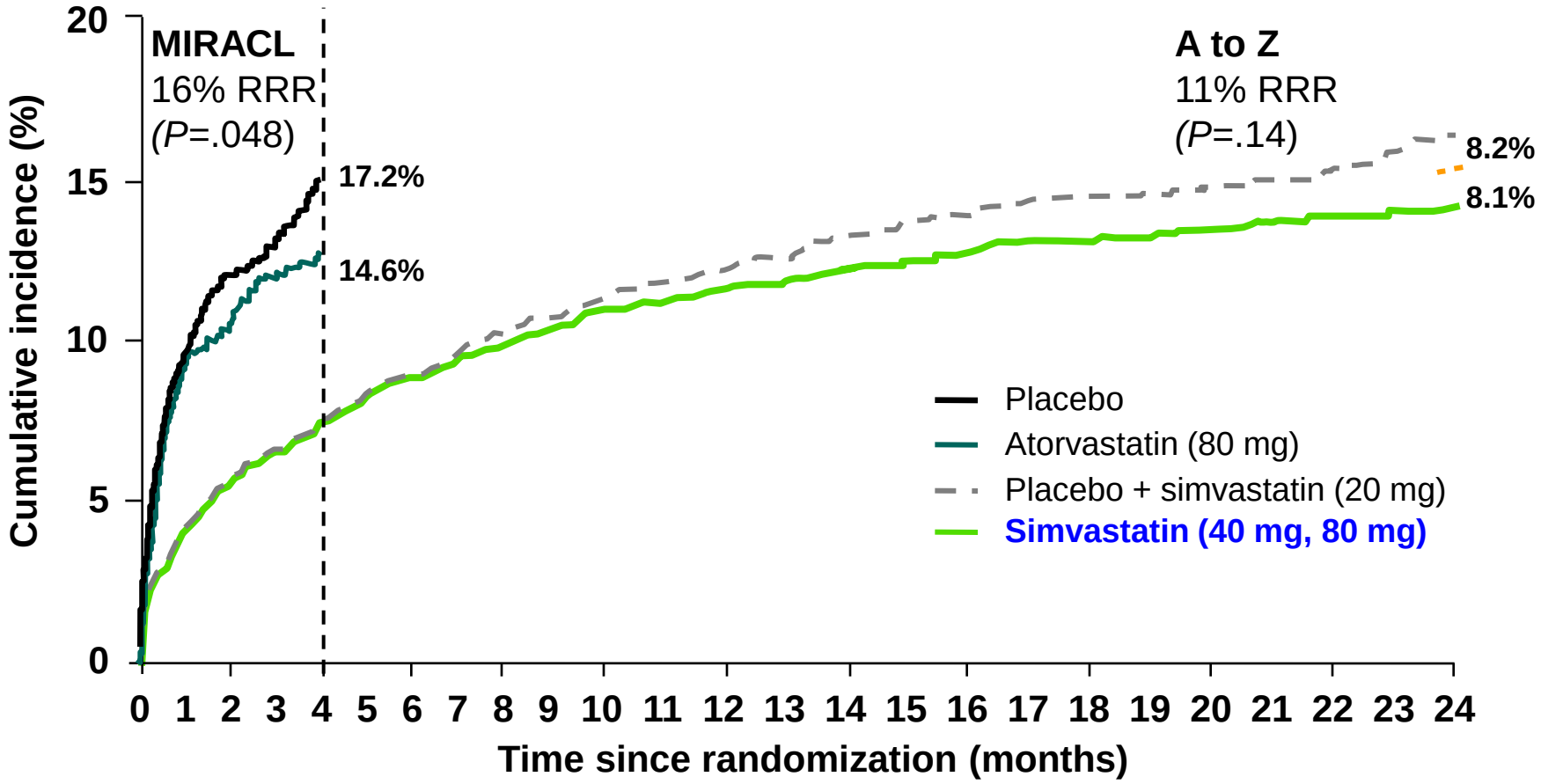
NS = not significant; RR = risk reduction.

Adapted from de Lemos et al. *JAMA*. 2004;292:1307, with permission.

Adapted from Schwartz et al. *JAMA*. 2001;285:1711, with permission.

Schwartz and Olsson. *Am J Cardiol*. 2005;96(suppl):45F.

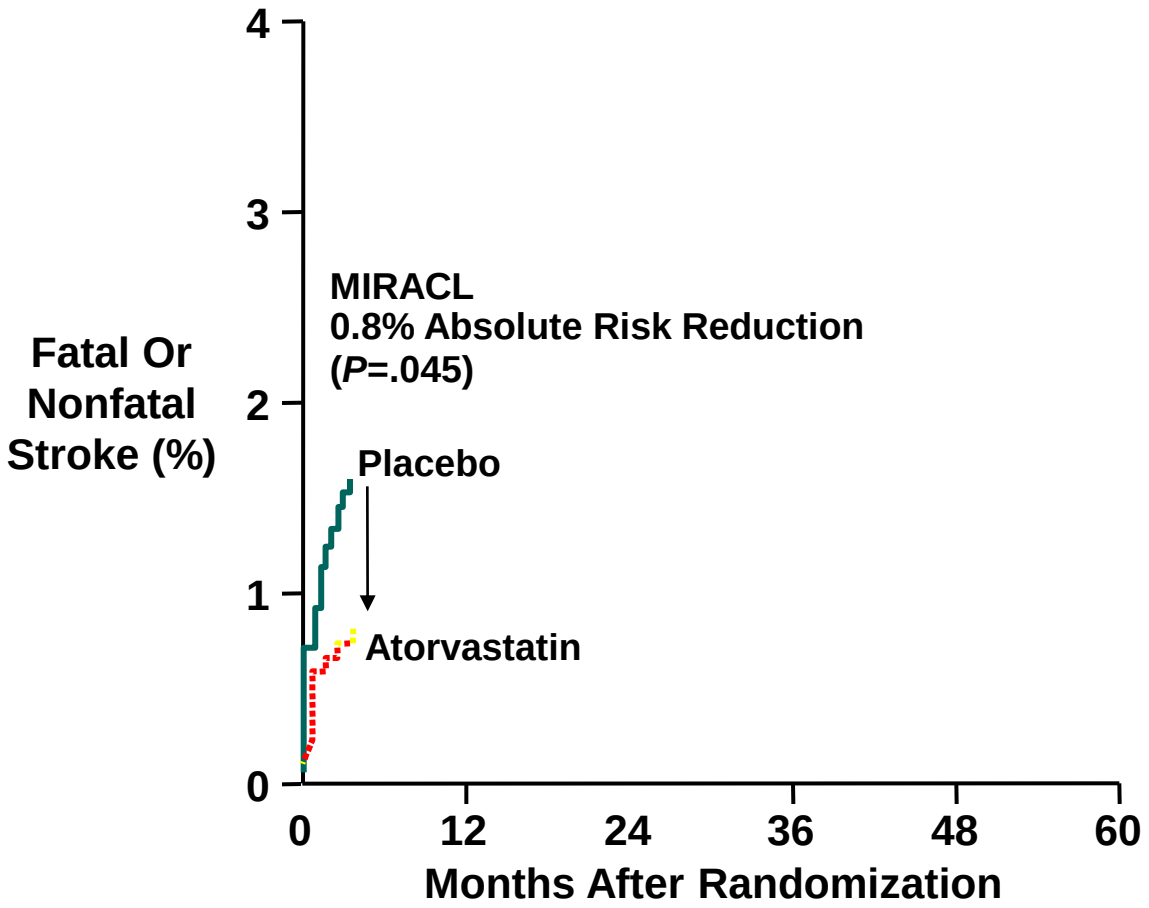
MIRACL: Intensive Atorvastatin Therapy Reduces Early Events within 16 weeks After AC



Occurrence of primary composite end point – MIRACL: death, nonfatal acute MI, cardiac arrest with resuscitation, or recurrent symptomatic myocardial ischemia requiring rehospitalization;
A to Z: the composite of CV death, nonfatal MI, readmission for ACS, and stroke.

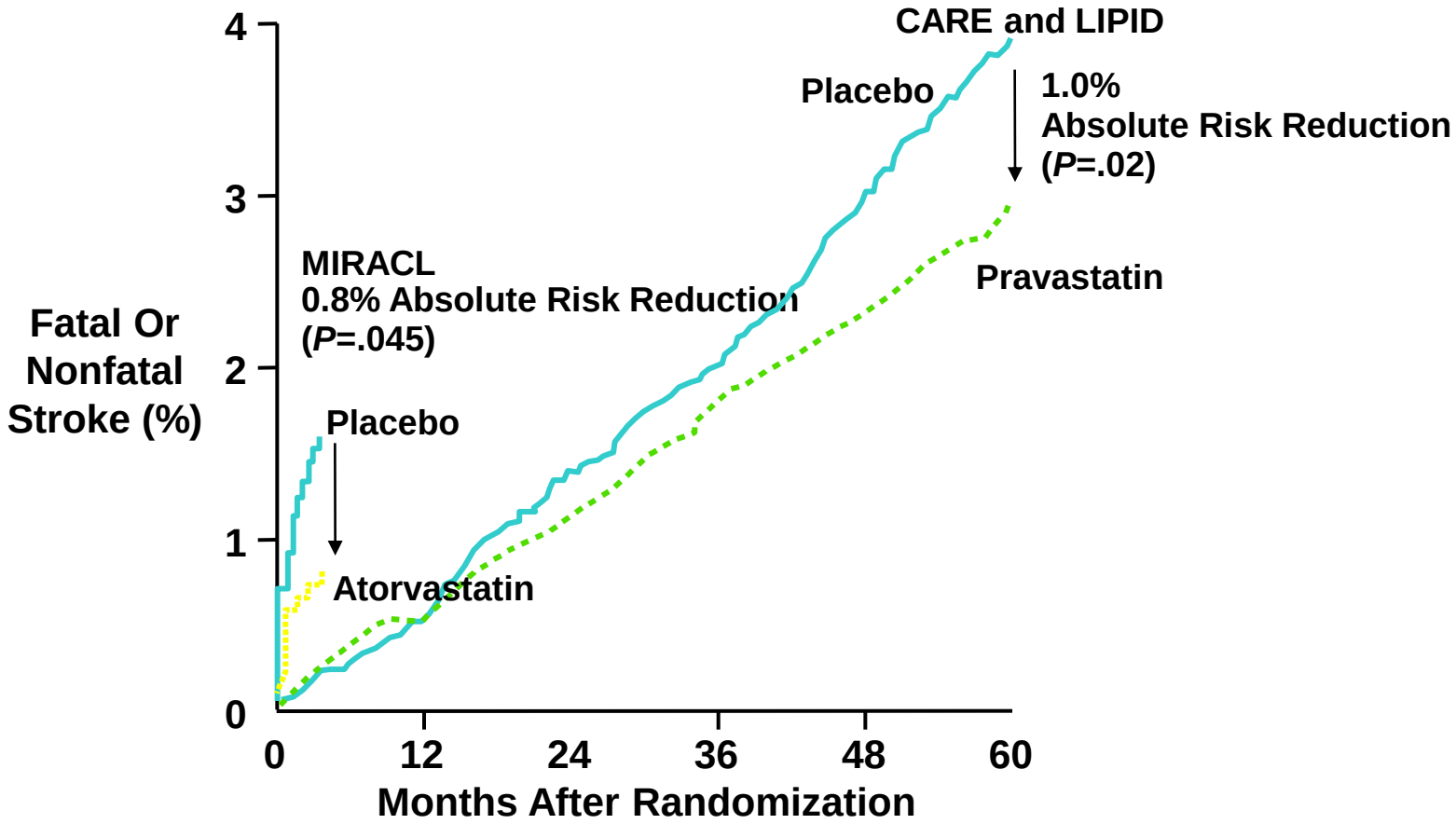
Schwartz GG et al. *JAMA.* 2001;285:1711-1718; de Lemos JA et al. *JAMA*. 2004;292:1307-1316.

MIRACL: Early Reduction In Fatal And Nonfatal Stroke



CARE = Cholesterol and Recurrent Events; LIPID = Long-Term Intervention with Pravastatin in Ischaemic Disease.
Atorvastatin dose = 80 mg; pravastatin dose = 40 mg/d.
Adapted from Byington et al. *Circulation*. 2001;103:387, with permission.
Adapted from Waters et al. *Circulation*. 2002;106:1690, with permission.
Schwartz and Olsson. *Am J Cardiol*. 2005;96(suppl):45F.

MIRACL: Early Reduction In Stroke Comparable To That Observed In Stable CAD



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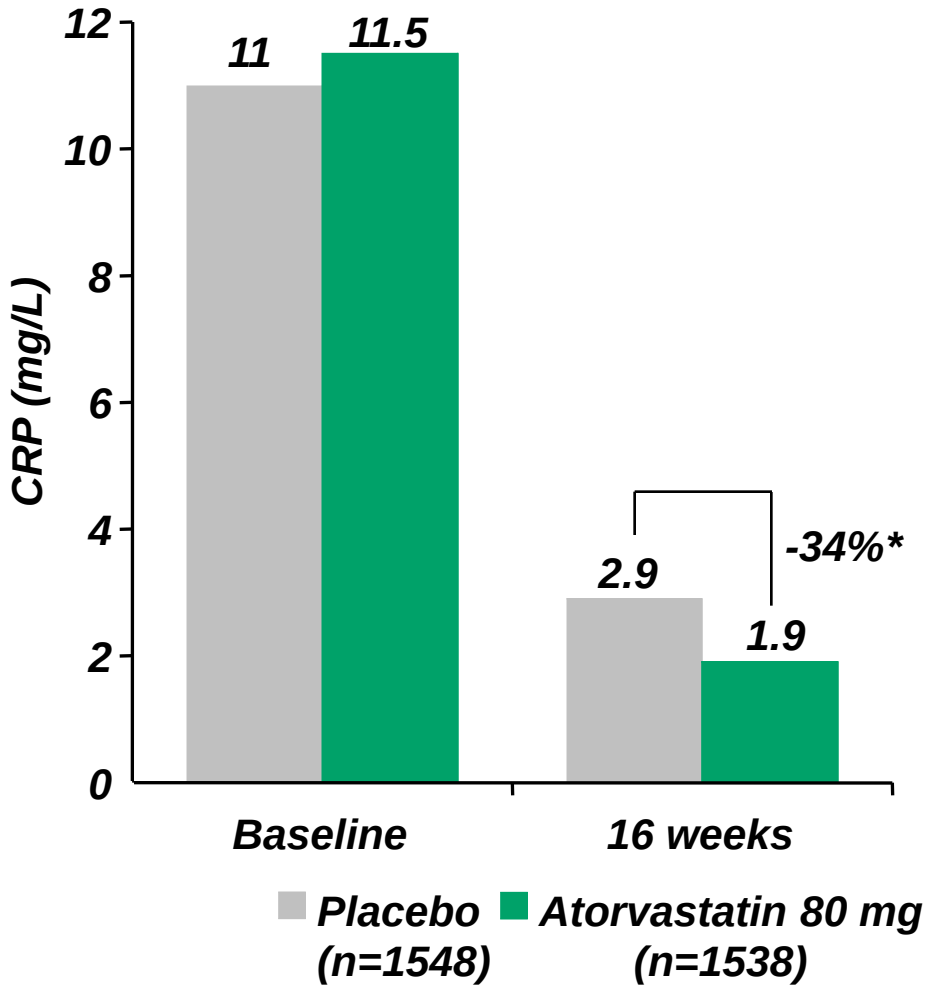
Adapted from Byington et al. *Circulation*. 2001;103:387, with permission.
Adapted from Waters et al. *Circulation*. 2002;106:1690, with permission.
Schwartz and Olsson. *Am J Cardiol*. 2005;96(suppl):45F.

MIRACL Sub-analysis: LDL-C Independent Reductions in CRP Were Seen in Patients Treated With Atorvastatin



*P<.0001.

Adapted from Kinlay S et al. Circulation. 2003;108:1560-1566.

MIRACL
Conclusions

- Intensive therapy with atorvastatin 80 mg *reduced early recurrent ischemic events* after ACS *at 4 months,*

    1. composite primary outcome reduced to 14.6%

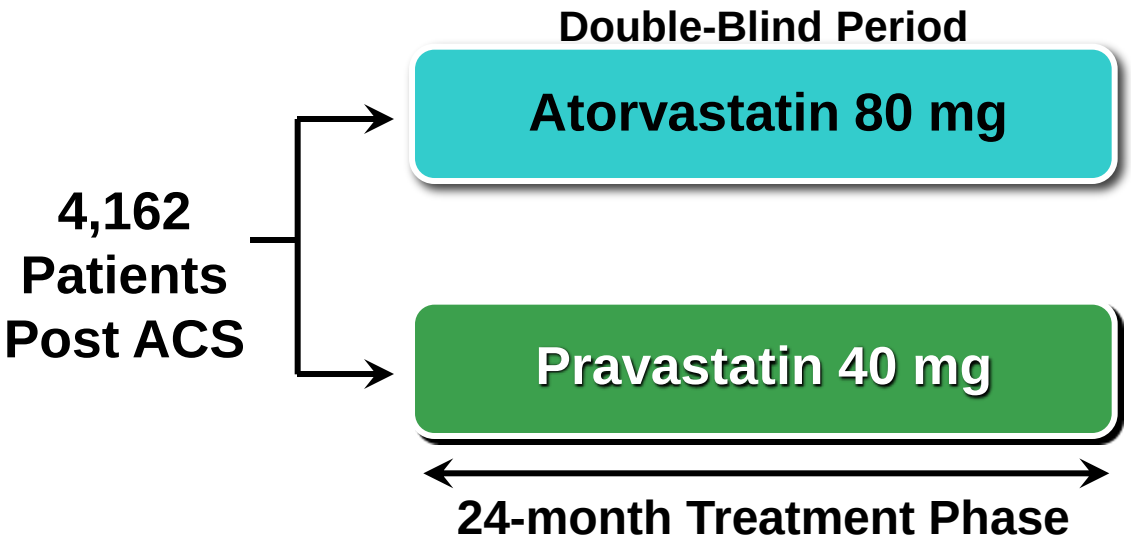
        vs 17.2% in placebo-treated patients (*P*=.048)

    2. stroke reduced to 0.8%

        vs 1.6% in placebo (*P*=.045)

Waters et al. *Circulation*. 2002;106:1690.

PROVE-IT*: Study Design



Patient Population

- 58 y (mean)
- TC <6.2 mmol/L
- Randomized within 10 days of ACS event (mean: 7 days)

Primary End Point

- Time to Occurrence of: Death, Nonfatal MI, Unstable Angina, Stroke, Revascularization

* PROVE-IT was sponsored by Bristol Myers Squibb and Sankyo

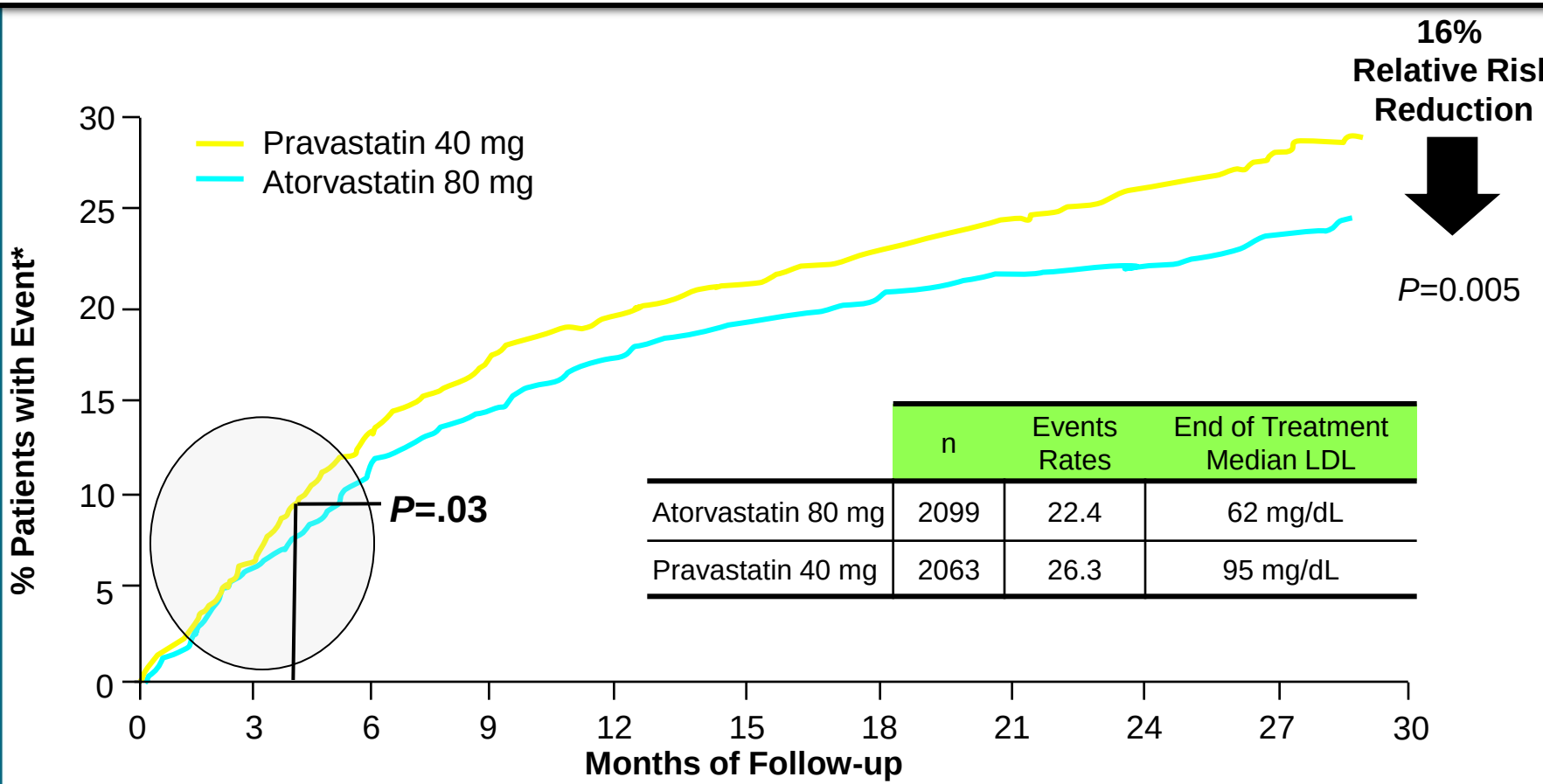
Atorvastatin is not indicated for secondary prevention of CHD in all countries

Adapted from Cannon CP, et al. *N Engl J Med*. 2004;350:1495-1504.

PROVE-IT*: Primary End Point

All-Cause Death, Non-Fatal MI, Unstable Angina
Requiring Hospitalization, Urgent Revascularization, and/or Stroke

Separation of the Curves Occurred Within 30 Days and Was Maintained over Follow-up. Statistical Significance was Reached at 180 Days



	n	Events Rates	End of Treatment Median LDL
Atorvastatin 80 mg	2099	22.4	62 mg/dL
Pravastatin 40 mg	2063	26.3	95 mg/dL

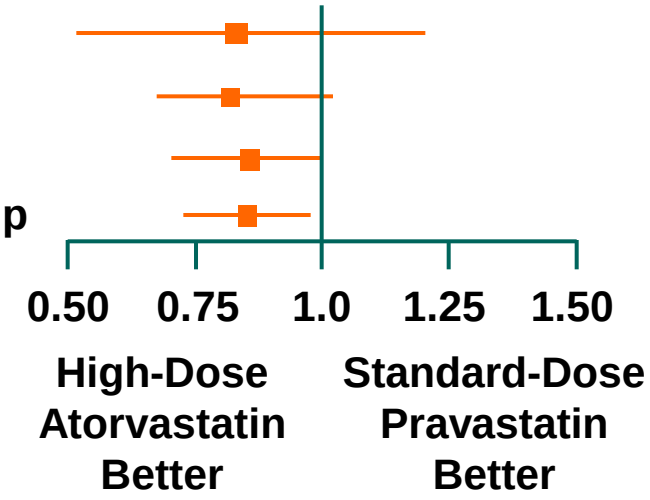
* PROVE-IT was sponsored by Bristol Myers Squibb and Sankyo

Atorvastatin is not indicated for secondary prevention of CHD in all countries

Adapted from Cannon CP, et al. *N Engl J Med*. 2004;350:1495-1504.

PROVE IT: A Major Cardiovascular Event Or Death From Any Cause At Different Censoring Times

Censoring Time	Hazard Ratio (95% CI)	Risk Reduction (%)	Event Rate (%)	
			Atorvastatin	Pravastatin
30 days		17	1.9	2.2
90 days		18	6.3	7.7
180 days		14	12.2	14.1
End of follow-up		16	22.4	26.3



Reproduced from Cannon et al. *N Engl J Med*. 2004;350:1495, with permission.

Ray and Cannon. *Am J Cardiol*. 2005;96(suppl):54F.

PROVE IT: Effect Of Different Statin Regimens On LDL Cholesterol And CRP

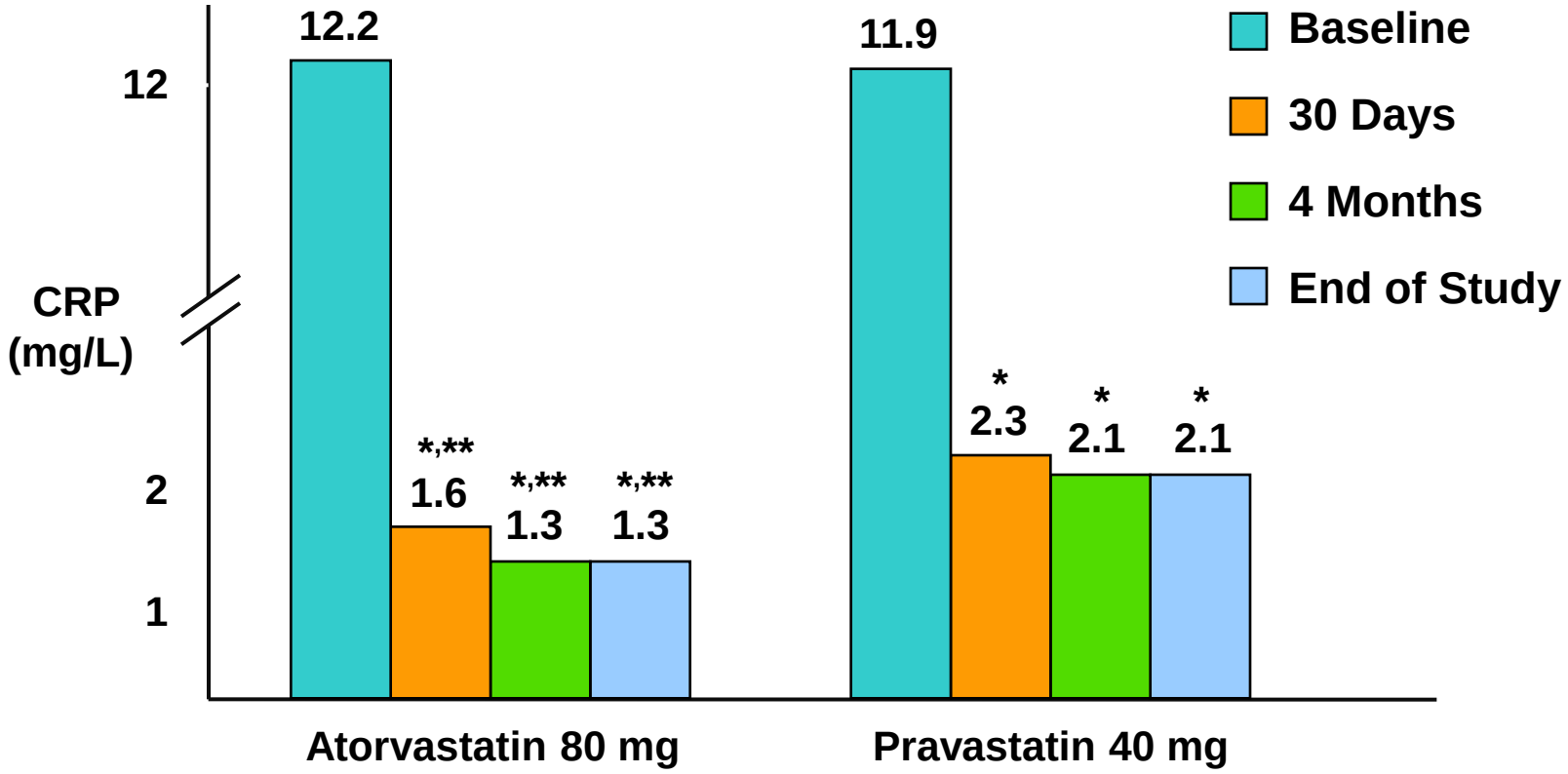
Biological Response	Statin Regimen	Baseline	30 Days	4 Months
LDL mg/dL (mean)	Pravastatin 40 mg	106	88	97
	Atorvastatin 80 mg	106	60	67
	P value	NS	<.001	<.001
CRP mg/L (median)	Pravastatin 40 mg	11.9	2.3	2.1
	Atorvastatin 80 mg	12.2	1.6	1.3
	P value	NS	<.001	<.001

Cannon et al. *N Engl J Med*. 2004;350:1495.

Ridker et al. *N Engl J Med*. 2005;352:20.

Reproduced from Ray and Cannon. *Am J Cardiol*. 2005;96(suppl):54F, with permission.

PROVE IT: CRP Levels At Enrollment And During Follow-Up



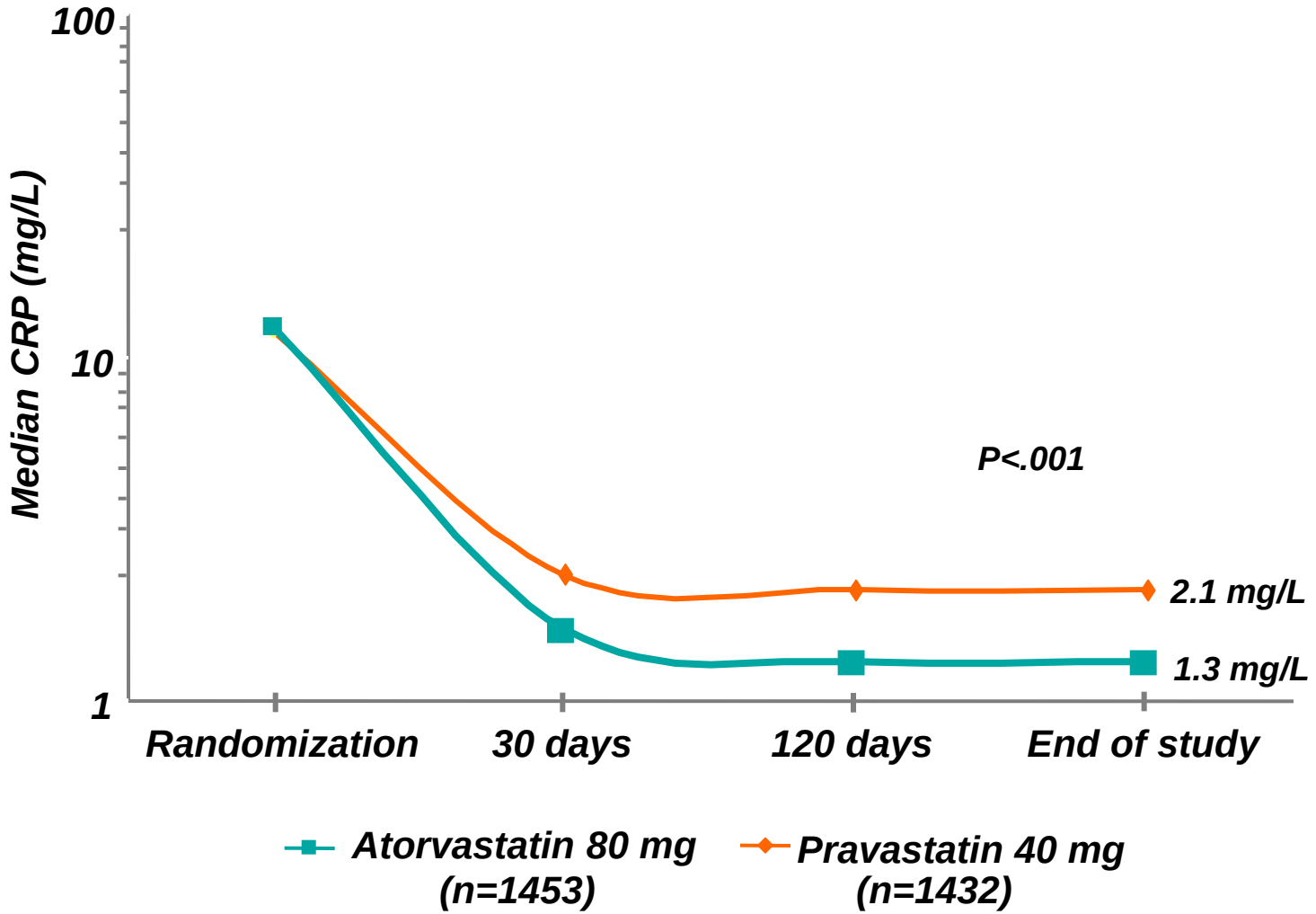
* *P*<.001 vs baseline.

** *P*<.001 vs pravastatin.

Ridker et al. *N Engl J Med*. 2005;350:20.

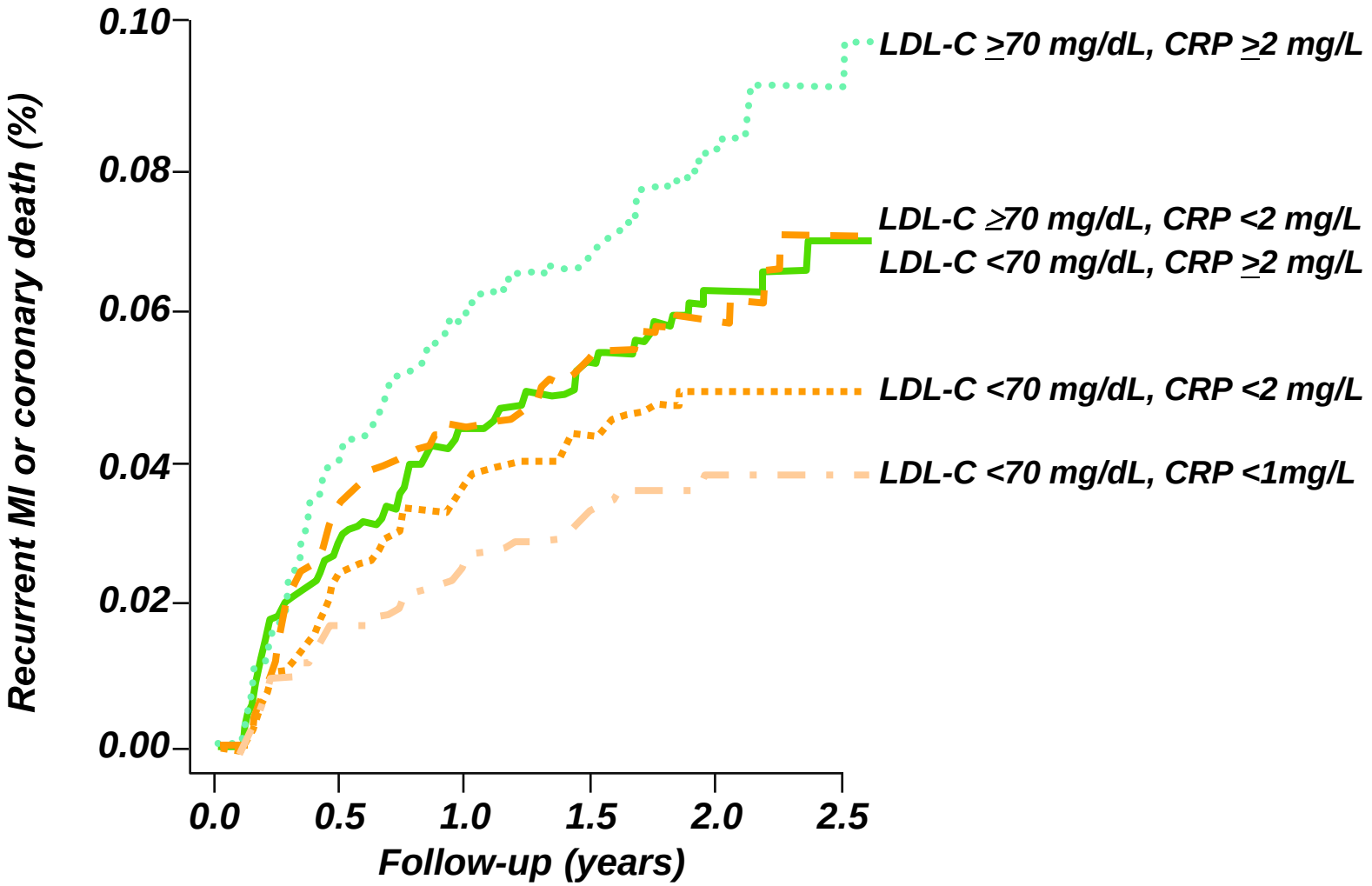
Reproduced from Ray and Cannon. *Am J Cardiol*. 2005;96(suppl):54F, with permission.

PROVE IT Subanalysis: Greater Reductions in CRP in Patients Treated With Atorvastatin Than in Those Who Received Pravastatin



Adapted from Ridker PM et al. N Engl J Med. 2005;352:20-28.

PROVE IT: Prognostic Value Of 30-Day Achieved LDL And CRP On Recurrent MI Or Death From Cardiovascular Causes



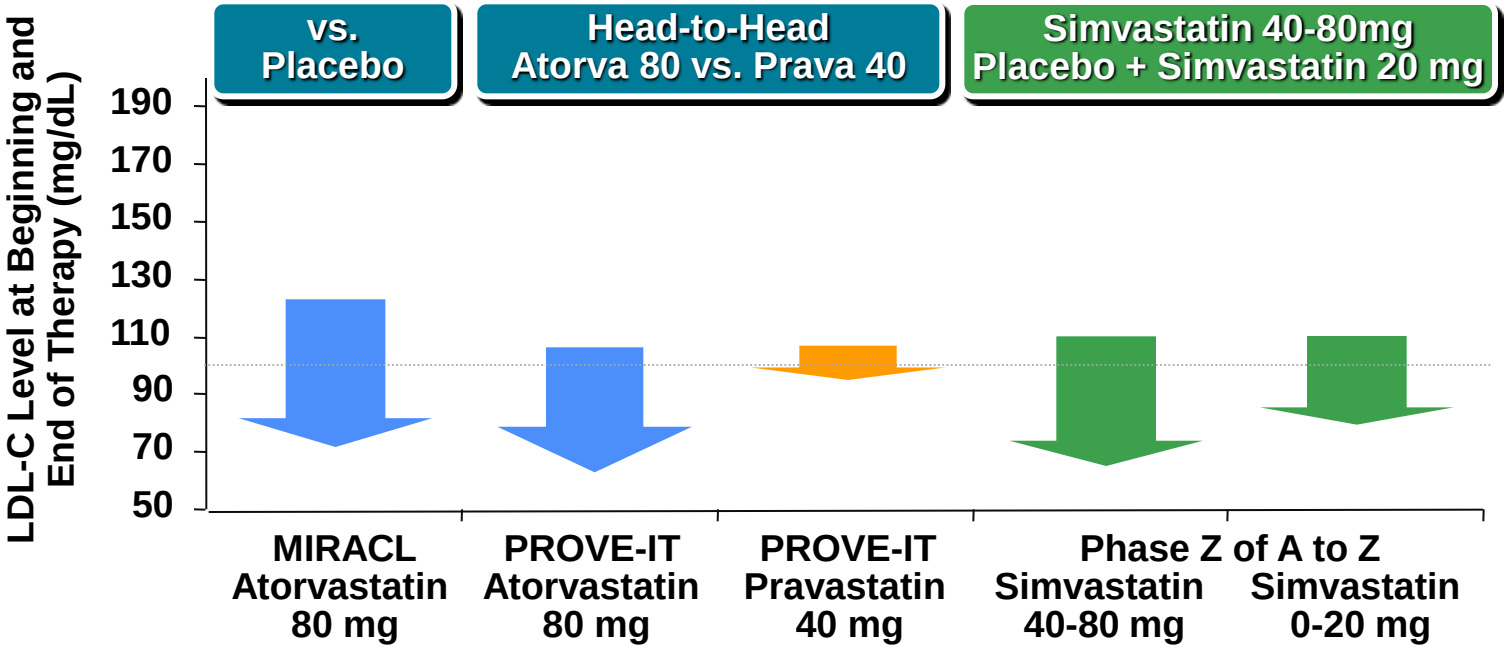
Reproduced from Ridker et al. *N Engl J Med*. 2005;352:20, with permission.

Ray and Cannon. *Am J Cardiol*. 2005;96(suppl):54F.

PROVE IT
Conclusions

- Intensive therapy with atorvastatin 80 mg resulted in apparent clinical benefit observed *as early as 30 days*
- Significant reduction in all-cause mortality, MI, unstable angina, revascularization ≥30 days, and stroke *apparent at 4 months (P=.03)*

Comparison of Reductions in LDL-C Levels by Intensive Statin Therapies in Patients with ACS



Patients	UA or AMI	ACS	ACS	ACS, MI	ACS, MI
Treatment period	16 weeks	24 months	24 months	24 months	24 months

Schwartz GG et al. *JAMA.* 2001;285:1711-1718
Cannon CP, et al. *N Engl J Med*. 2004;350:1495-1504
de Lemos JA et al. *JAMA*. 2004;292:1307-1316

Despite Similar Reductions in LDL-C, Significant Clinical Benefits Seen Only With Atorvastatin

	A to Z	MIRACL	PROVE IT
Treatment	Simva (40 mg, 80 mg) vs placebo + simva 20 mg	Atorva 80 mg vs placebo	Atorva 80 mg vs prava 40 mg
No. of patients randomized	4497	3086	4162
LDL-C difference mmol/L (mg/dL)			
Early*	1.61 (62)	1.63 (63)	0.85 (33)
Late	0.41 (15)	NA	0.73 (28)
Event reduction (%)			
Early*	0*	**16* (*P*=.048)**	**18†**
Late‡	11 (NS)	NA	**16 (*P*=.005)**

NS=not significant; NA=not applicable.
*Measured 120 days after randomization.
†Measured 90 days after randomization.
‡Measured at trial completion—24 months for A to Z and PROVE IT.
mmol/L = mg/dL × .0259

Adapted from Nissen SE. *JAMA*. 2004;292:1365-1367.

Intensive & early statin treatment

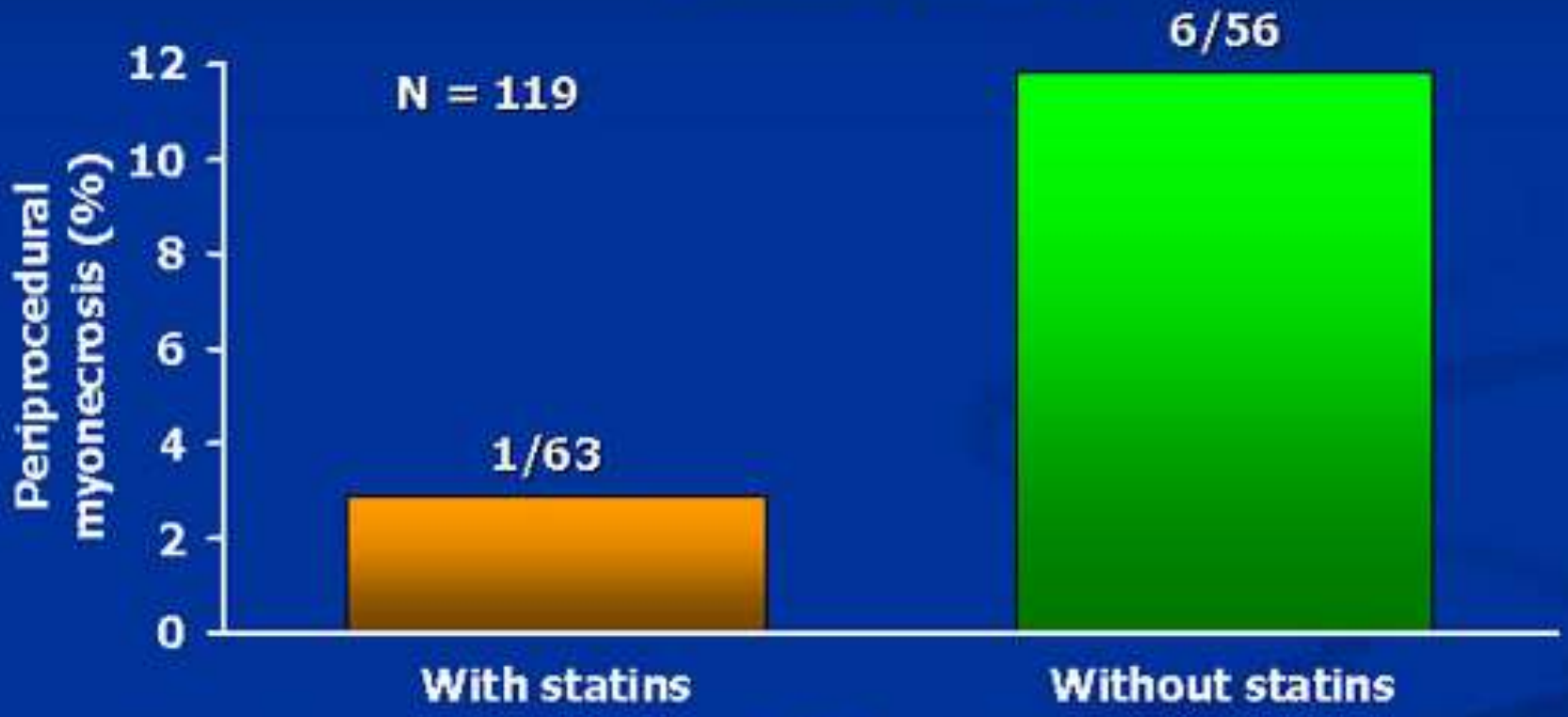
prior to PCI

for acute coronary syndrome

(ARMYDA-ACS)

Statins in ACS Patients Undergoing PCI: Observational Nonrandomized Data

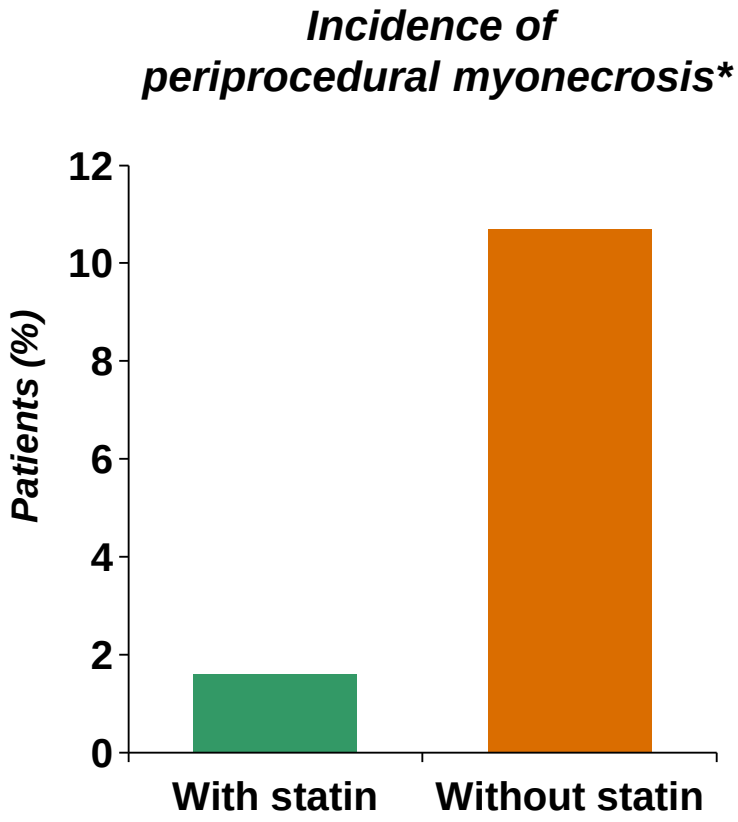
Peak elevation of CK–MB or CK > 3x ULN within 24 hours post-PCI

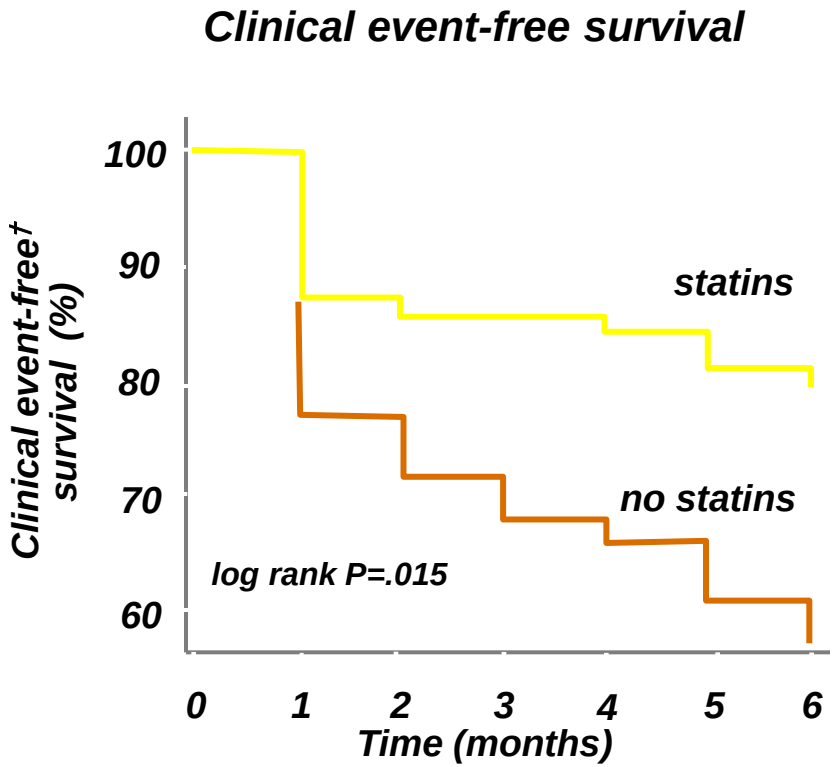


...but patients were treated with different statins at varying doses with unknown duration of previous treatment

Chang SM, et al. *Catheter Cardiovasc Interv.* 2004;62:193-197.

Background: Treatment With Statins Prior to PCI Improves Clinical Outcomes





Study of 119 patients undergoing nonprimary PCI who received (n=63) or did not receive (n=56) statins prior to procedure.
**Myonecrosis defined as elevations in creatine kinase-myocardial band (CKMB) or CK >3 times the upper limit of normal within 24 hours of PCI in patients without recent MI, or 25% increase from trough value in patients with an MI <72 hours before procedure.*
†Events defined as death, nonfatal MI unrelated to PCI, target vessel revascularization, and UA requiring hospitalization.

Chang SM et al. Catheter Cardiovasc Interv. 2004;62:193-197.

The Atorvastatin for

Reduction of MYocardial Damage

during Angioplasty

in Acute Coronary Syndromes

ARMYDA ACS Trial

ARMYDA – ACS Trial

Inclusion Criteria:

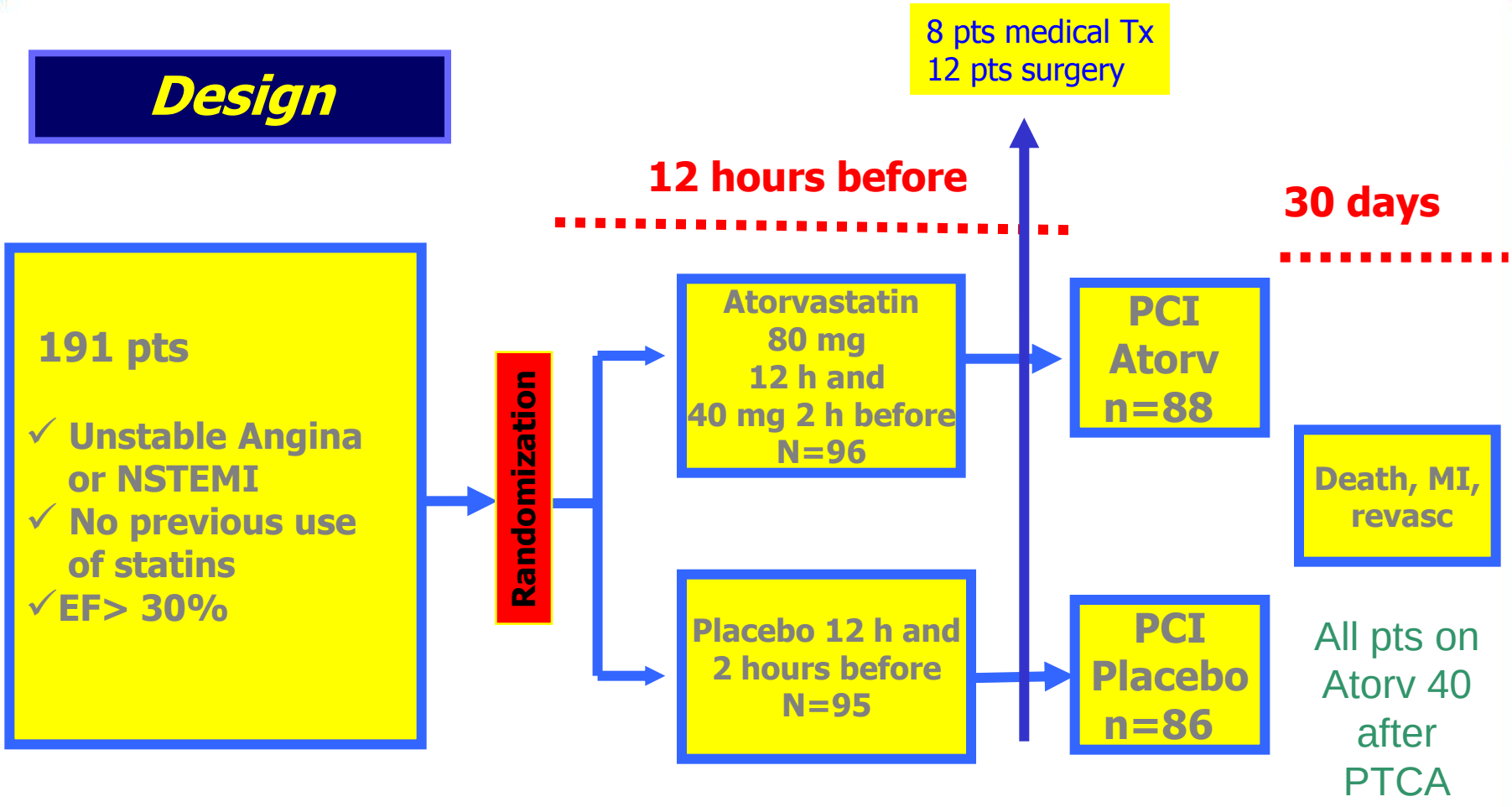
- ✓ Patients with NSTEMI or Unstable Angina
- ✓ treated with early invasive strategy (angio at 12-24 hours)

Exlusion Criteria:

- ✓ Previous or current statin therapy
- ✓ Need for emergency angio (<12 hours from admission)
- ✓ LVEF <30%
- ✓ Contraindications to statins, liver or renal failure

Patti G, et al. ***J Am Coll Cardiol. 2007;49:1272-1278***

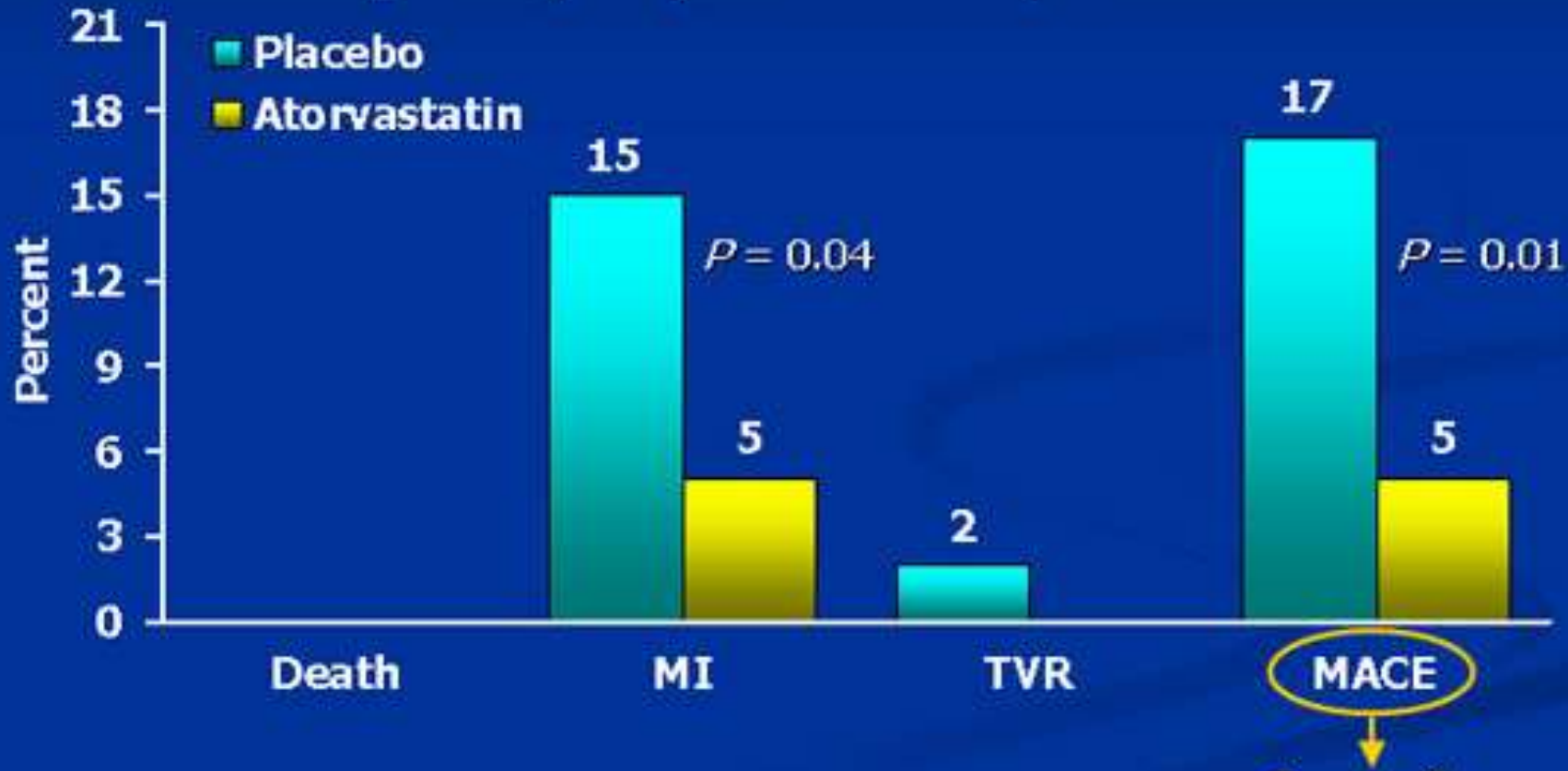
METHODS



Patti G, et al. *J Am Coll Cardiol. 2007;49:1272-1278*

ARMYDA–ACS
Results

Individual and combined outcome measures of the primary endpoint at 30 days



Patti G, et al. *J Am Coll Cardiol.* 2007;49:1272-1278.

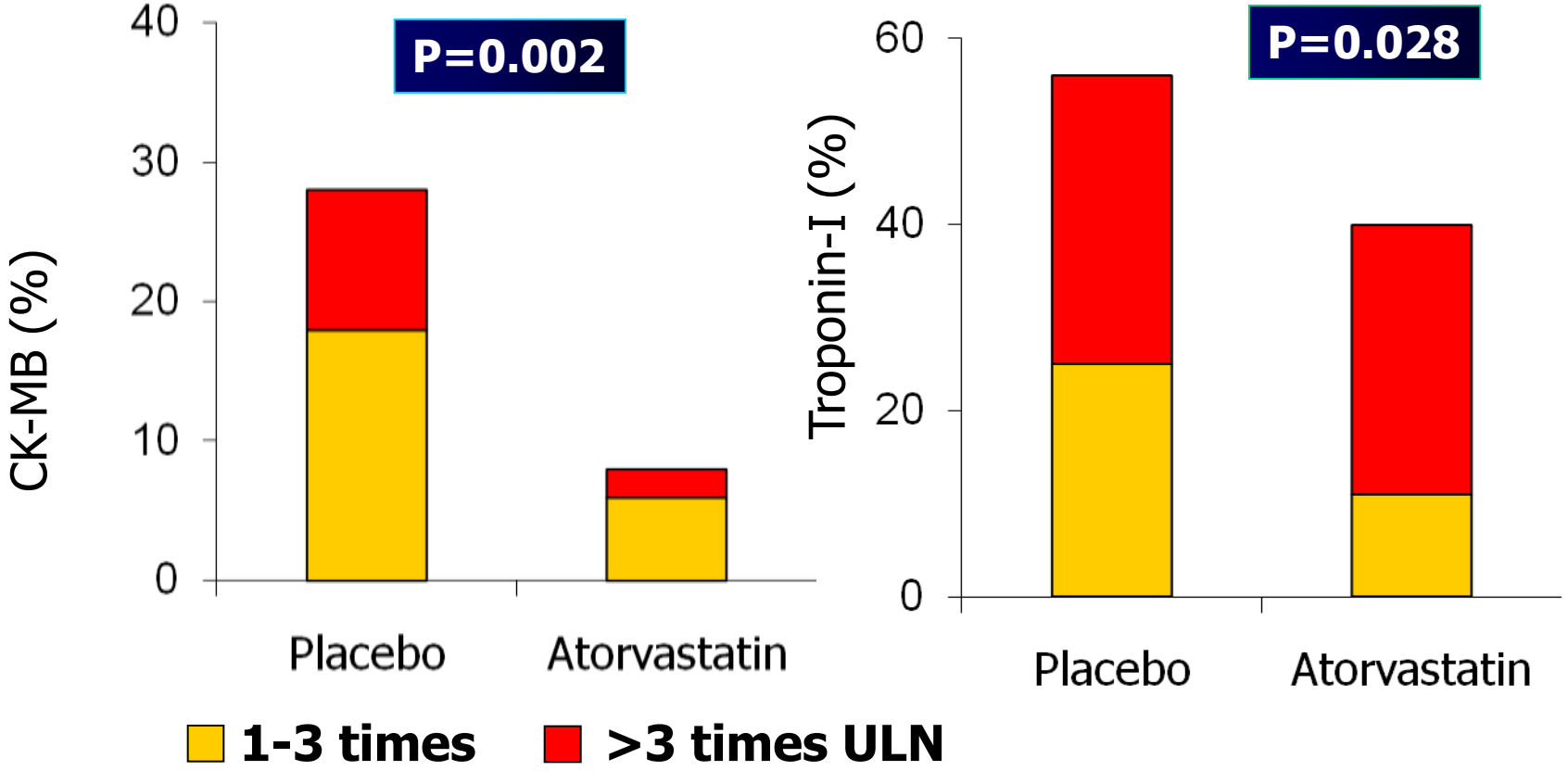
ARMYDA-ACS Trial:
Individual and Combined Outcome Measures of the Primary End Point at 30 days in the Atorvastatin and Placebo Groups

	Atorvastatin (N=86)	Placebo (N=85)	P
Death	-	-	
Myocardial infarction	4 (5%)	13 (15%)	0.04
Target vessel revascularization	-	1 (2%)	1
Total MACE	**4 (5%)**	**14(17%)**	**0.01**

Patti G, et al. ***J Am Coll Cardiol. 2007;49:1272-1278***

AMRYDA – ACS Secondary *End Points*

CK-MB or Troponin-I Increase



Patti G, et al. *J Am Coll Cardiol. 2007;49:1272-1278*

ARMYDA-ACS: CONCLUSIONS

❖ Short-term atorvastatin pretreatment prior to PCI reduce peri-procedural myocardial necrosis in patients with Unstable Angina and NSTEMI.

❖ 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 ACS under early invasive strategy

Patti G, et al. ***J Am Coll Cardiol. 2007;49:1272-1278***

Statins and Myocardial Proctection: Possible Mechanisms

- Effect Independent from cholesterol levels
- Plaque Stabilization (reduced microembolization)
- Improved Endothelial Function and Microcirculation
- Reduced Platelet Aggregation (?)
- Antinflammatory effect (reduced CRP)
- Direct Effcect on Myocardial Cells

Patti G, et al. ***J Am Coll Cardiol. 2007;49:1272-1278***

MUSTANG Study

Clinical Investigations

PREVENTION

Current Statin Usage for Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention: Multicenter Survey in Korea

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ABSTRACT

Background: Although high-dose statin therapy has been reported to improve outcomes in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI), patterns of statin usage for such patients have not been reported in real-world clinical practice.

Hypothesis: Some clinical factors would affect the pattern of statin usage in patients with ACS.

Methods: In the multicenter prospective registry, 3362 patients with ACS who underwent PCI were analyzed. High-dose statin treatment was defined as atorvastatin ≥40 mg or rosuvastatin ≥20 mg per day. The patterns of statin usage were investigated for 30 days after the index PCI.

Results: High-dose statins were administered prior to PCI to 13.7% and 19.6% of patients with unstable angina/non–ST-elevated myocardial infarction (UA/NSTEMI) and ST-elevated myocardial infarction (STEMI), respectively ($P < 0.001$). After PCI, 476 (14.2%) patients were maintained on high-dose statins, and 550 (16.4%) patients received no statins. Independent factors associated with high-dose statin usage after PCI were STEMI (odds ratio [OR]: 1.704, 95% confidence interval [CI]: 1.321–2.197, $P < 0.001$), high total cholesterol level (OR: 1.445, 95% CI: 1.136–1.837, $P = 0.003$), and current smoker (OR: 1.556, 95% CI: 1.206–2.008, $P < 0.011$). The absence of hypercholesterolemia was an independent factor determining the nonuse of statins (OR: 0.229, 95% CI: 0.148–0.353, $P < 0.001$).

Conclusions: In real-world clinical practice, high-dose statin treatment is being underused despite extensive evidence for patients with ACS undergoing PCI, particularly in UA/NSTEMI. Efforts are needed to ensure that clinical practice complies with evidence-based guidelines.

- **OBJECTIVES**

✓ Examination of statin treatment patterns in acute coronary syndrome(ACS) undergoing percutaneous coronary intervention(PCI)

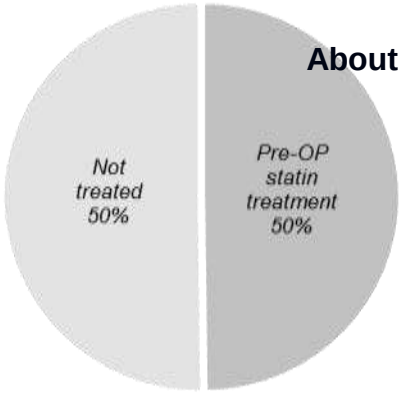
- **POPULATION and DATA COLLECTION**

✓ 3362 patients registered and followed for 30 days after enrollment from 48 hospitals

✓ diagnosed with unstable angina,(UA) non-ST-elevated MI(NSTEMI), or ST-elevated MI(STEMI)

✓ High dose: atorvastatin ≥40 mg or rosuvastatin ≥20 mg per day

83.6% of ACS undertreated with no or low statin



About a half were never treated with statin prior to PCI

high statin treatment: average 16.4%

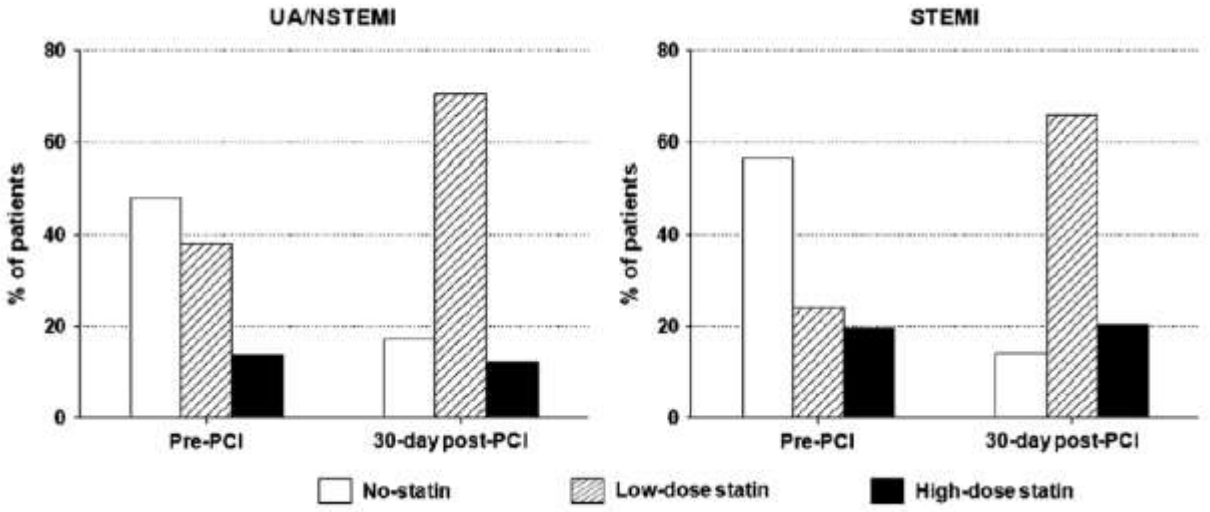
1)pre-OP: 16.7% (UA/NSTEMI: 13.7%, STEMI: 19.6%)

2)post-OP: 16.2% (UA/NSTEMI: 12.2%, STEMI: 20.1%)

associated factors w/high dose

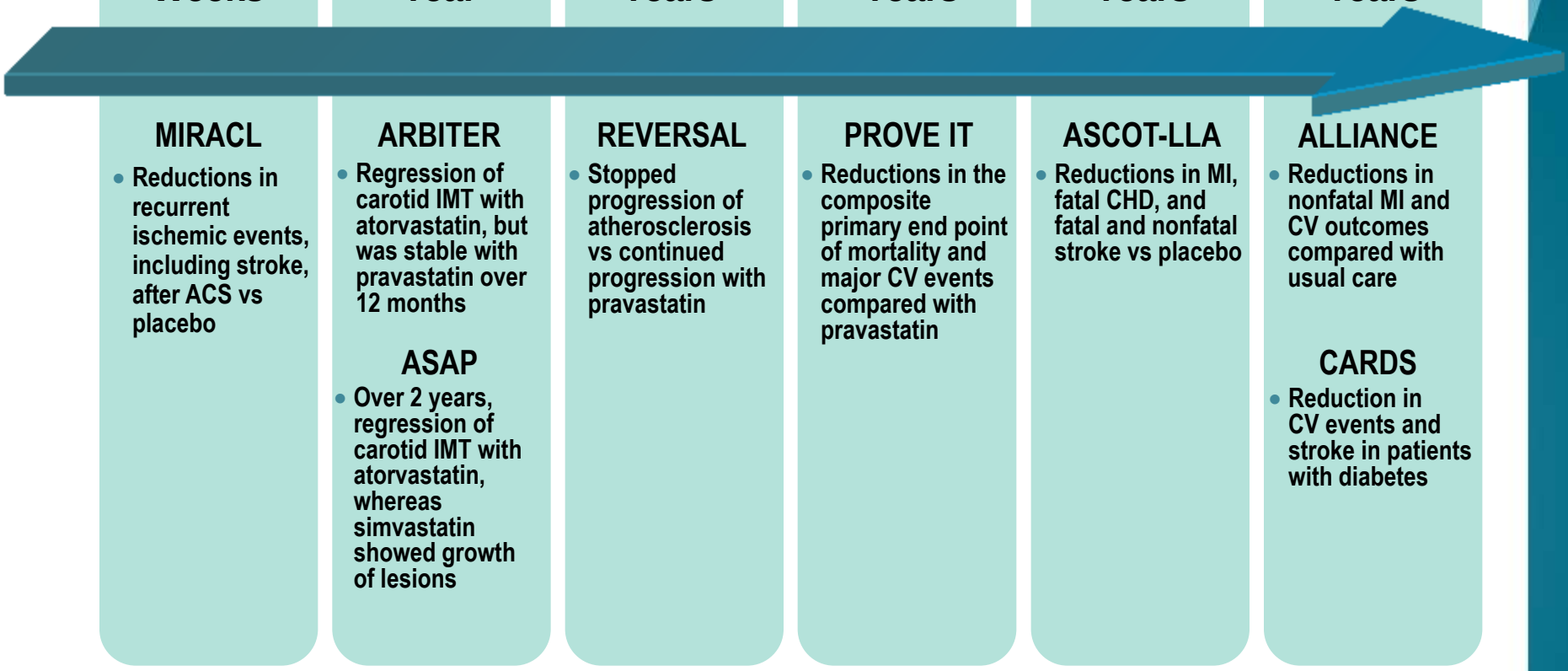
1)pre-OP: STEMI, current smoker

2)post-OP: STEMI, current smoker, hypercholesterolemia



Statin dosage used in pre-PCI and post-PCI period in patients with UA/NSTEMI and STEMI. Abbreviations: NSTEMI, non–ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; UA, unstable angina

Atorvastatin Shows Early and Rapid Effects in Hard and Surrogate End Point Trials



Schwartz GG et al for the Myocardial Ischemia Reduction With Aggressive Cholesterol Lowering (MIRACL) Study Investigators. *JAMA*. 2001;285:1711-1718. Taylor AJ et al. *Circulation*. 2002;106:2055-2060. Smilde TJ et al. *Lancet*. 2001;357:577-581. Nissen SE et al for the REVERSAL Investigators. *JAMA*. 2004;291:1071-1080. Cannon CP et al for the Pravastatin or Atorvastatin Evaluation and Infection Therapy—Thrombolysis in Myocardial Infarction 22 Investigators. *N Engl J Med*. 2004;350:1495-1504. Sever PS et al for the ASCOT Investigators. *Lancet*. 2003;361:1149-1158. Koren MJ et al on behalf of the ALLIANCE Investigators. *J Am Coll Cardiol*. 2004;44:1772-1779. Colhoun HM et al on behalf of the CARDS Investigators. *Lancet*. 2004;364:685-696.

Conclusions

- High recurrence rate in 30 days after ACS event.

→ urgent aggressive intervention and early statin benefits

- In MIRACL (ATV 80 vs placebo) and PROVE IT (ATV 80 vs PVS 40), significant reductions in the primary end point *observed at 4 months*
- In ARMYDA-ACS, even *a short-term atorvastatin pretreatment* prior to PCI may improve peri-procedural myonecrosis in patients with Unstable Angina and NSTEMI.
- Front-loaded Intensive statin therapy is safe and results in earlier time to benefit than standard-dose statin therapy.
- Early reduction in clinical events may be related more to pleiotropic effects (eg, greater reduction in inflammation).