Pre-procedural Statin Treatment in the Patients undergoing PCI or CABG

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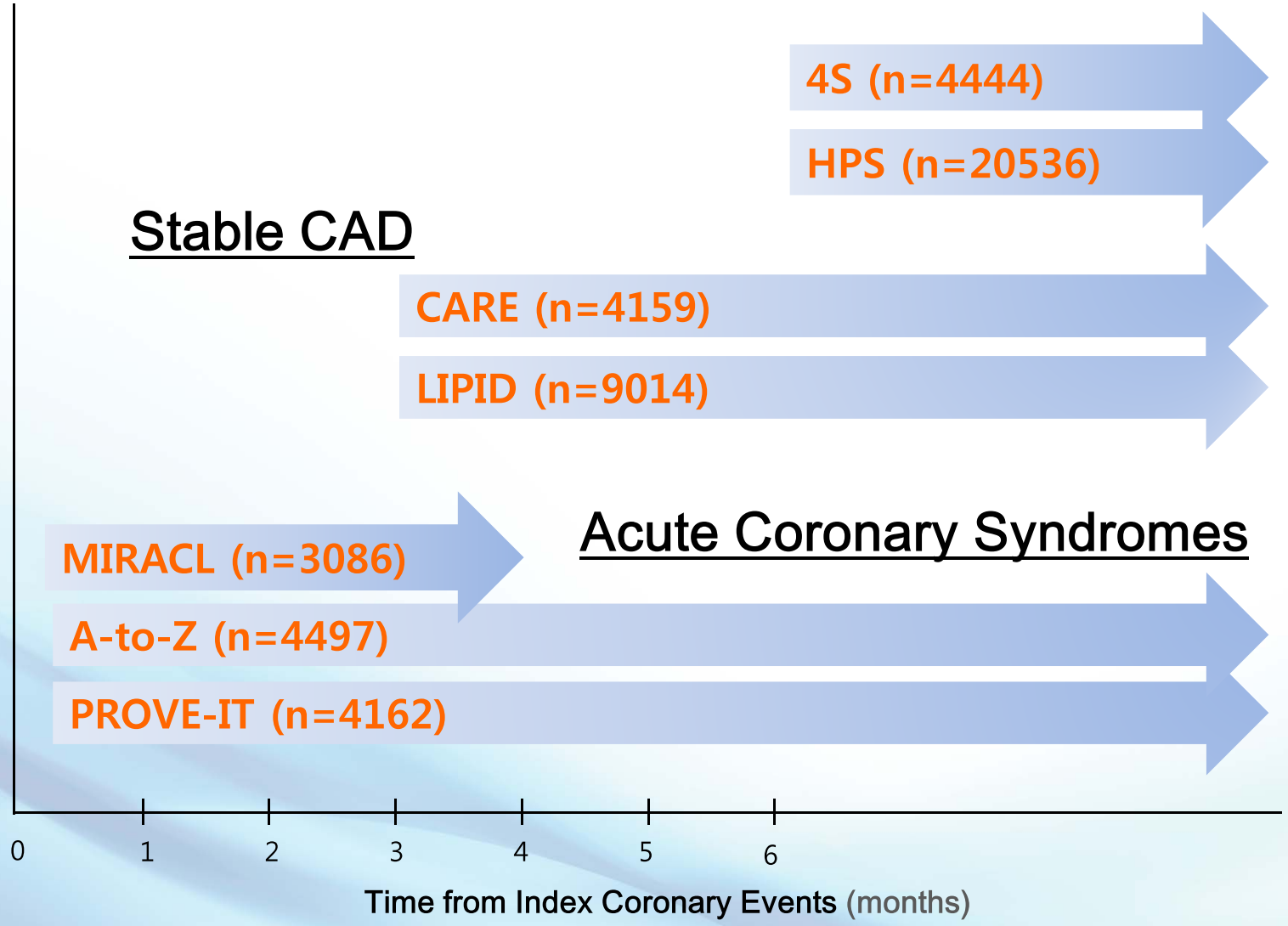
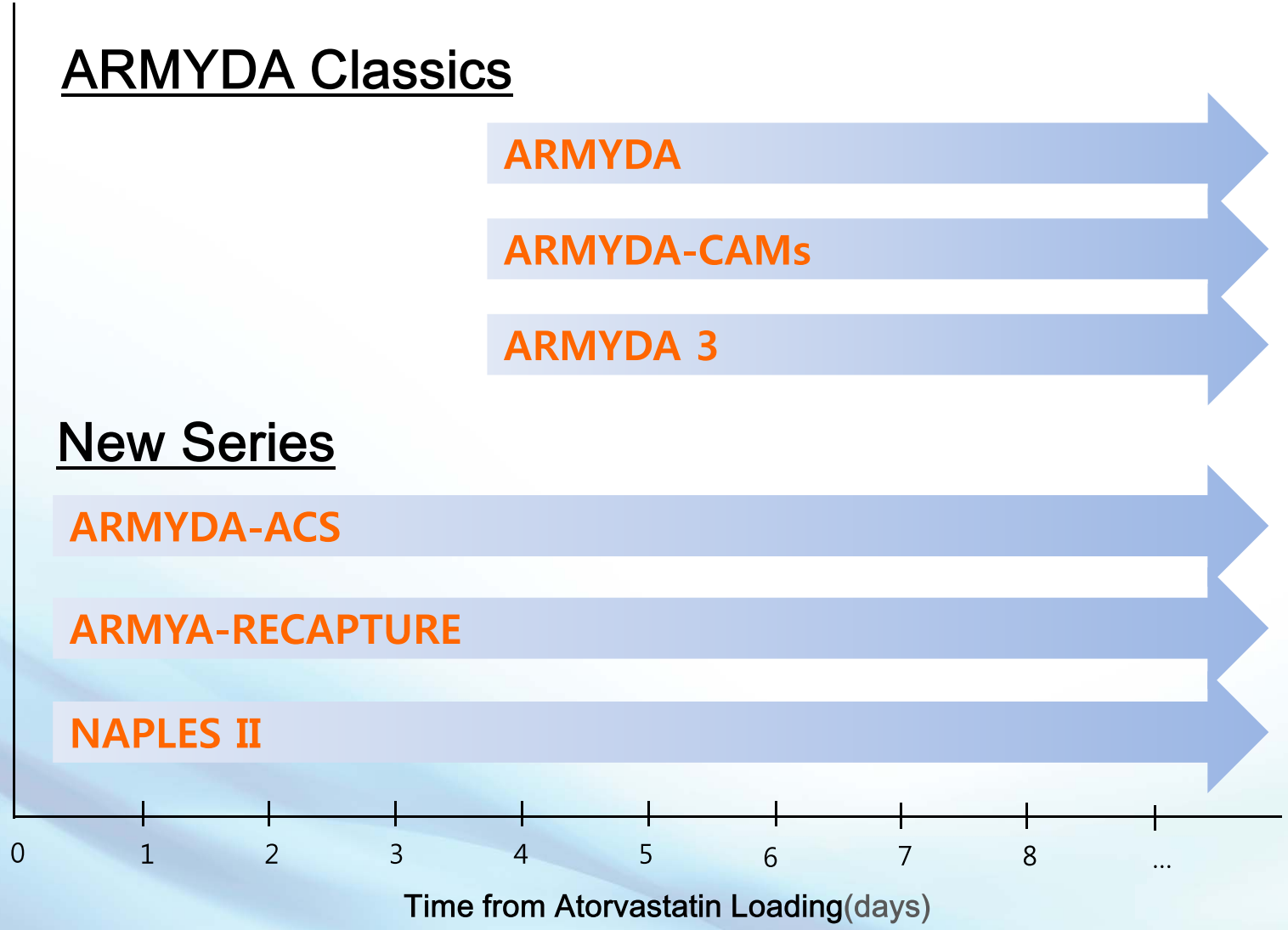
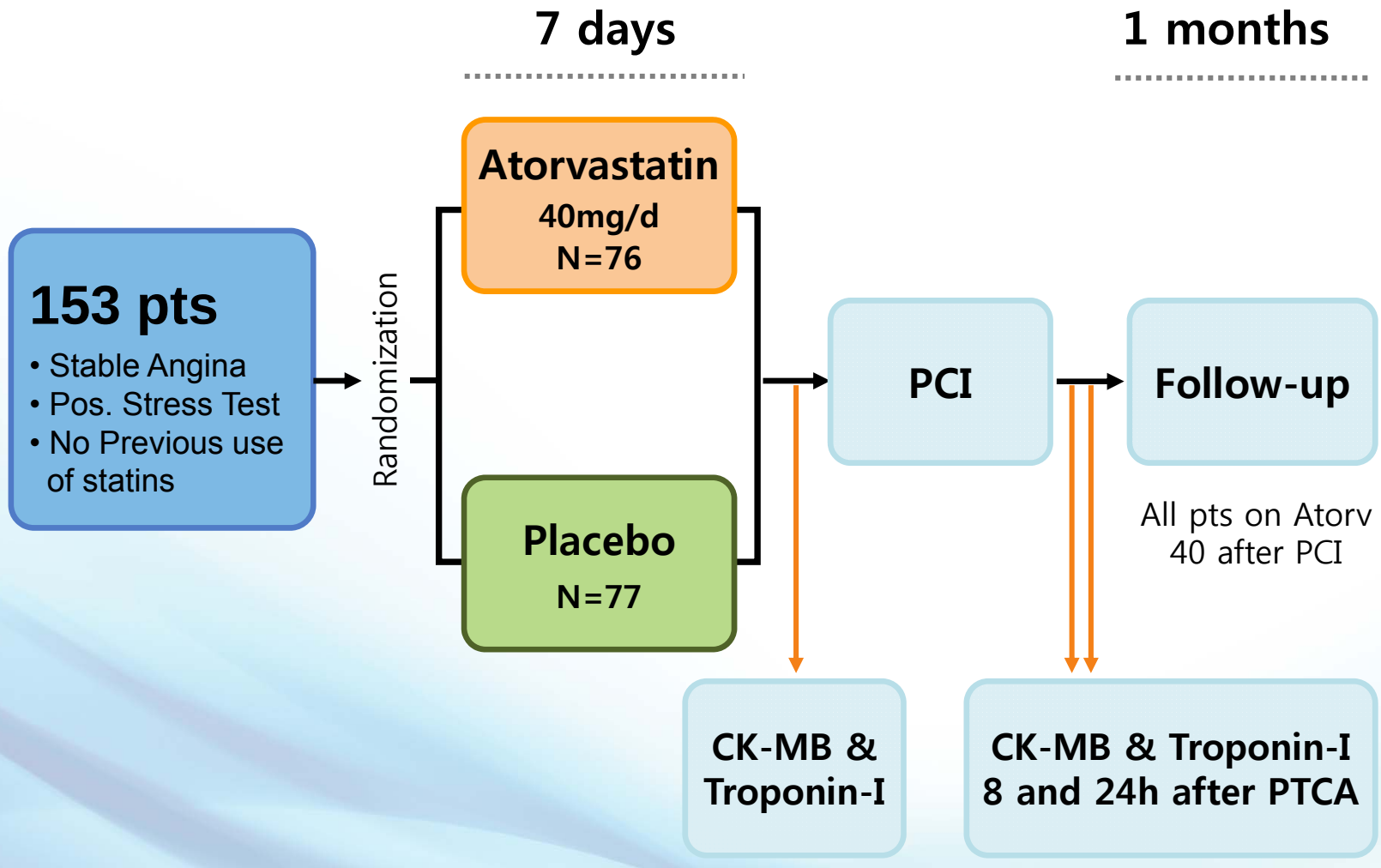
Randomized Controlled Studies of Lipid-Lowering Therapy



Latest Trials on ACS....



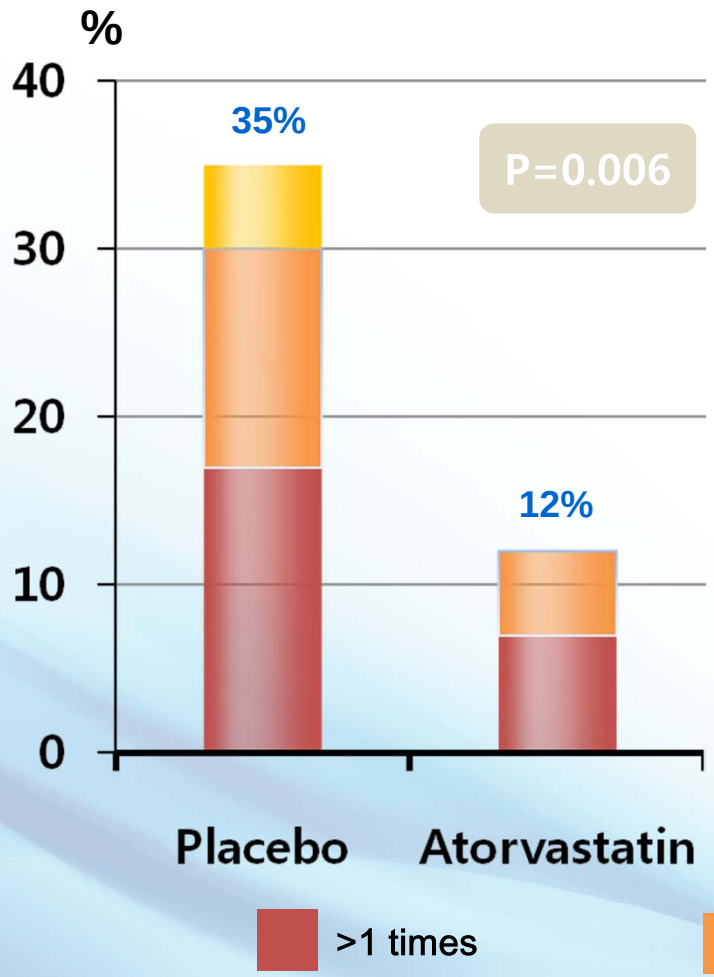
The Atorvastatin for Reduction of Myocardial Damage during Angioplasty(ARMYDA)



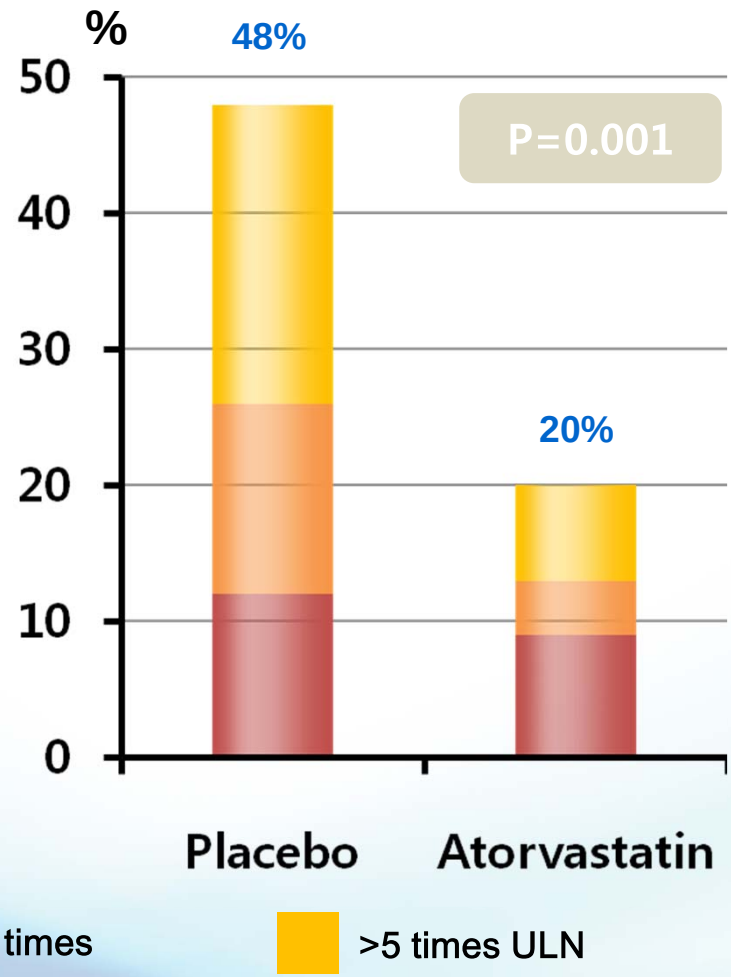
Pasceri V,et al. Circulation 2004;110:674-678

ARMYDA Study Results

CK-MB Increase



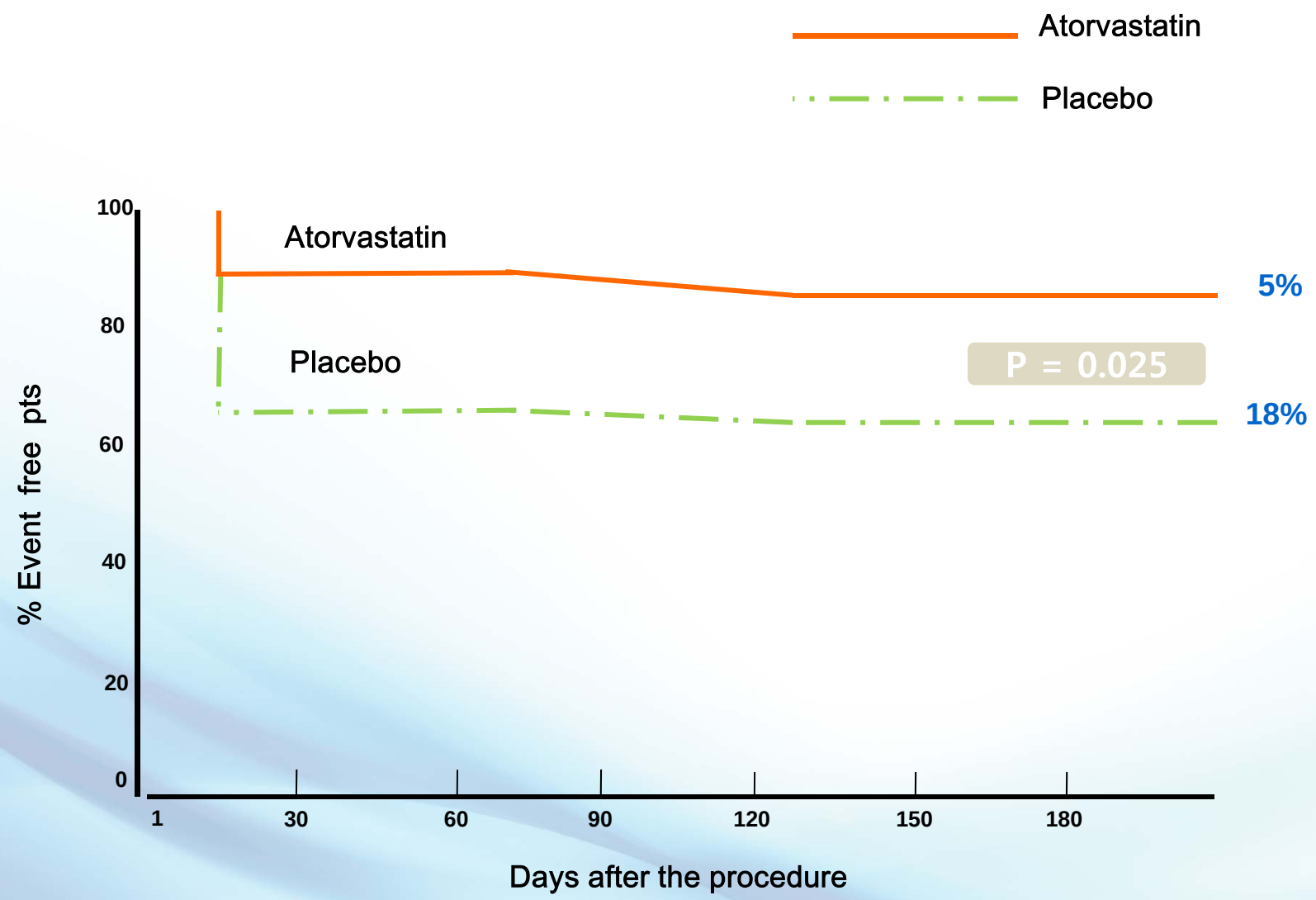
Troponin-I Increase



>1 times 2-5 times >5 times ULN

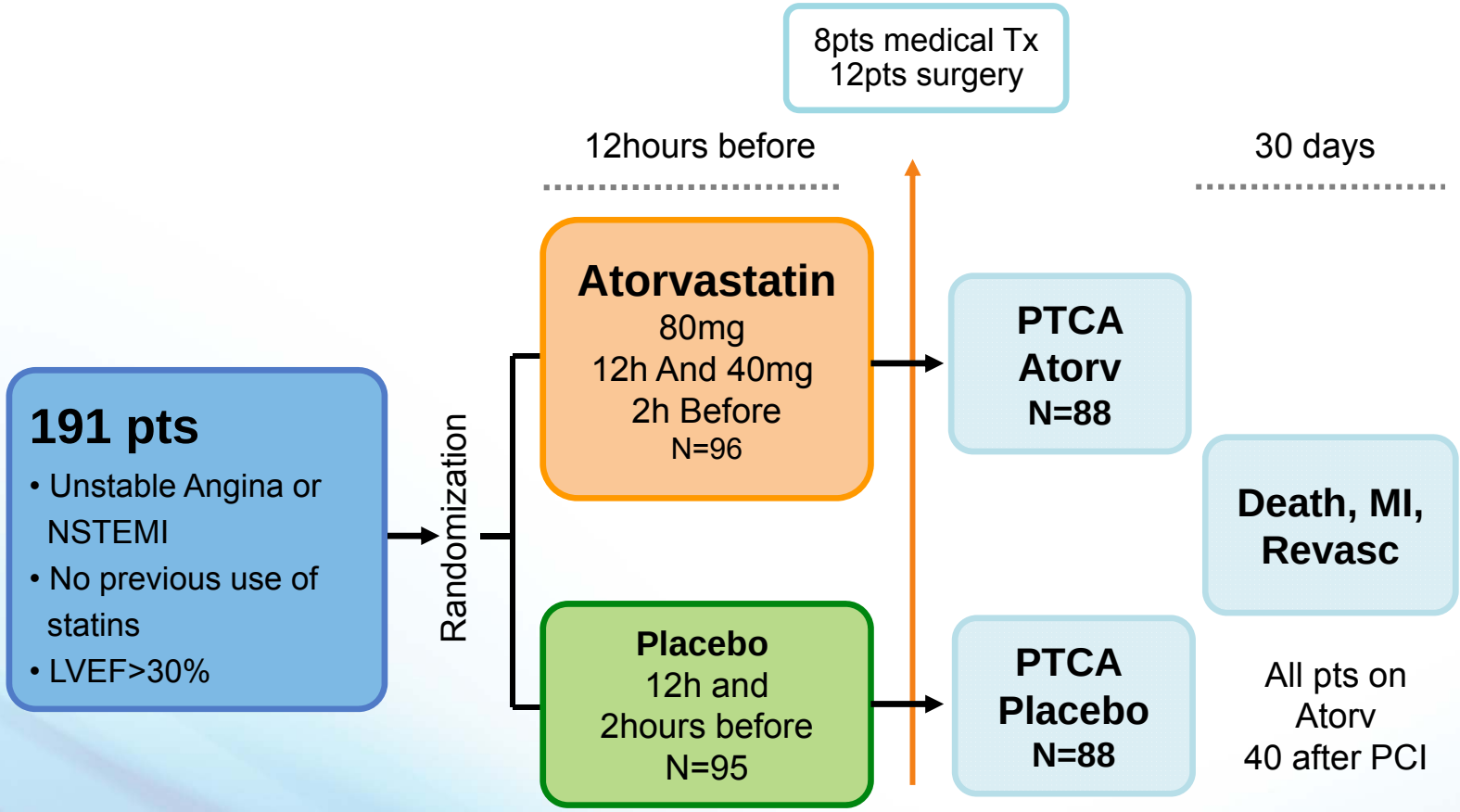
Pasceri V,et al. Circulation 2004;110:674-678

ARMYDA Result :MACE at 1 months



Pasceri V,et al. Circulation 2004;110:674-678

ARMYDA-ACS Study Design

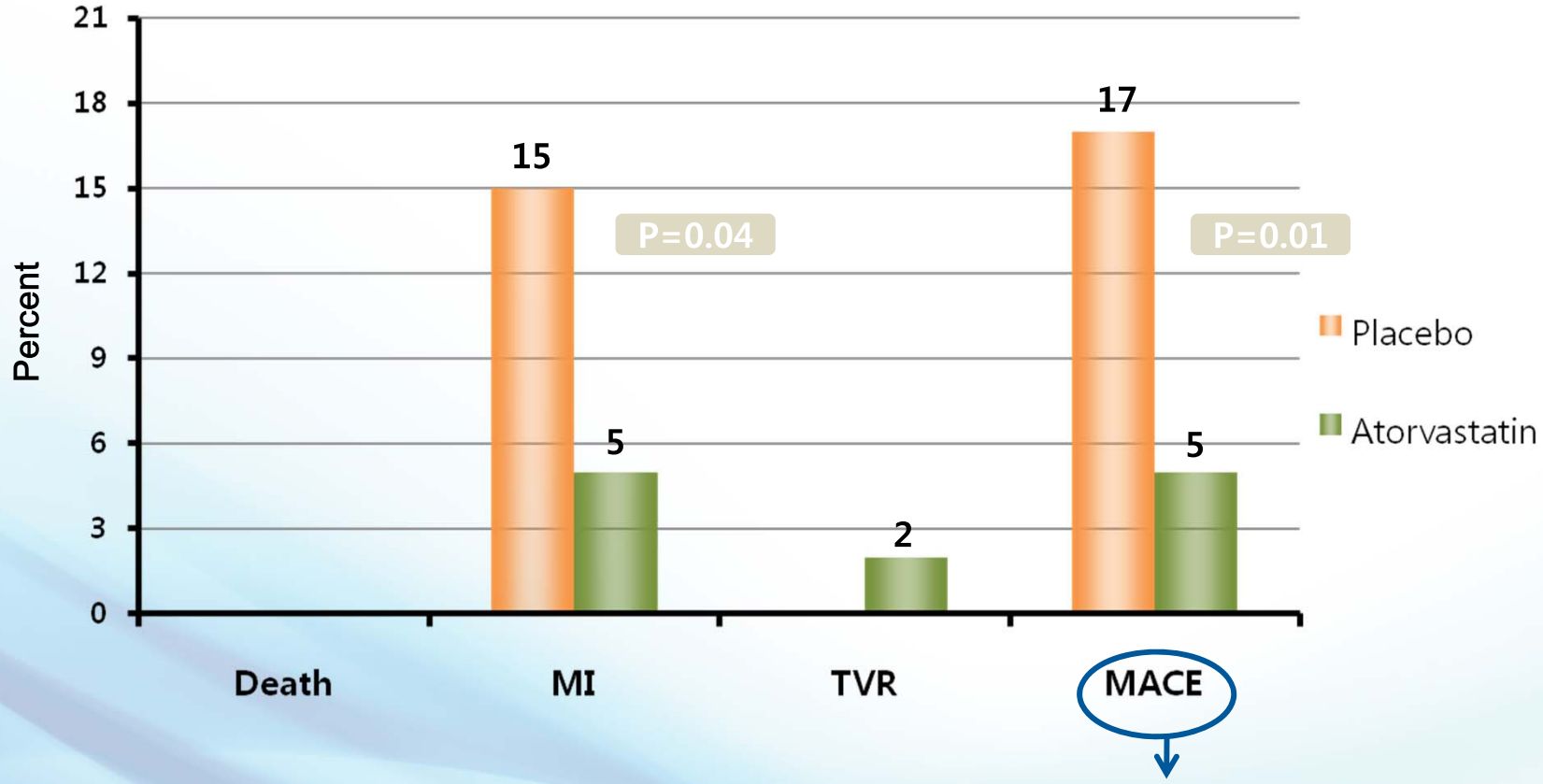


- Inclusion Criteria: Patients with NSTEMI or Unstable Angina treated with early invasive strategy (angio at 12-24hours)
- Exlusion Criteria: Previous or current statin therapy; Need for emergency angio (<12 hours from admission); LVEF <30%; Controindications to statins, liver or renal failure

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

ARMYDA-ACS Results

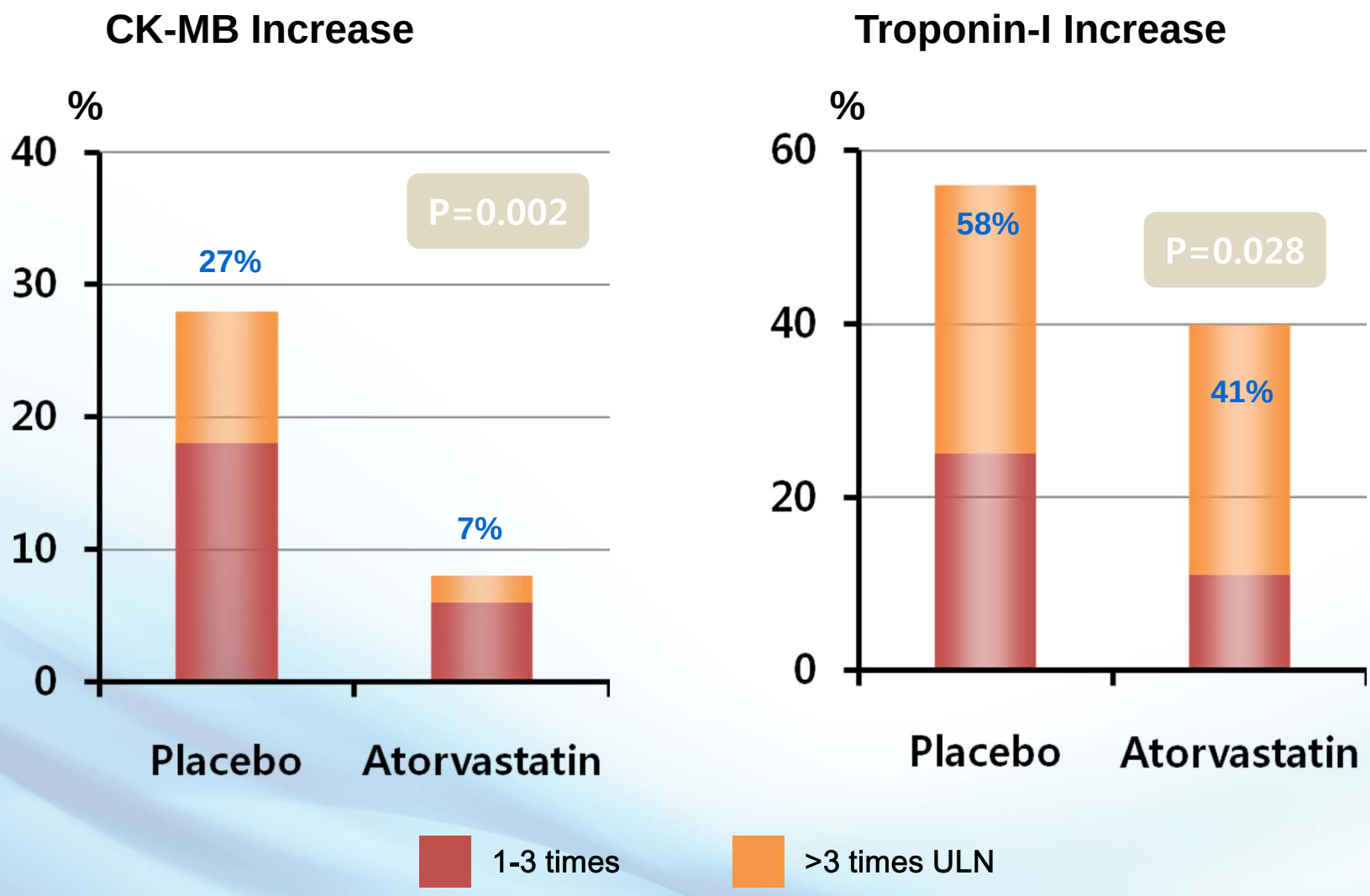
Individual and combined outcome measures of the primary end point at 30 days



Composit primary end point
88% RR at MV analysis

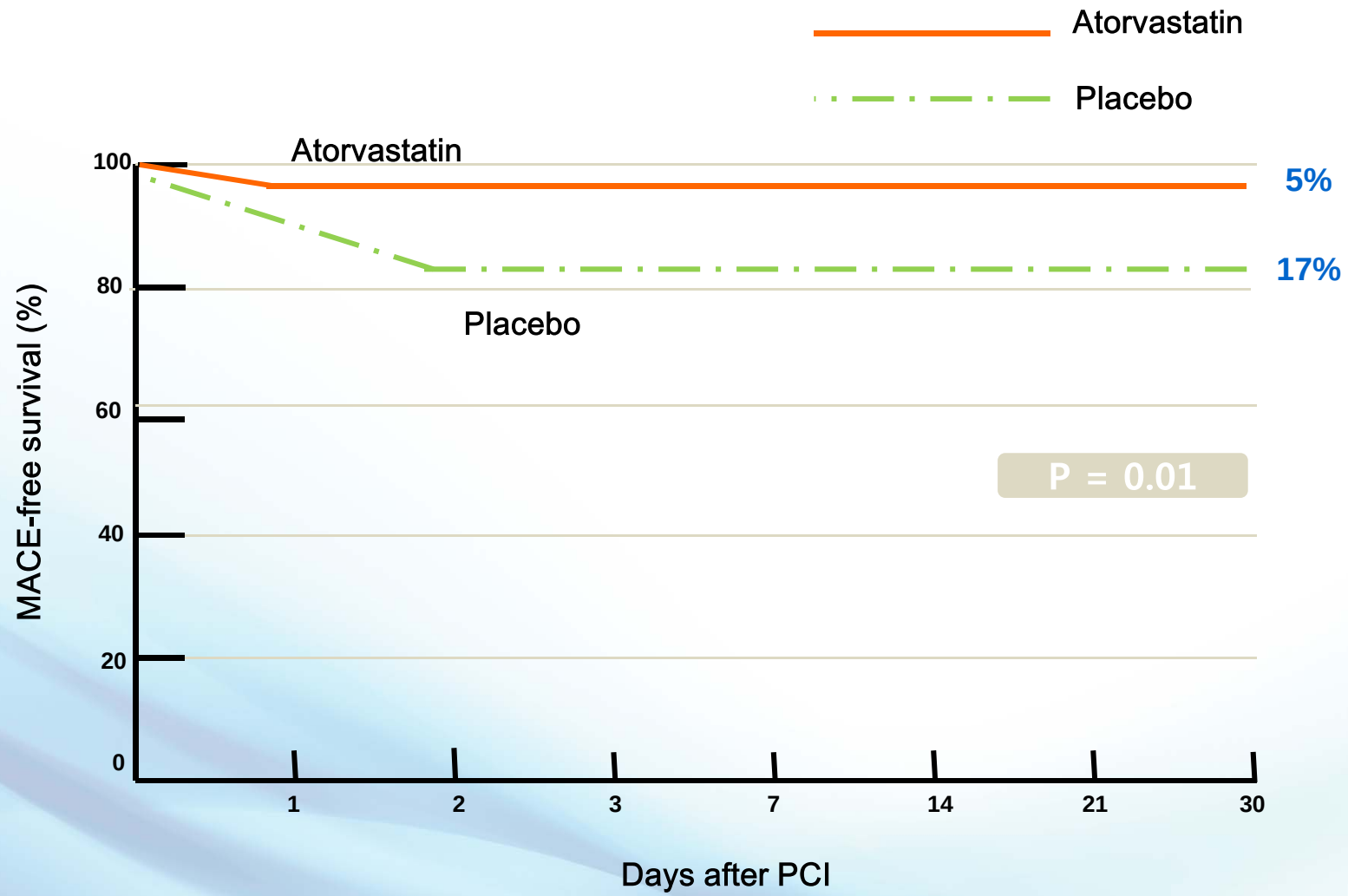
Patti G, et al. J Am coll Cardiol 2007;49:1272-1278

AMRYDA-ACS Result : Secondary End Points



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

AMRYDA-ACS : Survival Curves



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

ARMYDA-ACS Results

- 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.**

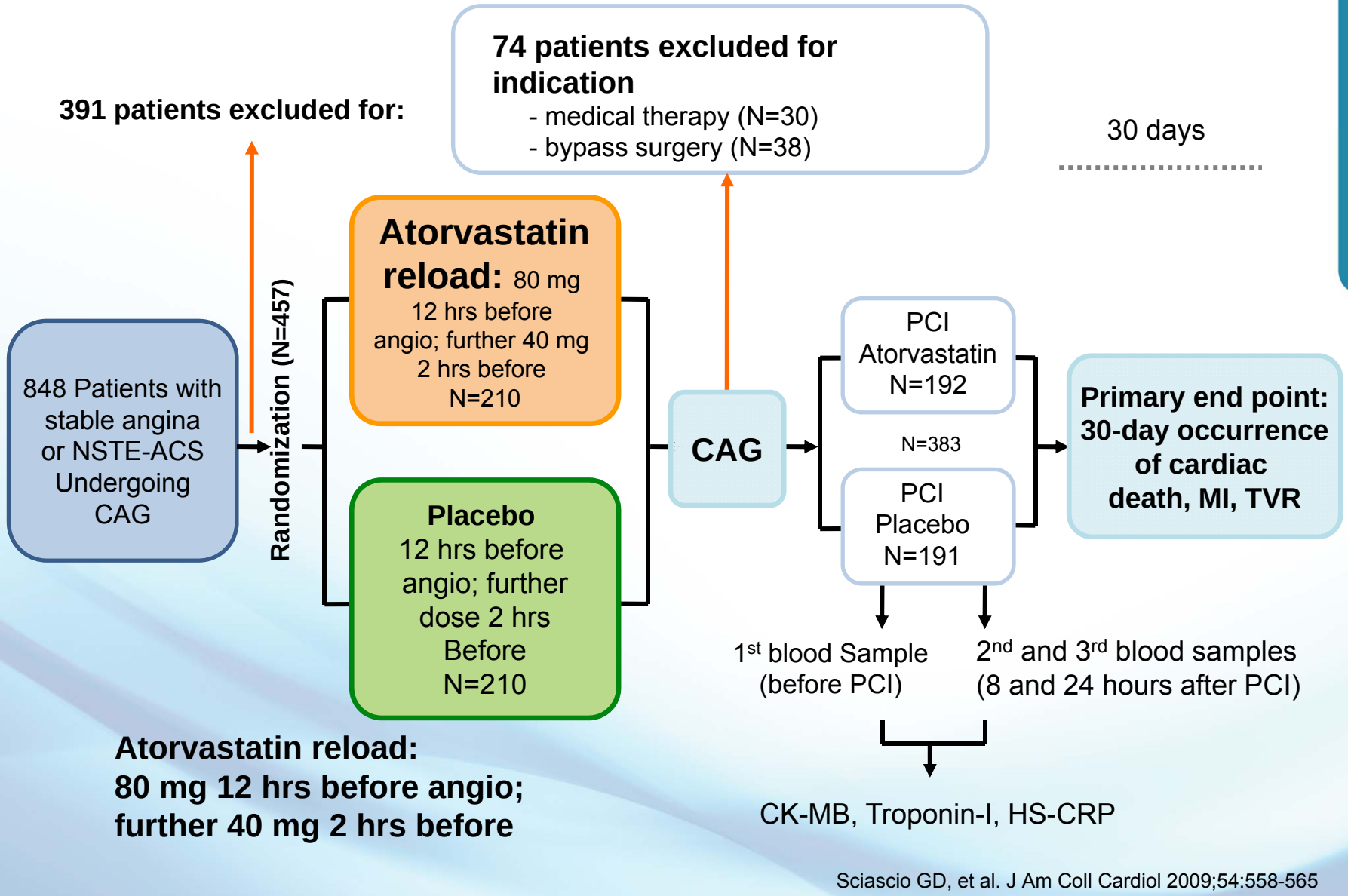
- This benefit is mostly driven by a reduction of peri-procedural MI (70% risk reduction)

- Lipid-independent **pleiotropic actions of atorvastatin may explain such effect.**

- Statins contribute to plaque stability and/or regression through a number of lipid-dependent and -independent (pleiotropic) mechanisms (e.g. ↓ inflammation).

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

ARMYDA-RECAPTURE: Study design



Sciascio GD, et al. J Am Coll Cardiol 2009;54:558-565

ARMYDA-RECAPTURE

Inclusion criteria:

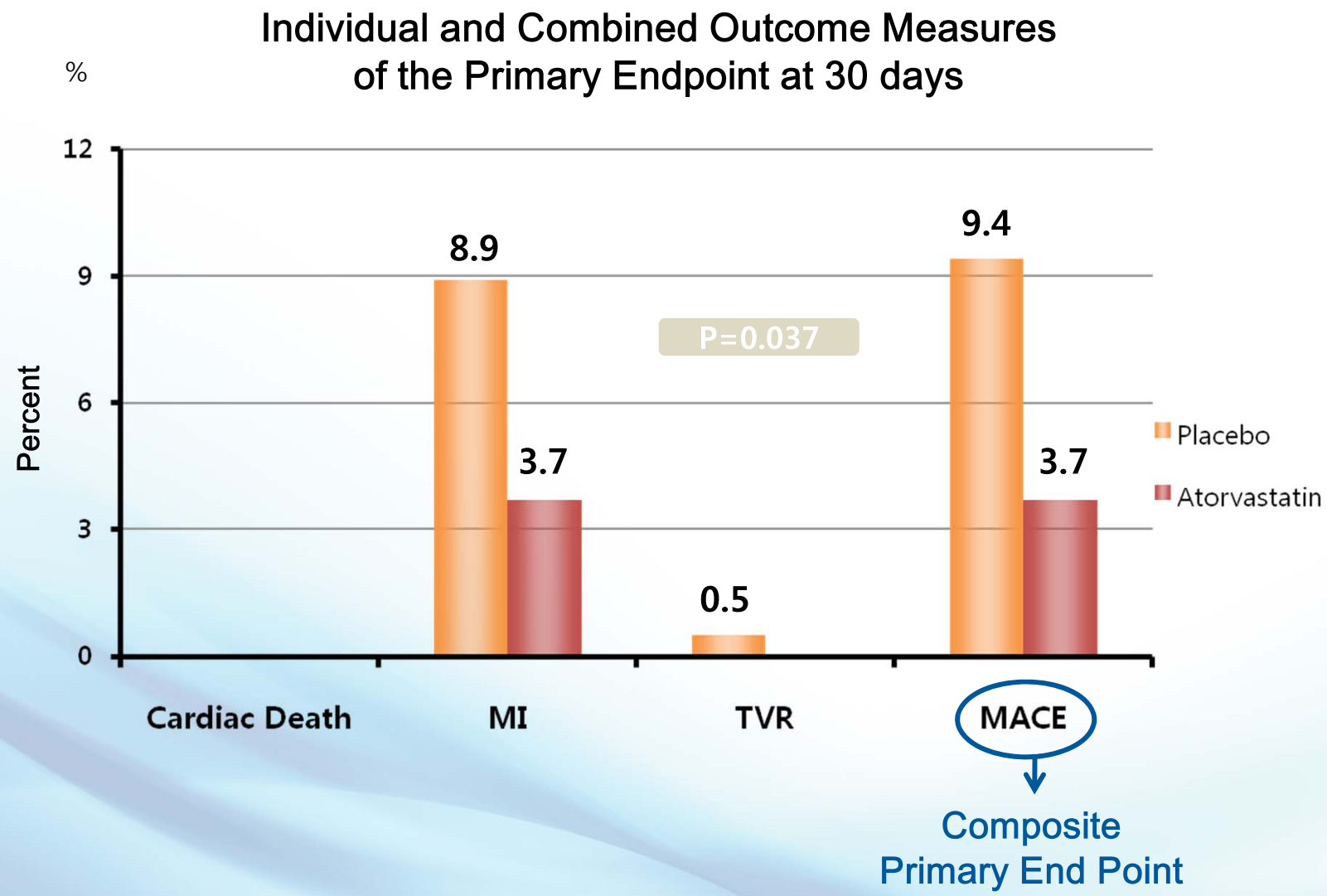
Patients on chronic (>30 days) statin therapy and stable angina or NSTE-ACS undergoing coronary angiography

Exclusion criteria:

- ST- segment elevation acute myocardial infarction
- Non ST-segment elevation acute coronary syndrome with high risk features warranting emergency coronary angiography (<2 hours)
- Any increase in liver enzymes (AST/ALT)
- Left ventricular ejection fraction <30%
- Severe renal failure with creatinine >3 mg/dl
- History of liver or muscle disease

Sciascio GD, et al. J Am Coll Cardiol 2009;54:558-565

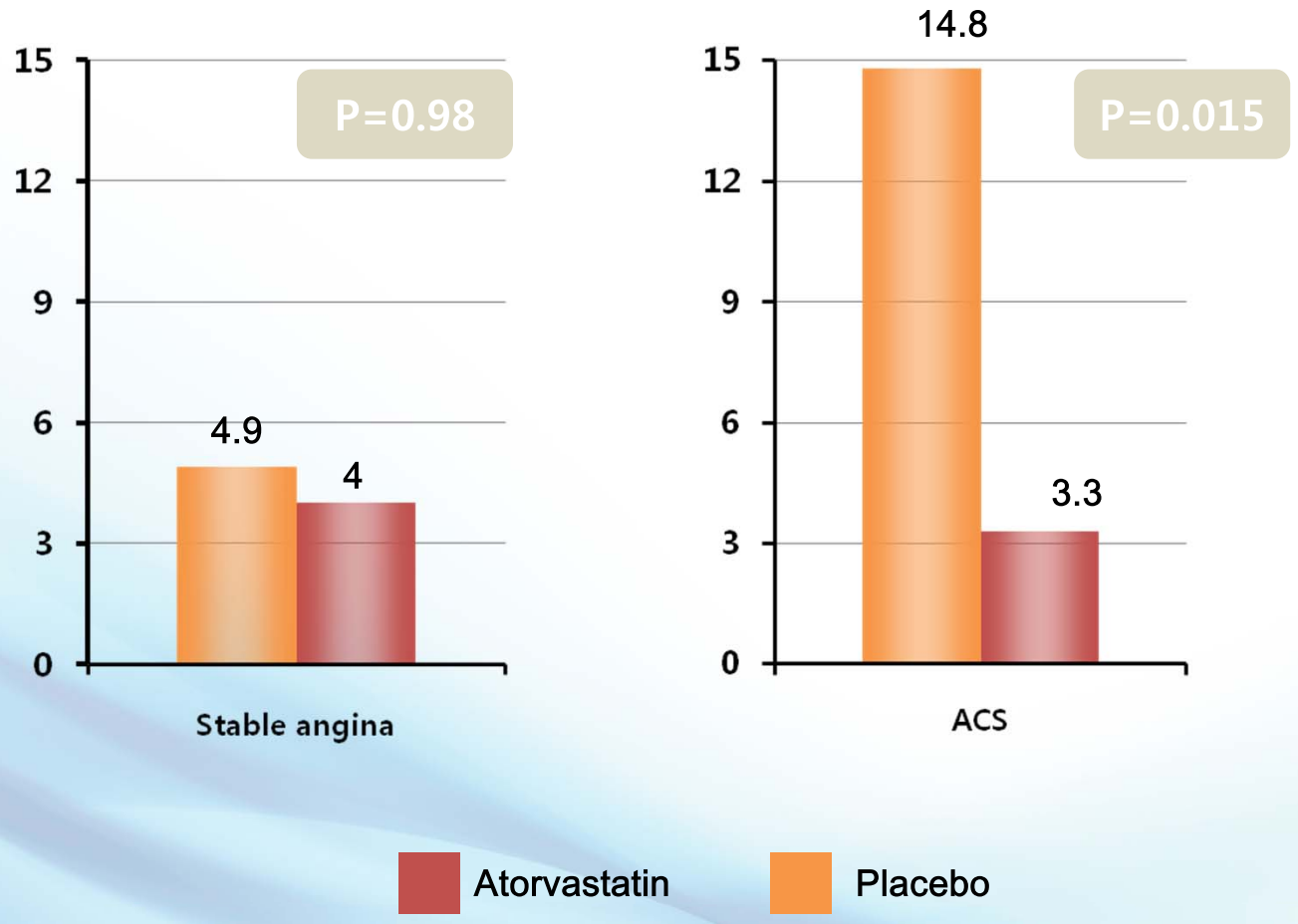
ARMYDA-RECAPTURE : RESULTS



Sciascio GD, et al. J Am Coll Cardiol 2009;54:558-565

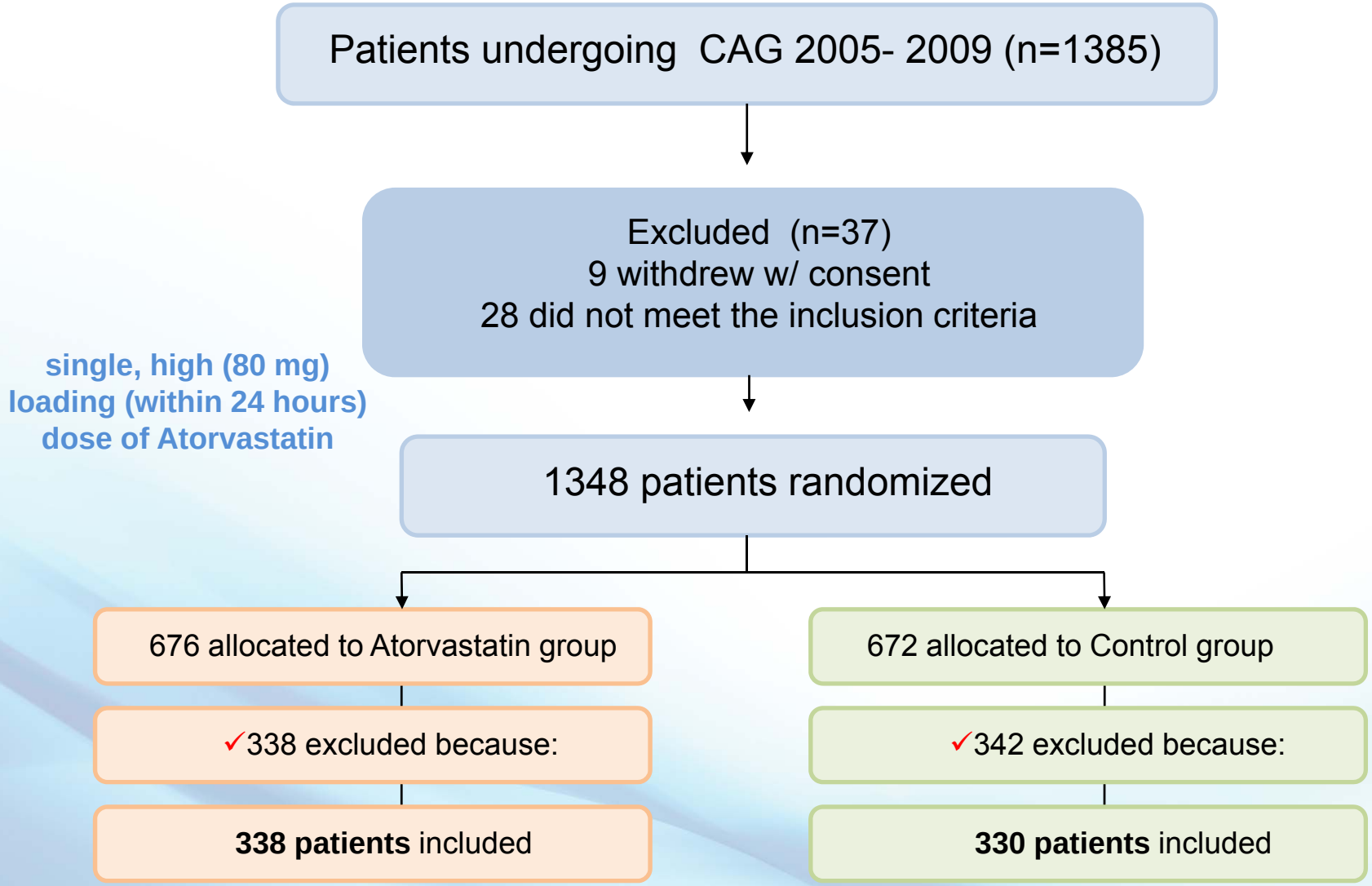
ARMYDA-RECAPTURE Secondary endpoints

MACE according to clinical presentation (stable angina or ACS)



Sciascio GD, et al. J Am Coll Cardiol 2009;54:558-565

NAPLES II : Study design



Briguori C, et al. J Am Coll Cardiol 2009;54

In-hospital Outcome

	Atorvastatin Group (N=338)	Control Group (N=330)	P value
Death	1 (0.3%)	0	NS
MI	33 (9.8%)	52 (15.8%)	0.014
Q-wave MI	1 (0.3%)	0	NS
Non Q-wave MI	32 (9.5%)	52 (15.8%)	0.014
Unplanned revasc	0	0	-
Stent thrombosis	2 (0.58%)	1 (0.30%)	0.57
Composite end point	34 (10%)	52 (15.7%)	0.029

- A single, high (80 mg) loading (within 24 hours) dose of atorvastatin reduces the incidence of periprocedural non Q wave MI in elective PCI.
- This cardioprotective effect seems to be more pronounced in patients with high CRP level at baseline.

Briguori C, et al. J Am Coll Cardiol 2009;54

Atorvastatin for Reduction of Myocardial Damage during Angioplasty (ARMYDA)	ARMYDA-ACS
Statin-naïve 한 153명의 chronic stable angina	Statin-naive한 171명의 stable angina 또는 NSTE-ACS 환자를.
Myocardial Infarction (MI)의 발생율 (MI는 CK-MB가 정상상한치(ULN: Uppler Limit of Normal)의 2배 이상 증가하는 경우로 정의되었다.)	PCI 시술 후 30일 동안 발생하는 주요 심혈관계 사건 (MACE: Death, Myocardial Infarction, Target Vessel Revascularization (bypass surgery, repeat PCI))
● Primary Endpoint: ❿ PCI시술 후 MI는 리피토군에서 5%, 위약군에서 18% 발생 (p=0.025). **● Secondary Endpoint:** ❿ CK-MB가 정상상한치(UNL)가 2배 이상 증가하는 환자의 비율은 리피토군에서 12%였던 반면, 위약군은 35% (p=0.001). ❿ 리피토군은 위약군에 비해 troponin-I와 myoglobin이 상승한 환자의 비율이 낮음. ✓Troponin-I: 위약군 (48%) vs. 리피토군 (20%) (p=0.0004) ✓Myoglobin: 위약군 (51%) vs. 리피토군 (22%) (p=0.0005) ❿ 리피토와 위약군 두 군에서 myocardial injury marker의 최고치는 유사했으며, 모두 정상 범위안에 들어감 ❿ 하지만 시술 후 리피토군의 myocardial injury marker 수치는 위약군에 비해 현저히 낮음 ✓CK-MB: 리피토군 (2.9±3ng/ml) vs. 위약군 (7.5±1.8ng/mL) (p=0.007) ✓Troponin I: 리피토군 (0.09±0.2ng/mL) vs. 위약군 (0.47±1.3ng/mL) (p=0.0008) ✓Myoglobin: 리피토군 (58±36ng/mL) vs. 위약군 (81±49ng/mL) (p=0.0002)	**● Primary Endpoint:** ❿ MACE는 리피토군의 5%, 위약군의 17% 발생 (p=0.01). ❿ MI는 리피토군의 5%, 위약군의 15%에서 발생 (p=0.04) **● Secondary Endpoint:** ❿ Myocardial infarction marker가 정상상한치를 넘는 환자군 ✓ CK-MB: 리피토군 (7%) vs. 위약군 (27%) (p=0.001) ✓ Troponin-I: 리피토군 (41%) vs. 위약군 (58%) (p=0.039) ✓ Myoglobin: 리피토군 (45%) vs. 위약군 (42%) (p=0.81) - 시술 전, 후 CRP 수치: 리피토군 (63±114%) vs. 위약군 (147±274%) (p=0.01)

ARMYDA-RECAPTURE	Novel Approaches for Preventing or Limiting Event Study (NAPLES) II
기존의 statin치료를 받은 총352명의 stable angina 또는 NSTE-ACS (Unstable Angina + NSTEIMI) 환자	Statin naive한 668명
PCI 시술 30일 동안 발생하는 주요 심혈관계 사건 (MACE: cardiac death, myocardial infarction 또는 unplanned revascularization)	PCI 시술 30일 이후 발생하는 per-procedural MI damage
▪Primary Endpoint: ▪ MACE는 리피토군의 3.4%, 위약군의 9.1%에서 발생 (p=0.045) ✓ Stable Angina환자 중 리피토를 복용한 환자에서 MACE는 감소하는 경향, 위약군에 비해 통계적으로 유의한 차이를 보이지 못함 ✓ 또한 NSTE-ACS환자에서 리피토를 복용한 2.4%의 환자, 그리고 위약군의 13.8%에서 MACE가 발생 (p=0.016). **▪Secondary Endpoint:** ▪ 시술 후 CK-MB와 Troponin-I 수치의 상승은 위약군 보다 리피토군에서 적게 발생했다. ✓ CK-MB: 리피토군(13%) vs. 위약군(23%) (p=0.023) ✓ Troponin-I: 리피토군 (36%) vs. 위약군 (47%) (p=0.032) ▪ CRP의 상승은 위약군 보다 리피토군에서 적게 발생하였다. ✓ CRP: 리피토군 (2.1±6.7mg/dL) vs. 위약군 (3.0±9.5 mg/dL) (p=0.12)	▪ Peri-procedural MI 발생: 리피토군 (9.5%) vs. 위약군 (15.7%) (p =0.027) ▪ Cardiac Troponin-I가 정상상한치보다 3배 이상 증가: 리피토군 (25.9%) vs. 위약군 (39.7%) (p <0.001)

Statin Therapy Before PCI : Summary

- Post-ACS period is associated with a high rate of serious recurrent events in 30 days after event. It shows an urgent need for more aggressive intervention and early statin benefits during the early post-ACS period.
- In ACS, early benefits become more important to choose statin with proven evidence (CV outcome) for recurrent events prevention post ACS.
- In ARMYDA, Recapture findings may support a strategy of *routine loading and reloading with high dose Atorvastatin* early before intervention.
- In ARMYDA-ACS & RECAPTURE Study, even *a short-term Atorvastatin pretreatment* prior to PCI may improve outcome in patients with Stable Angina and NSTE-ACS.
- A *single, high (80 mg) loading* (within 24 hours) dose of Atorvastatin reduces the incidence of periprocedural non Q wave MI in elective PCI.

Statin Therapy Before PCI : Conclusion

- *A short-term Atorvastatin pretreatment* prior to PCI may improve outcome in patients with Unstable Angina and NSTEMI.
- Reloading with high dose Atorvastatin is associated with improved clinical outcome in patients on chronic statin therapy undergoing PCI.
- Early reduction in clinical events may be related more to pleiotropic effects (eg, greater reduction in inflammation).
- Intensive statin therapy is safe and results in earlier time to benefit than standard-dose statin therapy.

Pre-Procedural Statin Therapy : A Meta-Analysis of Randomized Trials

First Author/Trial (Ref. #)	Year	Patients, n	Age, yrs	DM, %	Patient Population	Follow-Up Duration
Yun et al. (18)	2009	225/220	64/63	33/30	Urgent PCI for ACS	30 days
Veselka et al. (19)	2009	100/100	68/64	26/25	Elective PCI	1 day
NAPLES II (20)	2009	338/330	64/65	39/37	Elective PCI	1 day
Jia et al. (21)	2009	113/115	65/66	19/22	Urgent PCI for ACS*	1 day
ARMYDA-RECAPTURE (22)	2009	192/191	66/66	37/35	Elective PCI or urgent PCI for ACS†	30 days
ARMYDA-ACS (23)	2007	86/85	64/67	29/33	Urgent PCI for ACS	30 days
Kinoshita et al. (24)	2007	21/21	66/67	NR‡	Elective PCI	6 months
Bozbas et al. (25)	2007	29/34	57/62	17/21	Elective PCI	1 day
ARMYDA (12)	2004	76/77	64/65	27/19	Elective PCI	30 days
Briguori et al. (26)	2004	226/225	63/62	25/19	Elective PCI	1 day
Ji et al. (27)	2009	71/69	65/66	38/38	Elective off-pump CABG	13 days
Berkan et al. (28)	2009	23/23	65/68	35/39	Elective CABG	30 days
Mannacio et al. (29)	2008	100/100	61/59	0/0	Elective CABG	23 days
Song et al. (30)	2008	62/62	62/64	47/52	Elective off-pump CABG	30 days
Tamayo et al. (31)	2008	22/22	68/68	27/41	Elective CABG	2.5 days
ARMYDA-3 (32)	2006	101/99	66/67	32/42	Elective CABG	30 days
Chello et al. (33)	2006	20/20	66/64	0/0	Elective CABG	7 days
Christenson et al. (34)	1999	40/37	63/64	23/24	Elective CABG	12 days
DECREASE-III (13)	2009	250/247	66/66	22/17	Elective vascular surgery	30 days
DECREASE-IV (35)	2009	265/268	65/66	12/9	Elective noncardiac surgery	30 days
Durazzo et al. (36)	2004	50/50	66/68	18/16	Elective vascular surgery	6 months

Winchester DE, et al. J Am Coll Cardiol 2010

Pre-Procedural Statin Therapy : A Meta-Analysis of Randomized Trials

First Author/Trial (Ref. #)	Trial Primary Outcome	Generation of Treatment Assignment	Blinded Outcome Assessment	Completeness of Follow-Up (%)
Yun et al. (18)	Post-procedure MI	ND	ND	100/100
Veselka et al. (19)	Post-procedure MI	ND	No	100/100
NAPLES II (20)	Post-procedure MI	Computer-generated	ND	100/100
Jia et al. (21)	Post-procedure MI	ND	ND	100/100
ARMYDA–RECAPTURE (22)	Adverse events	Random number	Double blind*	100/100
ARMYDA–ACS (23)	Adverse events	Random number	Yes	100/100
Kinoshita et al. (24)	Post-procedure MI	ND	ND	95/100
Bozbas et al. (25)	Post-procedure MI	ND	ND	100/100
ARMYDA (12)	Post-procedure MI	ND	Double blind*	100/100
Briguori et al. (26)	Q-wave MI	Computer-generated	No	100/100
Ji et al. (27)	Atrial fibrillation	Computer-generated	Yes	100/100
Berkan et al. (28)	Inflammatory markers	ND	Double blind*	100/100
Mannacio et al. (29)	Post-operative MI	Computer-generated	Double blind*†	100/100
Song et al. (30)	Atrial fibrillation	Randomization table	ND	100/100
Tamayo et al. (31)	Inflammatory markers	ND	ND	100/100
ARMYDA-3 (32)	Atrial fibrillation	Computer generated	Yes	100/100
Chello et al. (33)	Inflammatory markers	ND	Double blind*†	100/100
Christenson et al. (34)	Thrombocytosis	ND	ND	100/100
DECREASE-III (13)	Myocardial ischemia	Computer-generated	ND†	ND
DECREASE-IV (35)	Adverse events	Computer-generated	No	ND
Durazzo et al. (36)	Adverse events	Computer-generated	Yes	100/100

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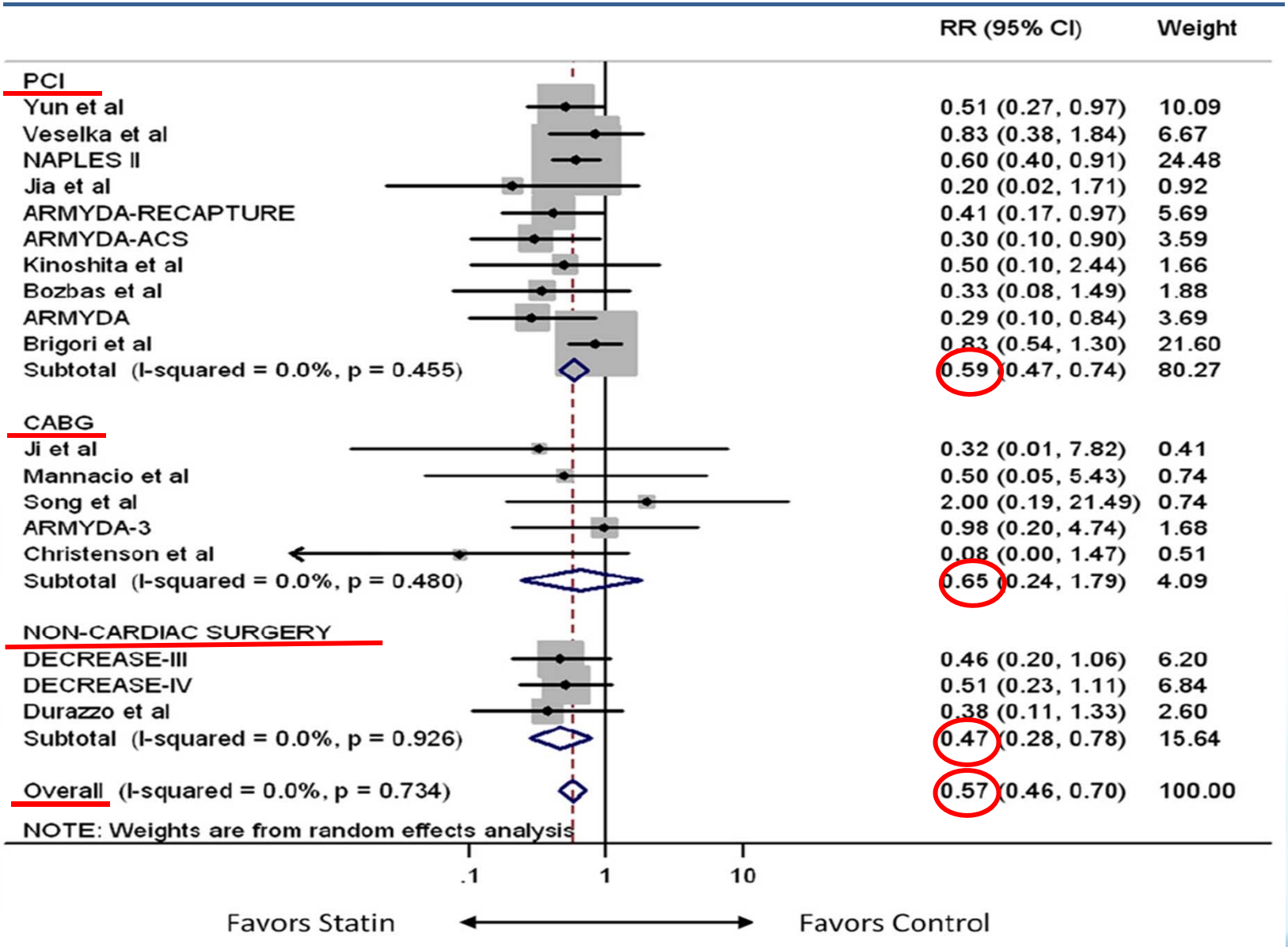
Post-Procedural Myocardial Infarction



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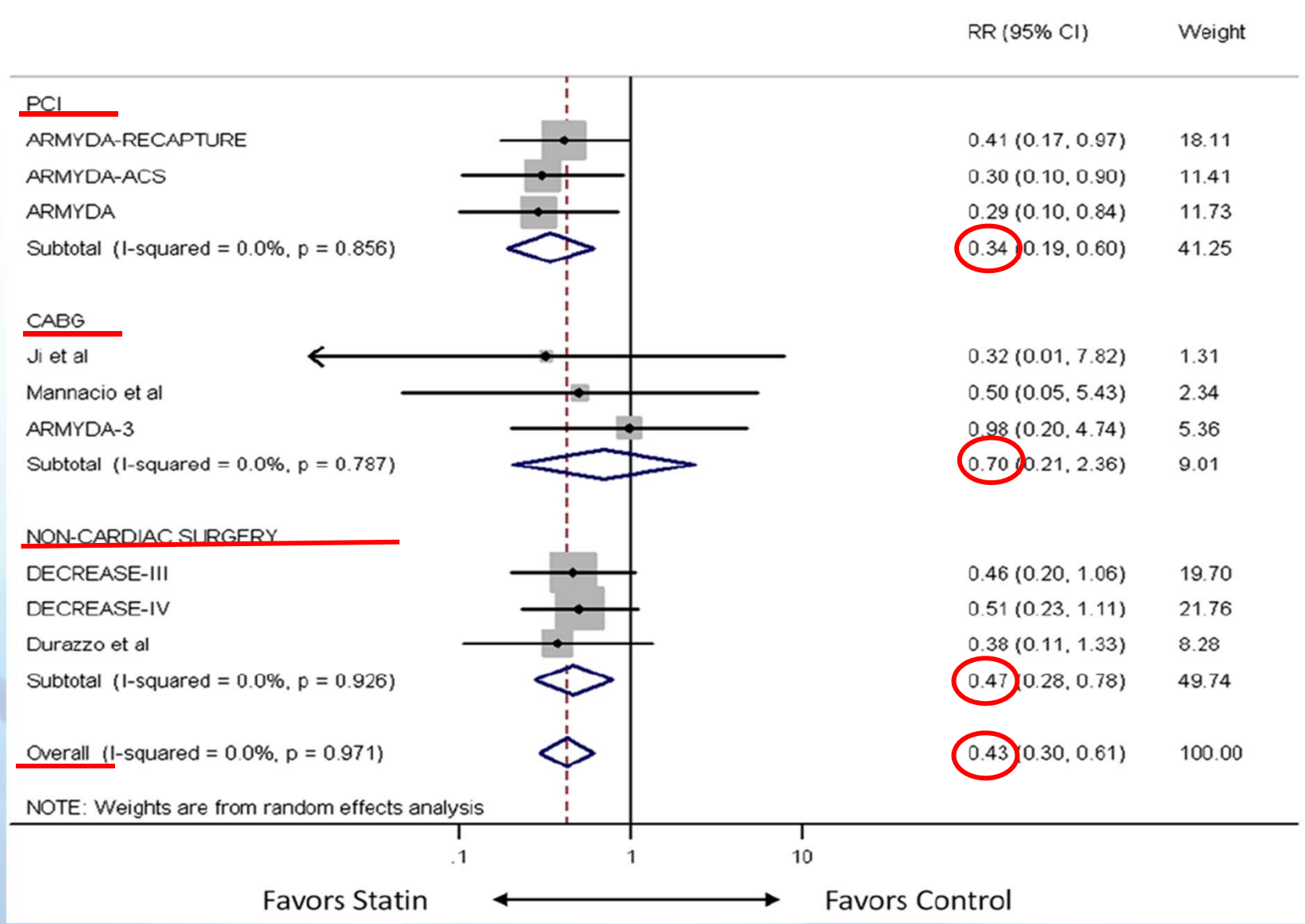
Post-Procedural Myocardial Infarction in Placebo-Controlled Trials



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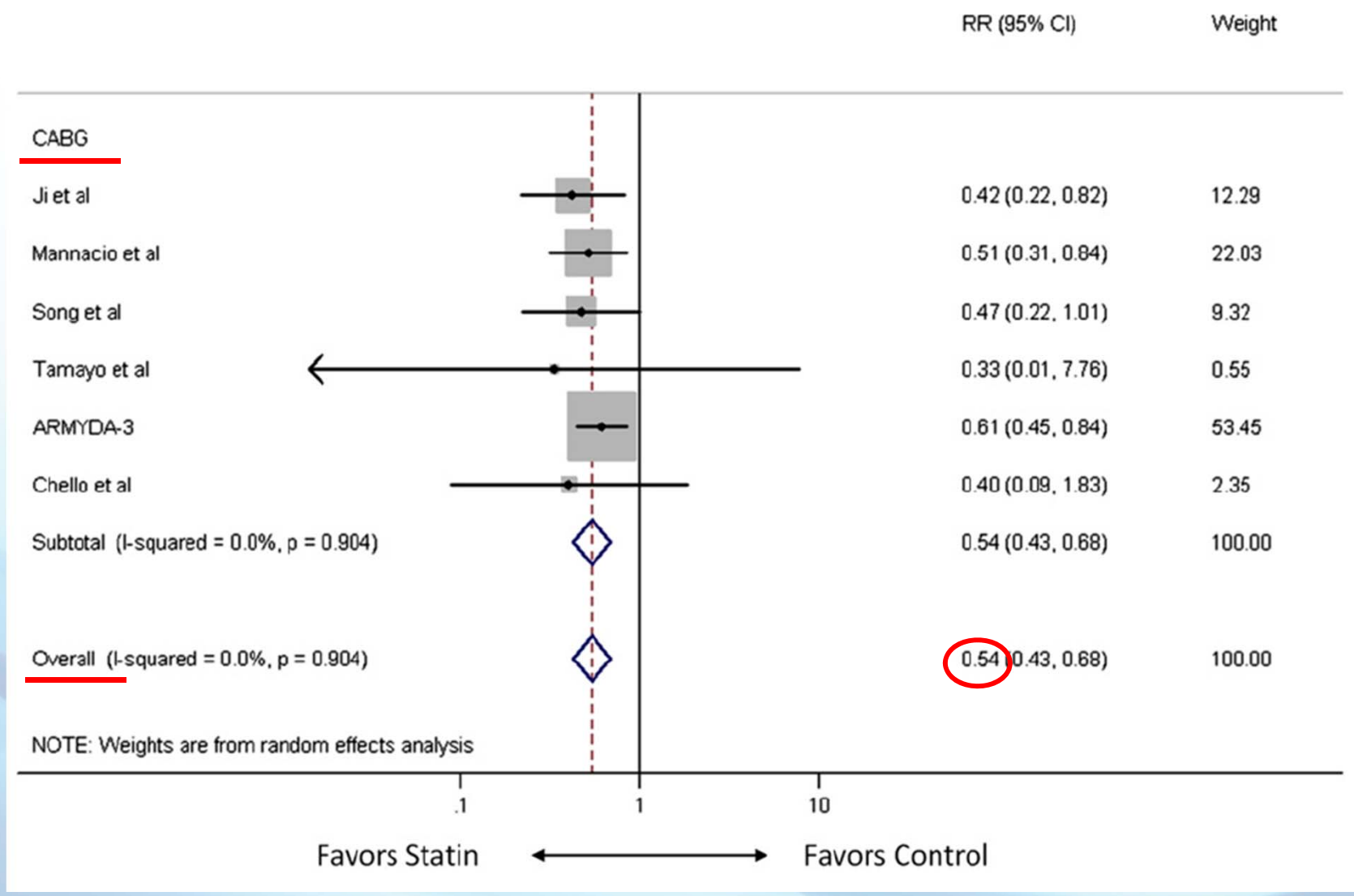
Post-Procedural Atrial Fibrillation



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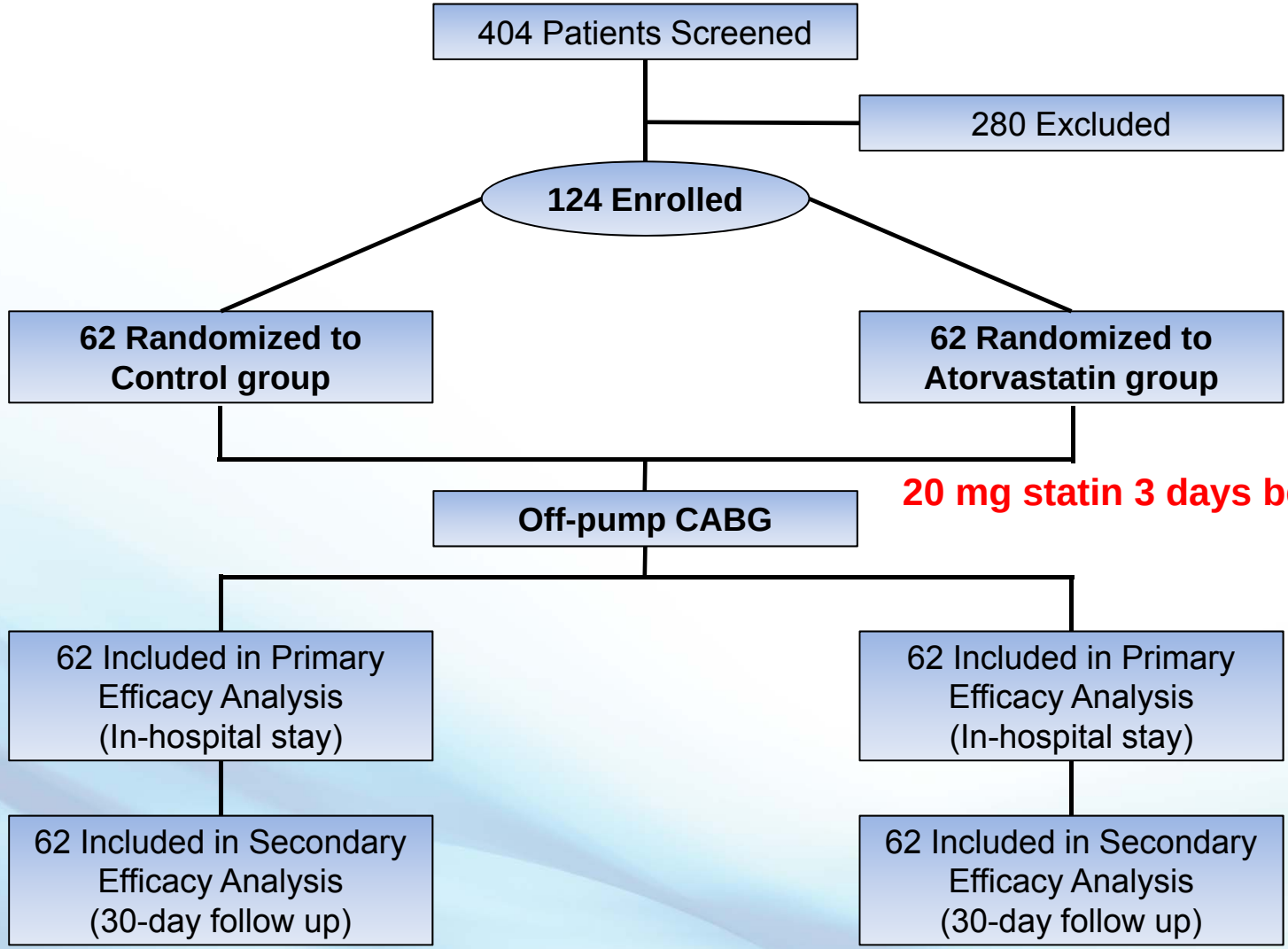
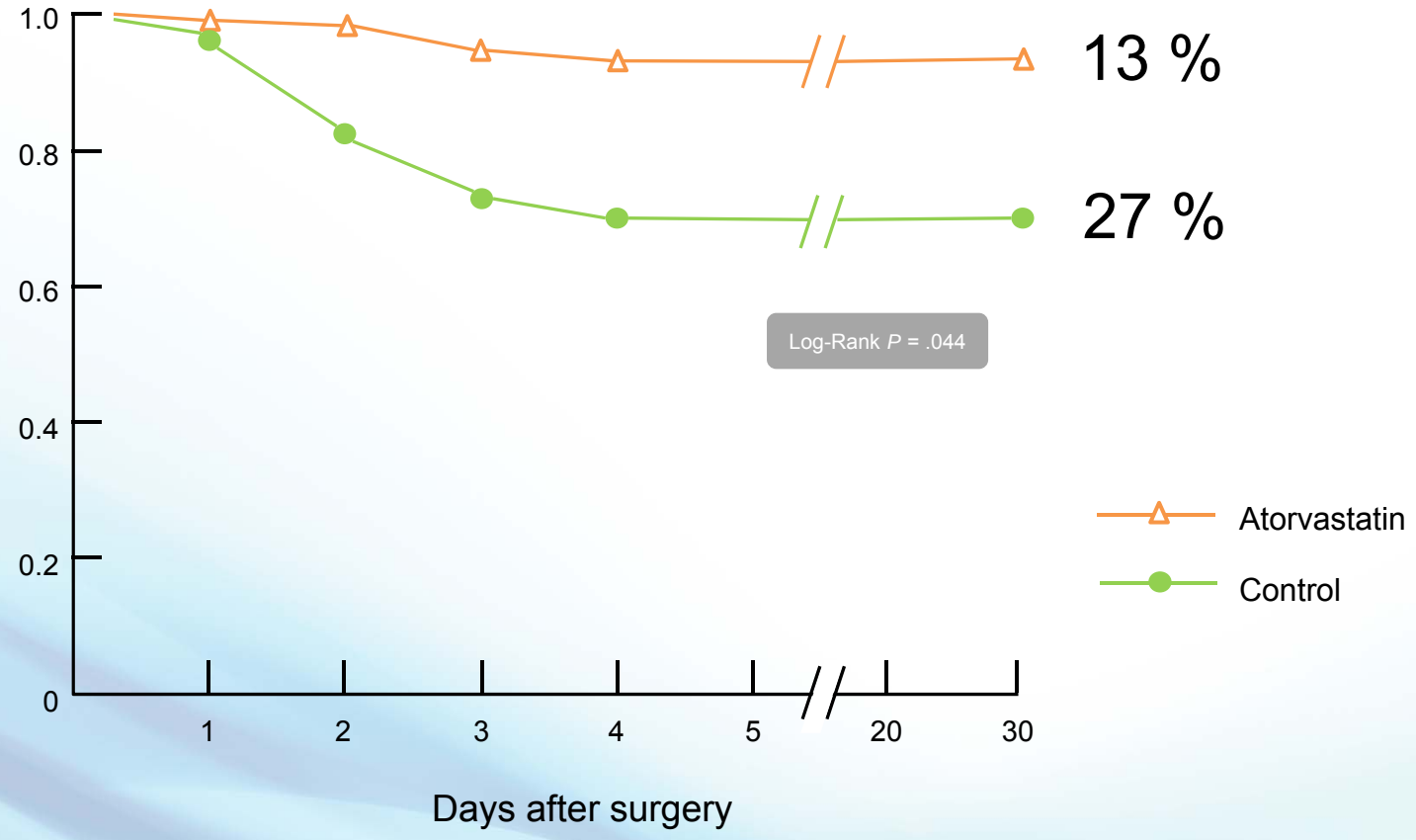
Postoperative AF after off-pump CABG



Song YB, et al. Am Heart J 2008;156:373

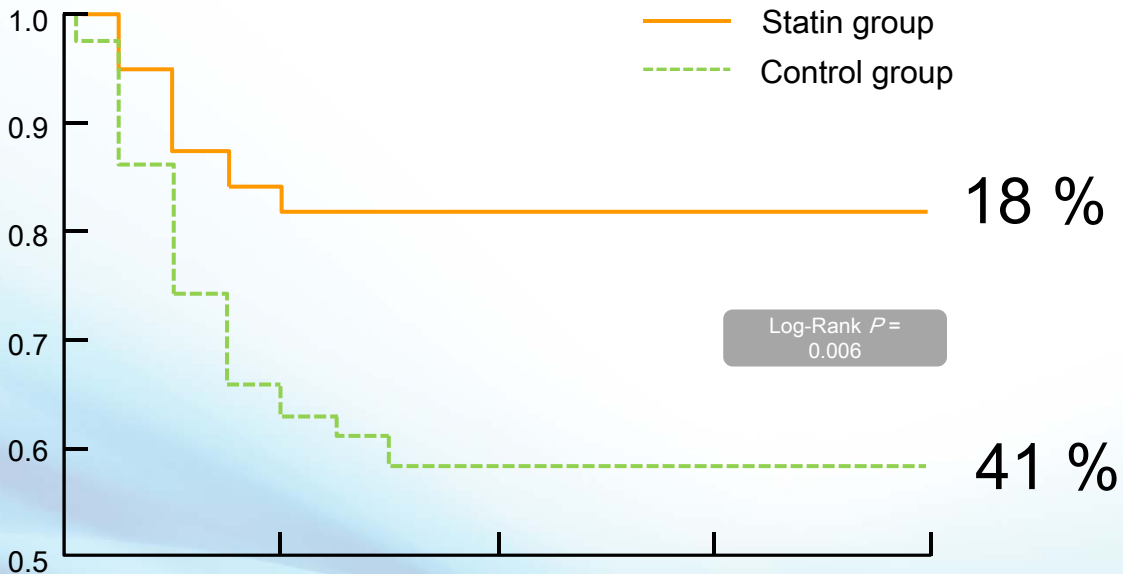
Kaplan-Meier plot of AF free after off-pump CABG



Song YB, et al. Am Heart J 2008;156:373

stoperative AF after CABG in China

patients with a mean age of 65 years (45~78 YO) who underwent
BG with cardiopulmonary bypass.
rvastatin 49 patients (20 mg, 7 days before op)
trol 51 patients (placebo)
nary end point: Atrial fibrillation



nclusions

tatins before invasive procedures significantly reduce the risk of post-procedural MI.

tatins reduce the risk of AF after CABG.

he use of statins before invasive procedures should be considered.