Comparison of high reloading ROsuvastatin and Atorvastatin pretreatment in patients undergoing elective PCI to reduce the incidence of MyocArdial periprocedural necrosis.

(ROMA II Reload) *(NCT01228227)*

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Potential conflicts of interest

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☐ **I have the following** potential conflicts of interest to report:

- ☐ Research contracts
- ☐ Consulting
- ☐ Employment in industry
- ☐ Stockholder of a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)

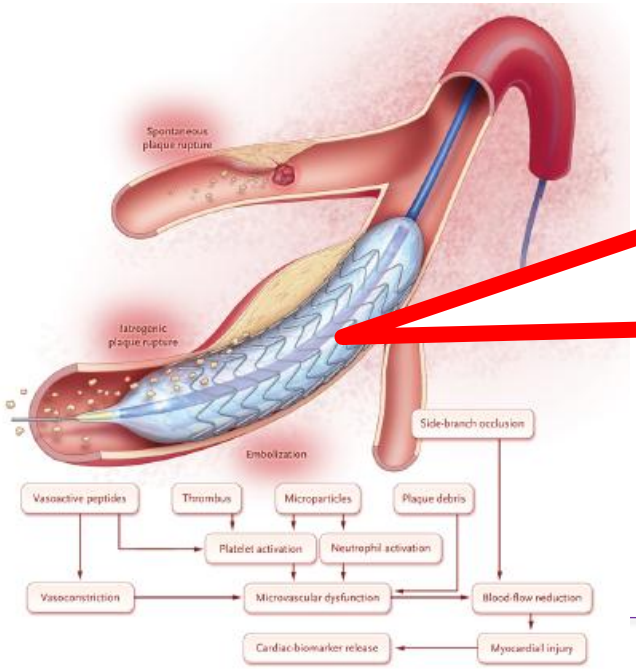
X I do not have any potential conflict of interest

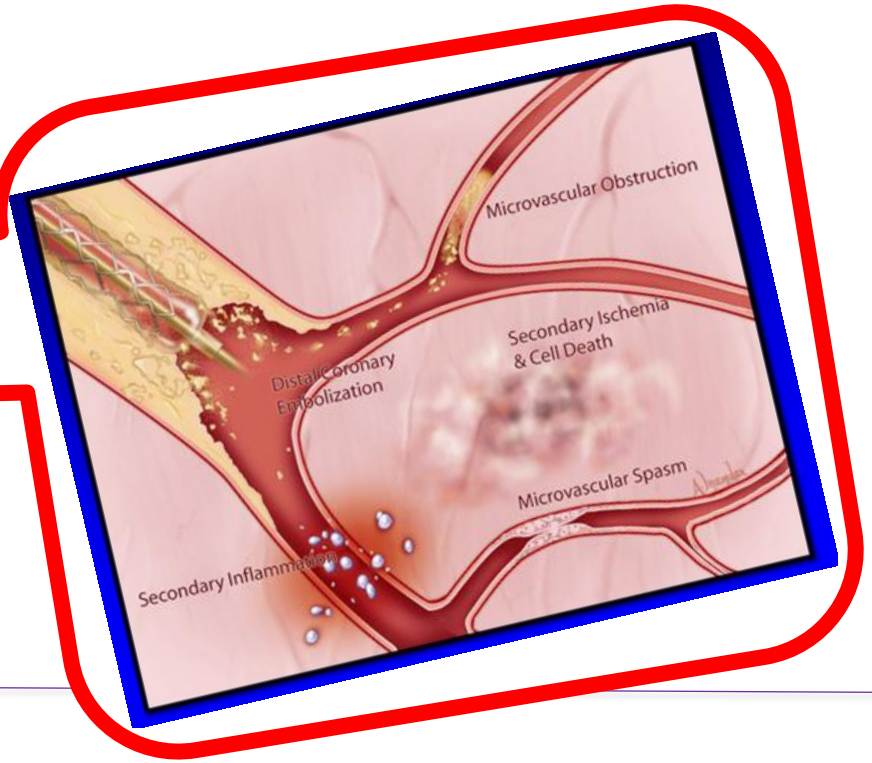
Universal definition of myocardial infarction

Type 4a: Myocardial infarction associated with PCI

- **PCI is associated with up to 30% incidence of myonecrosis, as reflected by elevation of cardiac enzymes even in a successful procedure.**

- **A part from technical complications, myonecrosis after PCI might be due to a distal embolization of atherogenic materials from plaque disruption,causing a secondary inflammation and finally a microvascular obstruction .**





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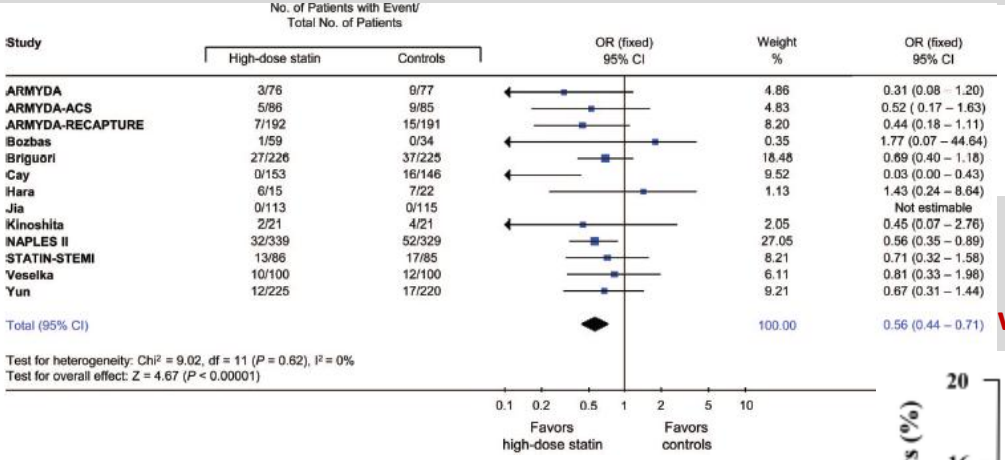
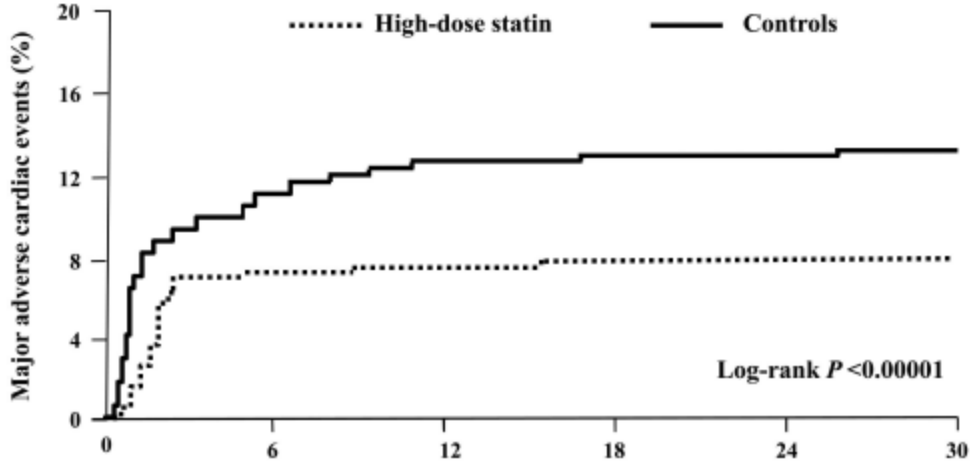
Impact of Statins pretreatment on procedural and clinical outcome

- The available data suggest that by an administration of either at least 3-7 days before and within 24 hours of elective PCI an high loading dose of statins prevents periprocedural MI

Post-procedural MI was reduced by pre-procedural statin therapy compared with control (OR: 0.40, 95% CI: 0.32 to 0.51, p < 0.00001)



All MACEs were significantly reduced with pre-procedural statin therapy compared with control (RR: 0.56, 95% CI: 0.44 to 0.71, p <0.00001)



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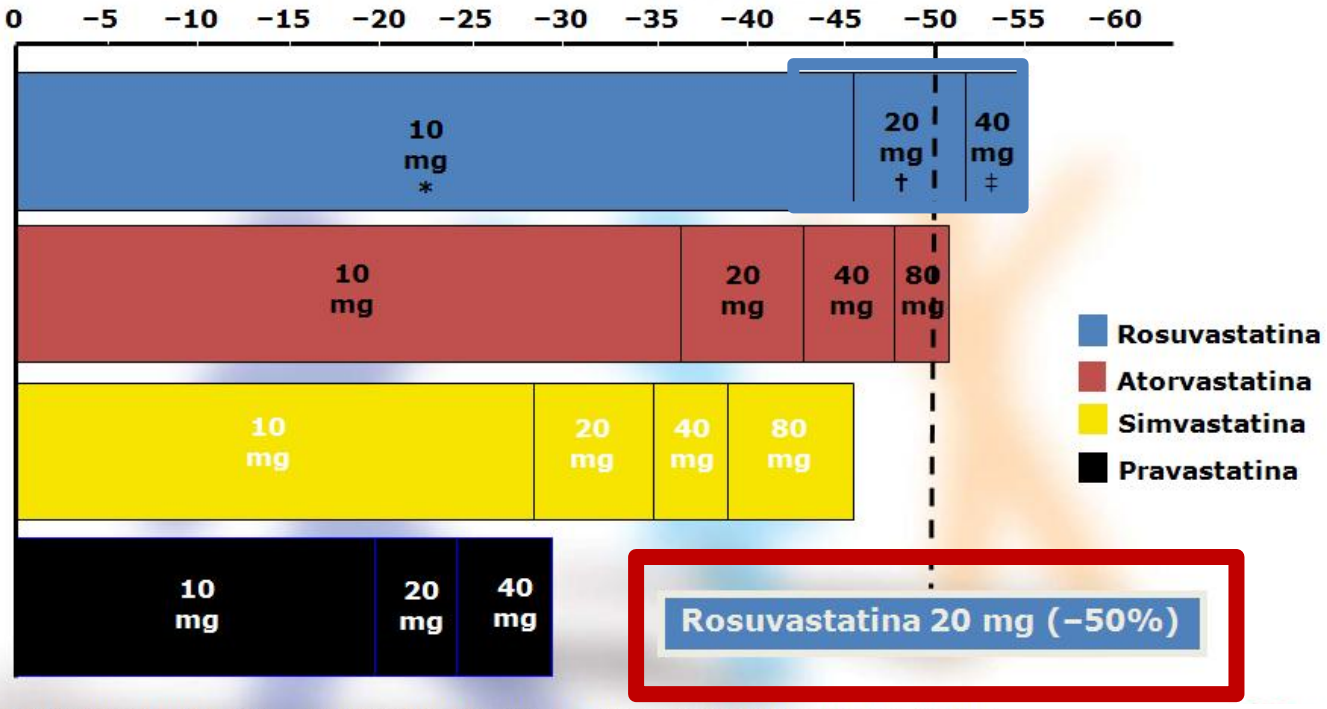
(G.Patti Circulation 2011 Vol.123,;1622-1632)

Comparison between different statins efficacy

C-LDL Reduction from basal value (%)



*p<0.002 vs atorvastatin 10 mg; simvastatin 10, 20, 40 mg; pravastatin 10, 20, 40 mg
†p<0.002 vs atorvastatin 20, 40 mg; simvastatin 20, 40, 80 mg; pravastatin 20, 40 mg
‡p<0.002 vs atorvastatin 40 mg; simvastatin 40, 80 mg; pravastatin 40 mg

Adapted from Jones PH et al. *Am J Cardiol* 2003;92:152–160

Rosuvastatin Pre-treatment in Patients Undergoing Elective PCI to Reduce the Incidence of Myocardial Periprocedural Necrosis. The ROMA Trial.

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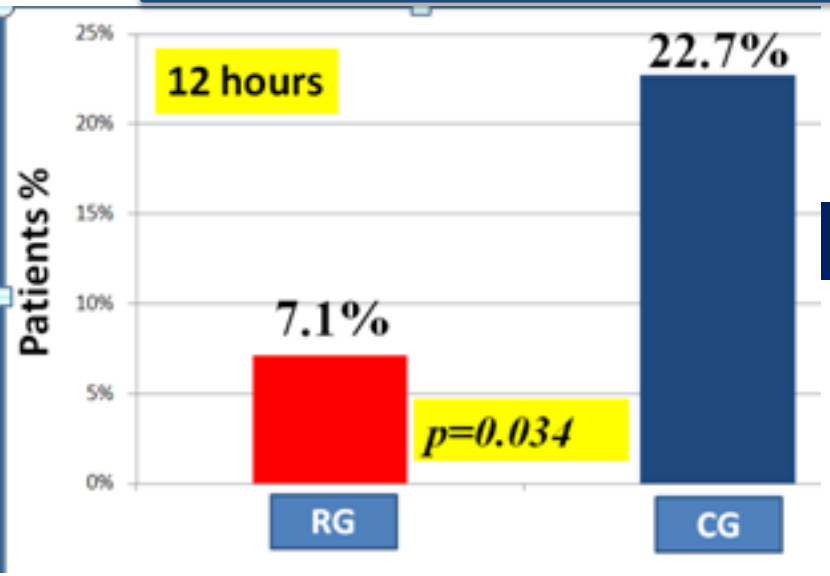
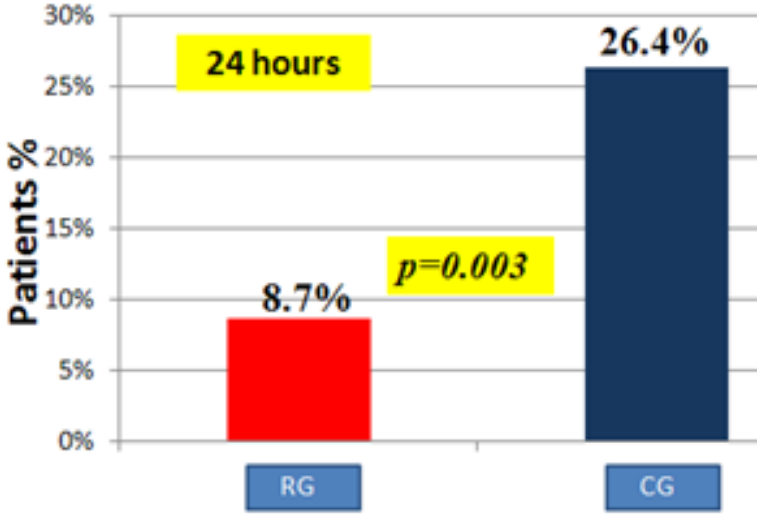
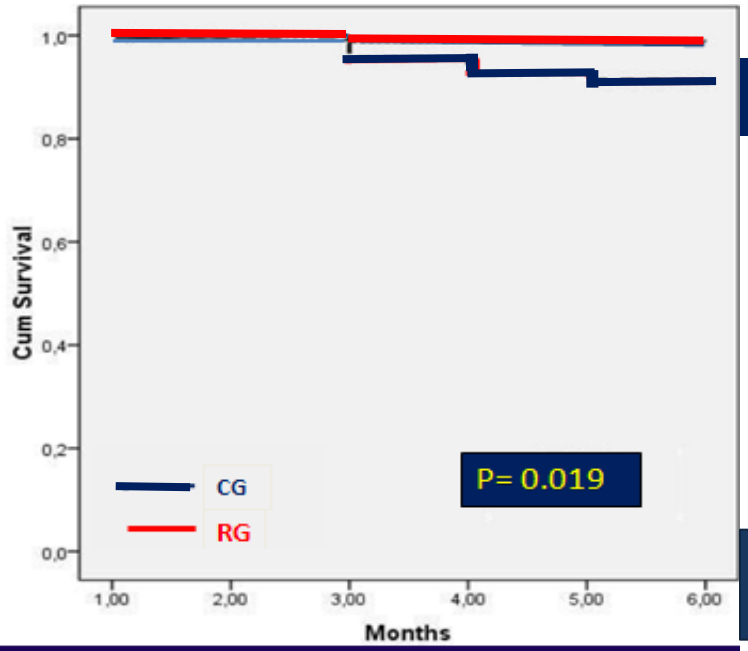
Catheterization and Cardiovascular Interventions

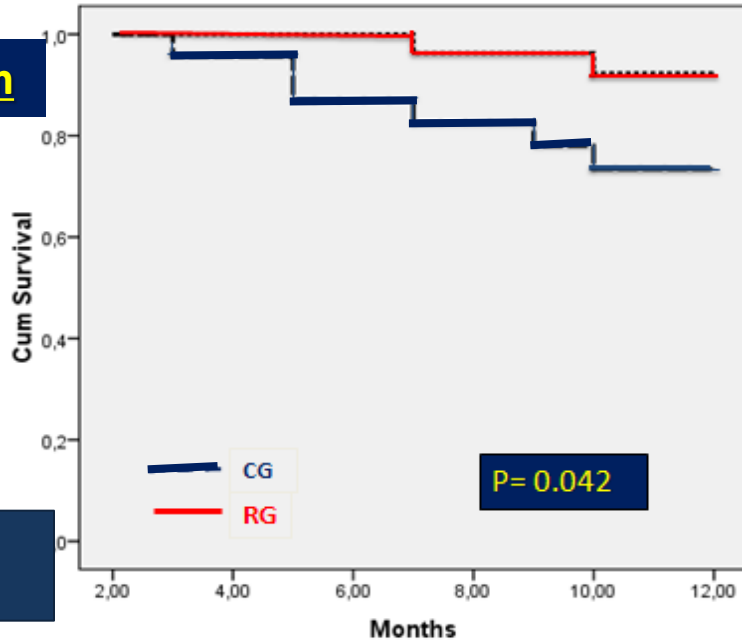


CK-MB> 3ULN



MACCE at 6-12 m





Sardella et al
CCI 2012 Apr 19

ROMA II Trial

Prospective,randomized, double-arm, single-center clinical, spontaneous study

AIM

*To compare a reloading dose of **Rosuvastatin (40mg)** and **Atorvastatin (80mg)** administered within 24h before the procedure in reducing the rate of **periprocedural myonecrosis (CKMB>3ULN)** in patients on chronic statin treatment undergoing elective non urgent coronary PCI.*

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ROMA II Trial

Patients on chronic statin tx suitable for elective PCI in native coronary artery with "de novo" lesions -Negative Biomarkers before intervention-

Randomization 1:1

Rosuvastatin Group (RG) 175pts	Atorvastatin Group (AG) 175pts	Control Group (CG) 100 pts
Standard therapy + Rosuvastatin 40mg within 24 hours before the procedure	Standard therapy + Atorvastatin 80mg within 24 hours before the procedure	Standard therapy -ASA -Clopidogrel 300 mg the day before/600mg <24 hours

Elective PCI

Blood samples for CK-MB (ng/ml) and other standard myocardial markers were collected at 12 and 24 h post PCI

1-6-12 months Follow-up

Primary End-point:

Incidence of myonecrosis after elective non urgent PCI (CK-MB >3x ULN) and

Clinical MACCE at 30 days 6 and 12 months

Principal Investigator:
Gennaro Sardella, MD

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Sample size

Hypothesis :

- To detect a difference in the incidence of **myonecrosis** and **MACCE** of **9%** between groups (from **12%** in the **Atorvastatin** [1-2] to **3%** in the **Rosuvastatin group**)

Sample size

- On the basis of a two-sided test size of 5% and a power of 80%, it was calculated that a minimum of 155 patients would need to be recruited in each group (310 pts. total).
- **350 pts**.(resulted by an increase of 10% to adjust for potential losses to follow-up) undergoing elective,non urgent PCI were randomized respectively to **RG and to AG.**
- In addition we analyzed a group of consecutive patients with SA on statins that were prospectively enrolled in the **Registry group (100 pts)**

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1 Di Sciascio et al. JACC 2009 Vol 54 n° 6 558-65
2 Patti G. et al. JACC 2007; 49; 1272-78

ROMA II Trial

Patients with stable CAD undergoing PCI from February 2009 to March 2011 in chronic statin treatment assessed for eligibility (n=550)

Excluded (n=57)
3 withdrew consent
54 did not meet the inclusion criteria

Rosuvastatin Group (RG) 193 pts.

✓18 excluded because:
✓13 had coronary angiography alone and not PCI
✓4 were referred for elective CABG
✓1 had PCI for ISR retsenosis

175 patients included

Atorvastatin Group (AG) 200 pts.

✓25 excluded because:
✓17 had coronary angiography alone and not PCI
✓6 were referred for elective CABG
✓2 had PCI for ISR retsenosis

175 patients included

Control Group (CG)*

100 patients prospectively enrolled in the Registry

***Treated within the same period and by the same medical team as the randomized patients**

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INCLUSION CRITERIA

- Age ≥18 y
- De novo lesion in a native coronary artery
- Elective PCI
- Normal cardiac biomarkers
- Current statin treatment

EXCLUSION CRITERIA

- Primary or rescue PCI
- ACS
- Basal elevated cardiac markers
- Previous myocardial infarction
- Renal failure (GFR < 60 ml/min)
- Restenotic lesion
- SVG or LIMA treatment
- CTO
- Not signed informed consent

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Clinical Characteristics

Variables	RG (n=175)	AG (n=175)	P value RG vs AG	CG (n=100)	P value RG or AG vs CG
Males % (Pts)	81.2 (142)	83.8 (146)	0.549	79 (79)	0.632
Age, mean±SD	67.8 ± 9.9	67.1 ± 9.3	0.521	68 ± 9.4	0.852
Diabetes Mellitus % (Pts)	22.5 (39)	26.4 (46)	0.428	19 (19)	0.235
- NIDDM % (Pts)	22.5 (39)	27.7(48)	0.295	21 (21)	0.096
- IDDM % (Pts)	0	0.6 (1)	0.316	1 (1)	0.699
Hypertension % (Pts)	89.6 (157)	85.8 (150)	0.298	79 (79)	0.256
Hypercholesterolemia % (Pts)	76.2 (133)	69.6(122)	0.201	70 (70)	0.658
Current smoker % (Pts)	40.0 (70)	47.1 (82)	0.207	47 (47)	0.524
Family history of CAD % (Pts)	62.6 (110)	58.1 (102)	0.416	57 (57)	0.315
LVEF %±SD	52.7±5.7	50.4 ±15.1	0.07	53.9±5.2	0.256
Clinical presentation Stable Angina% (Pts)	100 (175)	100 (175)	1	100 (100)	1

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Angiographic & Procedural Characteristics

Variables	RG (n=175)	AG (n=175)	P value RG vs AG	CG (n=100)	P value RG or AG vs CG
Type B_2/C %	60.8	59.3	0.578	51	0.091
mean lesion length, mm±SD	23±15.15	19.54 ± 16.5	0.071	19±13.3	0.852
mean RVD, mm±SD	2.92±0.36	2.85 ± 0.51	0.163	2.87±0.35	0.625
mean MLD, mm±SD	0.56±0.47	0.51 ± 0.39	0.308	0.51±0.32	0.356
mean diameter stenosis, %±SD	80.7±17.93	82.2 ± 12.62	0.394	81.6±10.6	0.635
mean stent length, mm±SD	26.5±17.15	27.5 ±12.9	0.562	20.8±12.5	0.079
Left anterior descending %	32.6	43.8	0.254	48.9	0.326
Left circumflex %	21.7	21.7	0.542	29.8	0.265
Right coronary artery %	30.4	28.5	0.752	27	0.826
GP IIb/IIIa inhibitor use %	0	4.3	0.162	4.1	0.183

Previous Statin Treatment

STATIN	RG (n=175)	AG (n=175)	P value RG vs AG	CG (n=100)	P value RG or AG vs CG
Atorvastatin % (Pts)	40.0%(70)	43.2% (76)	0.564	41% (41)	0.873
Rosuvastatin % (Pts)	19.3%(34)	16.1% (28)	0.457	22% (22)	0.608
Simvastatin % (Pts)	23.2%(40)	27.1% (47)	0.432	11% (11)	0.08
Other % (Pts)	17.4%(30)	13.5% (24)	0.346	26% (26)	0.09

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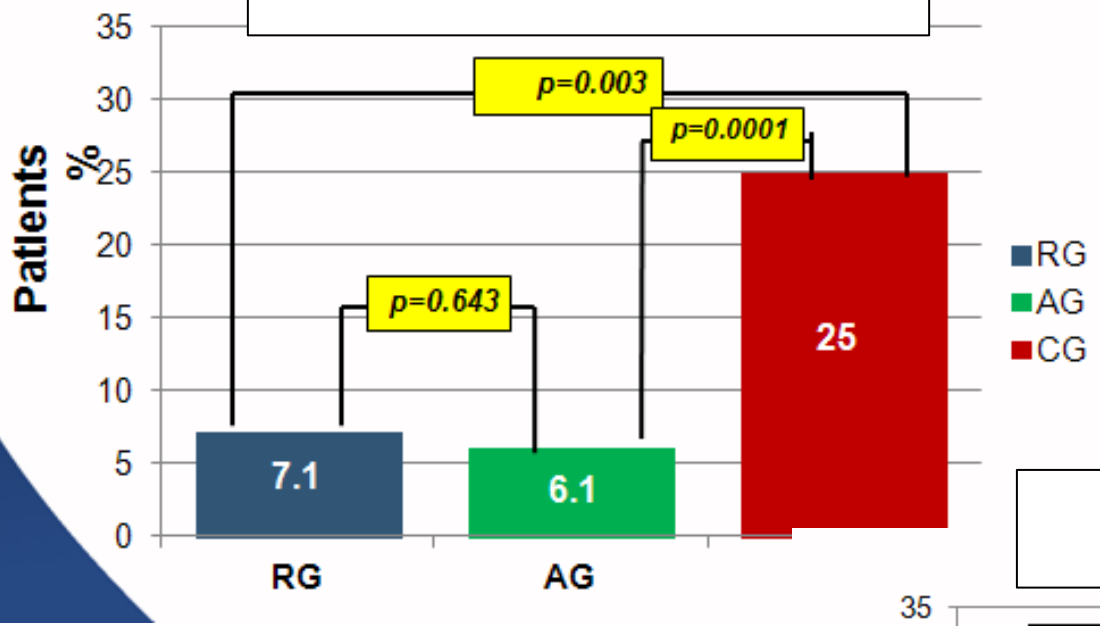
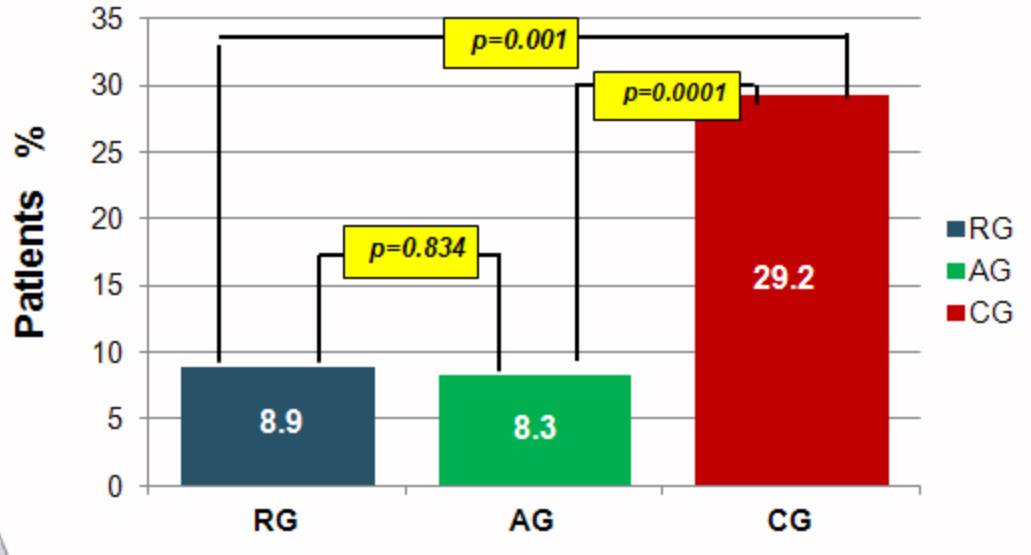
RESULTS
Primary End-Point

CK-MB 12 h



CK-MB> 3xULN

CK-MB 24 h



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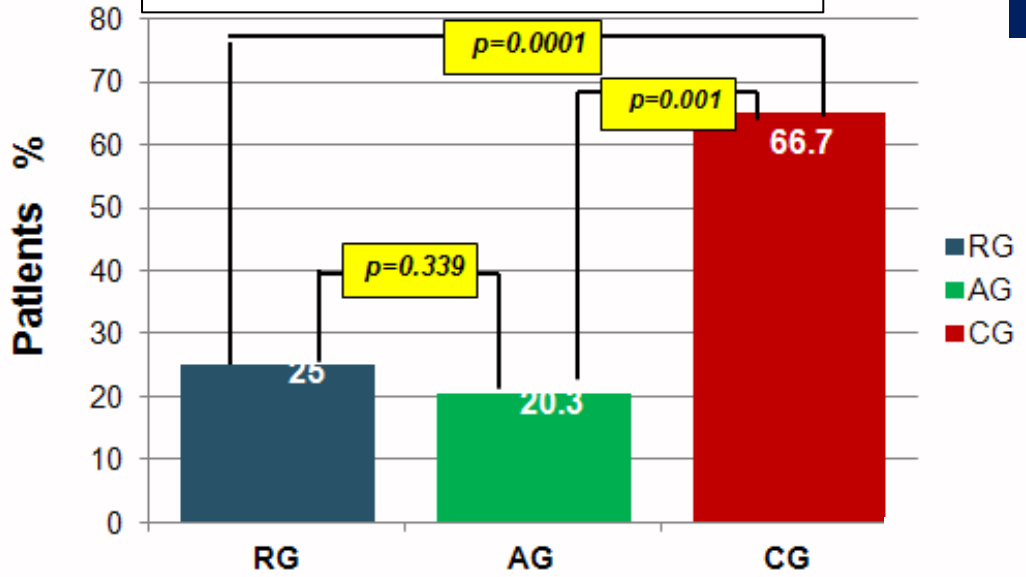
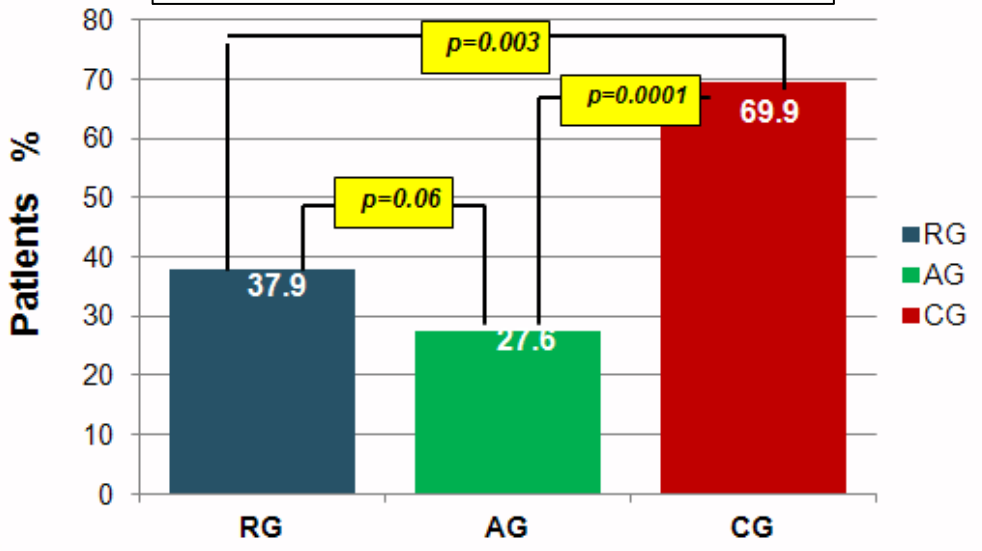
RESULTS

Tn-T 12 h



TnT > 0.1ng/ml ULN

Tn-T 24 h



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30 Days MACCE

Primary End-Point

Events %	RG (175 pts)	AG (175 pts)	p-value RG vs AG	CG (100 pts)	p-value RG or AG vs CG
Cumulative MACCE	8.9(16)	8.3(14)	0.702	33(33)	*0.0001* **
-Cardiac Death	0	0	-	1(1) *	0.185
-Peri-procedural MI	8.9(16)	8.3(14)	0.702	29(29)	*0.0001* **
-Spontaneous MI	0	0	-	1(1)	0.185
-TVR	0	0	-	1(1)	0.185
-Stroke	0	0	-	1(1)	0.185
Rehospitalization	0	0	-	3(3)	*0.030* **

* Ventricular fibrillation during acute heart failure episode

** p between CG and both Statins

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6 MONTHS MACCE

Primary End-Point

Events %	RG (175 pts)	AG (175 pts)	p-value RG vs AG	CG (100 pts)	p-value RG or AG vs CG
Cumulative MACCE	10.2(18)	8.9(16)	0.718	36(36)	*0.0001***
-Cardiac Death	0	0	-	1(1)*	0.185
-Peri-procedural MI	8.9(16)	8.3(14)	0.702	29(29)	*0.0001***
-Spontaneous MI	0.6(1)	0	0.316	2(2)	0.060
-TVR	0.6(1)	1.2(2)	0.562	2(2)	0.567
-Stroke	0	0	-	3(3)	*0.03***
-Rehospitalization	1.2(2)	0.6(1)	0.562	6(6)	*0.021***

* Ventricular fibrillation during acute heart failure episode
** p between CG and both Statins

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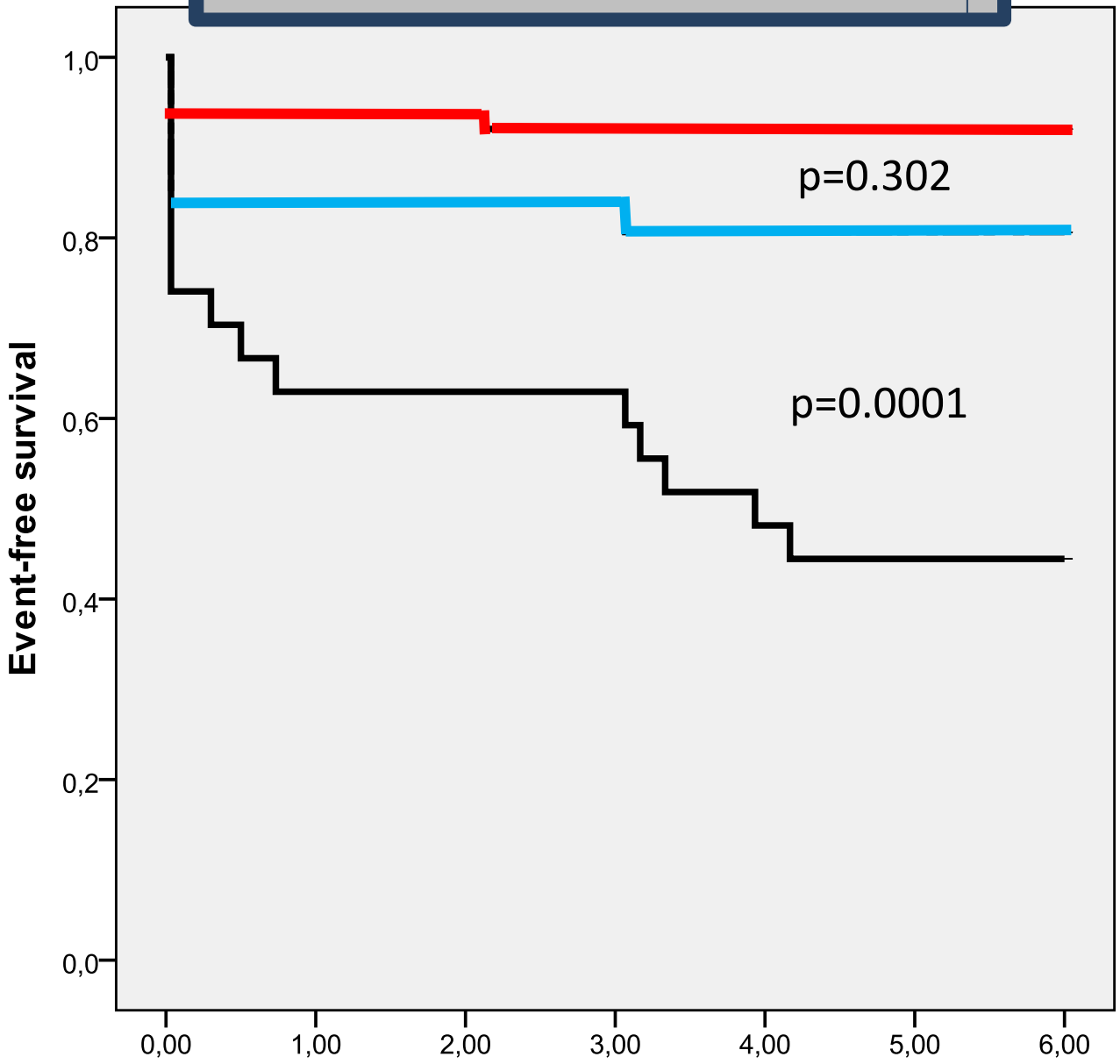
6 MONTHS MACCE



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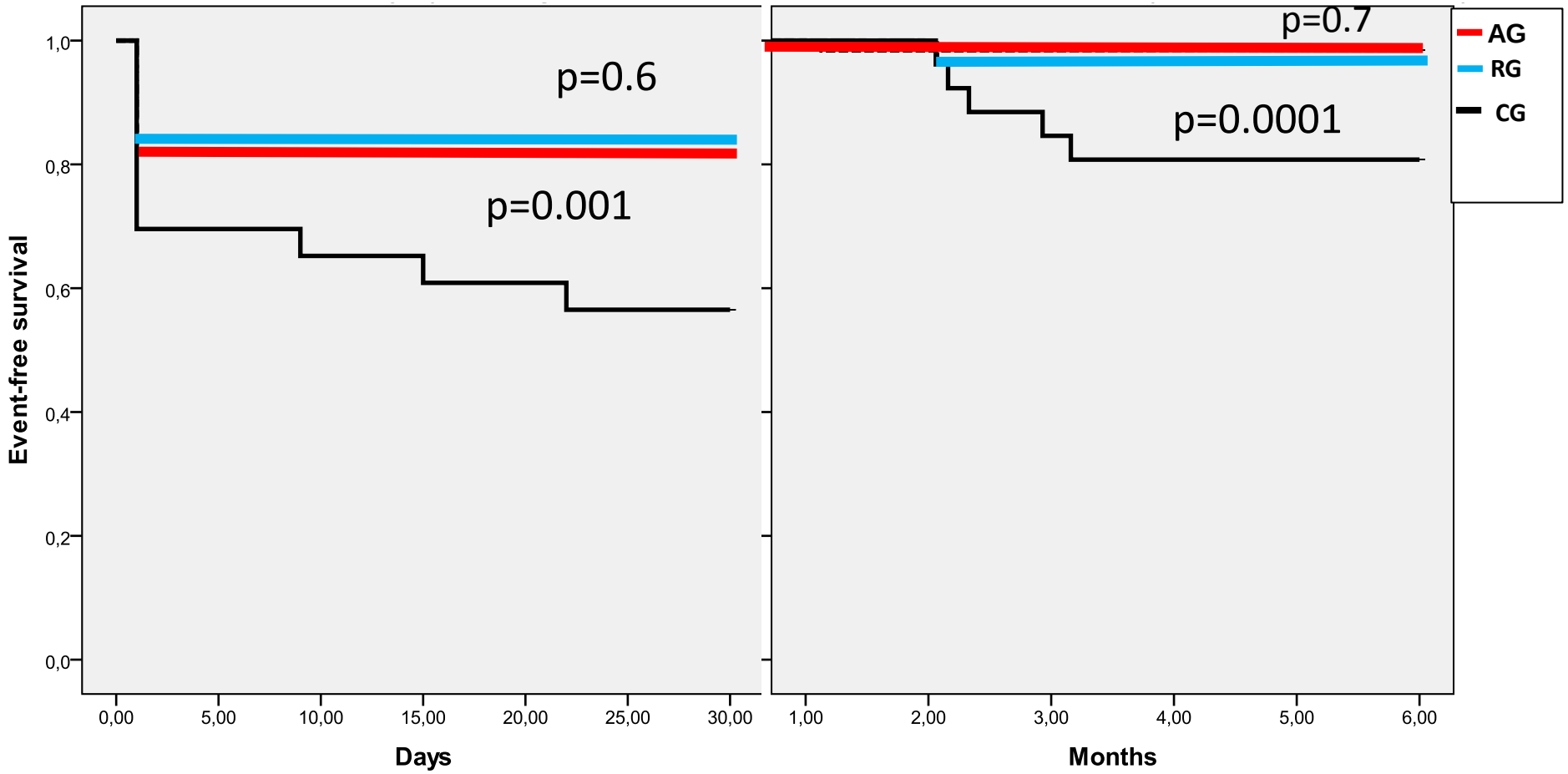
LANDMARK SURVIVAL ANALYSYS
6 MONTHS MACCE



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MULTIVARIATE ANALYSYS 6 MONTHS MACCE

Variables	Univariate Analysys HR (95% CI)	p-values	Multivariate Analysys HR (95% CI)	p-values
Reload of Atorvastatin or Rosuvastatin	0.181 (0.083-0.396)	*0.001*	0.222 (0.093-0.529)	*0.001*
Diabetes	1.304 (1.094-1.785)	0.016	-	-
Number of implanted stents	1.244 (0.996-1.554)	0.054	-	-
Multi-vessel disease	1.574 (0.689-3.598)	0.212	-	-

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12 months MACCE
Primary End-Point

Events %	RG (n=175)	AG (n=175)	p RG vs AG	CG (n=100)	p RG vs AG vs CG
Cumulative MACCE	11.4 (20)	12 (21)	0.868	41 (41)	*0.0001***
Cardiac Death	0.6 (1)	1.1 (2)	0.562	2 (2) *	0.562
Periprocedural MI	9 (16)	8.3 (14)	0.702	29 (29)	*0.0001***
Spontaneous MI	1.1 (2)	0	0.156	3 (3)	0.060
TVR	0.6 (1)	2.8 (5)	0.09	5 (5)	0.09
Stroke	0	0	-	3 (3)	*0.030***
-Rehospitalization	1.7(3)	3.4(6)	0.31	11(11)	*0.011***

*1 Ventricular fibrillation during acute heart failure episode
** p between CG and both Statins

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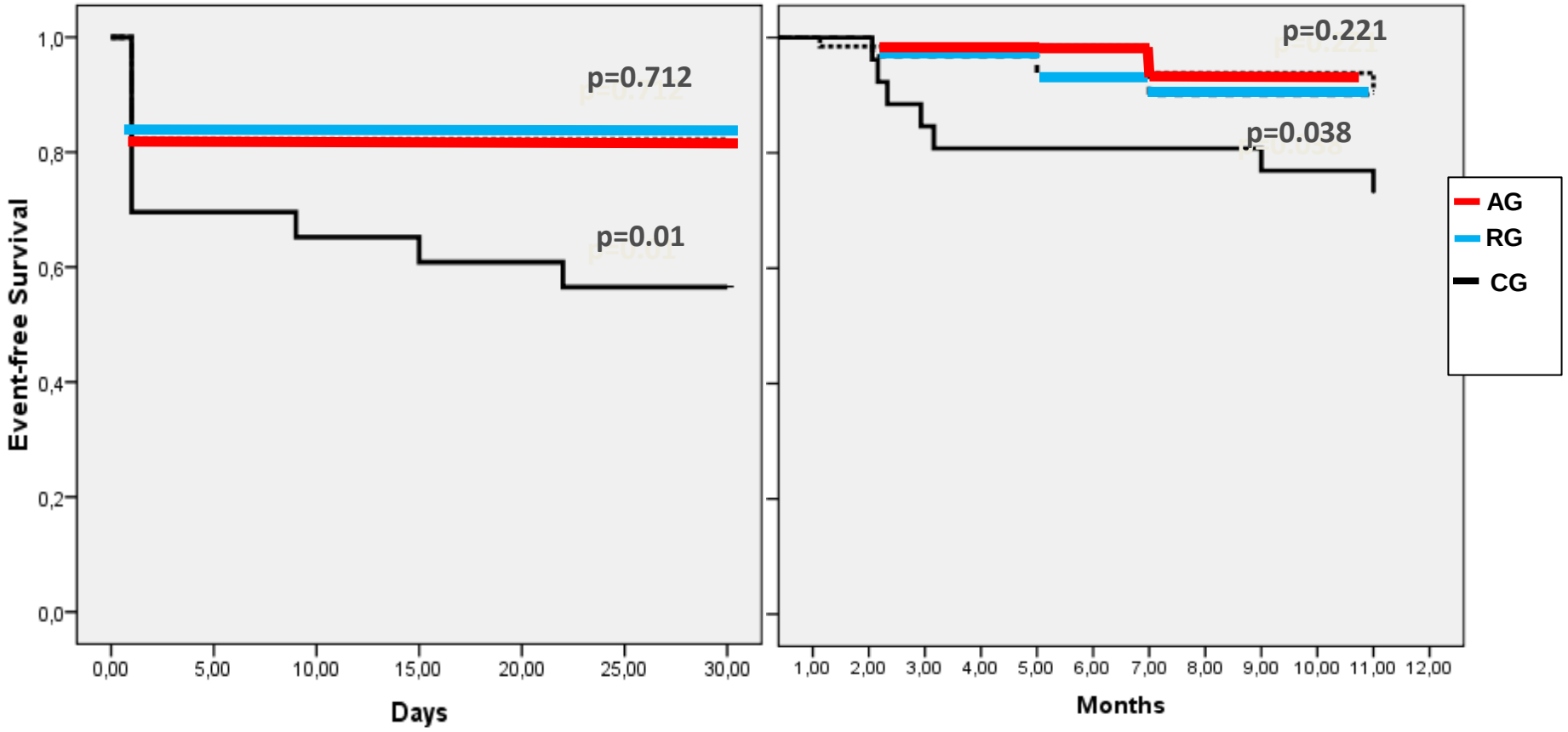
LANDMARK SURVIVAL ANALYSYS 12 MONTHS MACCE



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MULTIVARIATE ANALYSYS 12 MONTHS MACCE

Variables	Univariate Analysis HR (95% CI)	P values	Multivariate Analysis HR (95% CI)	p values
Atorvastatin or Rosuvastatin "reload"	0.198 (0.096-0.409)	*0.0001*	0.180 (0.081-0.401)	*0.0001*
Diabetes Mellitus	1.388 (1.160-1.842)	*0.036*		
Hypertension	1.785 (0.717-4.445)	0.213		
N° of stent implanted	1.188(0.955-1.478)	0.122		
Multivessel disease	1.628 (0.756-3.504)	0.214		

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Conclusions

- **The efficacy of statin pretreatment seems to improve the procedural and long term clinical outcome in stable PCI patients**

- **Our previous experience showed that Rosuvastatin loading dose administration before PCI (ROMA trial) improves clinical outcome at 1 year in naïve patients**

- **Comparison between Rosuvastatin and Atorvastatin loading dose in stable patients on chronic statin therapy before PCI showed similar effects on procedural and mid-long term outcome**

- **Both statins confirmed their beneficial effects compared with absence of statin pretreatment**

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THANK YOU !

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