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)

G. SARDELLA MD, FACC, FESC

O.U. of Invasive Cardiology
Department of Cardiovascular and Pulmonary Sciences
Policlinico Umberto I
“Sapienza” University of Rome

rino.sardella@uniroma1.it
Disclosure Statement of Financial Interest

I, GENNARO SARDELLA, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
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**.
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 (RR: 0.57, 95% CI: 0.46 to 0.70, p < 0.0001).

All-cause mortality was nonsignificantly reduced with pre-procedural statin therapy compared with control (RR: 0.66, 95% CI: 0.37 to 1.17, p = 0.15).

D.E. Winchester, JACC Vol. 56, No. 14, 2010
Comparison between different statins efficacy

C-LDL Reduction from basal value (%)
ROMA Trial: Prospective, randomized, double-arm, single-center clinical, spontaneous study in naïve pts.

- CK-MB > 3ULN
- MACCE at 6-12 m

G. Sardella TCT 2010
PCR 2011 submitted
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.
# ROMA II Trial

## Primary End-point:

**Incidence of myonecrosis after elective non urgent PCI**

- **CK-MB >3 X ULN**

## Secondary End-point:

**Clinical MACCE at 30 days 6 and 12 months**

Principal Investigator: Gennaro Sardella, MD

## Groups

- **Rosuvastatin Group (RG) 155pts**

- **Atorvastatin Group (AG) 155pts**

- **Control Group (CG) 100 pts**

## Treatments

- **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**

## Elective PCI

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

## Follow-up

1-6-12 months Follow-up
Hypothesis:

- To detect a difference in the incidence of myonecrosis and MACCE of 9% between groups (from 12% in the Atorvastatin\textsuperscript{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)

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

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 and restenosis

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
**INCLUSION CRITERIA**

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Age $\geq$ 18 y</td>
</tr>
<tr>
<td>- De novo lesion in a native coronary artery</td>
</tr>
<tr>
<td>- Elective PCI</td>
</tr>
<tr>
<td>- Normal cardiac biomarkers</td>
</tr>
<tr>
<td>- Current statin treatment</td>
</tr>
</tbody>
</table>
### EXCLUSION CRITERIA

- Primary or rescue PCI
- ACS
- Basal elevated cardiac markers
- Renal failure (GFR < 60 ml/min)
- Restenotic lesion
- SVG or LIMA treatment
- CTO
- Previous myocardial infarction
- Not signed informed consent
<table>
<thead>
<tr>
<th>Variables</th>
<th>RG (n=175)</th>
<th>AG (n=175)</th>
<th>P value RG vs AG</th>
<th>CG (n=100)</th>
<th>P value RG or AG vs CG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males % (Pts)</td>
<td>81.2 (142)</td>
<td>83.8 (146)</td>
<td>0.549</td>
<td>79 (79)</td>
<td>0.632</td>
</tr>
<tr>
<td>Age, mean±SD</td>
<td>67.8 ± 9.9</td>
<td>67.1 ± 9.3</td>
<td>0.521</td>
<td>68 ± 9.4</td>
<td>0.852</td>
</tr>
<tr>
<td>Diabetes Mellitus % (Pts)</td>
<td>22.5 (39)</td>
<td>26.4 (46)</td>
<td>0.428</td>
<td>19 (19)</td>
<td>0.235</td>
</tr>
<tr>
<td>- NIDDM % (Pts)</td>
<td>22.5 (39)</td>
<td>27.7 (48)</td>
<td>0.295</td>
<td>21 (21)</td>
<td>0.096</td>
</tr>
<tr>
<td>- IDDM % (Pts)</td>
<td>0</td>
<td>0.6 (1)</td>
<td>0.316</td>
<td>1 (1)</td>
<td>0.699</td>
</tr>
<tr>
<td>Hypertension % (Pts)</td>
<td>89.6 (157)</td>
<td>85.8 (150)</td>
<td>0.298</td>
<td>79 (79)</td>
<td>0.256</td>
</tr>
<tr>
<td>Hypercholesterolemia % (Pts)</td>
<td>76.2 (133)</td>
<td>69.6 (122)</td>
<td>0.201</td>
<td>70 (70)</td>
<td>0.658</td>
</tr>
<tr>
<td>Current smoker % (Pts)</td>
<td>40.0 (70)</td>
<td>47.1 (82)</td>
<td>0.207</td>
<td>47 (47)</td>
<td>0.524</td>
</tr>
<tr>
<td>Family history of CAD % (Pts)</td>
<td>62.6 (110)</td>
<td>58.1 (102)</td>
<td>0.416</td>
<td>57 (57)</td>
<td>0.315</td>
</tr>
<tr>
<td>LVEF %±SD</td>
<td>52.7±5.7</td>
<td>50.4 ±15.1</td>
<td>0.07</td>
<td>53.9±5.2</td>
<td>0.256</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stable Angina% (Pts)</td>
<td>100 (175)</td>
<td>100 (175)</td>
<td>1</td>
<td>100 (100)</td>
<td>1</td>
</tr>
</tbody>
</table>

**Clinical Characteristics**
### Angiographic & Procedural Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>R G (n=175)</th>
<th>A G (n=175)</th>
<th>P value RG vs AG</th>
<th>C G (n=100)</th>
<th>P value RG or AG vs CG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type B₂/C %</td>
<td>60.8</td>
<td>59.3</td>
<td>0.578</td>
<td>51</td>
<td>0.091</td>
</tr>
<tr>
<td>mean lesion length, mm±SD</td>
<td>23±15.15</td>
<td>19.54±16.5</td>
<td>0.071</td>
<td>19±13.3</td>
<td>0.852</td>
</tr>
<tr>
<td>mean RVD, mm±SD</td>
<td>2.92±0.36</td>
<td>2.85±0.51</td>
<td>0.163</td>
<td>2.87±0.35</td>
<td>0.625</td>
</tr>
<tr>
<td>mean MLD, mm±SD</td>
<td>0.56±0.47</td>
<td>0.51±0.39</td>
<td>0.308</td>
<td>0.51±0.32</td>
<td>0.356</td>
</tr>
<tr>
<td>mean diameter stenosis, %±SD</td>
<td>80.7±17.93</td>
<td>82.2±12.62</td>
<td>0.394</td>
<td>81.6±10.6</td>
<td>0.635</td>
</tr>
<tr>
<td>mean stent length, mm±SD</td>
<td>26.5±17.15</td>
<td>27.5±12.9</td>
<td>0.562</td>
<td>20.8±12.5</td>
<td>0.079</td>
</tr>
<tr>
<td>Left anterior descending %</td>
<td>32.6</td>
<td>43.8</td>
<td>0.254</td>
<td>48.9</td>
<td>0.326</td>
</tr>
<tr>
<td>Left circumflex %</td>
<td>21.7</td>
<td>21.7</td>
<td>0.542</td>
<td>29.8</td>
<td>0.265</td>
</tr>
<tr>
<td>Right coronary artery %</td>
<td>30.4</td>
<td>28.5</td>
<td>0.752</td>
<td>27</td>
<td>0.826</td>
</tr>
<tr>
<td>GP IIb/IIIa inhibitor use %</td>
<td>0</td>
<td>4.3</td>
<td>0.162</td>
<td>4.1</td>
<td>0.183</td>
</tr>
<tr>
<td>STATIN</td>
<td>RG (n=175)</td>
<td>AG (n=175)</td>
<td>P value RG vs AG</td>
<td>CG (n=100)</td>
<td>P value RG or AG vs CG</td>
</tr>
<tr>
<td>---------------</td>
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<td>------------</td>
<td>------------------------</td>
</tr>
<tr>
<td>Atorvastatin % (Pts)</td>
<td>40.0% (70)</td>
<td>43.2% (76)</td>
<td>0.564</td>
<td>41% (41)</td>
<td>0.873</td>
</tr>
<tr>
<td>Rosuvastatin % (Pts)</td>
<td>19.3% (34)</td>
<td>16.1% (28)</td>
<td>0.457</td>
<td>22% (22)</td>
<td>0.608</td>
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<tr>
<td>Simvastatin % (Pts)</td>
<td>23.2% (40)</td>
<td>27.1% (47)</td>
<td>0.432</td>
<td>11% (11)</td>
<td>0.08</td>
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<tr>
<td>Other % (Pts)</td>
<td>17.4% (30)</td>
<td>13.5% (24)</td>
<td>0.346</td>
<td>26% (26)</td>
<td>0.09</td>
</tr>
</tbody>
</table>
RESULTS
Primary End-Point

CK-MB 12 h

CK-MB > 3xULN

CK-MB 24 h
RESULTS

Tn-T 12 h
- Tn-T > 0.1 ng/ml ULN

Tn-T 24 h
- Tn-T > 0.1 ng/ml ULN

Patients %

<table>
<thead>
<tr>
<th></th>
<th>RG</th>
<th>AG</th>
<th>CG</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>20.3</td>
<td>66.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p=0.0001</td>
<td>p=0.001</td>
<td>p=0.339</td>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>RG</th>
<th>AG</th>
<th>CG</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>37.9</td>
<td>27.6</td>
<td>69.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>p=0.003</td>
<td>p=0.0001</td>
<td>p=0.06</td>
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</table>
## MACCE 30 DAYS Primary End-Point

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

* Ventricular fibrillation during acute heart failure episode
## MACCE 6 MONTHS
Primary End-Point

<table>
<thead>
<tr>
<th>Events %</th>
<th>RG</th>
<th>AG</th>
<th>p-value RG vs AG</th>
<th>CG</th>
<th>p-value RG or AG vs CG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cumulative MACCE</strong></td>
<td>10.2(18)</td>
<td>8.9(16)</td>
<td>0.718</td>
<td>36(36)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Cardiac Death</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>1(1)*</td>
<td>0.185</td>
</tr>
<tr>
<td>Peri-procedural MI</td>
<td>8.9(16)</td>
<td>8.3(14)</td>
<td>0.702</td>
<td>29(29)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Spontaneous MI</td>
<td>0.6(1)</td>
<td>0</td>
<td>0.316</td>
<td>2(2)</td>
<td>0.060</td>
</tr>
<tr>
<td>TVR</td>
<td>0.6(1)</td>
<td>1.2(2)</td>
<td>0.562</td>
<td>2(2)</td>
<td>0.567</td>
</tr>
<tr>
<td>Stroke</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>3(3)</td>
<td>0.03</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>1.2(2)</td>
<td>0.6(1)</td>
<td>0.562</td>
<td>6(6)</td>
<td>0.021</td>
</tr>
</tbody>
</table>

* Ventricular fibrillation during acute heart failure episode
LANDMARK SURVIVAL ANALYSIS
FOR MACCE 6 MONTHS

\[ p = 0.7 \]

\[ p = 0.6 \]

\[ p = 0.001 \]

\[ p = 0.0001 \]
<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate Analysys</th>
<th>p-values</th>
<th>Multivariate Analysys</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td></td>
<td>HR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Reload of Atorvastatin or Rosuvastatin</td>
<td>0.181 (0.083-0.396)</td>
<td>0.001</td>
<td>0.222 (0.093-0.529)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.304 (1.094-1.785)</td>
<td>0.016</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Implanted stents</td>
<td>1.244 (0.996-1.554)</td>
<td>0.054</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multi-vessel disease</td>
<td>1.574 (0.689-3.598)</td>
<td>0.212</td>
<td></td>
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</tr>
</tbody>
</table>
Conclusions

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

- Our 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 term outcome.

- Both statins confirmed their beneficial effects compared with absence of statin pretreatment.
THANK YOU!
CK-MB 24 h

Patients %

<table>
<thead>
<tr>
<th></th>
<th>Patients %</th>
</tr>
</thead>
<tbody>
<tr>
<td>RG</td>
<td>8.9</td>
</tr>
<tr>
<td>AG</td>
<td>8.3</td>
</tr>
<tr>
<td>CG</td>
<td>29.2</td>
</tr>
</tbody>
</table>

p=0.001

p=0.0001

p=0.834
Tn-T 12 h

- RG: 25 patients, p=0.339
- AG: 20.3 patients
- CG: 66.7 patients, p=0.001

Patients %
Tn-T 24 h

Patients %

<table>
<thead>
<tr>
<th></th>
<th>RG</th>
<th>AG</th>
<th>CG</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>37.9</td>
<td>27.6</td>
<td>69.9</td>
</tr>
</tbody>
</table>

- RG: p=0.003
- AG: p=0.0001
- CG: p=0.06

Legend:
- RG
- AG
- CG
Periprocedural non-Q MI (PPMI) is a frequent and prognostically important complication of PCI.\(^1\)

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

The majority of data in this field are shown regarding Atorvastatin and it is unknown the effect of different more recent statins on the occurrence of PPMI.

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