ARMYDA-RECAPTURE (Atorvastatin for Reduction of Myocardial Damage during Angioplasty) trial

Prospective, multicenter, randomized, double blind trial investigating efficacy of atorvastatin reload in patients on chronic statin therapy undergoing PCI

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ARMYDA-RECAPTURE

Background (statin-naïve pts)

ARMYDA trial

\[ \text{MI (\%)} \]

\[ \begin{array}{cc}
\text{Atorvastatin} & 18 \\
\text{Placebo} & 5 \\
\end{array} \]

\[ P = 0.025 \]

ARMYDA-ACS trial

\[ \text{MACE (\%)} \]

\[ \begin{array}{cc}
\text{Atorvastatin} & 17 \\
\text{Placebo} & 5 \\
\end{array} \]

\[ P = 0.01 \]


ARMYDA-RECAPTURE trial: Study design

793 Patients with stable angina or NSTE-ACS undergoing coronary angiography

Randomization (N=420)

Atorvastatin reload:
80 mg 12 hrs before angio; further 40 mg 2 hrs before
N=210

Placebo 12 hrs before angio; further dose 2 hrs before
N=210

Coronary angiography

PCI atorvastatin N=177
PCI placebo N=175

1st blood sample (before PCI)
2nd and 3rd blood samples (8 and 24 hours after PCI)

CK-MB, Troponin-I, HS-CRP

30 days

373 patients excluded for:
- 243 no chronic statin therapy (31%)
- 38 emergency angiography
- 82 ejection fraction <30%
- 10 severe renal failure

68 patients excluded for indication to:
- medical therapy (N=30)
- bypass surgery (N=38)

PCI atorvastatin
N=177

PCI placebo
N=175

Primary end point:
30-day occurrence of cardiac death, MI, TVR
Primary endpoint

- 30-day incidence of cardiac death, MI, TVR

- **MI definition**: according to the Consensus statement of the Joint ESC/ACCF/AHA/WHF Task Force, as a post-procedural increases of cardiac biomarkers (troponin or CK-MB) greater than 3 x 99th percentile of the upper reference limit in patients with normal baseline levels, and as a subsequent elevation of more than three-fold from baseline value in patients with raised baseline levels (Normal limits: CK-MB 3.6 ng/ml; Troponin-I 0.06 ng/ml)

Secondary endpoints

- Post-procedural increase of markers of myocardial injury above UNL (CK-MB, troponin I)
- Post-PCI variations from baseline of CRP levels in the 2 arms
- MACE incidence according to clinical syndrome (Stable Angina vs ACS)
**ARMYDA-RECAPTURE trial**

**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
## ARMYDA-RECATURE: Clinical Features

<table>
<thead>
<tr>
<th>Variable</th>
<th>Atorvastatin (N=177)</th>
<th>Placebo (N=175)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>133 (75)</td>
<td>147 (84)</td>
<td>0.054</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66±10</td>
<td>66±10</td>
<td>0.93</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>62 (35)</td>
<td>60 (34)</td>
<td>0.97</td>
</tr>
<tr>
<td>Systemic hypertension</td>
<td>138 (78)</td>
<td>148 (85)</td>
<td>0.15</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>147 (83)</td>
<td>147 (84)</td>
<td>0.92</td>
</tr>
<tr>
<td>Previous MI</td>
<td>56 (32)</td>
<td>65 (37)</td>
<td>0.33</td>
</tr>
<tr>
<td>LDL-cholesterol (mg/dL)</td>
<td>92±15</td>
<td>93±16</td>
<td>0.55</td>
</tr>
<tr>
<td>Duration of statin therapy (months)</td>
<td>9.1±8.8</td>
<td>9.2±9.1</td>
<td>0.87</td>
</tr>
<tr>
<td>Serum creatinine (mg/dL)</td>
<td>1.01±0.34</td>
<td>1.06±0.29</td>
<td>0.26</td>
</tr>
<tr>
<td>Clinical pattern</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic stable angina</td>
<td>95 (54)</td>
<td>94 (54)</td>
<td>0.92</td>
</tr>
<tr>
<td>NSTEMI-ACS</td>
<td>82 (46)</td>
<td>81 (46)</td>
<td>0.92</td>
</tr>
<tr>
<td>Multivessel coronary artery disease</td>
<td>83 (47)</td>
<td>93 (53)</td>
<td>0.29</td>
</tr>
<tr>
<td>Type of chronic statin therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>98 (55)</td>
<td>95 (54)</td>
<td>0.92</td>
</tr>
<tr>
<td>Simvastatin (+/- ezetimibe)</td>
<td>62 (35)</td>
<td>58 (33)</td>
<td>0.79</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>10 (6)</td>
<td>13 (7)</td>
<td>0.65</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>7 (4)</td>
<td>9 (5)</td>
<td>0.78</td>
</tr>
<tr>
<td>Other medical therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>176 (99)</td>
<td>175 (100)</td>
<td>1</td>
</tr>
<tr>
<td>Clopidogrel</td>
<td>177 (100)</td>
<td>175 (100)</td>
<td>-</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>73 (41)</td>
<td>66 (38)</td>
<td>0.57</td>
</tr>
<tr>
<td>Ace-inhibitors or ARBs</td>
<td>117 (66)</td>
<td>128 (73)</td>
<td>0.19</td>
</tr>
</tbody>
</table>
### ARMYDA-RECATURE: Procedural Features

<table>
<thead>
<tr>
<th>Variable</th>
<th>Atorvastatin (N=177)</th>
<th>Placebo (N=175)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vessel treated</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left main</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>0.63</td>
</tr>
<tr>
<td>Left anterior descending</td>
<td>90 (42)</td>
<td>93 (44)</td>
<td>0.72</td>
</tr>
<tr>
<td>Left circumflex</td>
<td>64 (30)</td>
<td>52 (25)</td>
<td>0.28</td>
</tr>
<tr>
<td>Right coronary artery</td>
<td>56 (26)</td>
<td>57 (27)</td>
<td>0.91</td>
</tr>
<tr>
<td>Saphenous vein grafts</td>
<td>2 (1)</td>
<td>6 (3)</td>
<td>0.27</td>
</tr>
<tr>
<td><strong>Restenotic lesions</strong></td>
<td>17 (10)</td>
<td>18 (10)</td>
<td>0.97</td>
</tr>
<tr>
<td>Lesion type B2/C</td>
<td>97 (55)</td>
<td>93 (53)</td>
<td>0.84</td>
</tr>
<tr>
<td>Multivessel intervention</td>
<td>32 (18)</td>
<td>32 (18)</td>
<td>0.93</td>
</tr>
<tr>
<td><strong>Type of intervention</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Balloon only</td>
<td>13 (7)</td>
<td>11 (6)</td>
<td>0.86</td>
</tr>
<tr>
<td>Stent</td>
<td>164 (93)</td>
<td>164 (94)</td>
<td>0.86</td>
</tr>
<tr>
<td>Bifurcations with kissing balloon</td>
<td>4 (2)</td>
<td>4 (2)</td>
<td>0.73</td>
</tr>
<tr>
<td>No. of stents per patient</td>
<td>1.4±0.8</td>
<td>1.3±0.7</td>
<td>0.23</td>
</tr>
<tr>
<td><strong>Use of drug eluting stents</strong></td>
<td>58 (33)</td>
<td>64 (37)</td>
<td>0.52</td>
</tr>
<tr>
<td><strong>Use of Glycoprotein IIb/IIIa inhibitors</strong></td>
<td>21 (12)</td>
<td>21 (12)</td>
<td>0.90</td>
</tr>
<tr>
<td>Anti-thrombin therapy during intervention</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unfractionated heparin</td>
<td>159 (90)</td>
<td>155 (89)</td>
<td>0.84</td>
</tr>
<tr>
<td>Bivalirudin</td>
<td>18 (10)</td>
<td>20 (11)</td>
<td>0.84</td>
</tr>
</tbody>
</table>
ARMYDA-RECAPTURE:

PRIMARY ENDPOINT (30-day MACE)

MACE (%)

- Placebo: 3.4%
- Atorvastatin: 9.1%

P = 0.045
ARMYDA-RECAPTURE: RESULTS

Individual and Combined Outcome Measures of the Primary Endpoint at 30 days

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Atorvastatin</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac death</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>MI</td>
<td>3.4%</td>
<td>3.4%</td>
</tr>
<tr>
<td>TVR</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>MACE</td>
<td>P=0.045</td>
<td>9.1%</td>
</tr>
</tbody>
</table>

Composite Primary End Point
**ARMYDA-RECAPTURE: Secondary endpoints**

Proportion of patients with any post-PCI cardiac markers elevation

- Creatine kinase-MB (%): Atorvastatin 13, Placebo 23, \( P=0.023 \)
- Troponin-I (%): Atorvastatin 36, Placebo 47, \( P=0.032 \)
ARMYDA-RECAPTURE: Secondary endpoints

Post-PCI increase of CRP levels from baseline

P=0.12

5
4
3
2
1
0

mg/L

Atorvastatin
Placebo

2.1 ± 6.7
3.0 ± 9.5
ARMYDA-RECAPTURE trial:

Event-free survival at 30 days in the atorvastatin reload vs placebo arm

MACE-free survival (%)

Days after PCI

P=0.045

Atorvastatin

Placebo
ARMYDA-RECAPTURE: Odds Ratio for 30-day MACE

- ACS: 1.8 (0.72-4.6)
- LVEF <40%: 2.1 (0.53-8.2)
- IIb/IIIa inhibitors: 3.2 (1.2-8.8)
- Multiple stents: 2.4 (1.1-5.4)
- Atorvastatin reload *: 0.52 (0.20-0.82)

* P=0.041
ARMYDA-RECAPTURE  Secondary endpoints

MACE  according to clinical presentation (stable angina or ACS)

Test for Interaction: z=2.0; P=0.022
ARMYDA-RECAPTURE: Odds Ratio for 30-day MACE in patients with ACS

- LVEF <40%: 2.2 (0.37-13.0)
- IIb/IIIa inhibitors: 2.7 (0.59-12.7)
- Multiple stents: 1.8 (0.48-7.0)
- Atorvastatin reload *: 0.17 (0.10-0.81)

* P=0.026
ARMYDA-RECAPTURE
Conclusions

- ARMYDA-RECAPTURE indicates that reloading with high dose atorvastatin is associated with improved clinical outcome in patients on chronic statin therapy undergoing PCI.

- Acute atorvastatin bolus 80 mg + 40 mg 12 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).

- 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 ARMDA-RECAPTURE may influence practice patterns for the acute care of non ST-segment elevation ACS.