

# **JUPITER: the Greatest but Not the Only In the Galaxy of Rosuvastatin Data**

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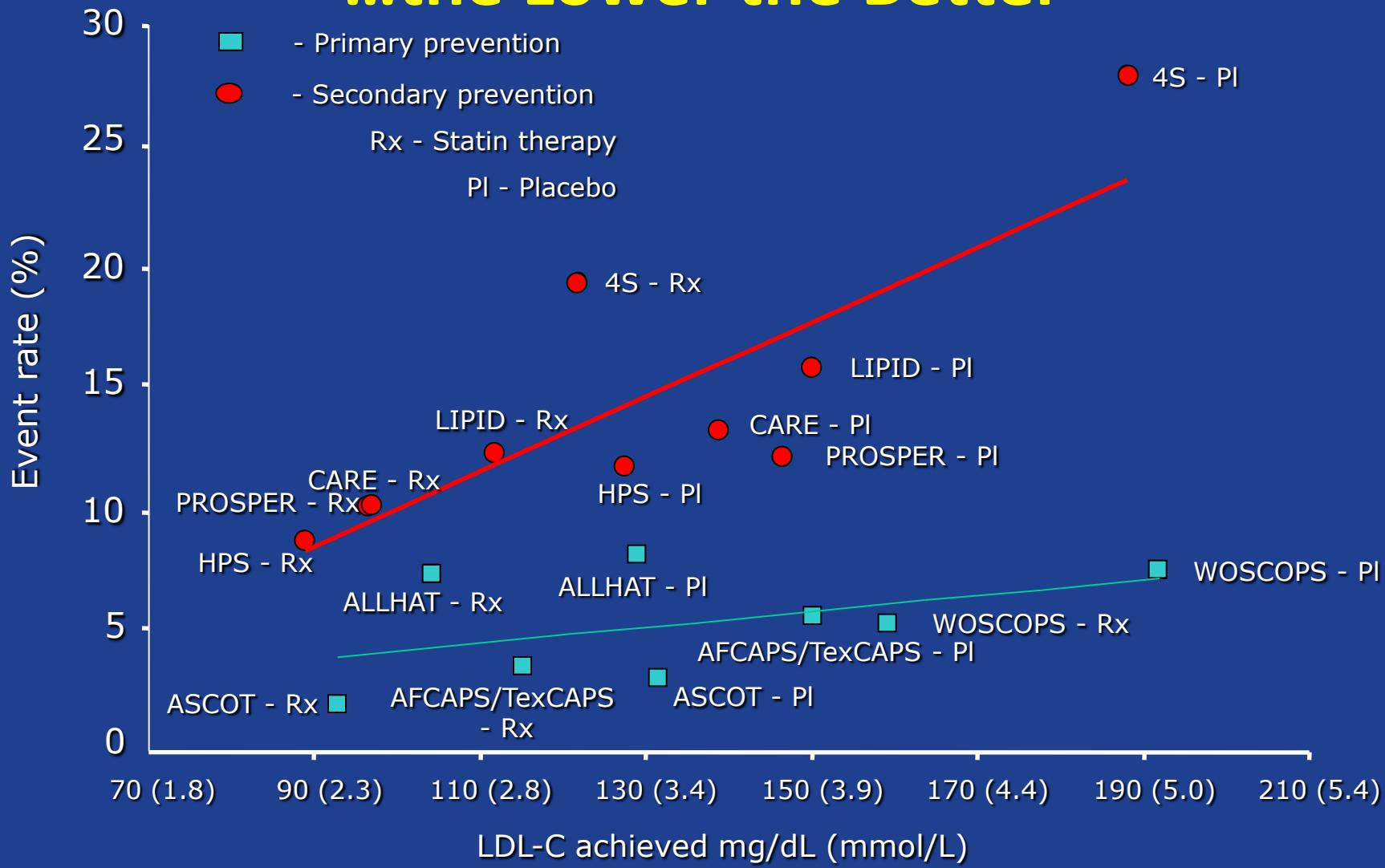
**Michal Vrablík**

***Centre for Preventive Cardiology  
3<sup>rd</sup> Department of Internal Medicine, 1<sup>st</sup> Faculty of  
Medicine, Charles University in Prague  
Czech Republic***

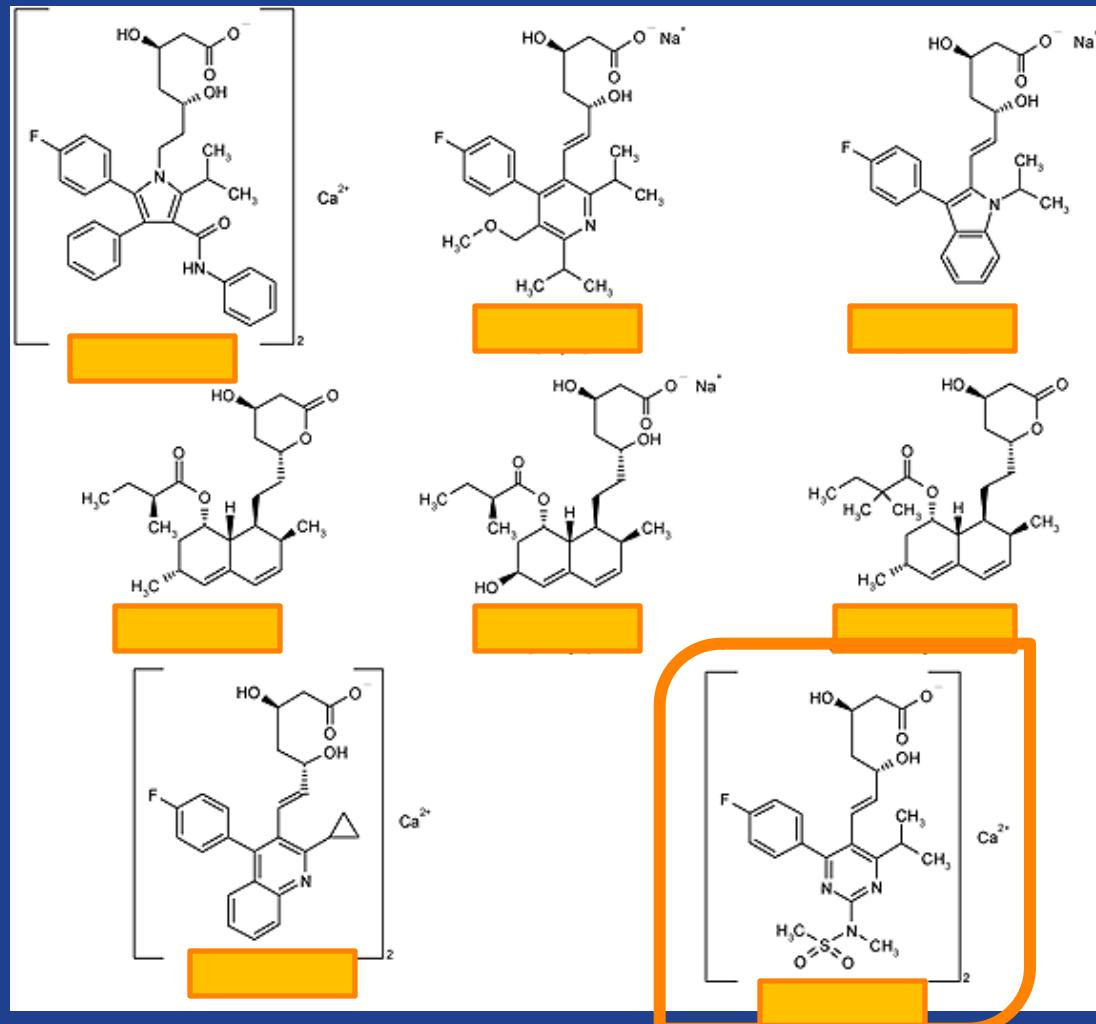
**CARDIONALE, November 26, 2010, Prague**

# Aggressive DLP Management Reduces Risk

...the Lower the Better



# Can you recognize them ?



Statins lower LDL-c and CVD risk across all high risk population groups

# **7 Properties of a Statin for the 21<sup>st</sup> Century**

1. Significant TC and LDL-c lowering efficacy
2. Positive impact on other lipoprotein classes
3. Slowing progression/regression of atherosclerosis
- 4. Reduction in CVD events/mortality**
5. Good safety profile
6. Added value
7. Acceptable cost

Does  
rosuvastatin  
fulfill these  
requirements

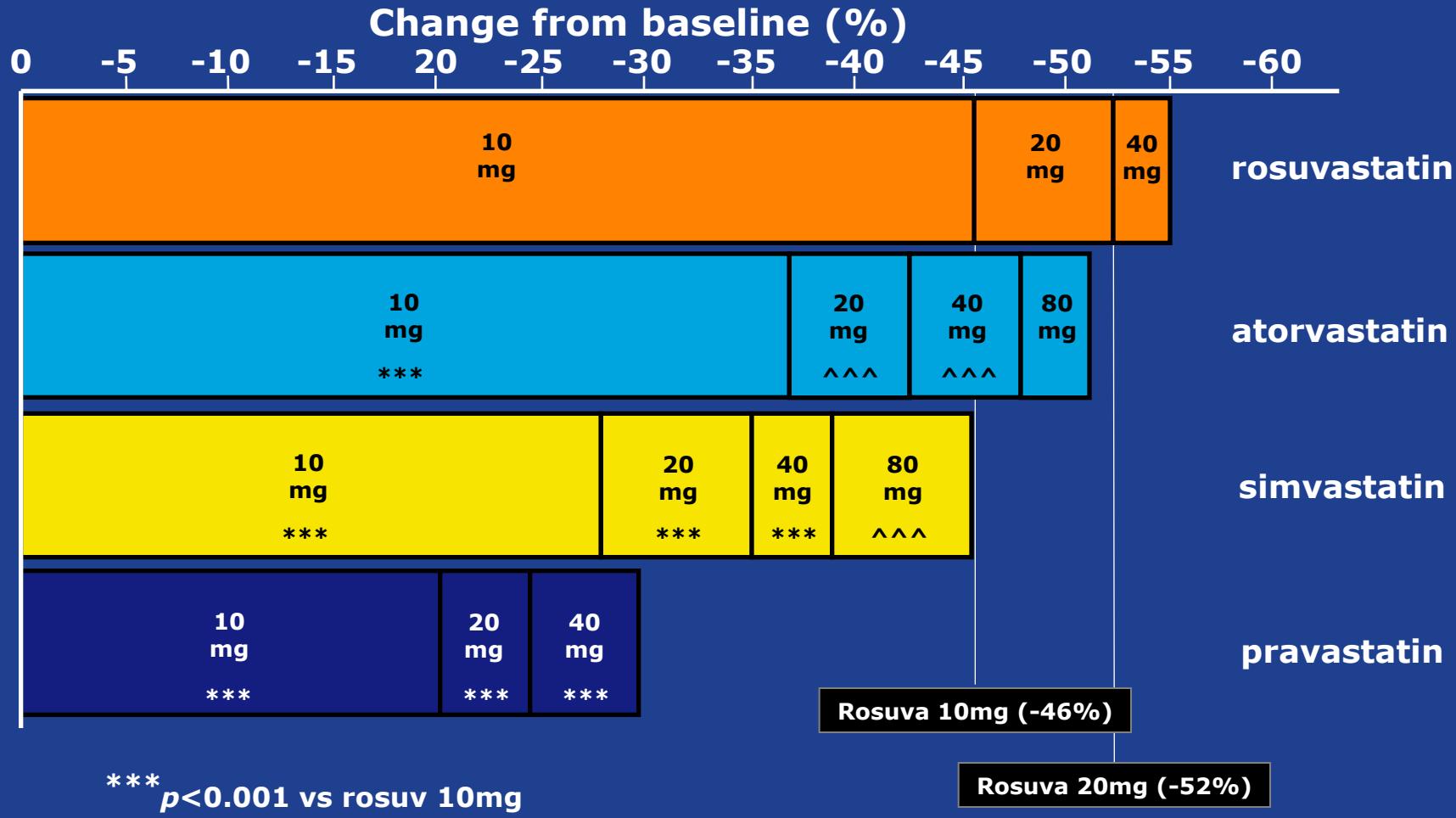
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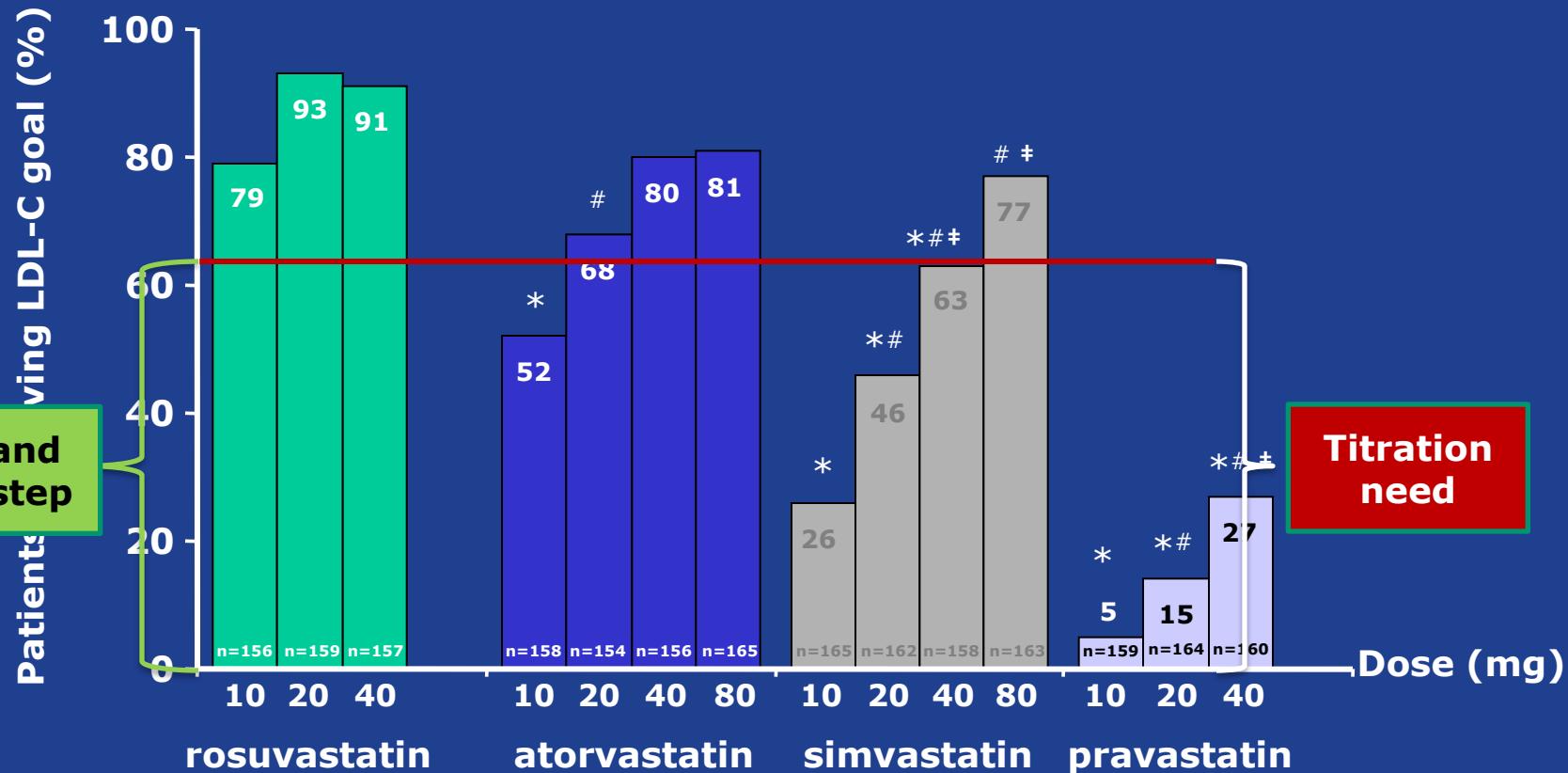
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# Stellar study: LDL-C: Percentage Change from Baseline at Week 6



Jones PH, Am J Cardiol. 2003 Jul 15;92(2):152-60

# Stellar Study: Percentage of Patients Achieving Joint European Recommendations LDL-C Goal at Week 6



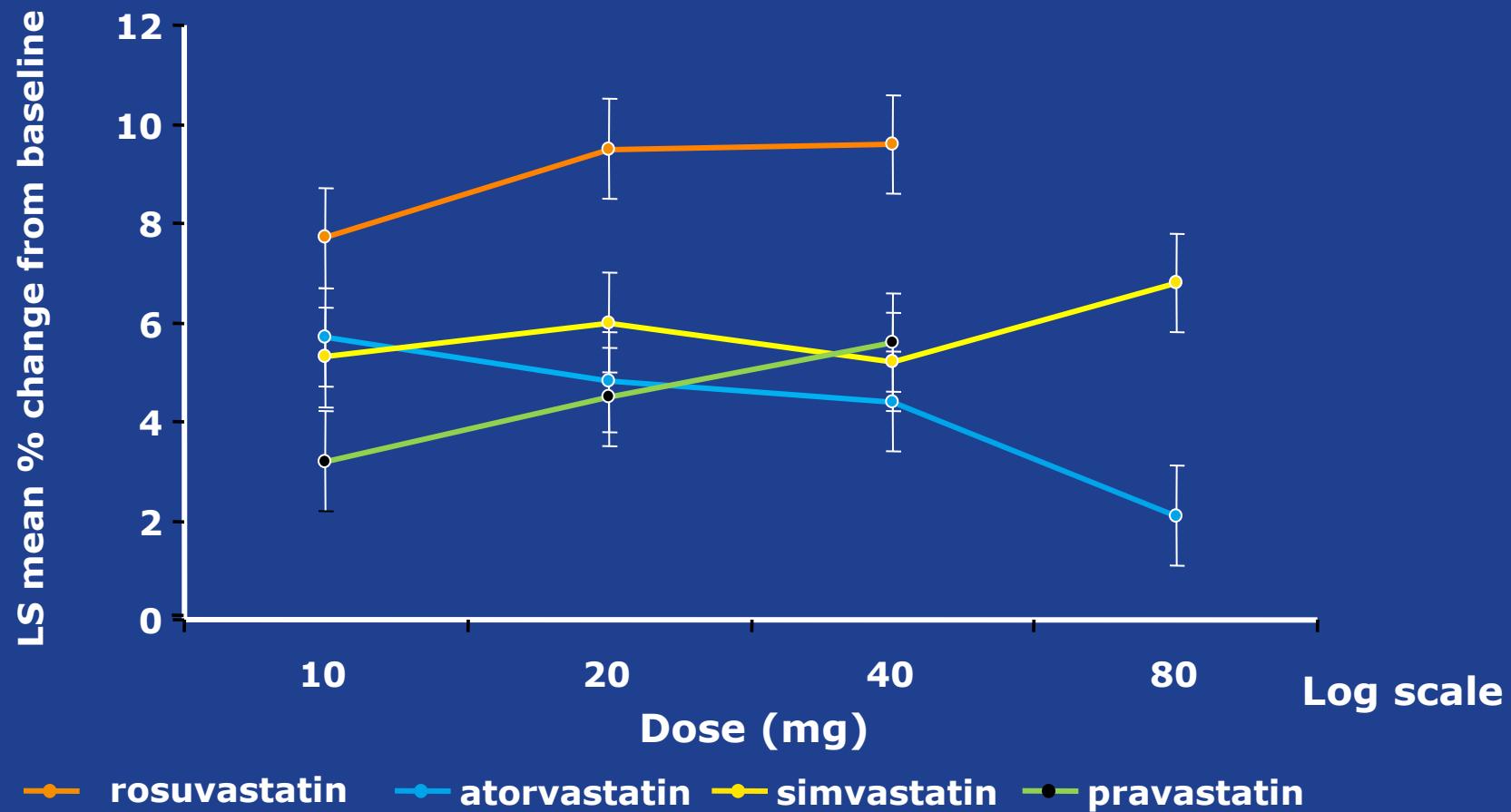
LDL-C goal: <116mg/dL (3.0 mmol/L)

\*  $p<0.001$  vs rosuva 10mg  
#  $p<0.001$  vs rosuva 20mg  
‡  $p<0.001$  vs rosuva 40mg

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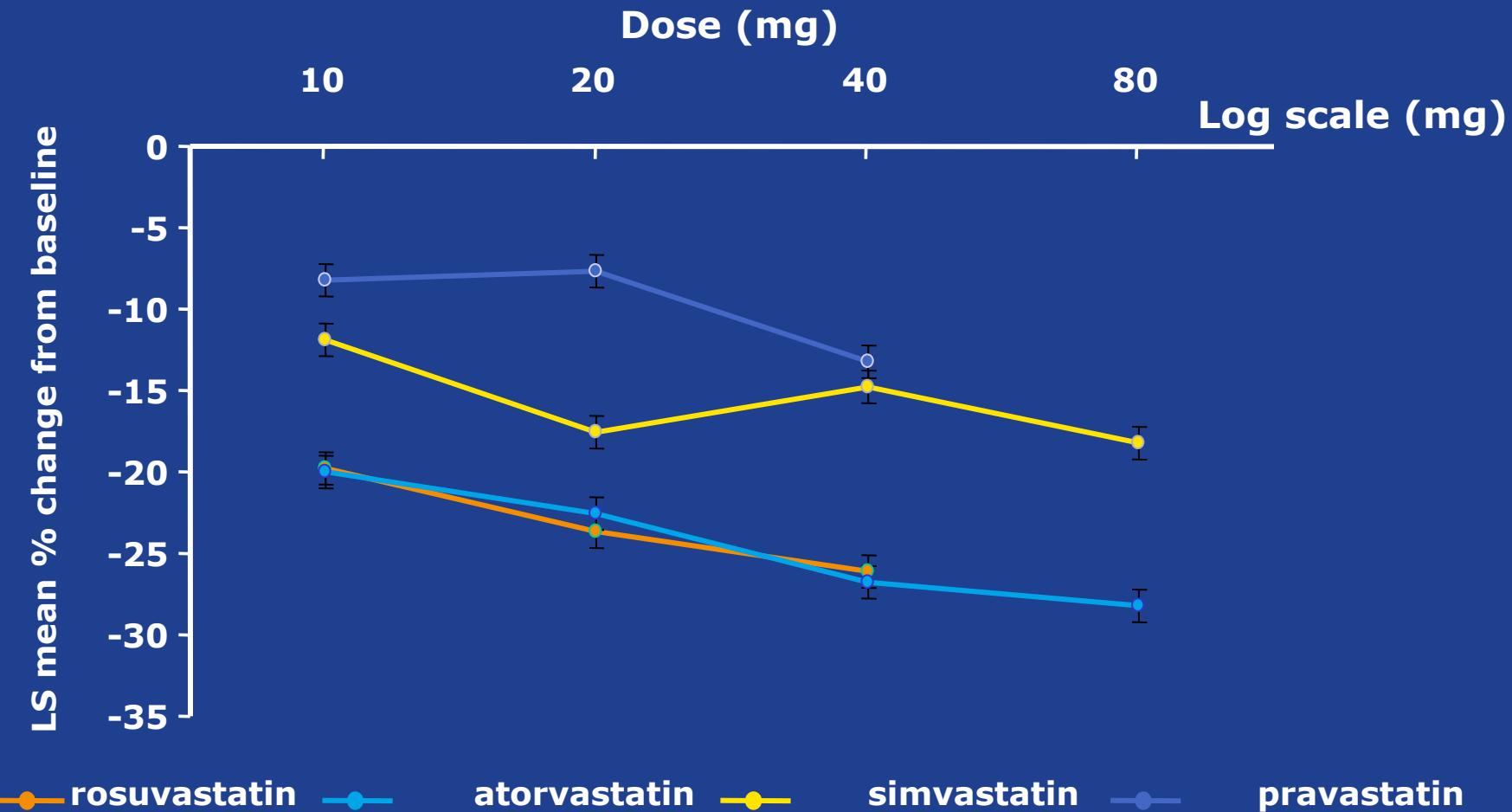
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# Stellar Study: HDL-C: Percentage Change from Baseline at Week 6



Jones PH, Am J Cardiol. 2003 Jul 15;92(2):152-60

# Stellar Study: TG: Percentage Change from Baseline at Week 6

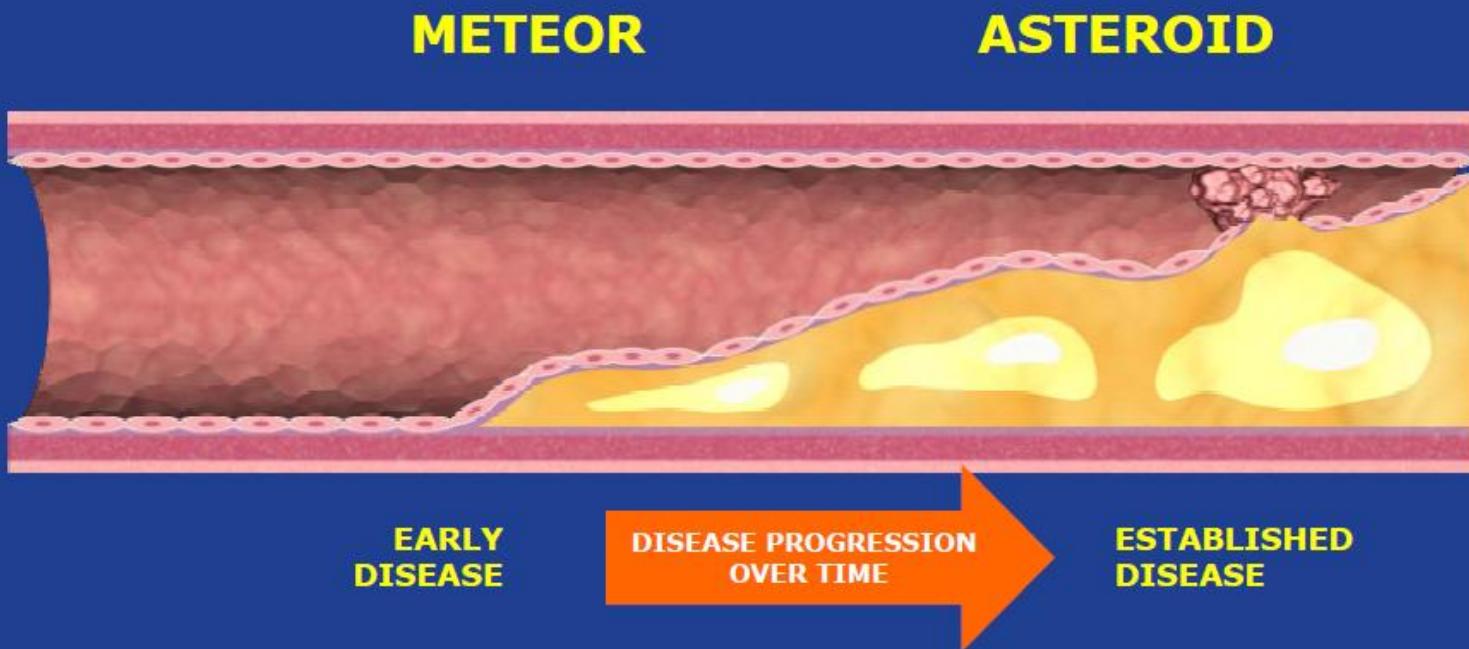


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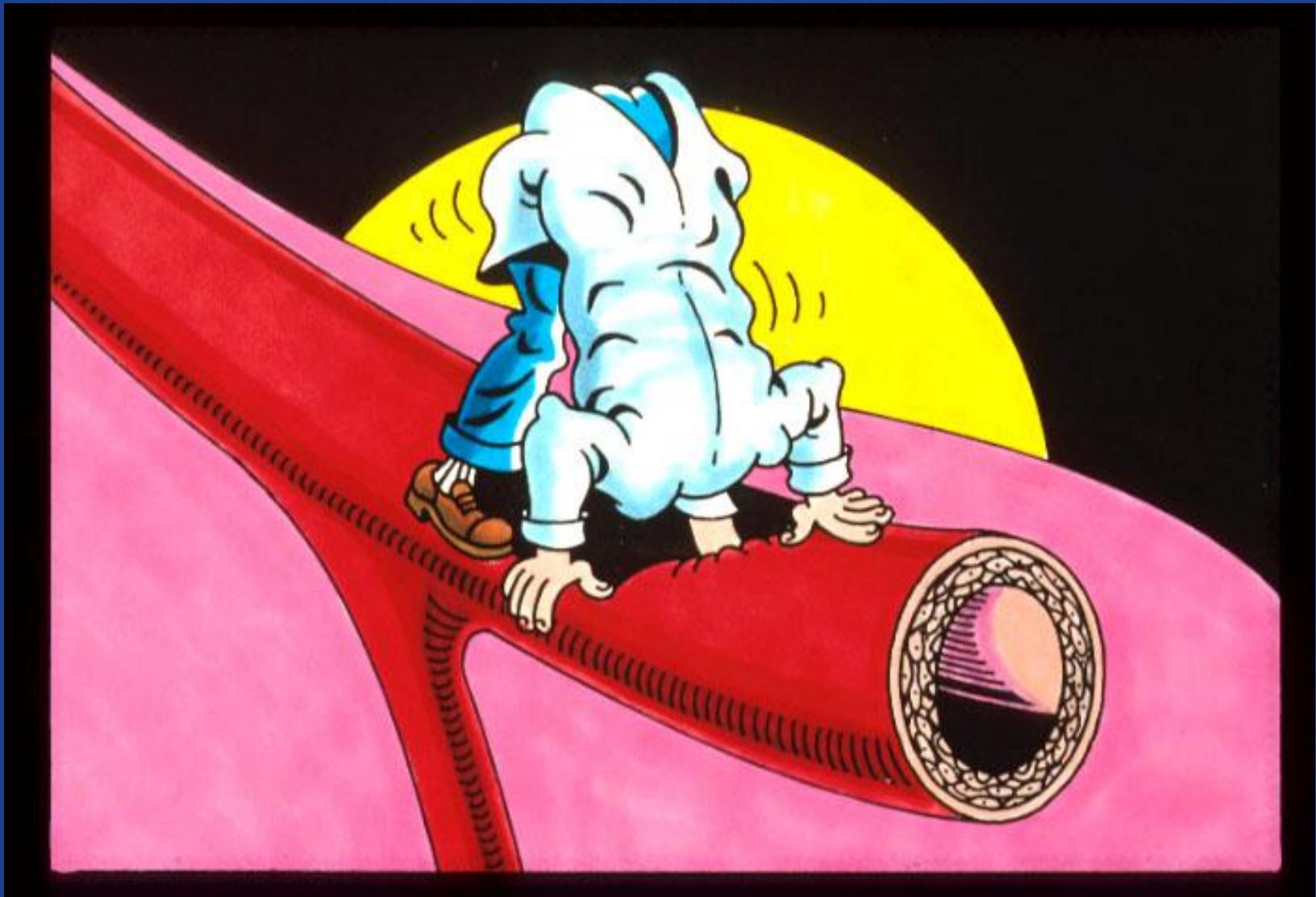
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# Rosuvastatin: Imaging Studies

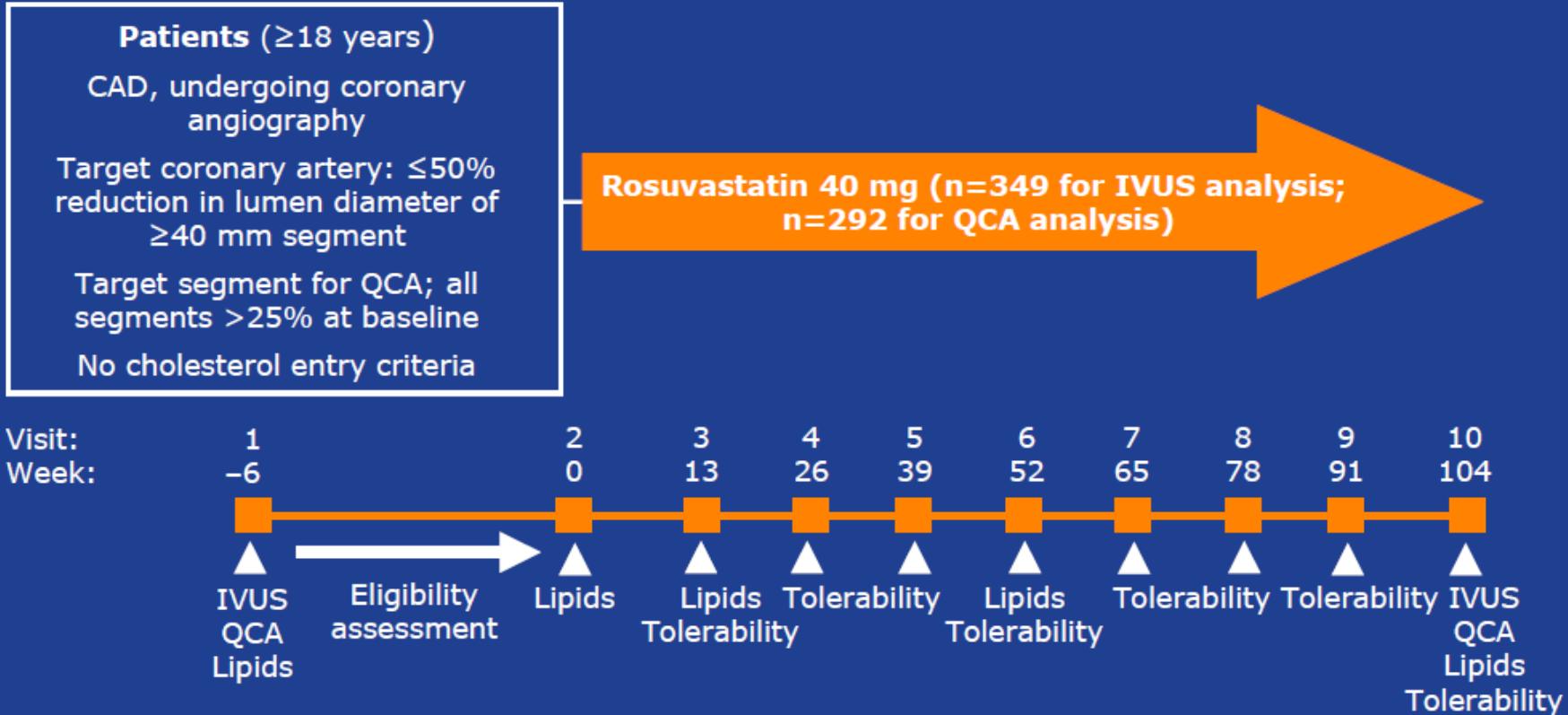


# Rosuvastatin: Asteroid Study

## Let Us Take a Look Inside



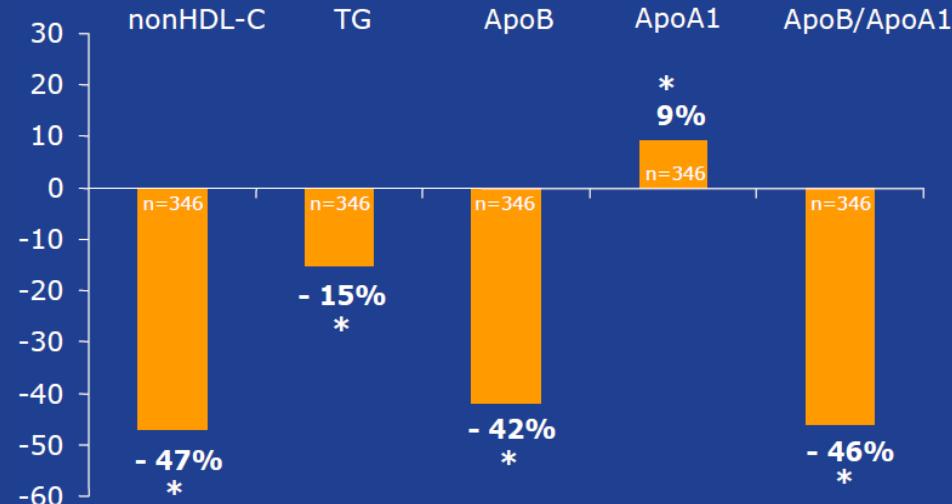
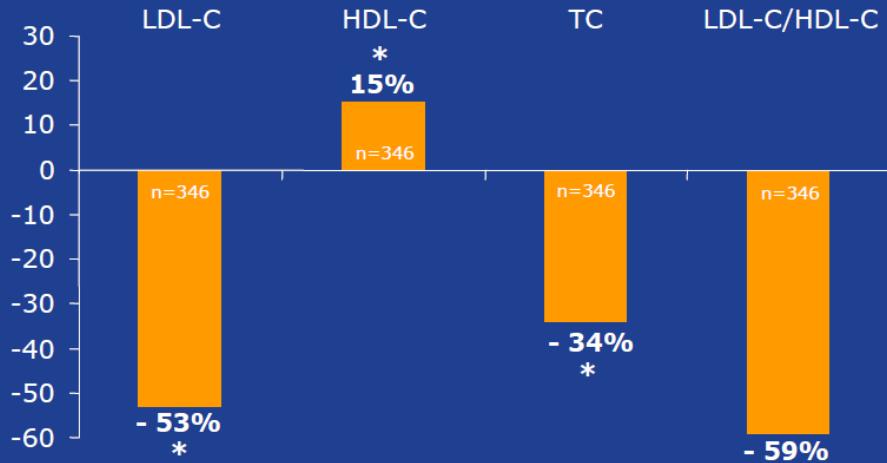
# Rosuvastatin: Asteroid - Design



CAD=coronary artery disease; PCI=percutaneous coronary intervention; IVUS=intravascular ultrasound; QCA=Quantitative coronary angiography

# Rosuvastatin: Asteroid

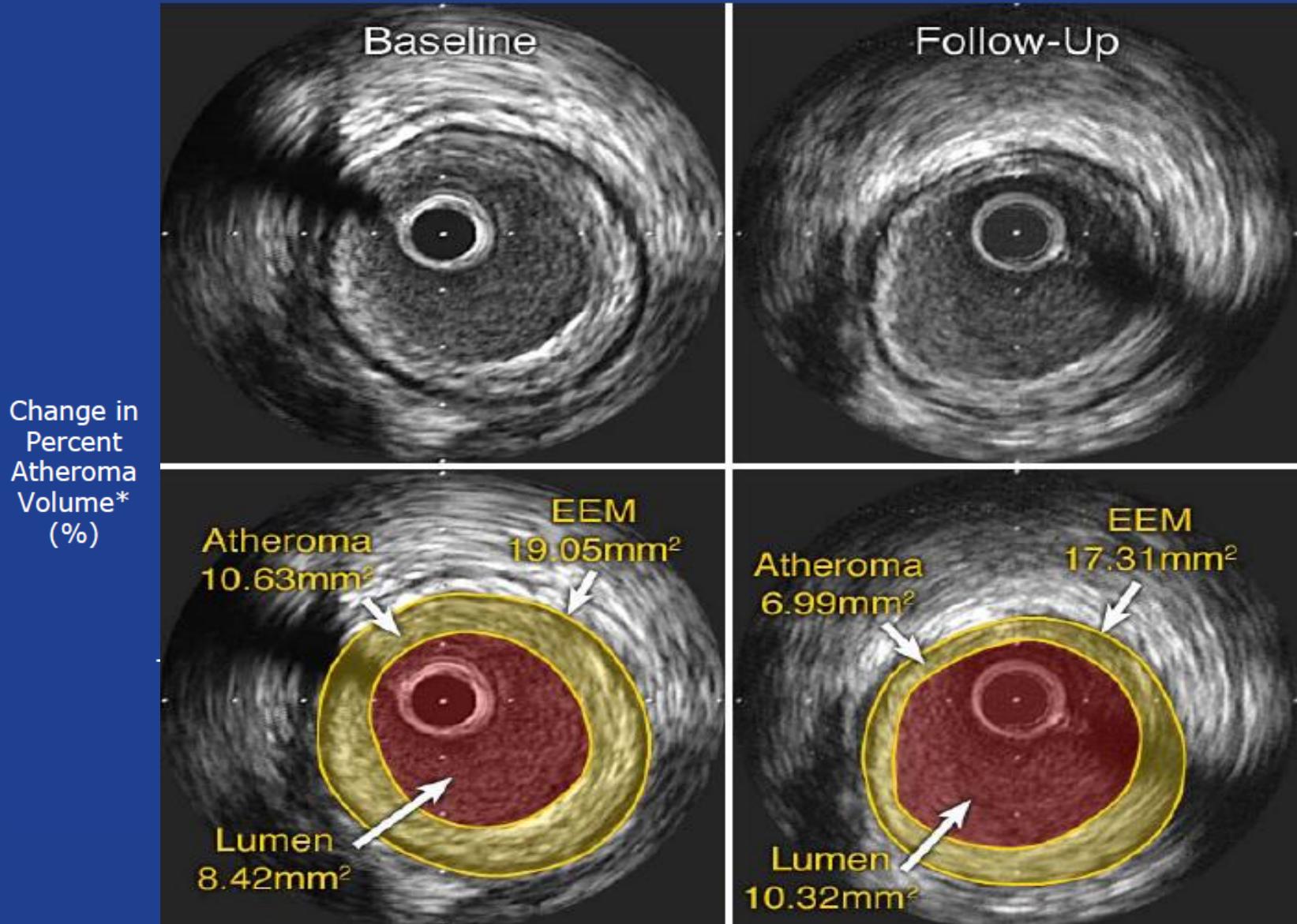
## Lipid changes



## EOS Lipid Levels

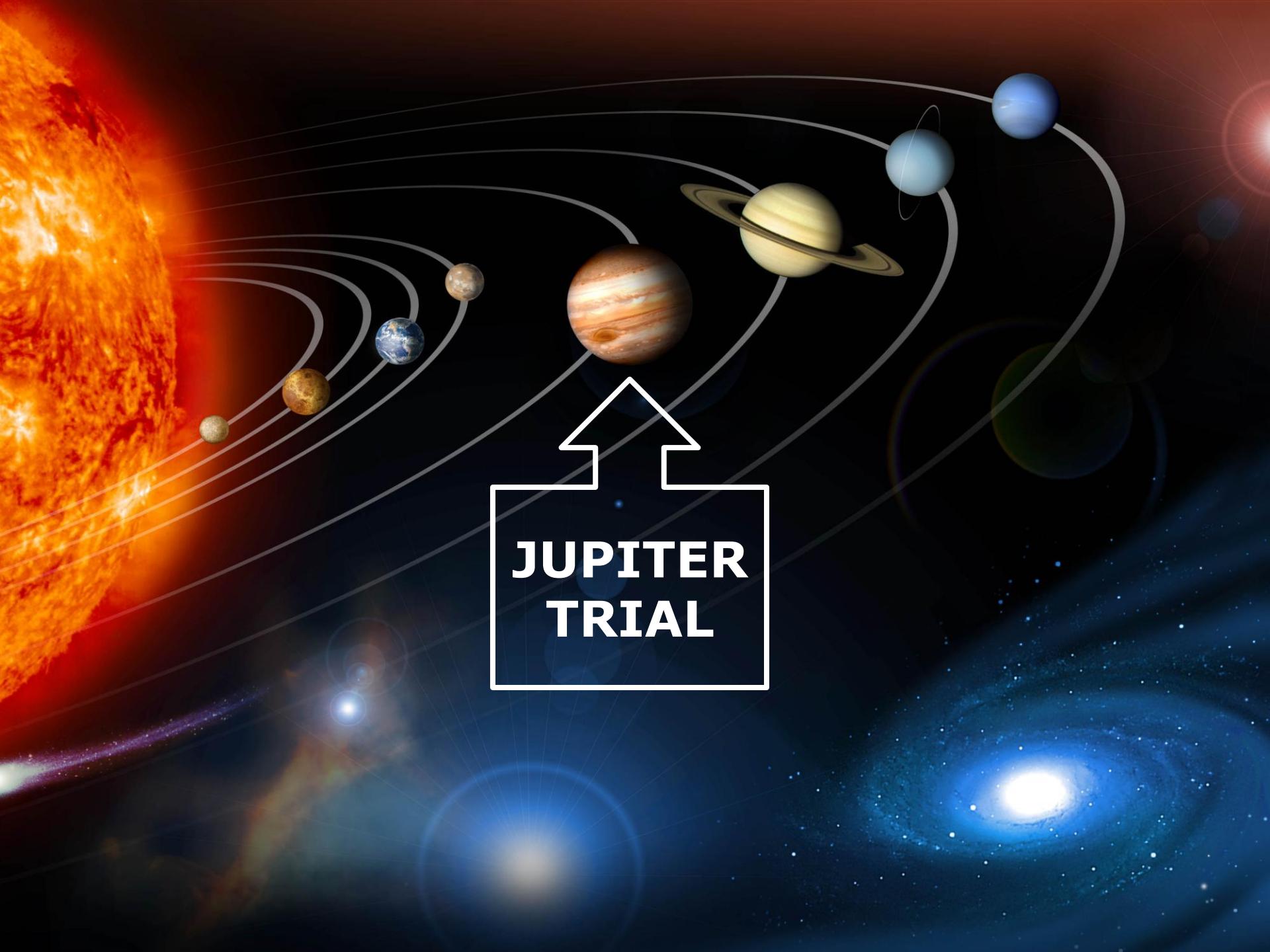
TC	TG	LDL	HDL	apoB
mmol/L				g/l
3, 4 ± 0,66	1, 37 ± 0,64	1, 57 ± 0,52	1, 27 ± 0,33	0, 75 ± 0,22

# And What About Atherosclerosis?



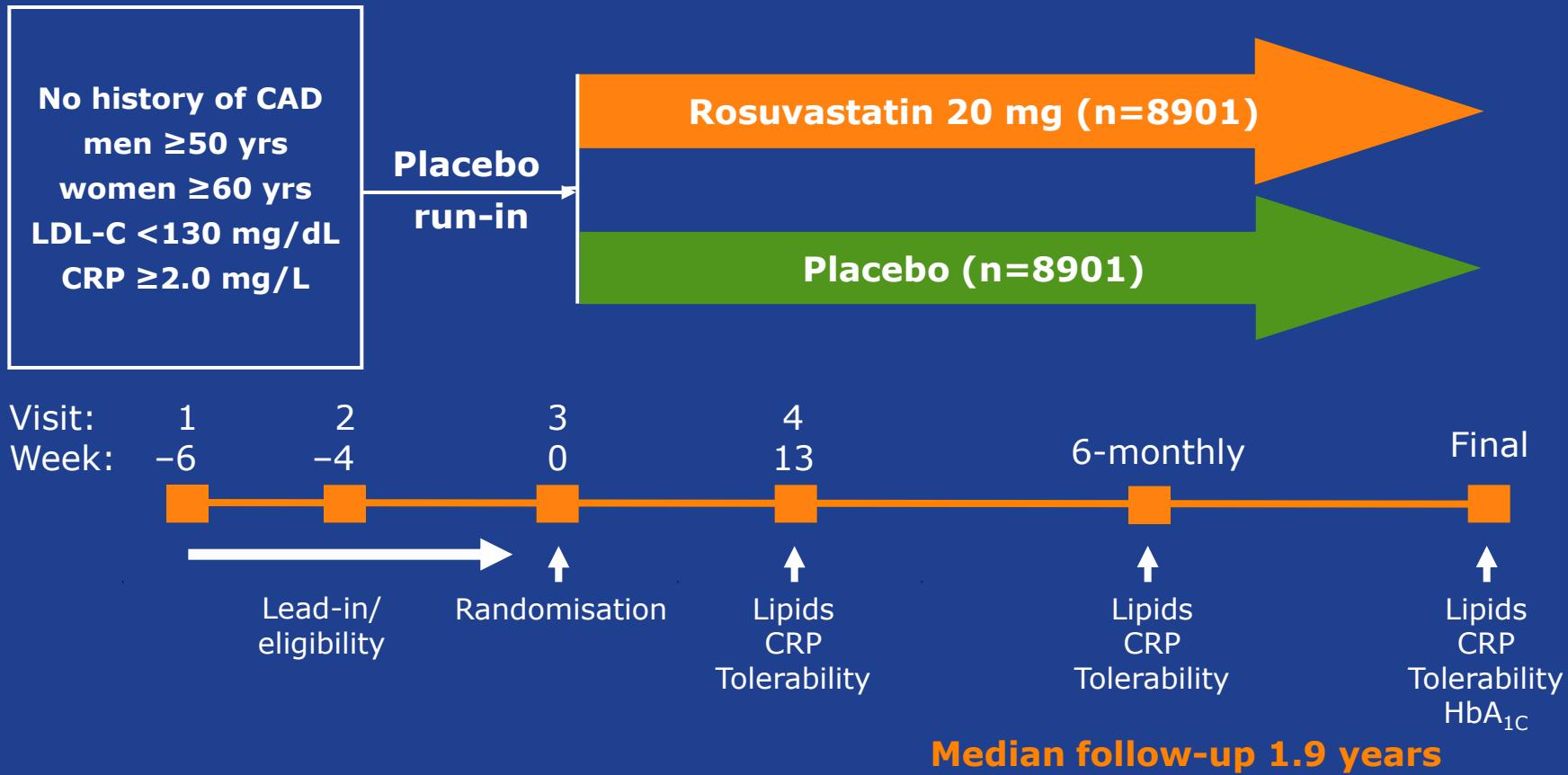
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**JUPITER  
TRIAL**

# JUPITER – study design



CAD=coronary artery disease; LDL-C=low-density lipoprotein cholesterol; CRP=C-reactive protein; HbA<sub>1c</sub>=glycated haemoglobin

# JUPITER - Study Endpoints

- Primary Endpoint
  - Time to the first occurrence of a major cardiovascular event, composite of:
    - cardiovascular death
    - Stroke
    - MI
    - unstable angina
    - arterial revascularisation
- Secondary Endpoints:
  - total mortality
  - non-cardiovascular mortality
  - development of diabetes mellitus
  - development of venous thromboembolic events
  - bone fractures
  - discontinuation of study medication due to adverse effects.

## JUPITER - Major inclusion criteria

- Men aged  $\geq 50$  years; women aged  $\geq 60$  years
- Fasting LDL-C levels  $< 130$  mg/dL (3.4 mmol/L) , CRP levels  $\geq 2.0$  mg/L and TG levels  $< 500$  mg/dL (5.7 mmol/L) on initial screening

# JUPITER - Baseline characteristics\*

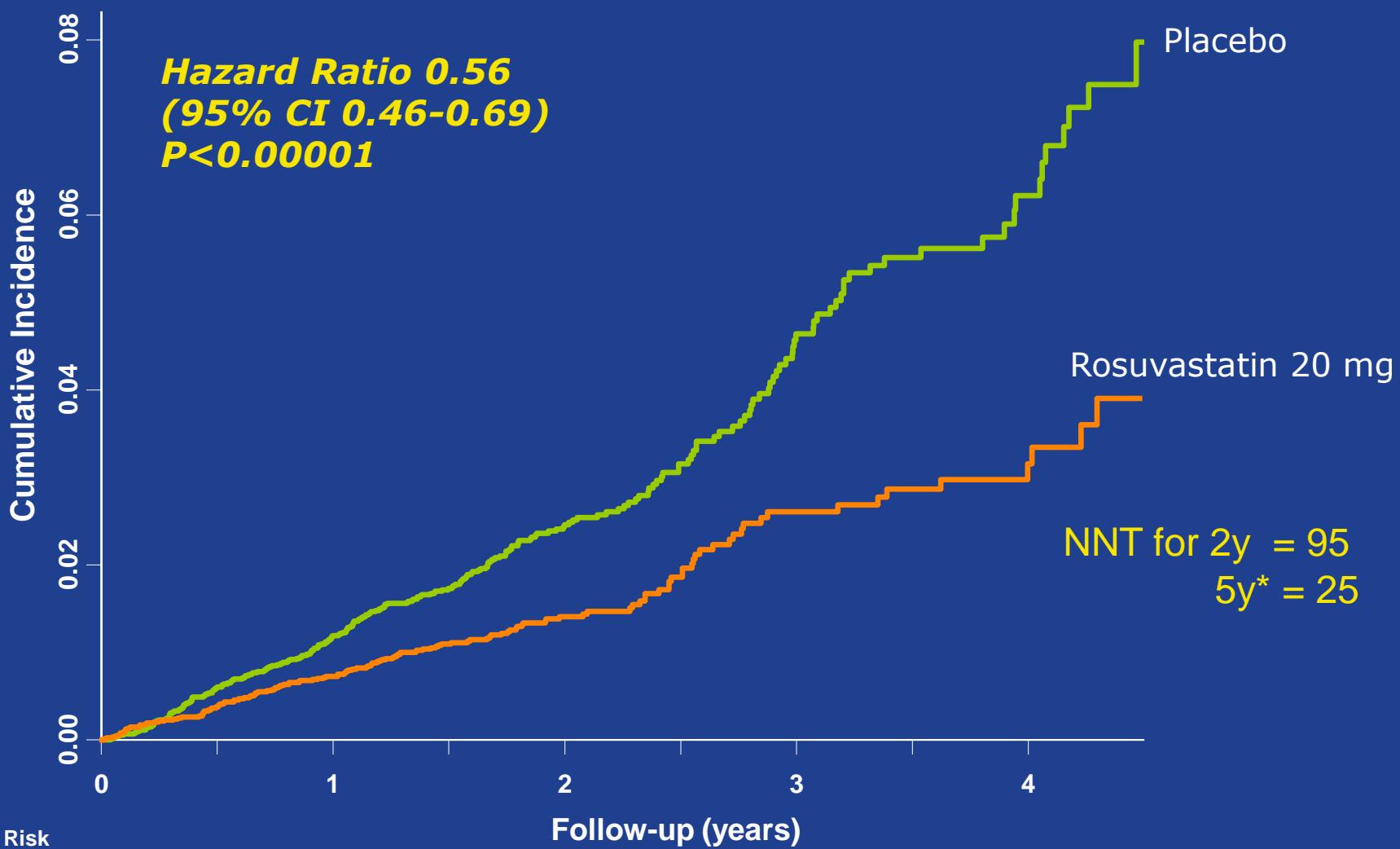
	Rosuvastatin n=8901	Placebo n=8901
Age (years)	66 (60-71)	66 (60-71)
Male sex (%)	61.5	62.1
BMI (kg/m <sup>2</sup> )	28.3 (25.3-32.0)	28.4 (25.3-32.0)
BP (mmHg)	134/80	134/80
TC (mg/dL/mmol/L)	186 (4,8)	185 (4,8)
LDL -c (mg/dL/mmol/L)	108 (2,8)	108 (2,8)
HDL - C (mg/dL/mmol/L)	49 (1,3)	49 (1,3)
Triglycerides (mg/dL/mmol/L)	118 (1,3)	118 (1,3)
hsCRP (mg/L)	4.2 (2.8-7.1)	4.3 (2.8-7.2)
Glucose (mg/dL/mmol/L)	94 (5,2)	94 (5,2)
HbA <sub>1c</sub> (%)	5.7 (5.4-5.9)	5.7 (5.5-5.9)

\*All values are median (interquartile range) or N (%).

Ridker P et al. *N Eng J Med* 2008;359: 2195-2207

# JUPITER - Primary Endpoint

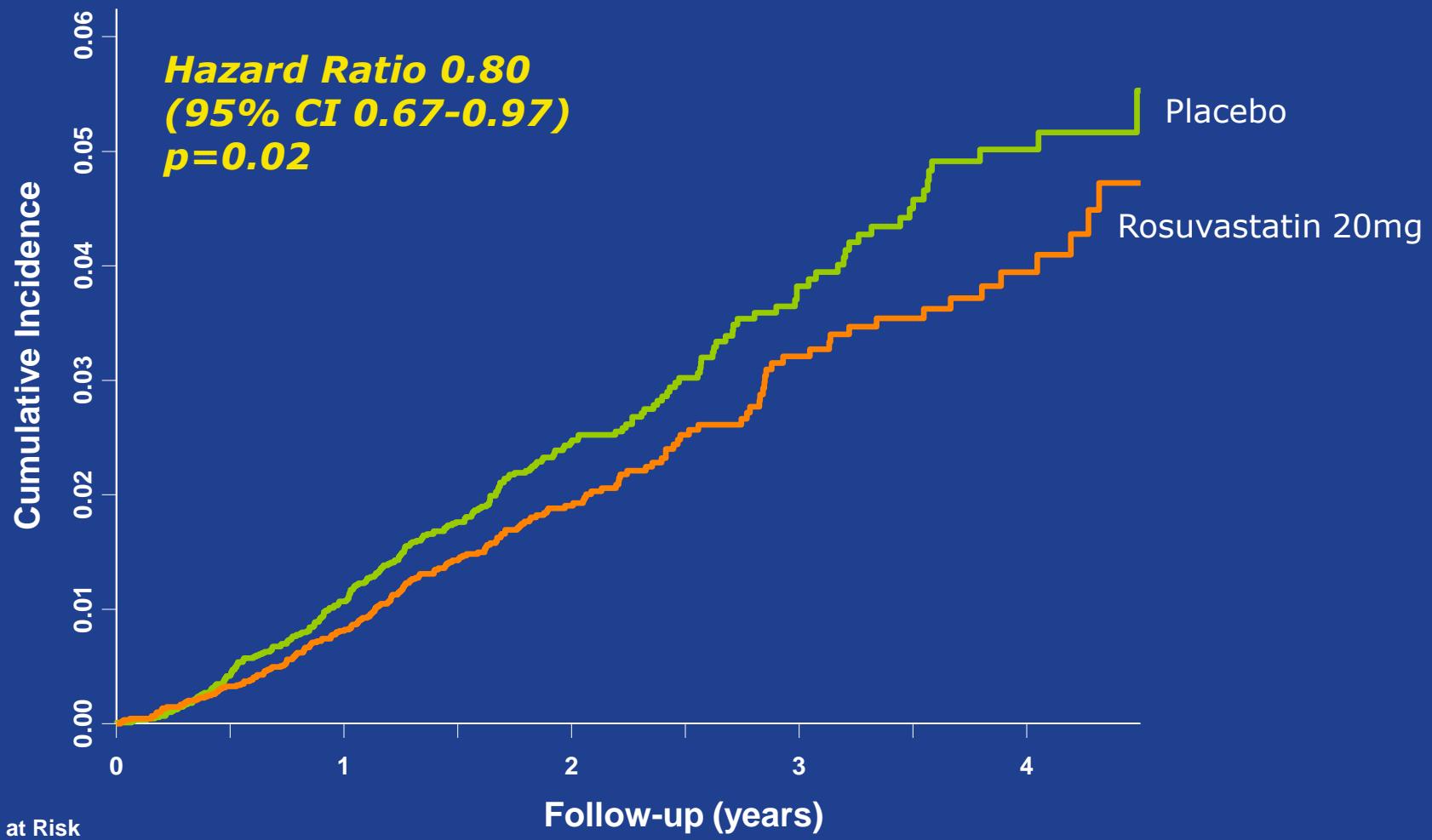
**Time to first occurrence of a CV death, non-fatal stroke, non-fatal MI, unstable angina or arterial revascularization**



\*Extrapolated figure based on Altman and Andersen method

# JUPITER - Total Mortality

*Death from any cause*



# JUPITER - Dual Treatment Target

**Hazard Ratios for Incident CV Events According to Achieved Concentrations of LDL-C and hsCRP**

Group	N (Event rate*)	HR**	95% CI	P-value
<b>Placebo</b>	<b>7832</b> (1.11)	<b>1.00</b>		
<b>Rosuvastatin</b>				
[Dual target: LDL-C < 70mg/dL, hsCRP < 2mg/L]				
Dual target achieved	<b>2685</b> (0.38)	<b>0.35</b>	0.23-0.54	
Dual target not achieved	<b>5031</b> (0.74)	<b>0.64</b>	0.49-0.84	
P-value (active treatment)				0.033
P-value (trend across groups)				<0.0001
LDLC ≥ 70mg/dL	<b>2110</b> (0.91)	<b>0.85</b>	0.60-1.21	
LDLC < 70mg/dL	<b>5606</b> (0.51)	<b>0.45</b>	0.33-0.59	
P-value (trend across hsCRP strata)				<0.0001
hsCRP ≥ 2mg/L	<b>4305</b> (0.77)	<b>0.68</b>	0.51-0.89	
hsCRP < 2mg/L	<b>3411</b> (0.42)	<b>0.36</b>	0.24-0.54	
P-value (trend across LDL-C strata)				<0.0001

**Conversion: LDL-C < 70 mg/dL = 1.8 mmol/L**

\* Rates are per 100 person years; \*\*Fully adjusted model controlled for age (years), baseline LDL-C (mg/dL), baseline hsCRP (mg/L), baseline HDL-C (mg/dL), blood pressure, gender, body mass index ( $\text{kg}/\text{m}^2$ ), smoking status and parental history of premature coronary heart disease.

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# JUPITER

## Tolerability and safety data

	Placebo [n=8901]	Rosuvastatin [n=8901]	p-value
<b>Adverse Events, (%)</b>			
Any serious adverse event	15.5	15.2	0.60
Muscle weakness, stiffness, pain	15.4	16.0	0.34
Myopathy	0.1	0.1	0.82
Rhabdomyolysis	0.0	<0.1*	----
Newly diagnosed cancer	3.5	3.4	0.51
Death from cancer	0.7	0.4	0.02
Gastrointestinal disorders	19.2	19.7	0.43
Renal disorders	5.4	6.0	0.08
Bleeding	3.1	2.9	0.45
Hepatic disorders	2.1	2.4	0.13
<b>Other events, (%)</b>			
Newly diagnosed diabetes**	2.4	3.0	0.01
Haemorrhagic stroke	0.1	0.1	0.44

\*Occurred after trial completion; \*\*physician reported newly diagnosed diabetes

Ridker P et al. N Eng J Med 2008;359: 2195-2207

# JUPITER

## Laboratory Safety Data

	Placebo [n=8901]	Rosuvastatin [n=8901]	p-value
<b>Laboratory Values, N (%)</b>			
Serum creatinine <sup>‡</sup>	10 (0.10)	16 (0.20)	0.24
ALT > 3 x ULN <sup>#</sup>	17 (0.20)	23 (0.30)	0.34
Glycosuria <sup>†</sup>	32 (0.40)	36 (0.50)	0.64
<b>Laboratory Values, median values (IQR)</b>			
GFR*, (mL/min/1.73m <sup>2</sup> )	66.6 (58.8-76.2)	66.8 (59.1-76.5)	0.02
% HbA1c**	5.8 (5.6-6.1)	5.9 (5.7-6.1)	0.001
Fasting plasma glucose**, (mg/dL)	98 (90-106)	98 (91-107)	0.12

GFR = Glomerular filtration rate, HbA1c = Haemoglobin A1c

# on consecutive visits, ‡ >100% increase from baseline, \*at 12 months, \*\*at 24 months, †>trace at 12 months

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# JUPITER – Venous Thromboembolic Events

## *Occurrence of Venous Thromboembolism by Study Group*

Endpoint	Placebo [n=8901] n (rate*)	Rosuvastatin [n=8901] n (rate*)	HR	95% CI	p-value
<b><i>Primary efficacy analysis, 94 cases</i></b>					
All cases of VTE	<b>60</b> (0.32)	<b>34</b> (0.18)	<b>0.57</b>	0.37-0.86	<b>0.007</b>
Unprovoked VTE	<b>31</b> (0.17)	<b>19</b> (0.10)	<b>0.61</b>	0.35-1.09	<b>0.09</b>
Provoked VTE	<b>29</b> (0.16)	<b>15</b> (0.08)	<b>0.52</b>	0.28-0.96	<b>0.03</b>
Pulmonary embolism	<b>22</b> (0.12)	<b>17</b> (0.09)	<b>0.77</b>	0.41-1.45	<b>0.42</b>
Deep vein thrombosis	<b>38</b> (0.20)	<b>17</b> (0.09)	<b>0.45</b>	0.25-0.79	<b>0.004</b>

Unprovoked VTE = occurred in absence of malignancy, trauma, hospitalization or surgery within 3 months before event.  
Provoked VTE = includes events that occurred in patients with cancer or during or shortly after trauma or surgery

\* Rates are per 100 person years

VTE – venous thromboembolism

HR – Hazard Ratio; CI – Confidence Interval

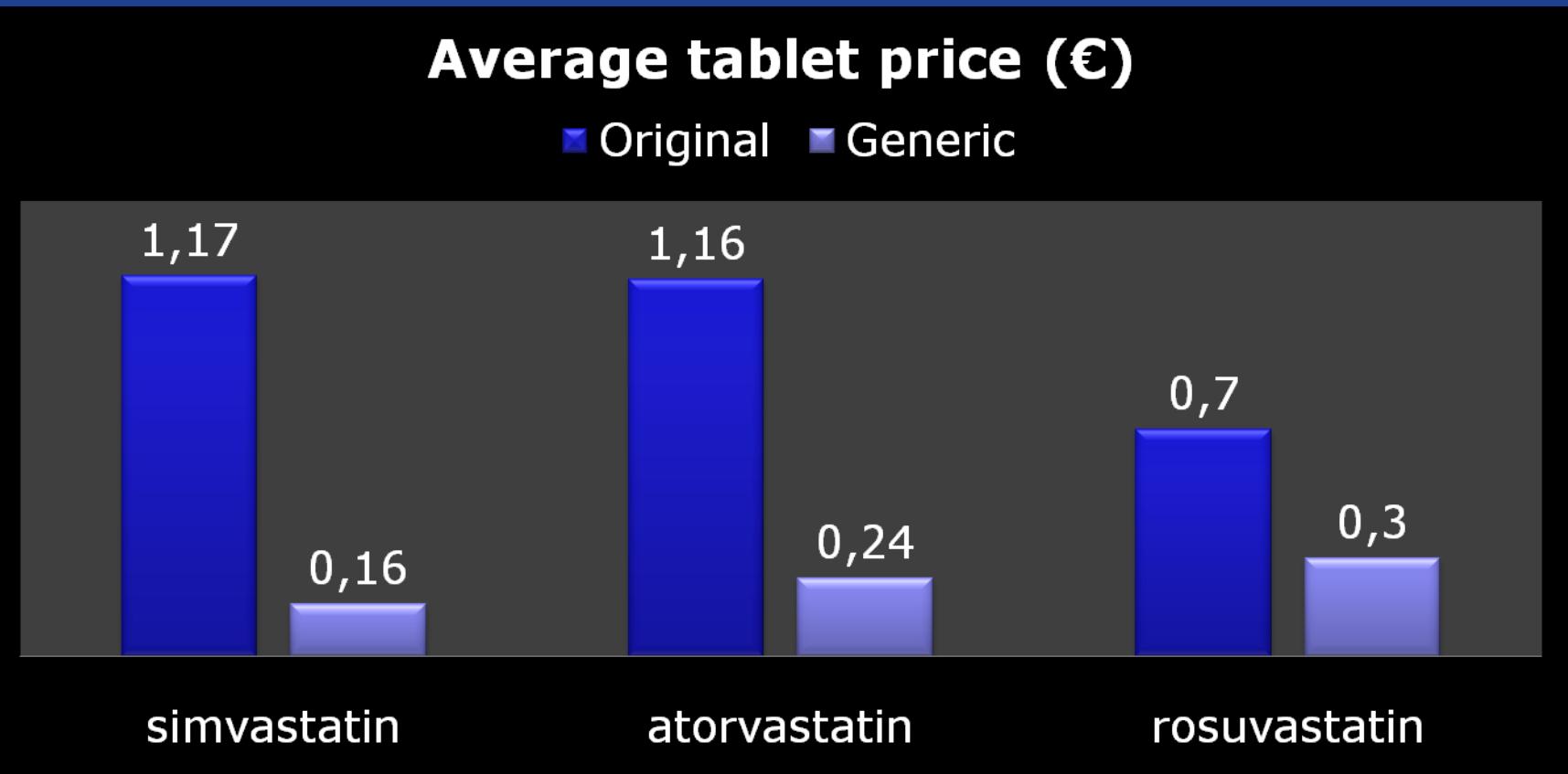
Glynn RJ et al. NEJM 2009; **360**: (10.1056/NEJMoa0900241)

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# Development of Statin Prices

*Comparison of Prices after First Introduction to Market and Current Situation*



# Rosuvastatin: a Galaxy of Evidence



**Most effective LDL-c lowering**



**Favourable impact on other lipoprotein classes (TG, HDL)**



**Evidence of slowing progression/inducing regression of atherosclerosis**



**Evidence of CVD risk reduction (JUPITER)**



**Satisfactory safety profile**