

# Comparison of the efficacy and safety of rosuvastatin versus atorvastatin, simvastatin, and pravastatin across doses (STELLAR Trial)

(Am J Cardiol 2003;93:152-60)

**Study Type:** Disease-oriented trial. The data focuses on markers for disease and not patient -oriented outcomes.

**Purpose:** Stellar trial compares the LDL cholesterol lowering effect of the FDA approved dose ranges for rosuvastatin versus atorvastatin, simvastatin and pravastatin.

**Study Duration:** 6 weeks, n = 2431 (~150 in each group)

**Trial Design:** Randomized, open-labeled trial; multicenter (182 centers in USA)

Patients were instructed to follow NCEP Step 1 diet; then randomized to 1 of 15 treatments taken once daily for 6 weeks

Fasting lipid panels were drawn at randomization and then at 4 weeks, and 6 weeks

**Drugs:** Rosuvastatin 10, 20, 40, 80 mg

atorvastatin 10, 20, 40, 80 mg

simvastatin 10, 20, 40, 80 mg

pravastatin 10, 20, 40 mg (the 80 mg was not approved by the FDA at the time of this trial)

**Patients:** 2431 patients, 86% white, 8% black, 50% male, mean age of 58 yrs, ~30% > 65 years, ~20% have a history of cardiovascular disease, 8% diabetics

**Inclusion:** patient compliance with diet; men & women with hypercholesterolemia  $\geq$  18 years; LDL baseline of >160 and < 250; triglycerides < 400 at all prerandomized visits

**Exclusion:** pregnant women; sensitivity to statins; serious unstable medical conditions; psychological instability; familial hypercholesterolemia; concomitant medication known to interact with the drugs or lipid profile; history of drug abuse; creatine kinase > 3 times normal; LFT's or bilirubin 1.5 times normal;

**Outcome Events:** Primary endpoints: % change in LDL from baseline to 6 weeks

Secondary endpoints: pair comparisons, safety assessment, getting to goal LDL as defined by National Cholesterol Education Program

## 1. Are the results valid?

Randomized? Yes

Blinded? No

Study groups similar at start? yes

Equal treatment of groups? yes

Proper accounting at end? yes

## 2. What are the results?

Dose	Rosuvastatin	Atorvastatin	Simvastatin	Pravastatin
10 mg	-46%	-37%	-28%	-20%
20 mg	-52%	-43%	-35%	-24%
40 mg	-55%	-48%	-39%	-30%
80 mg	n/a	-51.1%	-45.8%	n/a

**Primary Outcome:** Mean Change from Baseline in LDL Cholesterol

### Observations

- \* 10 mg dose of rosuvastatin was as effective in lowering LDL as 20 mg of the others (p < .001).
- \* 10 mg dose of rosuvastatin was as effective in lowering LDL as 10, 20, 40 mg atorvastatin (p<.001)
- \* 20 mg rosuvastatin was as effective as atorvastatin or simvastatin 80 mg.

Dose	Rosuvastatin	Atorvastatin	Simvastatin	Pravastatin
10 mg	+7.7%	+5.7%	+5.3%	+3.2%
20 mg	+9.5%	+4.8%	+6.0%	+4.4%
40 mg	+9.6%	+4.4%	+5.2%	+5.6%
80 mg	n/a	+2.1%	+6.8%	n/a

**Secondary Outcomes:** Mean Change from Baseline in HDL cholesterol

- \* low dose rosuvastatin was as effective in increasing HDL as other doses of the other agents

### Triglycerides

- \* Rosuvastatin lowered triglycerides by 20 points and are as good as atorvastatin and better than simvastatin and pravastatin.

### Percent reaching NCEP guidelines

- \* Highest proportion of patients reaching NCEP LDL cholesterol goals was 89% in the rosuvastatin group, 85% in atorvastatin group and 82% in the simvastatin group.

### Safety

- \* overall trial treatments were well tolerated
- \* 46% of all patients experienced some adverse effect
- \* Most common across all groups were: pain (6%); pharyngitis (5%), myalgia (4%); headache (3%)
- \* 80 mg rosuvastatin caused the most myalgia (7.3%)
- \* acute renal failure in 2 patients in the 80 mg rosuvastatin group, both recovered after discontinuation of therapy
- \* no cases of myopathy

### **3. Will the results help me?**

- \* 10 mg of rosuvastatin is as effective at lowering LDL as most other doses of the other drugs
- \* 20 mg of rosuvastatin is as effective at lowering LDL as 80 mg of atorvastatin or simvastatin
- \* More side effects with the 80 mg dose of rosuvastatin. Based on the chart of LDL lowering, the 80 mg dose is not needed and may be too potent.

#### **Perspective and spin:**

**Perspective:** Let's remember that this is a disease-oriented article. Treating cholesterol numbers does not mean that patients will get a positive benefit in outcomes that matter to patients, like heart attack, stroke and all-cause mortality.

**Spin doctor:** If the 10 mg dose is effective and potent, what about the 5 mg dose or even a 2.5 mg dose? Astra-Zeneca has shown efficacy data with a 1 mg dose. No wonder the 80 mg dose has lots of side effects. Any statin given at high doses can cause renal and other serious side effects. If 20 mg of rosuvastatin is equivalent to 80 mg of atorvastatin, then 80 mg of rosuvastatin is equivalent to 320 mg of atorvastatin.