2005]. "Widening the treatment target to include prevention of VTE in addition to arterial thrombosis will increase the benefits of statin use," Dr. Glynn concluded.

Paul Ridker, MD, Brigham and Women's Hospital, Boston, MA, discussed results of another prespecified subanalysis that compared clinical outcomes between JUPITER trial participants according to achieved levels of LDL and hsCRP. The findings established hsCRP as a biomarker of risk for cardiovascular disease not only in people with known risk factors but also in asymptomatic individuals who previously were considered at average or even low risk for MI, stroke, or death from cardiovascular causes [Ridker PM et al. *Lancet* 2009].

In this subanalysis (87% of full cohort), the clinical outcomes of JUPITER trial participants were evaluated according to achieved levels of LDL (≥70 or <70 mg/dL) and hsCRP (≥2 or <2 mg/L).

After adjusting for baseline variables, rosuvastatin-treated subjects who achieved a reduction in LDL levels to <70 mg/dL had a 55% reduction in cardiovascular events (HR, 0.45; 95% CI, 0.34 to 0.60; p<0.0001); those who achieved an hsCRP reduction <2 mg/L had a 62% reduction in event rate (HR, 0.38; 95% CI, 0.26 to 0.56; p<0.0001), and those who achieved both a reduction of LDL <70 mg/dL and hsCRP <2 mg/L had a 65% CV event reduction (HR, 0.35; 95% CI, 0.23 to 0.54; p<0.0001). In individuals who achieved an LDL reduction of <70 mg/dL and hsCRP reduction of <1 mg/L, there was a 79% event rate reduction (HR, 0.21; 95% CI, 0.09 to 0.52; p<0.001). Similar effects were observed in analyses that were based on apolipoprotein (Apo) B or ApoB:ApoA ratio rather than on LDL.

Dr. Ridker pointed out that the impact of hsCRP reduction appears to be independent of LDL, because less than 2% of the variance in achieved hsCRP was explained by the variance in achieved LDL. This fits with previous study results (PROVE IT-TIMI 22 and A to Z trials) that have indicated that in patients with acute coronary ischemia who were treated with statin therapy, greater clinical benefits were achieved when hsCRP levels were reduced to below 1 to 2 mg/L [Ridker PM et al. *N Engl J Med* 2005; Morrow DA et al. *Circulation* 2006].

Despite these encouraging results, Dr. Ridker stressed that for patients with raised LDL or raised hsCRP, initial interventions should include dietary restrictions, exercise, and smoking cessation. However, he estimated that applying the JUPITER screening and treatment strategy to the overall US population for 5 years could prevent more than 250,000 cardiovascular disease-related events.

Patients Receiving Hemodialysis for Treatment of End-Stage Renal Disease Did Not Benefit From Statin Therapy: Results of the AURORA Trial

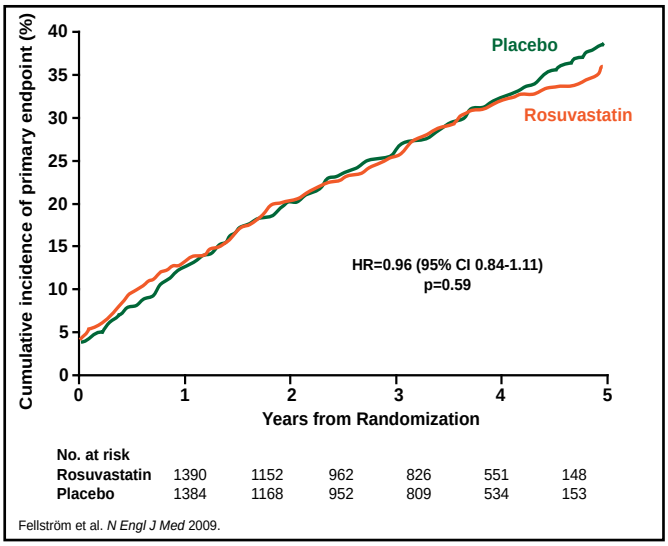
Rosuvastatin did not improve cardiovascular morbidity and mortality in patients who had end-stage renal disease (ESRD) and who were on hemodialysis, according to results of the large, randomized, placebo-controlled AURORA (A study to evaluate the Use of Rosuvastatin in subjects On Regular hemodialysis: an Assessment of survival and cardiovascular events; NCT00240331) trial. There was no difference between rosuvastatin 10 mg and placebo in reducing the combined endpoint of cardiovascular death, nonfatal stroke, and nonfatal myocardial infarction (MI) or any of the individual components of this endpoint when analyzed separately. The results were presented by Bengt Fellström, MD, University Hospital, Uppsala, Sweden [Fellström B et al. *New Engl J Med* 2009].

A number of studies have shown that statins lower the incidence of cardiovascular events in high-risk patients; however, it was unknown if they would have a similar effect in patients with ESRD who were on hemodialysis. A previous study with atorvastatin failed to demonstrate that statins have a statistically significant effect in reducing cardiovascular events in diabetic patients on hemodialysis with ESRD [Wanner C et al. *New Engl J Med* 2005].

Results from AURORA showed no statistically significant difference between the rosuvastatin 10 mg daily group and the placebo group in the primary endpoint of major cardiovascular event (defined as cardiovascular death, nonfatal MI, or nonfatal stroke). A major cardiovascular event occurred in 396 rosuvastatin-treated subjects and 408 subjects who received placebo (HR, 0.96; 95% CI, 0.84 to 1.11; p=0.59; Figure 1). There were no statistically significant differences in any of the secondary endpoints, including any death (p=0.51), noncardiovascular death (p=0.34), major cardiovascular event-/cause-specific death (p=0.30), atherosclerotic cardiac event (p=0.64), vascular access procedure for hemodialysis (p=0.19), and coronary or peripheral revascularization (p=0.88). Rosuvastatin achieved a 43% reduction in LDL cholesterol at 3 months, from a mean baseline level of 100 mg/dL (2.6 mmol/L), compared with a 1.9% reduction in the placebo group (p<0.001). Rosuvastatin reduced total cholesterol at 3 months by 26.6% from baseline, compared with a 0.5% reduction in the placebo group (p<0.001), and

triglyceride levels were reduced by 16.2% from baseline in the rosuvastatin group, compared with an increase of 0.9% in the placebo group (p<0.001). Adverse event rates were similar between the 2 groups. In the rosuvastatin group, 1140 (82.1%) subjects suffered a serious adverse event versus 1159 (84.1%) in the placebo group (p=0.80; Table 1). Drug-related adverse events occurred in 16 (1.2%) subjects in the rosuvastatin group and 11 (0.8%) subjects in the placebo group (p=0.35; Table 1). The baseline characteristics between the 2 groups were balanced. Mean duration of treatment was 2.4 years, and mean duration of follow-up was 3.2 years.

Figure 1. AURORA Primary Study Endpoint of Major Cardiovascular Event.



Fellström et al. *N Engl J Med* 2009.

The AURORA study was an international, multicenter, randomized, double-blind, prospective trial and was the largest and longest trial ever conducted on the efficacy of statins on cardiovascular events in persons with ESRD on hemodialysis. Patients with ESRD have advanced calcification of the arteries, and the lack of benefit on CV outcomes that was observed with statin therapy in 4D and AURORA suggests that cardiovascular disease in patients who receive chronic hemodialysis differs from that in other clinical settings. Inclusion criteria were men and women aged 50 to 80 years who had ESRD and were on hemodialysis for at least 3 months. Major exclusion criteria were taking a statin within the previous 6 months and needing a kidney transplant within the following year. The study design required 2750 subjects, and the study continued until 620 subjects had a major cardiovascular event. Assessment was every 3 months for the first year and every 6 months thereafter until the study's conclusion.

Table 1. Adverse Events for Rosuvastatin 10 mg vs Placebo.

	Rosuvastatin No. of patients (%)	Placebo No. of patients (%)	p Value
Any adverse event	1338 (96.3)	1332 (96.7)	0.56
Serious adverse events			
Any†	1140 (82.1)	1159 (84.1)	0.80
Requiring study drug discontinuation	438 (31.5)	443 (32.1)	0.78
Study drug-related	16 (1.2)	11 (0.8)	0.35
Leading to death **From CV causes** **From non-CV causes** **From unspecified causes**	640 (46.1) 324 (23.3) 248 (17.9) 68 (4.9)	662 (48.0) 324 (23.5) 267 (19.4) 71 (5.2)	0.49 0.92 0.34 0.77
Others			
Infection	976 (70.3)	956 (69.4)	0.16
Gastrointestinal disorder	814 (58.6)	788 (57.2)	0.26
Hepatic disorder	66 (4.8)	54 (3.9)	0.28
Musculoskeletal disorder	310 (22.3)	343 (24.9)	0.21
Newly diagnosed cancer	107 (7.7)	118 (8.6)	0.41

†Some patients suffered more than 1 serious adverse event; CV=cardiovascular; Source: Fellström B et al. *New Engl J Med* 2009.

During the question and answer session after the presentation, an audience member asked if the lack of efficacy resulted from the trial dose only being 10 mg. Dr. Fellström replied, "I wouldn't be surprised if it was a matter of dose."

Polypill May Offer Increased Protection Against Cardiovascular Disease in Patients With Average Risk Factors

Results of the Indian Polycap Study (TIPS; NCT00443794) indicate that it may be possible for individuals who have average risk factors for cardiovascular disease to significantly reduce their risk for heart disease and stroke through the use of a single pill—the Polycap™—which combines low doses of thiazide (12.5 mg), atenolol (50 mg), ramipril (5 mg), simvastatin (20 mg), and aspirin (100 mg). The results of TIPS were presented by the joint principal investigator of the study, Salim Yusuf, PhD, McMaster University, Hamilton, ON, Canada, at the