Five baseline variables were shown to be significant predictors of HF risk: treatment with rosiglitazone (HR, 2.25; 95% CI, 1.42 to 3.58), age ≥60 years (HR, 3.81; 95% CI, 2.34 to 6.20), waist circumference ≥104 cm (HR, 3.52; 95% CI, 2.08 to 5.98), the presence of microalbuminuria/proteinuria (HR, 3.35; 95% CI, 2.18 to 5.14; all p<0.001), and baseline beta-blocker therapy (HR, 1.86; 95% CI, 1.20 to 2.90; p=0.006).

"These findings support the current recommendation that rosiglitazone should not be used in patients with symptomatic HF and should not continue to be used in the presence of HF," said Prof. Komajda. Professor Kenneth Dickstein, MD, Stavanger University Hospital, Stavanger, Norway, the discussant for the presentation, noted that subjects with a history of treatment for HF were excluded from RECORD and that use of RSG in such patients also should be avoided.

A second analysis by Home et al. (*Lancet* 2009) also evaluated the first occurrence of MI as an endpoint and showed no difference between the RSG group and the control (HR, 1.14; 95% CI, 0.80 to 1.63) from the RECORD trial. Professor John McMurray, University of Glasgow, Glasgow, Scotland, presented results of a post hoc analysis that was focused on more broadly defined coronary events, including an analysis of time to the first of three expanded coronary endpoints in the overall trial cohort, total (including recurrent) events, and events that occurred among those subjects who experienced a "first MI" during the trial. The three additional composite outcomes were: any acute coronary syndrome ([ACS], defined as fatal MI, sudden death, or hospitalization for cardiac arrest, acute MI, or unstable angina [UA] pectoris); any ACS or hospitalization with "other" angina (defined as ACS plus "other" CV hospitalization attributed to angina pectoris); and any ACS, "other angina," or coronary revascularization.

Similar to the results of the MI analysis in the RECORD study, no difference was observed between the RSG group and the control group for any of the newly analyzed composite outcomes (Table 1).

There were a total of 15 deaths in the RSG group (7 acute MI; 8 sudden cardiac deaths) versus 22 in the control group (10 acute MI; 12 sudden cardiac deaths). Total coronary events (cardiac arrest, acute MI, UA, other angina, or revascularization) also were similar between groups, wherein 221 events were experienced by 127 subjects in the RSG group versus 230 events in 128 subjects in the control group. Overall numbers of recurrent events in subjects who had a first MI also did not differ between treatment groups. Among the 60 survivors of a first MI in the RSG group, there were 7 recurrent MIs, 3 cases of UA, and 11 deaths (7 CV deaths). Among the 52 survivors of a

first MI in the control group, there were 11 recurrent MIs, 2 cases of UA, and 12 deaths (10 CV deaths).

Table 1. Time-to-First Event Composites.

Outcome	RSG Group[1] n=2220	Control Group[2] n=2227	Hazard Ratio	95% CI	p value
First acute MI (fatal/nonfatal)	64	56	1.14	0.80-1.63	0.47
First ACS[3]	92	88	1.14	0.78-1.40	0.77
First ACS or stable angina	109	113	0.96	0.74-1.25	0.78
First ACS, stable angina, or revascularization	127	128	0.99	0.78-1.27	0.94

Rosiglitazone + metformin or + a sulfonylurea; Metformin + a sulfonylurea; ACS = fatal MI, sudden death, or hospitalization for cardiac arrest, acute MI, or unstable angina pectoris

"In the RECORD trial, contrary to the meta analysis published by Nissen and Wolski [Nissen SE and Wolski K. *N Engl J Med* 2007]," said Prof. McMurray, "we did not see statistically significant increase in coronary outcomes, an excess of recurrent coronary events, or an excess of total or cardiovascular mortality in subjects treated with rosiglitazone compared with those receiving conventional therapy."

JUPITER Subgroup Analysis Provides Convincing Evidence for Statin Therapy as Primary Prevention for CV Events in Older Individuals

Results of a subgroup analysis from the JUPITER trial (NCT00239681), presented by Robert Glynn, MD, PhD, Brigham and Women's Hospital, Boston, MA, showed a significant reduction in major cardiovascular (CV) events in older, apparently healthy individuals who were treated with rosuvastatin compared with placebo.

The JUPITER study comprised 17,802 apparently healthy men aged ≥50 years and women aged ≥60 years with LDL <130 mg/dL who were at increased vascular risk due to elevated high-sensitivity C-reactive protein (hsCRP; ≥2 mg/L). The primary endpoint of the study was major CV events, which were defined as the combined risk of myocardial infarction (MI), stroke, arterial revascularization, hospitalization for unstable angina, or death from CV causes. JUPITER was stopped early after a median follow-up of 1.9 years, on the basis of overwhelming evidence of efficacy with respect to the

primary endpoint. The results of JUPITER have been previously published [Ridker et al. *N Engl J Med* 2008].

The current analysis was based on the subgroup of 5695 subjects who were aged ≥70 years (median 74 years; range 70 to 97) at the time of enrollment. When compared with younger patients, those who were aged ≥70 years were more frequently female (51% vs 32%), less often obese (body mass index ≥30 kg/m^2, 32% vs 40%), less frequently current smokers (8% vs 19%), and more frequently had a Framingham risk score >10 (69% vs 41%). Overall, the relative treatment effects of rosuvastatin in individuals ≥70 years were comparable with those seen in the younger patient group. There was no difference between the age groups in the achieved lipid or hsCRP levels (Table 1). There was a significant 39% risk reduction in the primary composite endpoint of CV death, MI, stroke, unstable angina, or revascularization) (HR, 0.61; 95% CI, 0.46 to 0.82; p<0.001) in older patients who were randomized to rosuvastatin compared with those on placebo. Significant reductions were also seen for MI (HR, 0.55; 95% CI, 0.31 to 1.0; p=0.046), stroke (HR, 0.55; 95% CI, 0.33 to 0.93; p=0.023), and the incidence of revascularization or unstable angina (HR, 0.51; 95% CI, 0.33 to 0.80; p=0.003). The older subgroup was at higher risk for the primary endpoint (incidence rate 1.99/100 person-years vs 1.06/100 person-years in younger group) and showed a greater rate of difference on therapy compared with placebo (0.77/100 person-years vs 0.52/100 person-years in the younger group), with an estimated number needed to treat (NNT) for 5 years of 19 versus 29 for subjects aged <70 years to prevent 1 primary endpoint event.

Table 1. Achieved Lipid and hsCRP levels by Age.

Biomarker	Age	36 months	
hsCRP (mg/L)	≥70	2.0 (1.1-4.2)	3.3 (1.8-6.1)
	<70	2.0 (1.2-3.7)	3.6 (1.9-5.9)
LDL (mmol/L	≥70	1.4 (1.1-1.8)	2.7 (2.3-3.1)
	<70	1.4 (1.1-1.8)	2.8 (2.4-3.1)
HDL (mmol/L)	≥70	1.4 (1.1-1.7)	1.4 (1.1-1.7)
	<70	1.3 (1.0-1.5)	1.2 (1.0-1.5)
Triglycerides (mmol/L)	≥70	1.1 (0.9-1.5)	1.3 (1.0-1.8)
	<70	1.3 (0.9-1.7)	1.5 (1.1-2.1)

hsCRP=high-sensitivity C-reactive protein; LDL=low-density lipoprotein; HDL=high-density lipoprotein

The overall risk of serious adverse events was similar for the older subgroup (HR, 1.05; 95% CI, 0.93 to 1.17; p=0.44), with the exception of incident diabetes, for which the risk that was associated with treatment was significant in younger subjects (HR, 1.26; 95% CI, 1.02 to 1.56; p=0.03) but not in the older subgroup (HR, 1.25; 95 % CI, 0.90 to 1.74; p=0.18).

Overall, these results provide reassuring data regarding the efficacy and safety of statin therapy in elderly patients. The trial discussant, Professor Philippe Gabriel Steg, MD, INSERM U-698, Paris, France, said that the trial provides "solid evidence that the benefit seen from rosuvastatin in the overall trial is seen in the elderly subgroup, including a reduction in stroke." Prof. Steg did offer caution that these findings "pertain to a special population: high-risk CV patients with low LDL and elevated hsCRP" and asked whether the results could be extended to patients without elevated hsCRP and to very elderly patients.

A Subpopulation Analysis from the TRITON-TIMI 38 Study

Michelle O'Donoghue, MD, Brigham and Women's Hospital, Boston, MA, reported the results of an analysis of data from a subgroup of patients in the TRITON-TIMI 38 study [NCT00097591; Wiviott et al. *N Engl J Med* 2007] who were receiving proton pump inhibitor (PPI) therapy in addition to a thienopyridine (prasugrel or clopidogrel). The results showed no association between PPI use and an increased risk of cardiovascular (CV) events [O'Donoghue M et al. *Lancet* 2009].

The TRITON-TIMI 38 trial randomized 13,608 subjects with acute coronary syndrome (ACS) and planned percutaneous coronary intervention (PCI) to prasugrel or clopidogrel, in addition to standard therapy. The use of a PPI was at the discretion of the treating physician and was captured on the case report forms. The primary outcome of the study was CV events (defined as CV death, myocardial infarction [MI], or stroke).

At randomization, 4529 (33%) of the subjects were being treated with a PPI. The most frequently used PPIs were pantoprazole (40%) and omeprazole (37%). Subjects who were on a PPI were slightly older than those who were not on a PPI (median age 61 vs 60 years) and were more likely to be women. The PPI group was also more likely to be white, be enrolled at a center in Western Europe or North America, have a history of peptic ulcer disease or lower baseline hemoglobin (all p<0.001), or have an index diagnosis of unstable angina or non-ST-segment MI (p=0.007).

There was no association between the use of a PPI and an increase in the primary endpoint of a major CV event for either clopidogrel or prasugrel (Table 1).

Similarly, the use of a PPI was not associated with an increased risk of MI, stent thrombosis, or urgent revascularization or a decreased risk of bleeding for