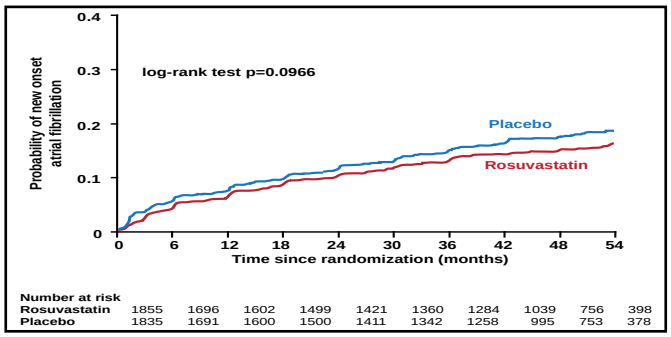
failure (HF) patients who were treated with rosuvastatin. The aim of the subanalysis was to assess the effect of n-3 PUFA and rosuvastatin compared with placebo in patients with chronic HF who were not in AF at study entry.

GISSI-HF was a double-blind, placebo-controlled trial in patients with chronic HF. Patients were randomized to daily treatments of n-3PUFA (1 g) or placebo (n=6975), and to rosuvastatin (10 mg) or placebo (n=4574). Patients were followed for nearly 4 years. Primary endpoints were all-cause mortality or cardiovascular (CV) hospitalizations. The study comprised men and women aged 18 years or older with clinical evidence of HF New York Heart Association class II-IV. Left ventricular ejection fraction (LVEF) was measured within 3 months of enrollment. AF occurrence was defined as the presence of AF on the electrocardiogram (ECG) that was performed at each visit during the trial, AF as a cause of worsening HF, hospital admission, or as an event during hospitalization.

Of the patients without AF at baseline, a total of 15.0% developed AF during a median follow-up of 3.7 years. AF occurred in 16% of the placebo and 13.9% of rosuvastatin patients with a 13.2% RRR and 2.1% absolute risk reduction. This difference was not significant when an unadjusted analysis (p=0.097; Figure 1) or multivariable analysis that adjusted just for clinical variables (p=0.067) was performed. However, it became significant when an adjustment was made for clinical variables and laboratory examinations (p=0.039) and for clinical variables, laboratory examinations, and background therapies (p=0.038).

Figure 1. Kaplan-Meier Curves for Time to New Onset of AF.



Maggioni A et al. *Eur Heart J* 2009. By permission of Oxford University Press.

Patients who experienced AF during the study were significantly (p≤0.03) older (aged >70 years) and had higher BMI, systolic blood pressure, heart rate, NYHA class, and percent LVEF than those who did not experience an AF. They also had significantly (p<0.05) higher frequencies of prior admission for HF, previous stroke, history of hypertension, pacemaker, history of paroxysmal AF, chronic obstructive pulmonary disorder, and more drug treatment.

Although this post hoc analysis showed some evidence of rosuvastatin's superiority over placebo in reducing the occurrence of AF, it should be noted that the trial was not powered to assess the effect of rosuvastatin on AF occurrence. The effect of a statin treatment that is conducted for a longer period of time or in a larger population of patients should be evaluated to confirm the findings of our study.

The discussant, Professor Harry Crijns, MD, Maastricht University Medical Centre, Maastricht, The Netherlands, agreed that rosuvastatin was not very effective in preventing incidence of AF in this study and suggested that there are a number of unanswered questions, including "whether statins prevent AF progression and reduce the burden of AF" and "whether prevention of AF by statins improves CV morbidity/mortality."

Full article available at: http://eurheartj.oxfordjournals.org/cgi/content/full/ehp357.

New Data from the RECORD Study

Two analyses from the RECORD (Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycemia in Diabetes) study [NCT00379769; Home PD et al. *Lancet* 2009] of cardiovascular (CV) outcomes in patients who were treated with rosiglitazone were presented at the European Society of Cardiology 2009 Annual Congress. The first evaluated rates of CV death or CV hospitalization, and the second evaluated rates of coronary events.

The first analysis showed no difference in the primary endpoint of CV hospitalization or CV death but did demonstrate increased rates of heart failure (HF) that led to hospitalization or death in subjects who were randomized to rosiglitazone plus metformin or a sulfonylurea (RSG) compared with a control group that was treated with a combination of metformin and a sulfonylurea.

Professor Michel Komajda, MD, Université Pierre et Marie Curie, France, Paris, presented the results of the post hoc analysis, showing that over the 5.5 years of follow-up in the RECORD study, subjects in the RSG group experienced similar rates of the primary endpoint (HR, 0.99; 95% CI, 0.85 to 1.16; p=0.93) compared with those on control, meeting the criteria for noninferiority. There were, however, significantly more fatal/nonfatal HF events in the RSG group (61 events in the RSG group vs 29 in the control group; HR, 2.10; 95% CI, 1.35 to 3.27; p = 0.001). The HF event rates for the two groups began to diverge early and continued to diverge throughout the trial.

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