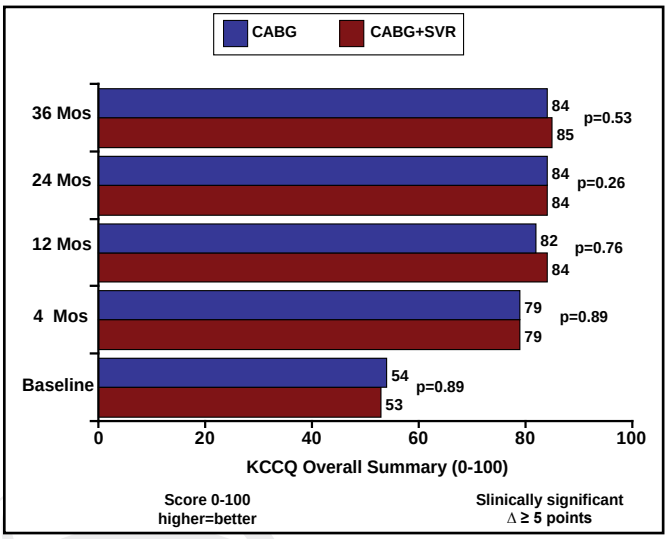
compared with baseline, the scores did not differ between the 2 treatment groups at any follow-up interval (Figure 1).

Figure 1. STICH QoL Substudy: KCCQ Overall Summary Score.



Operating times were longer for subjects in the combination group (5.5 hours vs 4.9 hours in the CABG-only group; p<0.001), as was the time on bypass (124 minutes vs 99 minutes in the CABG-only group; p<0.001). Subjects who received the combination surgery also required more postoperative care (eg, endocardial intubation and acute care) than subjects who received CABG alone. In a subset of United States patients who had cost information, the SVR procedure substantially increased the costs of the operation and postoperative care by an average of more than $14,500.

The investigators concluded that SVR is not justified in the population that was studied. Additional analyses are planned to determine if there are patient characteristics that may be associated with benefit or harm from adding SVR to CABG. The STICH study also has a second component that comprises subjects who were randomly assigned to receive either medical therapy alone or medical therapy plus CABG. This part of the study is ongoing.

"Our findings emphasize the importance of taking what appear to be medical breakthroughs and subjecting them to very rigorous comparisons with the best available therapy," said Dr. Jones.

The clinical results of the STICH trial were published online in *The New England Journal of Medicine* on March 29, 2009. The QoL and economic analysis was published online in the *American Heart Journal* on March 30 2009.

Relaxin Reduces Dyspnea, Cardiovascular Death, and Rehospitalization in Acute Heart Failure

Relaxin, a naturally occurring vasodilator, improves symptoms and lessens the risk of cardiovascular death and heart failure rehospitalization in patients hospitalized with acute heart failure, according to findings from the Preliminary Study of Relaxin in Acute Heart Failure (Pre-RELAX-AHF; NCT00520806).

Relaxin is a peptide hormone that increases in serum concentration in pregnant women to facilitate the hemodynamic adjustments of pregnancy, including increased cardiac output and decreased vascular resistance. The phase 2 Pre-RELAX-AHF trial was designed to evaluate the effects of relaxin in patients with similar physiologic changes due to heart failure. John R. Teerlink, MD, University of California San Francisco, CA, presented results from Pre-RELAX-AHF, which were simultaneously published online in *The Lancet*.

The trial enrolled 234 patients with acute heart failure characterized by dyspnea and congestion on chest X-ray, normal or elevated systolic blood pressure (>125 mm Hg), impaired renal function (CrCl 30-75 mL/min) and elevated brain natriuretic peptide (BNP). After receiving intravenous furosemide and within 16 hours of presentation, patients were randomly assigned to treatment with intravenous placebo (n=62) or relaxin 10 µg/kg (n=40), 30 µg/kg (n=43), 100 µg/kg (n=39), or 250 µg/kg (n=50) for 48 hours. Pre-RELAX-AHF had no prespecified primary endpoint and assessed clinical outcomes such as relief of dyspnea, in-hospital worsening of heart failure, renal impairment and hospital stay, among others.

Relaxin showed a preferential vasodilatory effect, providing a greater blood pressure reduction compared with placebo among patients with baseline systolic blood pressure >140 mm Hg (p=0.04), but not in those with systolic blood pressure ≤140 mm Hg (p=0.73).

Patients in the 30 µg/kg dosing group appeared to benefit the most from relaxin treatment. Compared with placebo, patients in the 30 µg/kg group reported a moderate or marked improvement in dyspnea (Likert scale) at 6, 12, and 24 hours (p=0.044), which was sustained through Day 14 (p=0.053). Relaxin 30 µg/kg also numerically reduced the mean length of hospital stay by nearly 2 days (12.0 vs 10.2 days; p=0.18).

Relaxin improved clinical outcomes following hospital discharge as well. Compared with placebo, relaxin 30 µg/kg reduced the risk of cardiovascular death or rehospitalization due to heart failure or renal failure by 87% at 60 days (HR, 0.13; p=0.053). No patients died because of cardiovascular causes in the Relaxin 30 µg/kg group at 180 days (p<0.05).

Relaxin had a favorable safety profile, with a similar proportion of patients reporting any adverse event in the placebo and relaxin groups. Compared with placebo, relaxin 30 µg/kg was associated with a nonsignificant increase in the incidence of bronchitis (0 vs 2.4%), stroke (1.6% vs 4.8%), renal failure (1.6% vs 2.4%), and hypotension (9.8% vs 11.9%). No cases of severe hypotension were reported in the placebo or relaxin 30 µg/kg groups, though 2 cases (4.1%) were reported in the relaxin 250 µg/kg group. Relaxin 250 µg/kg, but not 30 µg/kg, was associated with a nonsignifcant doubling in the incidence of worsening renal dysfunction (≥0.3 mg/dL increase in serum creatinine) compared with placebo (15% vs 7%, p=0.19).

Based on these findings, Dr. Teerlink and colleagues have chosen the 30 µg/kg dose for evaluation in the upcoming international phase 3 trial of relaxin in acute heart failure (RELAX-AHF-1).

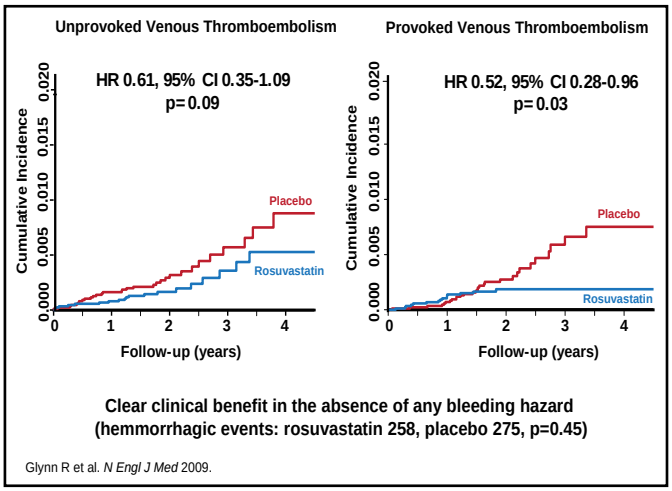
JUPITER Study Continues to Make News

A number of presentations highlighted new analyses from the Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER; NCT00239681) study, the results of which are expected to have a significant impact on the screening and treatment of cardiovascular disease (CVD). JUPITER was a primary preventive, prospective, randomized trial that included 17,802 men (aged ≥50 years) and women (aged ≥60 years) with no CVD or diabetes mellitus, and low-density lipoprotein (LDL) cholesterol and high-sensitivity C-reactive protein (hsCRP) levels <130 mg/dL and ≥2 mg/L, respectively. Subjects received either rosuvastatin (20 mg/day) or placebo. The trial was stopped prematurely after a median follow-up of 1.9 years due to clear and significant treatment benefits, wherein rosuvastatin produced a 44% reduction in the primary study endpoint (cumulative incidence rate of myocardial infarction [MI], stroke, arterial revascularization, hospitalization for unstable angina, or cardiovascular death) compared with placebo (HR, 0.56; 95% CI, 0.46 to 0.69; p<0.00001) [Ridker PM et al. *N Engl J Med* 2008].

Robert Glynn, PhD, Brigham and Women's Hospital, Boston, MA, presented findings from another prespecified analysis of the JUPITER data, assessing the effect of rosuvastatin on symptomatic venous thromboembolism (VTE), which occurred about as often as MI or stroke in the JUPITER study. Compared with placebo, rosuvastatin was associated with a 43% reduction (HR, 0.57; 95% CI, 0.37 to 0.86; p=0.007) in risk of VTE and no increase in bleeding [Glynn RJ et al. *N Engl J Med* 2009].

Rosuvastatin reduced the occurrence of both provoked (p=0.03) and unprovoked (p=0.09) VTE (Figure 1). Although the incidence of both pulmonary embolism and DVT was reduced, DVT alone was significantly reduced (p=0.004). The benefit of rosuvastatin was consistent across patient subgroups, based on baseline variables, while VTE reduction was independent of a prior cardiovascular event. Among patients who had VTE as the first event, there was a significant 43% reduction in risk (HR, 0.57; 95% CI, 0.37 to 0.86; p=0.007), similar to the 44% reduction in risk that was associated with rosuvastatin for the prevention of a first cardiovascular event.

Figure 1. JUPITER Venous Thromboembolism—Unprovoked versus Provoked.



When questioned regarding the likely underlying mechanisms of rosuvastatin, Dr. Glynn said he believed that the most likely candidate was an anticoagulant effect, noting that statins downregulate the blood coagulation cascade through decreased tissue factor expression, leading to reduced thrombin formation, as reported by Undas et al [Undas A et al. *Arterioscler Thromb Vasc Biol*