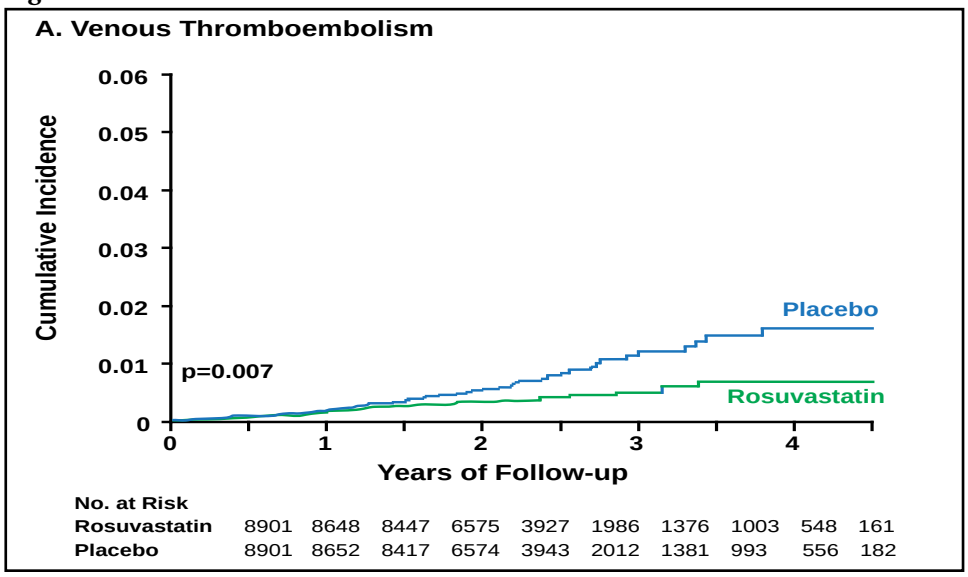
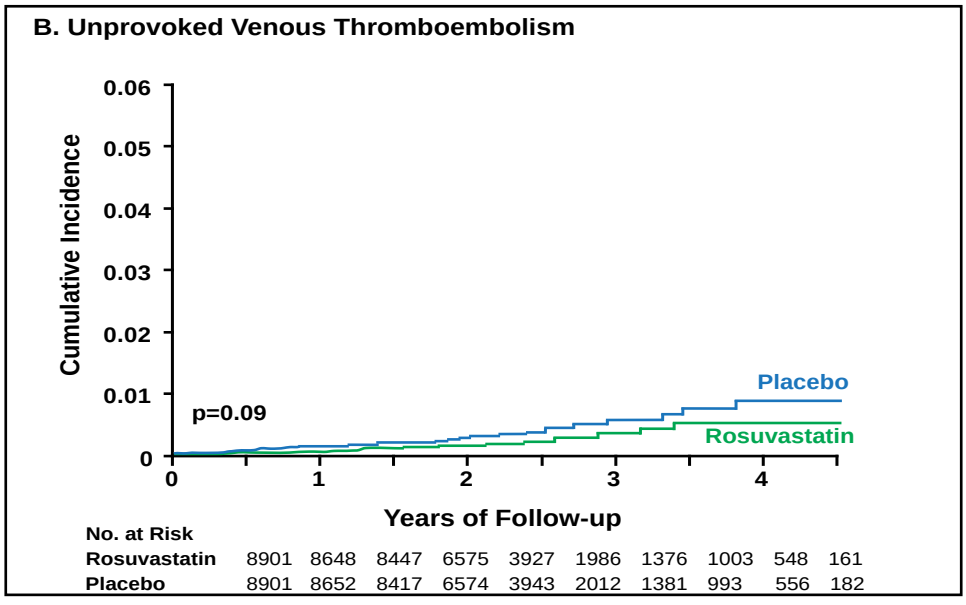
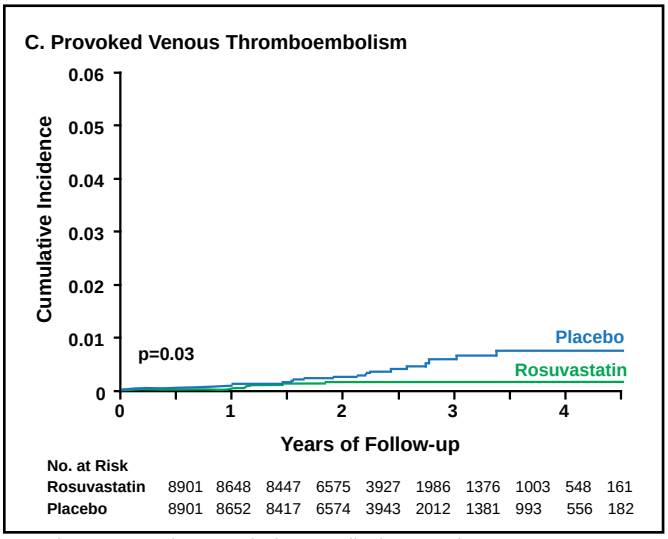
Rosuvastatin in the Prevention of Stroke Among Men and Women with Elevated Levels of C-Reactive Protein: The JUPITER Trial

Evidence from the Justification for the Use of statins in Prevention: an Intervention Trial Evaluating Rosuvastatin (JUPITER; NCT00239681) trial [Ridker PM et al. *N Engl J Med* 2008] provides support for the use of statins to prevent strokes in healthy individuals with low LDL cholesterol but elevated high-sensitivity C-reactive protein (hsCRP) levels. Robert Glynn, PhD, Brigham and Women's Hospital, Boston, MA, presented results that showed that rosuvastatin (20 mg/day) reduced the incidence of stroke by 48% after 1 year of treatment compared with placebo (Figure 1). The benefits occurred across all subgroups, including patients at higher risk, with no evidence of an increased risk for hemorrhagic stroke.

Figure 1. Cumulative Incidence of Venous Thromboembolism.







Although lipid levels are significant risk determinants for ischemic stroke and coronary vascular disease (CVD), several studies have shown that individuals with high levels of hsCRP are at increased risk for stroke [Rost NS et al. *Stroke* 2001; Ballantyne CM et al. *Arch Intern Med* 2005; Everett B et al. *JACC* 2006]. The objective of this study was to determine if rosuvastatin would reduce stroke rates among individuals with low levels of cholesterol but elevated levels of hsCRP.

JUPITER enrolled 17,802 apparently healthy men and women at 1315 sites in 26 countries. Patients were required to have LDL levels <130 mg/dL and hsCRP levels >2.0 mL, be aged ≥50 years (men) or ≥60 years (women), and have no CVD or diabetes. The primary endpoint was the first major cardiovascular event (nonfatal myocardial infarction, nonfatal stroke, arterial revascularization, hospitalization for unstable angina, or cardiovascular death).

Median age of the study population was 66 years; 38% was women; 12% was black and 12% was Hispanic; mean blood pressure was 134/80 mm Hg; 16% smoked; and 17% used aspirin. After 12 months, rosuvastatin reduced LDL cholesterol levels by 50% (sustained for the course of the trial), hsCRP by 37% (sustained), triglycerides by 17%, and HDL by 4% compared with placebo.

The trial was stopped after a median follow-up of 1.9 years, because a significant (p<0.00001) change in the HR (0.56; 95% CI, 0.46 to 0.69) of the primary endpoint was reached. Overall, rosuvastatin was associated with a 44% reduction in the composite endpoint. There were 33 stroke events in the rosuvastatin group and 64 in the placebo group, a 48% reduction in HR (0.52; 95% CI, 0.34 to 0.79; p=0.002). For nonfatal stroke, the HR was 0.52 (95% CI, 0.33 to 0.80; p=0.003); ischemic stroke HR was 0.49 (95% CI, 0.30 to 0.81; p=0.004). There was no increase in the risk of hemorrhagic stroke (HR 0.67; 95% CI, 0.24 to 1.88; p=0.44). The secondary endpoint, all-cause mortality, decreased 20% with rosuvastatin (HR 0.80; 95% CI, 0.67 to 0.97; p=0.02).

These results were consistent across all subgroups with patients in high-risk groups (hypertension, smokers, high Framingham risk factors), showing substantial benefits from rosuvastatin treatment. Except for cancer deaths (higher in the placebo group) and the incidence of diabetes (higher in the rosuvastatin group), adverse events were similar between the treatment groups.

Compared with previous trials (WOSCOPS and AFCAPS), the JUPITER trial showed significant positive effects on stroke reduction. Dr. Glynn suggested that these benefits may be due to JUPITER's larger patient population, patient characteristics (more women and lower LDL levels in the JUPITER trial and higher smoking and lipid levels in the WOSCOPS trial), or the treatment (rosuvastatin in JUPITER, pravastatin in WOSCOPS, and lovastatin in AFCAPS).

Whole Genome Association of Intracranial Aneurysm Identifies Susceptibilty Loci

A genome wide genotyping study has identified genetic loci that contribute to intracranial aneurysm (IA) formation and rupture. Single nucleotide polymorphisms (SNPs) on chromosomes 2q, 8q, and 9p showed significant association with IA (p values ranging from 10^{-8} to 10^{-10} and odds ratios 1.24 to 1.36) [Bilguvar et al. *Nat Genet* 2008]. Murat Gunel, MD, Yale University School of Medicine, New Haven, CT, reported that 2 of the loci, 2q and 8q, are novel, while the 9p locus previously has been associated with coronary artery disease and, more recently, with aortic aneurysm and IA.

IA affects 2% to 5% of the population and commonly occurs between the ages of 40 and 60 years, typically with no antecedent event or warning. There is no reliable way to identify at-risk individuals. Genetic identification of these subjects would make it possible to identify individuals before an IA rupture for preventive treatment. The etiology and pathogenesis of intracranial