

## Webcast Highlights

# Heart Protection Study Finds Simvastatin Reduces Vascular Risk in a Wide Range of High-Risk Patients

**S**imvastatin at a daily dose of 40 mg safely reduces the risk of myocardial infarction (MI), stroke, and the need for revascularization procedures by at least one third over 5.5 years, said Rory Collins, MB BS, Professor of Medicine and Epidemiology and Co-Director of the Clinical Trial Service Unit and Epidemiological Studies Unit at the University of Oxford in England.

In presenting the results of the MRC/BHF Heart Protection Study, the largest study of people at risk for death from these conditions, Dr. Collins noted that lipid-lowering therapy with simvastatin prevented between 70 and 100 major cardiovascular events over 5 years. "If 10 million additional people take a statin regimen such as this one, 50,000 lives would be saved each year and even more people would be saved from having an MI or stroke," he emphasized.

The 2 x 2 factorial design study, which was coordinated by the Clinical Trial Service Unit at the University of Oxford in 69 British hospitals, evaluated the effects of cholesterol lowering with simvastatin 40 mg/day versus placebo

and antioxidant vitamin therapy versus placebo in 20,536 high-risk patients with previous MI, other coronary heart disease (CHD), stroke, peripheral vascular disease, and diabetes. Approximately 6000 patients with diabetes, about 4000 of whom had no evidence of CHD at baseline, and 5082 women with previous disease were included in the study. All patients were between 40 and 80 years of age at study entry, and all had total cholesterol levels above 135 mg/dL.

Despite a huge body of observational epidemiologic evidence that antioxidant vitamins could protect against heart disease and cancer, the study found that an "antioxidant cocktail" of vitamin C, vitamin E, and beta carotene did not reduce total mortality or vascular or nonvascular causes of death, nor did it have any effect, either beneficial or adverse, on cancer incidence or mortality, Dr. Collins remarked. The study also found that the cocktail did not reduce the risk of total CHD, stroke, or the need for coronary or noncoronary revascularization procedures.

Simvastatin produced a highly significant reduction versus placebo in

total mortality, reflecting a substantial reduction of about 25% in vascular mortality, but no effect, either beneficial or adverse, on nonvascular causes of death.

The study demonstrated unequivocally that cholesterol lowering reduced the risk of stroke, particularly ischemic stroke, by at least one third.

—Rory Collins, MB BS

The big surprise of the study, he observed, was the effect of simvastatin on stroke. Although epidemiologic studies suggest that cholesterol levels are not strongly related to stroke risk, the Heart Protection Study demonstrated unequivocally, for the first time, that cholesterol lowering reduced the risk of stroke, particularly ischemic stroke, by at least one third. The reduction in risk of hemorrhagic stroke also favored simvastatin treatment, but was not

significant. The reduction in risk for MI, CHD, stroke, and the need for revascularization emerges over time, Dr. Collins said, with a further reduction in risk seen year after year.

In addition to the major clinical benefits demonstrated in this study, simvastatin was also found to be very well tolerated. There was no significant excess of liver enzyme abnormalities with simvastatin versus placebo, and the rate of reported muscle pain was the same in both groups—5%. There were 9 cases of markedly elevated creatine kinase levels in the simvastatin group versus 5 cases in the placebo group.

What is most remarkable, Dr. Collins said, is that the proportional reduction in risk for MI, stroke, and need for revascularization was consistent for all ages, for both genders, and across all cholesterol levels, even in patients whose levels of low-density lipoprotein cholesterol (LDL-C) were below 120 mg/dL at baseline and further reduced with therapy to less than 80 mg/dL during the study. Reducing LDL-C to below-target levels in this subgroup produced a substantial reduction in the risk of vascular events. ■

Rory Collins, MB BS, has provided no disclosure information.