NODM was similar between the 2 treatment arms, with 720 patients developing NODM in the ezetimibe plus simvastatin group compared with 694 in the placebo plus simvastatin group (HR, 1.04; 95% CI, 0.94 to 1.15; $P = .46$).

A breakdown of the primary outcome by the defining criteria for NODM showed similar percentages of NODM in the 2 treatment groups. A sensitivity analysis using 4 alternate NODM definitions and an alternate exclusion definition for prior diabetes was performed. The alternate definitions were as follows: (1) initiation of a hypoglycemic drug; (2) 2 consecutive fasting glucose levels ≥ 7 mmol/L; (3) diabetes-related adverse event reporting; and (4) either no. 1 or 3. The alternate definition for diabetes exclusion at randomization included investigator-reported diabetes in the case report form. These analyses found no significant difference in the numbers of NODM in the ezetimibe plus simvastatin vs the simvastatin groups using any of the alternate definitions.

These analyses of the IMPROVE-IT trial provide new information on the effects of ezetimibe on patients with diabetes and the potential for risk of NODM with the use of ezetimibe. The first analysis showed that patients with diabetes had a higher risk for cardiovascular events than patients without diabetes. This translated to a greater relative and absolute benefit from the addition of ezetimibe to simvastatin in patients with diabetes as compared with patients without diabetes. The increased benefit in patients with diabetes was driven by reductions in MI and ischemic stroke. The safety profile of ezetimibe plus simvastatin was similar to that of placebo plus simvastatin in both diabetes and nondiabetes groups. The second analysis showed that the rates of NODM at 75 months' follow-up were similar in the groups treated with simvastatin plus ezetimibe and simvastatin plus placebo.

Bleeding Risk Scores Identified Patients With DVT or PE at Low Risk of Bleeding

Written by Mary Mosley

Four bleeding risk scores identified patients with deep vein thrombosis (DVT) or pulmonary embolism (PE) who had a low rate of major bleeding at 30 days when treated with rivaroxaban, according to Jeffrey A. Kline, MD, Indiana University School of Medicine, Indianapolis, Indiana, USA.

The investigators hypothesized that the rate of major bleeding associated with rivaroxaban treatment would be < 1% when using a bleeding risk scoring system derived to predict a low risk of bleeding in patients with venous thromboembolism (VTE) treated with a vitamin K antagonist. They used pooled data from the EINSTEIN-DVT and EINSTEIN-PE studies and found a low rate of major bleeding in the patients treated with rivaroxaban (1%; 40 of 4150 patients) [Prins MH et al. *Thromb J*. 2013]. Rivaroxaban was given at 15 mg twice daily for 21 days and then 20 mg once daily for 3 to 12 months.

The 4150 rivaroxaban-treated patients were stratified as low, moderate, or high risk using each of the 4 bleeding risk scores [Ruiz-Gimenez N et al. *Thromb Haemost*. 2008; Kuijer PM et al. *Arch Intern Med*. 1999; Beyth RJ et al. *Am J Med*. 1998; Landefeld CS et al. *J Clin Epidemiol*. 1989]. SMQ codes were used to extract data from the case report forms and any missing data were considered normal. The ISTH definition of major bleeding was used.

The primary outcome was the rate of major bleeding at 30 days and for the total treatment duration. During the critical 30-day period after discharge, there was a low rate of major bleeding in the low-risk patients and the confidence intervals were < 1 at 30 days and for the entire study period. The proportion of patients defined as low risk ranged from 28.7% to 63.6% depending on the score.

The characteristics associated with low risk were age < 65 years, no history of bleeding, and no comorbid conditions (current cancer, renal insufficiency, diabetes mellitus, anemia, prior stroke or myocardial infarction). These criteria identified a subgroup of patients in the EINSTEIN studies who were at low risk of bleeding and had a rate of major bleeding of < 0.5% at 30 days. Thus, patients with VTE aged < 65 years with no bleeding history or significant comorbidities can be counseled that they have a < 1 in 100 chance of experiencing a major bleeding event during the first 30 days of treatment with rivaroxaban, concluded Dr Kline. Dr Kline postulated that these bleeding risk scores could be applied in the emergency room to identify low-risk patients who may be safely discharged from the emergency department with a novel oral anticoagulant.