

In subgroup analyses, clazosentan reduced mortality/vasospasm-related morbidity in patients with poor WFNS grade ( $\geq$ III) (RRR, 33%; 95% CI, 8% to 51%) and diffuse thick SAH (diffuse thick clot on baseline [CT] scan; RRR, 25%; 95% CI, 5% to 41%); however, no effect was observed on GOSE. Rescue therapy, a primary endpoint component, was used in 11% of clazosentan-treated and 16% of placebo-treated patients.

Treatment-emergent lung complications, anemia, and hypotension occurred in 34%, 22%, and 12% of clazosentan-treated patients versus 18%, 15%, and 4% of placebo-treated patients, respectively. Mortality was similar between the two groups (6%).

## Severity of Deficit Strongly Predicts Long-Term Survival Among Stroke Survivors

Results of a long-term follow-up study in patients with atrial fibrillation (AF), presented by Margaret C. Fang, MD, PhD, University of California, San Francisco, California, demonstrated that deficit severity is a strong predictor of long-term poststroke survival.

AF increases the risk for ischemic stroke approximately 5-fold and causes an estimated 15% of all strokes in the United States [Wolf PA et al. *Stroke* 1991]. Studies of AF-related stroke typically describe only short-term (ie, 30-day) mortality. The goal of this long-term follow-up was to estimate the impact of ischemic stroke on the survival of patients with AF beyond the initial 30-day period.

The Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study is a cohort of 13,559 patients with diagnosed nonvalvular AF who were enrolled in an integrated health care delivery system for a median of 6 years. Incident ischemic strokes were identified using computerized databases and validated by medical record review. Functional status at discharge was obtained through chart review and was measured using a modified Rankin severity scale. Warfarin status at stroke presentation was obtained through chart review. Mortality was obtained from health plan databases and the State Death Index. The survival of patients with and without ischemic stroke was compared using multivariable Cox regression models, adjusted for clinical factors.

A total of 1025 incident ischemic strokes, occurring over 66,717 person-years of follow-up, were identified. A

comparison of baseline characteristics of the 1025 cohort members who developed stroke with 12,534 cohort members who did not develop stroke showed several significant ( $p < 0.01$ ) differences. At 5 years, >70% of subjects without stroke were still alive compared with fewer than 40% of those who had a stroke. Subjects who were taking warfarin at the time of their stroke had less severe strokes (44% vs 47%), lower 30-day mortality rates (19.6% vs 27.7%;  $p < 0.01$ ), and lower rates of ischemic stroke (1.2% per year vs 2%).

Compared with cohort members without stroke, subjects who experienced a stroke had worse long-term survival (adjusted HR, 3.4; 95% CI, 3.1 to 3.7). Stroke severity at the time of discharge was a strong predictor of worse survival.

“The effects of stroke on mortality in patients with AF persist far beyond the initial event,” Dr. Fang said, noting the results of this study highlight the importance of preventing strokes and reducing the severity of strokes when they do occur.

## Apixaban Associated With Reduction in Stroke and SE in Patients Unsuitable for VKA Therapy

Hans-Christoph Diener, MD, University Hospital, Essen, Germany, presented the results of the Apixaban Versus Acetylsalicylic Acid to Prevent Strokes (AVERROES; NCT00496769) Study on behalf of the steering committee and the investigators. The study revealed clear evidence of a clinically important reduction in stroke and systemic embolism (SE) with apixaban over aspirin in patients with atrial fibrillation (AF) who were intolerant or otherwise considered unsuitable for vitamin K antagonist (VKA) therapy.

Patients with AF have an increased risk of stroke, and although VKA therapy is effective in reducing stroke, it is complex to manage and is associated with an increased risk of hemorrhage. For patients who are unsuitable for VKA therapy, the only alternative treatment is aspirin, which provides insufficient protection from stroke in high-risk patients (RR, 22%). Apixaban is an investigational oral anticoagulant that selectively inhibits factor Xa. It is efficacious as prophylaxis for venous thromboembolism and has a favorable risk-benefit ratio compared with low-molecular-weight heparin.

The purpose of the AVERROES Study was to evaluate apixaban for the prevention of stroke or SE patients