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New agent to prevent strokes in patients with atrial fibrillation shown in major study

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In the primary result from the largest double-blind study ever completed to assess a drug's effect in the prevention of stroke in patients with atrial fibrillation, a common heart rhythm abnormality, rivaroxaban, an anti-clotting drug, was shown to be superior to warfarin, the current standard for treatment of atrial fibrillation, while patients in the study were taking study drug. However, the full intention-to-treat analysis, which includes patients who discontinued study drug, showed that rivaroxaban was non inferior to warfarin for the prevention of stroke or blood clots but did not demonstrate statistical superiority.

The findings, presented by a research team from the Duke Clinical Research Institute, were highlighted today at the featured late-breaker sessions at the annual American Heart Association's Scientific Sessions meeting.

"Warfarin has been a standard treatment for decades, but requires a rigorous monitoring schedule to ensure therapeutic dosing levels, and is subject to the potential of food and drug interactions that present treatment obstacles for patients and doctors alike," said Kenneth W. Mahaffey, MD, associate professor of medicine at Duke University School of Medicine, who presented the trial today. "The results of this large global trial have convincingly shown rivaroxaban to be an alternative to warfarin in treating patients with atrial fibrillation and, importantly, with no increase in bleeding."

Atrial fibrillation is the most common abnormal heart rhythm disorder in

the U.S. and is characterized by an unusual and dangerously fast heart beat. It can cause blood to pool in the heart resulting in the formation of clots that may become lodged in the artery to the brain resulting in a stroke, or in formation of non-central nervous system blood clots. Approximately 2.2 million Americans suffer from atrial fibrillation, which increases a person's stroke risk by four to six times on average.

Warfarin has been documented over the years to reduce the rate of stroke for those who have atrial fibrillation by approximately one-half to two-thirds, at the cost of increased bleeding.

"In addition to addressing an important therapeutic need for patients with atrial fibrillation, ROCKET AF provides a model for how clinical trials of investigational therapies should be conducted to assess safety and efficacy prior to FDA submission. The sponsors of the study should be congratulated for taking this approach in which an international committee of leaders in the field designed the trial and provided independent oversight, including an independent analysis of the trial results," said Robert M. Califf, MD, study co-chair and vice chancellor for clinical research at Duke University School of Medicine, and director of the Duke Translational Medicine Institute.

The ROCKET AF (Rivaroxaban Once daily oral direct Factor Xa inhibition Compared with vitamin K antagonism for prevention of stroke and Embolism Trial in Atrial Fibrillation) study included 14,264 patients with atrial fibrillation who had a history of stroke or additional independent risk factors for future stroke and were randomized to receive either rivaroxaban or warfarin. The trial included more than 1,100 centers in 45 countries.

In the study, rivaroxaban was superior to warfarin for the primary efficacy endpoint while patients were taking study drug, showing a 21 percent relative risk reduction for stroke and non-CNS systemic

embolism in the pre-specified, on-treatment population (event rates = 1.71 vs. 2.16, p=0.018).

Rivaroxaban also showed numerically fewer myocardial infarctions (event rates = 0.9 vs. 1.1), and study investigators observed reduction in rates of all-cause mortality compared to warfarin (event rates = 4.5 vs. 4.9) though these differences were not statistically significantly different.

In the analysis of the intent to treat population, patients followed from the time of entry and throughout the full study duration, even if they discontinued study medication, rivaroxaban was not inferior to warfarin (p