Edoxaban effective in preventing stroke, reducing bleeding and cardiovascular death in patients with atrial fibrillation

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According to the United States Centers for Disease Control and Prevention, over 800,000 Americans die each year from heart disease and stroke. Stroke is the leading cause of serious long-term disability and death in the US. In addition to lifestyle changes, medications such as anti-blood clotting drugs are helpful in the prevention of stroke.

A late-breaking clinical trial to be presented at the American Heart Association Scientific Sessions on November 19, 2013 and published simultaneously online in the *New England Journal of Medicine*, demonstrates that high- and low-dose edoxaban were at least as effective in preventing stroke or systemic embolism (blood clot), while significantly reducing bleeding and cardiovascular death, compared to warfarin.

"Our study findings represent good news for patients and health care providers," said Robert Giugliano, MD, SM, FACC, FAHA, BWH Cardiovascular Division, lead study author. "We believe that once-daily edoxaban represents a new, effective, safe and convenient treatment to prevent stroke for many patients with atrial fibrillation, with the benefits of less bleeding and cardiovascular death, compared to standard therapy with warfarin."

Edoxaban and warfarin are anti-blood clotting medications. Edoxaban is a once-daily oral factor Xa inhibitor currently being studied in clinical

trials. Warfarin is a common drug prescribed to prevent the formation of blood clots, and has been the standard oral blood thinner for over five decades.

Led by the TIMI (Thrombolysis In Myocardial Infarction) Study Group at Brigham and Women's Hospital (BWH) and Harvard Medical School, the ENGAGE AF-TIMI 48 trial was the largest (21,105 participants) and longest (2.8 years average follow-up) trial of a novel anticoagulant to date in patients with atrial fibrillation. The study compared two dose-regimens of once-daily edoxaban versus warfarin.

Researchers recruited participants with atrial fibrillation (irregular heart rate) who were at moderate-to-high risk for stroke. The trial was conducted at 1,393 centers in 46 countries. Participants were enrolled from November 2008 to November 2010.

Patients had an equal chance to receive warfarin, high-dose edoxaban (60 milligrams/day), or low-dose edoxaban (30 milligrams/day), although knowledge of which treatment they were assigned was not revealed until after the end of the study.

About one-quarter of the patients had the dose of edoxaban lowered at the start of the trial based on their individual profile to ensure the desired blood level of the drug. To ensure patients treated with warfarin had the proper degree of blood-thinning, blood tests were performed at least monthly in each group, although such testing is not necessary with edoxaban.

The primary goals of the study were to assess the combined outcome of stroke or systemic embolism (primary efficacy outcome), as well as bleeding.

During the treatment period, the rate of stroke or systemic embolism

was 1.50 percent per year for participants on warfarin, and 1.18 percent per year for those on high-dose edoxaban. This represents a 21 percent reduction in the risk of stroke or systemic embolism with high-dose edoxaban compared to warfarin.

Moreover, annualized rates of major bleeding were 3.43 percent with warfarin and 2.75 percent with high-dose edoxaban, representing a 20 percent reduction in bleeding. There were also fewer cardiovascular deaths with edoxaban compared to warfarin: high-dose edoxaban 2.74 percent per year compared to warfarin 3.17 percent per year.

The favorable results with edoxaban were achieved despite excellent management with warfarin in this study (blood tests were in range more than two-thirds of the time, a higher rate than that seen in other similar studies).

Future research with edoxaban will investigate if patients with other conditions treated with warfarin might benefit from edoxaban. Additional research will also help doctors determine how to measure the blood-thinning effect of edoxaban and how to quickly reverse the effect if needed.

Provided by Brigham and Women's Hospital