Success stops drug trial

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The data monitoring committee of the AVERROES study, seeing overwhelming evidence of the success of apixaban in the prevention of stroke in patients with atrial fibrillation who are unsuitable for the conventional treatment of warfarin, has recommended early termination of this study. The decision came after repeated review and careful consideration of all efficacy and safety data.

The study leaders, principal investigator Dr. Stuart J. Connolly, chairman of the steering committee Dr. Salim Yusuf, and project officer Dr. John Eikelboom, have accepted this recommendation, as have the study sponsors, Bristol-Myers Squibb and Pfizer.

Results of the study were presented by Connolly at the annual European Society of Cardiology Congress in Stockholm, Sweden, on August 31.

The AVERROES study enrolled 5,600 patients with atrial fibrillation at risk for stroke who were unsuitable for therapy with a Vitamin K antagonist such as warfarin. These patients were randomized, double-blind, to receive either apixaban or the standard therapy which is Aspirin. The primary efficacy outcome of the AVERROES study was a composite of stroke or systemic embolism and the major safety outcome was major bleeding.

The data monitoring committee observed a relative risk reduction for stroke and systemic embolism of more than 50 per cent, which was highly statistically significant and which met the highly conservative monitoring boundaries of the AVERROES study. There was only a

modest increase in major hemorrhage that was not statistically significant.

"The results of AVERROES are truly impressive," said Connolly, a professor of medicine at the Michael G. DeGroote School of Medicine at McMaster University. "The reduction in stroke and systemic embolism is very important and the increased risk of hemorrhage is small. It appears that apixaban will be an excellent treatment for the many patients with atrial fibrillation who are unsuitable for warfarin. These findings will reduce the burden of stroke in society."

Atrial fibrillation is a common heart rhythm disorder, in which the upper chamber of the heart beats improperly. Patients with atrial fibrillation are at increased risk of stroke due to the formation of blood clots in the upper chamber of the heart. The standard therapy for the prevention of stroke and other embolic events in atrial fibrillation is to use a type of anticoagulant known as a Vitamin K antagonist. The most common Vitamin K antagonist is warfarin, which is very effective for reducing stroke but is a difficult drug to use because of numerous interactions with food and other drugs and due to a need for long-term monitoring each patient's blood coagulation.

There are many patients who are unsuitable for warfarin and for them the only effective therapy for prevention of stroke in atrial fibrillation is aspirin, which is not very effective. The purpose of the AVERROES study was to test whether the new Factor Xa inhibitor, apixaban, is superior to aspirin for the prevention of stroke in these patients, with an acceptable risk of bleeding.

Apixaban is a new type of anticoagulant known as a Factor Xa inhibitor, which is being jointly developed by Bristol-Myers Squibb and Pfizer. This agent blocks the coagulation system and can be used without the need for monitoring necessary in traditional treatments. It has been

studied and shown promising results in patients with deep vein thrombosis, in patients with recent orthopedic surgery and after acute coronary syndrome. It had not previously been studied in patients with atrial fibrillation.

AVERROES investigators have been informed of the decision to stop follow up of patients in AVERROES, and soon they will be informing their patients who are participating in the study. All patients in AVERROES who are still receiving study medication will be offered a long-term, open-label extension phase of the study in which they will receive apixaban, once the extension has been approved by regulatory bodies and local ethics committees.

Provided by McMaster University