Study contradicts reports of problems with blood-thinner

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New findings by McMaster University researchers contradict earlier reports that people with a certain genetic make-up don't benefit from the blood-thinner clopidogrel, also known as Plavix.

After researchers from the United States, France and Germany reported clopidogrel is less effective in some patients, the Food and Drug Administration (FDA) in the United States issued a black box warning to physicians on the drug's package insert.

"(Our findings) add a further layer of complexity to the FDA 'black box' warning and show that reported genetic variants have no effect in certain patient populations," said Dr. Guillaume Pare, lead researcher and assistant professor of pathology and molecular medicine at the Michael G. DeGroote School of Medicine.

Clopidogrel is the world's second best-selling prescription drug with global sales of more than $6 billion annually. It is used in 110 countries by millions of people to reduce the risk of heart attack and stroke.

Following the FDA's warning, clopidogrel became the focus of on-going debates within cardiology circles. Some American cardiologists initially called the FDA's actions irresponsible. Others complained they were left without any appropriate direction on how to manage their patients.

About 20 per cent of the population carry the loss-of-function version of the gene involved in the clopidogrel controversy.

To assess the influence genetics might have on patients prescribed clopidogrel, Paré and colleagues from McMaster University conducted a genetic sub-study of 6,000 participants from two major clinical trials (CURE and ACTIVE). The CURE (Clopidogrel in Unstable Angina to Prevent Recurrent Ischemic Events) trial of 12,562 patients with acute coronary syndrome in 28 countries found clopidogrel significantly reduces the risk of heart attack stroke and dying. The ACTIVE (Atrial Fibrillation Clopidogrel Trial with Irbesartan for the Prevention of Vascular Events) trial of 7,554 patients with atrial fibrillation in 30 countries found clopidogrel added to Aspirin significantly reduced the risk of cardiovascular events, and particularly stroke. Both trials were supported by Sanofi-Aventis and Bristol-Myers Squibb.

"We found the previously reported genetic variants had no effect at all (for patients) in either the CURE or ACTIVE trials," said Pare. He will present these findings at the European Cardiovascular Society Congress meeting in Stockholm, Sweden, on August 29. The study will also be simultaneously published online in the New England Journal of Medicine.

Paré said the positive results from McMaster's genetic sub-study come from studying different patient populations. "Also, our study design was a bit stronger from an epidemiology point of view."

Beyond clopidogrel, he said there is a broader message of the need for cautiousness as genetics becomes more and more integrated into patient care.

Provided by McMaster University

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