

Novel anti-platelet therapy reduces risk of cardiac events in patients with history of heart attack

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According to new research from Brigham and Women's Hospital (BWH), adding vorapaxar, an investigational platelet blocker, to standard antiplatelet therapy significantly reduces the longterm risk of recurrent cardiovascular events beyond one year in patients with a history of a prior heart attack. Researchers also identify a lowbleeding risk group among whom the clinical benefit of vorapaxar was particularly favorable. This research is presented at the European Society of Cardiology Congress 2012 and published simultaneously in the Lancet.

For more than a million Americans who survive a heart attack each year, doctors routinely prescribe a daily aspirin to help prevent the formation of clopidogrel, which also serve this purpose, are often added for up to a year, but the scientific evidence is unclear about whether adding platelet blockers to aspirin beyond this timeframe is clinically useful. Despite such therapies, these patients have an almost 15 percent chance of having another atherosclerosis-related event that brings them to the hospital within a year.

"There continues to be substantial uncertainty regarding the benefit of long-term antiplatelet therapy in addition to aspirin in patients with prior heart attacks," said Benjamin M. Scirica, M.D., M.P.H., investigator at the TIMI Study Group, a cardiologist at BWH, and one of the study's investigators. "This is the first study to show convincingly that continued, long-term, therapy beyond one year with more potent antiplatelet therapy reduces the risk of having another cardiovascular event." Previous studies in secondary prevention did not show this benefit.

Researchers from the TIMI Study Group at BWH

have shown, for the first time, that adding vorapaxar, a new antiplatelet medication, on top of standard therapy which includes aspirin, is effective for long-term secondary prevention in stable patients with a prior heart attack. When used with aspirin and other standard antiplatelet therapy in a broad group of patients with previous heart attack, vorapaxar reduced the risk of cardiovascular death, heart attack or stroke by an additional 20 percent.

This randomized, double blind, placebo-controlled, multinational study followed 26,449 patients for more than two years while receiving standard antiplatelet therapy for established atherosclerosis, including previous heart attack, stroke or atherosclerotic narrowing in the arteries of the legs. blood clots in the arteries which can frequently lead Participants were randomly assigned to receive the to another heart attack. Other platelet blockers, like investigational platelet blocker (2.5 mg orally once daily) with standard therapy, or a placebo with standard therapy. The overall trial results, which were presented and published in March 2012, demonstrated a 13 percent reduction in the risk of cardiovascular death, heart attack or stroke. These new findings focus specifically on the 17,779 patients with a prior heart attack.

> Vorapaxar is the first of a new class of investigational Protease Activated Receptor 1 (PAR-1) thrombin receptor antagonists. Unlike other antithrombotic drugs, vorapaxar blocks thrombin from stimulating platelets to stick together and create clots. In addition to the benefit of reducing future cardiac events, researchers also report that this new therapy was found to increase the risk of moderate or severe bleeding in patients with prior heart attacks. Intracranial hemorrhage tended to be higher but did not differ significantly between vorapaxar than placebo (0.6 vs. 0.4 percent at 3 years),

Researchers caution that if vorapaxar becomes



available for clinical use, clinicians will have to balance the antithrombotic efficacy versus the risk of bleeding for the individual patient.

"Of the groups we studied, the greatest net clinical benefit was observed in those patients who are less than 75 years old, have no history of stroke or transient ischemic attacks, and weigh at least 60 kilograms," said Scirica. "In this group of 14,909 patients, 84 percent of the group with prior heart attacks, vorapaxar reduced the risk of cardiovascular death, heart attack, or stroke by 25 percent and cardiovascular death alone by 27 percent."

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