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New platelet blocker reduces blood clots, artery-opening procedures

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A new investigational platelet blocker reduces the rate of clotted arteries and the need for artery-opening revascularization procedures in the legs in people with peripheral artery disease (PAD), according to new research presented in the American Heart Association's Emerging Science Series webinar.

"Much of the focus on PAD therapies has been on lowering patients' risk of heart attack and stroke, but this shows that there can be therapies that reduce limb-threatening blood clots and the need for revascularization procedures in the legs," said Marc P. Bonaca, M.D., M.P.H., Instructor of medicine at Harvard Medical School and Brigham and Women's Hospital in Boston, Mass., and an investigator with the Thrombolysis in Myocardial Infarction (TIMI) study group.

In the study, researchers randomized 3,787 patients with PAD to receive standard care or standard care plus vorapaxar, the first in a new class of anti-platelet drugs called PAR-1 antagonists. Participants were part of the 26,449-patient TRA2P-TIMI 50 trial testing 2.5 milligrams per day (mg/day) of vorapaxar in people with a history of heart attack, stroke or PAD. The TRA2P-TIMI 50 trial main results presented earlier this year showed a statistically significant reduction in cardiovascular events including heart attack, stroke, and cardiovascular death with vorapaxar. In this substudy focused on participants with PAD, 11.3 percent of those taking vorapaxar experienced these major cardiovascular events compared with 11.9 percent of those taking a placebo – a numeric reduction consistent with the overall trial findings that did not reach

statistical significance on its own. However, they found benefits of vorapaxar on limb events. Compared to those not receiving the drug:

- Fewer vorapaxar patients were hospitalized for blood clots in the limbs (2.3 percent vs. 3.9 percent).
- Fewer vorapaxar patients required revascularization to restore full blood flow in narrowed or blocked vessels in the limbs (18.4 percent vs. 22.2 percent).

“This is the first outpatient therapy that has been shown to reduce the risk of blood clots and the need for artery opening revascularization procedures in the legs in patients with PAD,” Bonaca said. The reduction in both urgent blood clots as well as the need for surgery to treat worsening atherosclerosis suggests that the drug may be working in more than one way. “The target for this therapy is expressed on platelets but also on cells in the artery walls that are important for normal artery function. The benefits observed may be due to drug activity at both sites,” noted Bonaca.

Moderate and severe bleeding was increased in patients on vorapaxar compared to those on standard care (7.4 percent vs. 4.5 percent consistent with the overall trial); however, there was no increase in fatal bleeding. “For clinicians and researchers, these data show the potential for therapies that can reduce leg problems in patients with PAD rather than just overall cardiovascular risk,” Bonaca said.

The investigators are analyzing whether vorapaxar treatment improves circulation in the lower body, or allows patients to walk further without pain due to insufficient blood flow to leg muscles (claudication). All of the PAD patients in the study initially had symptoms of claudication, and either poor leg circulation or a previous vessel-opening procedure.

Co-authors are David A. Morrow, M.D., M.P.H., and Eugene Braunwald, M.D. Merck funded the study.

Provided by American Heart Association

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