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Long-term ticagrelor cuts risk of future events after heart attack

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Adding the antiplatelet drug ticagrelor to aspirin as long-term therapy after a heart attack significantly reduced the rate of subsequent death from cardiovascular causes, heart attack or stroke, with the benefit appearing to accrue for nearly three years, according to a study presented at the American College of Cardiology's 64th Annual Scientific Session.

The double-blind PEGASUS-TIMI 54 trial recruited 21,162 patients who had experienced a heart attack in the previous one to three years. Each had another factor, such as age or diabetes, that put them at risk for a second heart attack. The patients, from 1,144 sites in 31 countries, were randomly assigned to a twice-daily regimen of ticagrelor at 90 mg, ticagrelor at 60 mg or placebo.

Both ticagrelor doses reduced the chances of cardiovascular death, heart attack or stroke, the study's primary endpoint, with a 15 percent reduction in the 90-mg group and a 16 percent reduction in the 60-mg group compared to the placebo group.

"The benefit we saw was remarkably consistent across the individual components of the endpoint and in all the major subgroups of patients," said Marc S. Sabatine, M.D., M.P.H., chair of the TIMI Study Group, a senior physician in the Cardiovascular Division at Brigham and Women's Hospital and Harvard Medical School in Boston, and the study's principal investigator. "Moreover, we followed patients for an average of just under three years, and our event curves continue to spread out over time, suggesting that the benefit continues to accrue over time."

After a heart attack, standard practice calls for putting patients on a lifetime regimen of daily aspirin to prevent clotting and reduce the chance of another heart attack. Previous studies have shown a benefit in adding a second antiplatelet drug like ticagrelor, from a class called P2Y12 inhibitors, but they investigated the additional therapy for only a year, leaving unanswered the question of whether patients would benefit from continuing this treatment longer.

The twice-daily 90-mg dose of ticagrelor is already approved for patients with acute coronary syndrome. Researchers included a lower dose in this study, to study whether platelet inhibition needed two years after a heart attack might be different from what is needed two hours after a heart attack. Findings from a pharmacokinetic and pharmacodynamic substudy comparing the two dose levels will be presented at a later date.

With blood thinners such as ticagrelor, bleeding is the major side effect, and excess bleeding was seen in both treatment arms, though bleeding into the brain and fatal bleeding were not more common with ticagrelor, Sabatine said. Shortness of breath, called dyspnea, was more common with ticagrelor than placebo. Bleeding led to discontinuation of ticagrelor in about 7 percent of patients on the study drug, and dyspnea led to discontinuation of the study drug in about 5 percent of patients on the drug.

"Efficacy was virtually identical with both ticagrelor doses," Sabatine said. "Risk of bleeding and dyspnea tended to be, as predicted, a bit more with the 90-mg than the 60-mg dose, but the trial wasn't designed to compare those two dose levels."

"Now that we have the evidence, when faced with a patient who has had a heart attack, based on these data, I would continue treatment with ticagrelor as long as the patient tolerated it," Sabatine said.

Provided by American College of Cardiology