新たなクラスの血小板阻害薬は有効であることがphase IIIトライアルで証明された

TRA 2°P-TIMI 50：標準的な抗血小板療法にvorapaxarを加えることにより再発性心血管イベントのリスクが軽減する

TRA 2°P-TIMI 50: Adding vorapaxar to standard antiplatelet therapy reduces risk of recurrent cardiovascular events

治験段階の抗血小板薬vorapaxarを標準的な抗血小板薬に追加することにより、既知の動脈硬化を有する患者の再発性心血管イベントリスクを軽減することができると第61回American College of Cardiology学会において発表され、同時にNew England Journal of Medicineに掲載された。この無作為化二重盲検プラセボコントロール多国籍試験では、26,449人の患者において過去の心筋梗塞（17,779例）、脳卒中（4,883例）または下肢動脈の動脈硬化性狭窄（3,787例）などの確定した動脈硬化に対し標準的な抗血小板薬を投与し2年以上追跡した。参加者は標準療法と試験用血小板阻害薬（経口2.5mg1日1回）または標準療法とプラセボのいずれかを内服する群に無作為に割り付けられた。Vorapaxarは心血管死、MIまたは脳卒中をさらに13%（3年後に9.3%対10.5%、p<0.001）低下させた。この新たな心血管イベントの低下はMI既往を有する患者で最大であり、彼らにおいてはこれらのイベントが20%低下した（p<0.001）。

Full Text

Adding vorapaxar, an investigational platelet blocker, to standard antiplatelet therapy significantly reduces the risk of recurrent cardiovascular events in patients with known atherosclerosis according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

Doctors routinely prescribe aspirin therapy to help prevent blood clot formation post-myocardial infarction. Other platelet blockers, such as clopidogrel, are often added for as long as a year but it is unclear whether adding any platelet blocker to aspirin beyond this timeframe is useful. Despite such therapies, survivors of myocardial infarction (MI) have an almost 15 percent chance of having another atherosclerosis-related event that brings them to the hospital within a year.

Now, researchers led by the TIMI Study Group at Brigham & Women's Hospital in Boston, Mass. have shown, for the first time, that adding a new antiplatelet agent on top of standard therapy, including aspirin, is effective for long-term secondary prevention in stable patients with a prior MI. When used with aspirin and other standard antiplatelet therapy in a broad group of patients with previous MI, stroke or peripheral arterial disease, vorapaxar reduced the risk of cardiovascular death, heart attack or stroke by an additional 13 percent (9.3 vs. 10.5 percent at three years, p<0.001). This reduction in new cardiovascular events appeared greatest in patients with prior heart attack, among whom there was a 20 percent decline in these events (p<0.001).

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. Blood thinners, like Coumadin, and other antiplatelets like aspirin or clopidogrel, do not directly target these same actions of thrombin.

"In the lab, we have seen very compelling science showing the importance of thrombin's action on platelets causing blood clots in arteries," said David A. Morrow, MD, MPH, senior investigator at the TIMI Study Group, director of the Samuel A. Levine Cardiac Unit at Brigham & Women's Hospital, and the study's lead investigator. "This is the first study to show definitively that blocking this pathway reduces the risk of suffering another cardiovascular event."

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 MI (n=17,779), stroke (n=4,883), or atherosclerotic narrowing in the arteries of the legs (n=3,787). Participants were randomly assigned to either take the investigational platelet blocker (2.5 mg orally once daily) with standard therapy, or a placebo with standard therapy.

"It's exciting to find clearly that we can reduce the risk of a recurrent thrombotic event by adding another platelet inhibitor to aspirin over the long-term," Dr. Morrow said. "Adding this new class of antiplatelet therapy reduced the risk of new cardiac events in stable patients, especially among the subset of patients with a prior heart attack."

Dr. Morrow commented that if vorapaxar becomes available for clinical use, it does not appear suitable for everyone with atherosclerosis. "Of the groups we studied, the benefit was compelling to us only in patients with a prior MI," said Dr. Morrow. In addition, this new therapy was found to increase the risk of severe bleeding, including intracranial bleeding. The risk of intracranial bleeding was highest among patients who have suffered from previous strokes; vorapaxar would likely not be appropriate for stroke victims or patients at high risk of bleeding. Stroke patients who were enrolled in the study ended their participation early after advice by the study's data and safety monitoring board.

Patients who took vorapaxar had significantly more bleeding events (GUSTO moderate or severe bleeding at three years 4.2 percent with vorapaxar vs. 2.5 percent with placebo, p<0.001). Intracranial hemorrhage was higher with vorapaxar than placebo (1.0 vs. 0.5 percent, p<0.001) with lower overall rates in patients with no history of stroke (3 years: 0.6 percent with vorapaxar vs. 0.4 percent with placebo, p=0.049).

Dr. Morrow and his team look forward to learning more from this very rich dataset to identify the patients who may have the best balance of benefit vs. bleeding risk with this agent.

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This study was simultaneously published in New England Journal of Medicine.

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