ACSに対するotamixabanの有効性の複合結果

SEPIA-ACS1 TIMI 42：otamixabanは非ST上昇急性冠症候群患者の治療薬として有望である

SEPIA-ACS1 TIMI 42: Otamixaban shows promise for the treatment of patients with non-ST-elevation acute coronary syndromes

ESC 2009で発表された静注抗凝固治験薬otamixabanのphase IIトライアルの結果、急性冠症候群（ACS）の現在の標準治療薬と比較し、死亡、二度目の心筋梗塞（MI）、または他の冠動脈疾患のリスクを軽減する可能性が示された。このスタディ（SEPIA-ACS1 TIMI 42）は、世界36ヵ国のACS患者3,241人（平均年齢61歳、女性31%）を組み入れた。患者は5つの用量のotamixaban群またはヘパリンと比較対照薬（静注抗血小板薬eptifibatideの併用）の群に無作為に割り付けられた。患者は7日間（一次エンドポイント）およびその後6ヵ月間にわたり追跡された。最も低用量の群を除いた全てのotamixaban群においてヘパリンとeptifibatide併用群よりも死亡率、二度目のMI、または他の冠疾患発現率が低い傾向にあった。特に、中等用量のotamixaban投与群患者においては、死亡または虚血性合併症発現率がヘパリンとeptifibatide併用群と比較し、40%低かった。これらの有益性は180日間にわたり持続した。中等用量otamixaban投与群における出血発現率はヘパリンeptifibatide併用群と同等であった。

Full Text

Data from a phase II trial of an investigational intravenous drug designed to block the formation of blood clots shows potential to reduce the risk of death, a second heart attack, or other coronary complications compared with the current standard of care in patients presenting with acute coronary syndromes.

Otamixaban inhibits the activity of Factor Xa, a key enzyme involved in the process of blood coagulation. It has already shown promising results when tested in patients undergoing elective angioplasty. In this trial, otamixaban was studied in high-risk patients with acute coronary syndromes (ACS). Otamixaban was compared with heparin, a standard and very commonly used blood thinner for acute coronary syndromes. Heparin, however, has many limitations, including thinning the blood to an unpredictable degree and therefore needing frequent monitoring. "There is intense interest in finding a more effective, reliable, and safe replacement for heparin," said study lead Marc S. Sabatine, MD, MPH, an Investigator in the TIMI Study Group and a cardiologist at Brigham and Women's Hospital, who presented the findings at the European Society of Cardiology meeting in Barcelona.

Sabatine, along with Professor Eugene Braunwald, Chairman of the TIMI Study Group, and colleagues studied the use of otamixaban in 3241 patients from 36 countries around the world who presented with ACS. The study (called SEPIA-ACS1 TIMI 42) was designed to identify the optimal dose of otamixaban. Patients were randomized into one of 5 doses of otamixaban or a comparator of heparin plus the intravenous platelet inhibitor eptifibatide. Researchers tracked the incidence of death, a second heart attack, additional coronary complications, and bleeding through 7 days (the primary endpoint) as well as over the following 6 months.

At the end of the study, Dr. Sabatine and colleagues found that in all of the otamixaban arms except the lowest one, the rate of death, a second heart attack, or additional coronary complications tended to be lower with otamixaban than with heparin plus eptifibatide. Specifically, patients receiving intermediate doses of otamixaban had a significant, 40% lower rate of death or ischemic complications compared with treatment with heparin plus eptifibatide. These benefits persisted through 180 days. The rates of bleeding in intermediate doses of otamixaban were similar to the rate in patients treated with heparin plus eptifibatide.

"The data show that intermediate doses of otamixaban may offer a substantial reduction in major coronary complications in patients presenting with an acute coronary syndrome, with bleeding rates comparable to current therapy," says Sabatine. "These findings will need to be tested in a large phase III trial to establish the definitive role of otamixaban in the treatment of acute coronary syndromes." Otamixaban is under development at sanofi-aventis, the company that sponsored the study. Dr. Sabatine has received honoraria and consulting fees from sanofi-aventis and honoraria from Bristol-Myers Squibb. Dr. Braunwald has received research support from Johnson & Johnson and honoraria and consultant fees from sanofi-aventis.

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