Anticoagulant does not reduce rate of ischemic events among certain patients undergoing PCI

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Use of the novel anticoagulant otamixaban did not reduce ischemic events compared with unfractionated heparin plus eptifibatide but increased bleeding among patients with non–ST-segment elevation acute coronary syndromes undergoing a percutaneous coronary intervention (PCI; procedures such as balloon angioplasty or stent placement used to open narrowed coronary arteries), according to a study published by *JAMA*. The study is being released early online to coincide with its presentation at the European Society of Cardiology Congress 2013

"Major progress has been made in the management of non–ST-segment elevation [a certain pattern on an electrocardiogram] acute coronary syndromes (NSTE-ACS) because of the availability of potent combinations of oral antiplatelet agents, injectable anticoagulants, and increasing use of an invasive strategy. Nevertheless, the risk of adverse outcomes remains substantial, and there is no consensus on a single optimal injectable anticoagulant that can be used across the continuum of care from the emergency setting through revascularization (when applicable)," according to background information in the article. The synthetic intravenous drug otamixaban inhibits thrombin [an enzyme that acts on fibrinogen in blood causing it to clot] generation in a dose-dependent manner. A phase 2 trial showed a reduction in the combined outcome of death or myocardial infarction (heart attack) in patients treated with otamixaban compared with unfractionated heparin (UFH) plus eptifibatide (an antiplatelet drug) and showed similar bleeding rates

with otamixaban at midrange doses.

Philippe Gabriel Steg, M.D., of the Université Paris-Diderot, Sorbonne-Paris Cité, Paris, and investigators with the TAO trial compared the clinical efficacy and safety of otamixaban with that of unfractionated heparin plus eptifibatide in 13,229 patients with NSTE-ACS and a planned early invasive strategy. The trial was conducted at 568 active sites in 55 countries between April 2010 and February 2013. Eligible participants were randomized to otamixaban or unfractionated heparin plus, at the time of PCI, eptifibatide.

The primary outcome of death or new myocardial infarction through day 7 occurred in 5.5 percent of the patients treated with otamixaban vs. 5.7 percent of the patients treated with UFH plus eptifibatide. Otamixaban did not significantly reduce the risk of any of the components of the primary outcomes, either death or heart attack, or of any of the secondary efficacy outcomes, including procedural thrombotic complications. Analysis of the primary outcome by 30 days confirmed the absence of a reduction with otamixaban.

In the lower-dose otamixaban group, discontinued by the data monitoring committee for futility based on the interim analysis, the rate of the primary outcome at day 7 was 6.3 percent.

Patients in the otamixaban group had about double the rate of the primary safety outcome of Thrombosis in Myocardial Infarction major or minor bleeding at day 7 compared with patients in the combination of UFH-plus-eptifibatide group (3.1 percent vs. 1.5 percent). Otamixaban consistently increased all types of bleeding events, regardless of the severity or bleeding classification scheme used. Study anticoagulant was discontinued because of bleeding in 242 patients (4.7 percent) in the otamixaban group and in 95 patients (1.7 percent) in the UFH-plus-eptifibatide group.

"Otamixaban did not reduce ischemic events compared with UFH plus eptifibatide but increased bleeding among patients with NSTE-ACS and a planned invasive strategy. These findings do not support the use of otamixaban for patients with NSTE-ACS undergoing planned early percutaneous coronary intervention," the authors conclude.

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