Heparin-Eptifibatide Combination Fails to Impress

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WASHINGTON — The adjunctive use of eptifibatide in antithrombotic regimens that are given to patients undergoing primary percutaneous coronary interventions for acute ST-segment elevation myocardial infarction significantly increases the rate of bleeding, compared with heparin alone, according to a small randomized trial.

This increased rate of bleeding—plus a lack of any added therapeutic benefit with eptifibatide in the trial—raises the question of whether treatment with a glycoprotein (GP) IIb/IIIa inhibitor is necessary when a patient has been pretreated for primary PCI with a high loading dose of clopidogrel (Plavix), Dr. Michel R. Le May

Adjunctive eptifibatide led to significantly more major and minor bleeding events combined than did heparin alone.

DR. LE MAY

said at Transcatheter Coronary Therapeutics 2008.

The trial, called ASSIST (A Safety and Efficacy Study of Integrilin-Facilitated PCI in ST Elevation Myocardial Infarction), is the first randomized trial to compare eptifibatide against a control group in the setting of a high (600-mg) loading dose of clopidogrel, said Dr. Le May, director of the Coronary Care Unit Research Group at the University of Ottawa Heart Institute.

Previously, another GP IIb/IIIa inhibitor, abciximab (ReoPro), was shown to have no benefit over unfractionated heparin when patients with a STEMI (ST-segment elevation myocardial infarction) were pretreated with a 600-mg loading dose of clopidogrel before undergoing primary PCI.

Dr. Le May noted that "in many centers in the United States, eptifibatide is now the preferred treatment for primary angioplasty, mostly because it's cheaper. It runs about $800, and abciximab is about twice the price."

In the open-label trial, 201 patients who took eptifibatide in addition to unfractionated heparin experienced a rate of events in the composite 30-day end point of death, reinfarction, or recurrent severe ischemia that was similar to the rate in patients who received unfractionated heparin alone (6.5% vs. 5.5%, respectively). At 6 months, the similarity between rates persisted (8% and 7.1%, respectively).

Eptifibatide-treated patients experienced significantly more major and minor bleeding events combined in the first 30 days after PCI than did patients who received unfractionated heparin alone (22.4% vs. 14.6%).

However, the differences between the groups in the rates of major bleeding alone or minor bleeding alone did not reach statistical significance, according to the TIMI (Thrombolysis in Myocardial Infarction) score.

The trial was performed after the establishment of an integrated, citywide rapid STEMI response system, which helped to achieve a median time from hospital arrival to PCI of 95 minutes in Ottawa.

All of the patients (mean age, about 60 years) were required to have felt symptoms less than 12 hours before admission. In the unfractionated heparin–only arm of the trial, 3% received eptifibatide and 4% received abciximab as a bail-out treatment.

The higher rate of bleeding during eptifibatide treatment—in addition to a lack of an improvement in effectiveness, compared with unfractionated heparin alone—may necessitate another trial in STEMI patients. In this trial, it would make sense to compare unfractionated heparin against bivalirudin (Angiomax) during primary PCI, given that in the HORIZONS-AMI (Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction) trial, bivalirudin reduced all-cause mortality and rates of major bleeding significantly more than did unfractionated heparin and adjunctive eptifibatide or abciximab, Dr. Le May said.

The ASSIST trial was funded by Schering-Plough Canada Inc. and Medtronic of Canada, although Dr. Le May said that he and his associates initiated the trial independently of industry. Schering-Plough has exclusive U.S. marketing rights to eptifibatide. ■