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Lamifiban

A Viewpoint by Robert A. Harrington

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Atherosclerotic plaque rupture with resultant coronary thrombosis and vessel occlusion are the pivotal events in the pathophysiology of the acute coronary syndromes (unstable angina and myocardial infarction) and of the ischaemic complications of percutaneous coronary intervention. Since arterial thrombi are composed of platelets within a fibrin and erythrocyte meshwork, standard therapy for the treatment of these platelet-dependent diseases has included both antiplatelet and anticoagulant therapies, typified by oral aspirin and intravenous heparin. Oral antiplatelet therapy has proven to be especially effective in reducing the morbidity and mortality associated with the acute coronary syndromes and with percutaneous coronary intervention.[1]

Despite the benefits of current antiplatelet strategies, these diseases carry substantial risks and, because of their prevalence, have a global public health impact. Aspirin is a weak platelet inhibitor that works on only 1 pathway by which platelets are activated. A new class of platelet inhibitors, the glycoprotein (GP) IIb/IIIa inhibitors, has been developed for the treatment of unstable angina and acute myocardial infarction and during percutaneous coronary intervention.[2] These drugs inhibit fibrinogen from binding to the GP IIb/IIIa receptor complex, leading to an inhibition of platelet aggregation. Randomised clinical trials involving more than 30 000 patients have demonstrated the clinical benefits of this class of drugs, which includes a monoclonal antibody fragment (abciximab), a peptide (eptifibatide) and nonpeptides (tirofiban and lamifiban).[3]

Lamifiban is a nonpeptide inhibitor of GP IIb/IIIa currently under clinical investigation for use in acute coronary syndromes without persistent ST segment elevation. Smaller, dose-finding studies have suggested an optimal dosage range at which clinical benefit may be maximised and bleeding risks minimised.[4] This concept, unique to lamifiban development, is being tested in ongoing clinical trials.

Although 3 drugs are available in the US for use in acute coronary syndromes without persistent ST segment elevation (eptifibatide and tirofiban) and during percutaneous coronary intervention (abciximab and eptifibatide), many questions regarding their clinical use remain. These questions include the optimal level and duration of platelet inhibition, whether the clinical benefit is confined to patients undergoing coronary intervention, and whether there is a need for concomitant therapy with aspirin and heparin.

The ongoing lamifiban project, PARAGON B, is designed to confirm that lamifiban improves patient outcomes in acute coronary syndromes without persistent ST segment elevation. Using a patient-based dose adjustment, PARAGON B will attempt to demonstrate that achievement of an 'optimal' dosing level will lead to clinical improvements superior to those seen with the other agents. ▲

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