Abciximab (c7E3 Fab)
A Review of its Pharmacology and Therapeutic Potential in Ischaemic Heart Disease

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Summary

Synopsis

Abciximab (c7E3 Fab) is a chimaeric human-murine monoclonal antibody Fab (fragment antigen binding) fragment. It binds to the platelet glycoprotein IIb/IIIa receptor and inhibits platelet aggregation. In two double-blind placebo-controlled trials, abciximab therapy reduced the incidence of ischaemic complications...
during the initial postoperative period (30 days or until hospital discharge) in high-risk patients undergoing percutaneous coronary angioplasty or directional atherectomy. It also reduced the incidence of clinical restenosis compared with placebo during longer term (6 months) follow-up of these patients. Although abciximab delayed the need for coronary artery bypass graft surgery, it did not reduce the proportion of patients ultimately requiring this procedure. The drug was generally well tolerated in clinical trials, with bleeding complications being the major adverse event.

Abciximab is at an early stage of its clinical introduction and, not surprisingly, some aspects of its use remain to be further assessed. Nevertheless, results show the addition of abciximab to standard aspirin plus heparin therapy during coronary angioplasty or directional atherectomy improves the outcome of the revascularisation procedure in patients with a high risk of subsequent acute ischaemic complications. The results of further trials defining the optimum dosage of heparin when administered with abciximab, and evaluating the role of abciximab in a wider range of patients, are eagerly awaited.

Abciximab (c7E3 Fab) is a chimaeric human-murine monoclonal antibody Fab (fragment antigen binding) fragment that binds to the platelet glycoprotein (GP) IIb/IIIa receptor. It has shown greater antithrombotic activity than aspirin or heparin in animal models. Dose-dependent blockade of GPIIb/IIIa receptors and inhibition of platelet function were observed in patients with ischaemic heart disease receiving the drug. Maximum effects occurred after intravenous bolus administration of abciximab 0.25 mg/kg (corresponding to approximately 80% blockade of GPIIb/IIIa receptors) and were maintained during continuous intravenous infusion of abciximab 10 µg/min for 12 hours.

Free plasma abciximab is cleared rapidly from the circulation but platelet-bound drug persists for several days. Human-antichimaeric antibodies develop in about 6% of abciximab recipients.

The results of two well-designed, double-blind trials in high-risk patients undergoing percutaneous coronary angioplasty or directional atherectomy indicate that abciximab significantly reduces the incidence of ischaemic complications (a composite end-point including death, nonfatal myocardial infarction or recurrent ischaemia requiring urgent intervention) compared with placebo. There was a 35% reduction in ischaemic complications occurring within 30 days of randomisation in patients receiving abciximab bolus plus infusion (8.3% of 708 patients) compared with placebo recipients (12.8% of 696 patients) in the pivotal phase III trial; after 6 months clinical restenosis had occurred in 27 and 35% of patients, respectively. The need for coronary artery bypass graft surgery was delayed in abciximab recipients but the proportion of patients ultimately requiring this procedure was not reduced. The smaller phase II trial had similar results, with ischaemic complications occurring in 1 of 30 patients receiving abciximab compared with 7 of 30 receiving placebo before hospital discharge.

Abciximab administration has also stabilised cyclic variations in coronary blood flow occurring after coronary angioplasty.

Major bleeding complications occurred more frequently in patients receiving intravenous abciximab bolus plus infusion (14%) than in placebo recipients (7%) in the phase III trial. However, the risk of haemorrhagic complications was not increased in patients who subsequently required coronary artery bypass graft