

Review: Glycoprotein IIb/IIIa inhibitors reduce MI and urgent revascularization but increase bleeding in PCI

Brown DL, Fann CS, Chang CJ. Meta-analysis of effectiveness and safety of abciximab versus eptifibatide or tirofiban in percutaneous coronary intervention. *Am J Cardiol.* 2001 Mar 1;87:537-41.

QUESTION

In patients who are having percutaneous coronary interventions (PCIs), do glycoprotein (GP) IIb/IIIa inhibitors as a class or as individual drugs (abciximab, eptifibatide, and tirofiban) have different rates of clinical outcomes?

DATA SOURCES

Studies were identified by searching MEDLINE with the terms platelet inhibitors, angioplasty, and stent; lists of conference abstracts; and bibliographies of relevant studies.

STUDY SELECTION

Randomized, double-blind, placebo-controlled trials were selected if patients were scheduled to have PCI, a parenteral GP IIb/IIIa inhibitor was studied, and 30-day outcomes were reported (death, myocardial infarction [MI], urgent or emergent revascularization, or major bleeding).

DATA EXTRACTION

Data were extracted on study characteristics, inclusion criteria, drug dosage and duration, use of other drugs, timing of PCI, and outcomes.

MAIN RESULTS

8 trials met the inclusion criteria. 8876 of 14 644 patients received a GP IIb/IIIa inhibitor (5022 received abciximab). The random-

effects model was used with an intention-to-treat analysis. Data for eptifibatide and tirofiban were combined. Treatment was started from 24 hours before to just before PCI, and duration was from 1 to 36 hours after PCI. Mortality was not reduced for all GP IIb/IIIa inhibitors (0.8% for GP IIb/IIIa inhibitors vs 1.1% for placebo), abciximab (0.8% vs 1.1%), or eptifibatide and tirofiban combined (0.7% vs 1.0%). The rate of MI was lower for all GP IIb/IIIa inhibitors and for abciximab ($P \leq 0.001$) (Table) than for placebo but not for eptifibatide and tirofiban combined. Urgent revascularization was reduced for all comparisons (Table). The risk for major bleeding was

increased for all GP IIb/IIIa inhibitors and for abciximab ($P \leq 0.01$) (Table).

CONCLUSIONS

The use of glycoprotein IIb/IIIa inhibitors in patients who are having percutaneous coronary interventions does not reduce mortality but does decrease the need for urgent revascularization. Abciximab, but not eptifibatide or tirofiban, is associated with a reduced rate of recurrent myocardial infarction.

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For correspondence: Dr. D.L. Brown, Division of Cardiovascular Medicine, Albert Einstein College of Medicine, 1825 Eastchester Road, Bronx, NY 10461, USA. FAX 718-918-1984. ■

Glycoprotein (GP) IIb/IIIa inhibitors (abciximab or eptifibatide and tirofiban [E+T] combined) as a class or individually vs placebo for percutaneous coronary interventions*

Outcomes at 30 d	GP inhibitors	Active drug	Placebo	RRR (95% CI)	NNT (CI)
Myocardial infarction	All	5.0%	7.8%	40% (24 to 51)	33 (26 to 53)
	Abciximab	4.3%	8.5%	49% (39 to 58)	25 (21 to 31)
Revascularization	All	3.4%	5.9%	41% (25 to 51)	42 (33 to 69)
	Abciximab	2.7%	6.2%	56% (45 to 137)	29 (12 to 36)
	E+T	4.2%	5.5%	23% (4 to 8)	80 (48 to 480)
				RRI (CI)	NNH (CI)
Major bleeding	All	5.5%	4.0%	43% (7 to 90)	58 (28 to 327)
	Abciximab	5.8%	3.8%	50% (3 to 84)	53 (31 to 115)

*Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

COMMENTARY

Brown and colleagues provide a systematic overview of the 30-day results for the 3 agents evaluated during the 1990s in placebo-controlled trials of adjunctive GP IIb/IIIa inhibitor therapy during PCI. Abciximab clearly reduced periprocedural MI and urgent revascularization. The initially observed increased risk for major bleeding with abciximab has been eliminated with appropriate heparin dosing. Although no significant mortality benefit has been shown at 30 days, longer-term follow-up has shown a reduction in mortality with abciximab therapy (1).

With a higher dose of eptifibatide than was used in the IMPACT (Integrilin to Minimise Platelet Aggregation and Coronary Thrombosis) trials (2, 3), the recent ESPRIT (Enhanced Suppression of the Platelet IIb/IIIa Receptor with Integrilin Therapy) trial (4) shows convincingly greater reductions in periprocedural MI in patients who received stents and who were treated with eptifibatide than in patients in the placebo group who received relatively low-dose heparin. Unlike with abciximab, however, a reduction in mortality was not shown at 1-year follow-up.

TARGET (Tirofiban and Reopro Give Similar Efficacy Outcomes Trial) (5) is the first major comparative trial of GP IIb/IIIa inhibitors. At the dose studied, tirofiban was inferior to abciximab in preventing

periprocedural MI. In the PCI setting, higher initial doses of tirofiban deserve study.

On the basis of the meta-analysis and the more recent studies, abciximab remains the gold standard for reducing periprocedural MI, urgent revascularization, and subsequent mortality, particularly in diabetic and high-risk patients. Whether the substantially higher initial cost of abciximab over eptifibatide is justified across all patient groups remains controversial.

William B. Hillegass, MD, MPH

Gregory D. Chapman, MD

*University of Alabama at Birmingham
Birmingham, Alabama, USA*

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