Abciximab did not reduce death or myocardial infarction in the acute coronary syndrome without early revascularization


**Question**
In patients with the acute coronary syndrome and non-ST elevation without early revascularization, does abciximab reduce death or myocardial infarction (MI)?

**Design**
Randomized (allocation concealed*), blinded (clinicians, patients, and outcome assessors),* trial with 30-day follow-up.

**Setting**
458 hospitals in 24 countries.

**Patients**
7800 patients ≥ 21 years of age (mean age 65 y, 62% men) with the acute coronary syndrome and non–ST-segment elevation. To be included, patients needed to have had ≥ 1 episode of angina lasting ≥ 5 minutes within the previous 24 hours and positive cardiac troponin T or I test results or ≥ 0.5 mm of new transient or persistent ST-segment depression not caused by coexisting disorders or medication. For patients who had an MI event in the past 10 days, inclusion criteria were new ST-segment depression and elevated creatine-kinase MB levels. Exclusion criteria included MI not caused by atherosclerotic coronary artery disease, MI with persistent ST-segment elevation, new left-bundle branch block, and percutaneous coronary intervention in the past 14 days. Follow-up was 100%.

**Intervention**
Patients were allocated to receive infusions of abciximab for 48 hours (n = 2612), matching placebo for 48 hours (n = 2598), or abciximab for 24 hours and then matching placebo for 24 hours (n = 2590). Abciximab was given first as a 0.25 mg/kg of body weight bolus and then as a 0.125 µg/kg per min infusion to a maximum of 10 µg/min for 24 hours. All patients received aspirin and either unfractionated or low-molecular-weight heparin.

**Main outcome measures**
All-cause mortality, MI, bleeding, and thrombocytopenia.

**Main results**
Analysis was by intention to treat. At 30 days, groups did not differ for the composite outcome of all-cause mortality or MI (Table) or for the single outcomes of all-cause mortality or MI. Bleeding and thrombocytopenia rates were low overall but higher among patients who received abciximab.

**Conclusion**
In patients with the acute coronary syndrome and non-ST elevation without early revascularization, abciximab did not reduce death or myocardial infarction.

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**Commentary**

The GUSTO IV study adds to the body of data on platelet glycoprotein IIb/IIIa blockers in patients with the acute coronary syndrome with non-ST elevation. It was designed to broaden the use of abciximab beyond the interventional catheterization laboratory to include “upstream” medical therapy. However, the surprisingly negative findings, even in patients with positive troponin levels (a group previously shown to benefit from glycoprotein IIb/IIIa blockers), have confused experts and practitioners. We know that abciximab works well as an adjunct to coronary interventions in patients who have unstable and stable acute coronary syndromes (1), but we now find that a deliberate noninterventional strategy with 24 or 48 hours of treatment with abciximab shows no benefit. In contrast, eptifibatide and tirofiban are often effective medical treatments and useful with subsequent intervention (1). However, a new meta-analysis pooling results from the 5 small-molecule trials plus GUSTO IV has shown a modest but significant and worthwhile reduction in death and MI in patients treated with a conservative medical strategy (2).

Potential reasons for the discrepancies between GUSTO IV and other studies include differences in trial design, patient populations, dosing regimens, and possibly the biological profile among all 3 agents. Recent consensus guidelines have weakly recommended tirofiban or eptifibatide for patients with high-risk acute coronary syndromes or with planned intervention, but new revisions using more recent data will probably strengthen the recommendation. GUSTO IV will reinforce the conviction that abciximab should be initiated in the catheterization laboratory and not before, but it should not deter a broader use of small molecules in the emergency department or hospital, with continuation to the interventional laboratory.

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**Reference**
