GUSTO IV Trial
Lancet 2001; 357: 1915-24

Purpose: To study the effect of the glycoprotein IIb/IIIa blocker abciximab on patients with acute coronary syndromes who were not undergoing early revascularization.

Design: Randomized, multicenter trial

Methods:
- 7800 pts admitted to hospital with chest pain and either ST-segment depression or raised troponin T or I concentrations.
- 2598 were randomized to PL, 2590 an abciximab bolus and 24 h infusion, and 2612 an abciximab bolus and 48 h infusion; all patients received aspirin and either unfractionated or low-molecular-weight heparin.

Endpoint: primary was 30 day death or MI

Results:
209 (8.0%) patients on placebo, 212 (8.2%) on 24 h abciximab, and 238 (9.1%) on 48 h abciximab died or had a MI before day 30 (odds ratio 1.0 [95% CI 0.83 – 1.24], for difference between placebo and 24 h abciximab, and 1.1 [0.94 – 1.39] for difference between placebo and 48 h abciximab.)

Bleeding rates were low, but increased with abciximab, particularly when continued for 48 h.

Additionally, thrombocytopenia was more frequent with abciximab.

Interpretation: Although the explanations for our findings are unclear, this study indicates that abciximab is not beneficial as first-line medical treatment in patients admitted with acute coronary syndromes.

GUSTO IV Trial cont.

Lancet 2001; 357: 1915-24

ASSENT III Trial
Lancet 2001; 358: 605-13

Purpose: To compare the efficacy and safety of TNKase plus enoxaparin or abciximab, with that of TNKase plus weight-adjusted UH in patients with AMI.

Methods: 6095 patients with AMI of less then 6 h were randomly assigned one of three regimens:
- full-dose TNKase with enoxaparin for 7 days (enoxaparin group; n=2040)
- half-dose TNKase with weight-adjusted low-dose UH and a 12 h infusion of abciximab (abciximab group; n=2017),
- or full-dose TNKase with weight-adjusted UH for 48 h (UH group; n=2038).

Endpoints:
1) efficacy endpoint)- Composite 30-day mortality, in hospital refractory ischemia
2) efficacy plus safety endpoint- the above plus in-hospital intracranial hemorrhage or in-hospital major bleeding complications

Results:
significantly fewer efficacy endpoints in the enoxaparin and abciximab groups than in the UH group: 233/2037 (11.4%) vs. 315/2038 (15.4%; relative risk 0.74 [95% CI 0.63-0.87], p=0.0002) for enoxaparin, and 223/2017 (11.1%) vs. 315/2038 (15.4%; 0.72 [0.61-0.84], p=0.0001) for abciximab.

The same was true for the efficacy plus safety endpoint: 280/2037 (13.7%) vs. 347/2036 (17.0%; 0.81 [0.70-0.93], p=0.0057) for enoxaparin, and 287/2016 (14.2%) vs. 347/2036 (17.0%; 0.84 [0.72-0.96], p=0.01416) for abciximab.

Interpretation: The TNKase plus enoxaparin or abciximab regimens studied here reduce the frequency of ischemic complications of an acute myocardial infarction. In light of its ease of administration, TNKase plus enoxaparin seems to be an attractive alternative reperfusion regimen that warrants further study.

ASSENT III Trial cont.

Lancet 2001; 358: 605-13

GUSTO V Trial
Lancet 2001; 357: 1905-14

Purpose: To compare the effect of reteplase alone with reteplase plus abciximab in patients with acute myocardial infarction.

Methods: 16588 patients in the first 6 h of evolving ST-segment elevation myocardial infarction were randomly assigned standard-dose reteplase (n=8260) or half-dose reteplase and full-dose abciximab (n=8328).

Endpoint: The primary endpoint was 30-day mortality, and secondary endpoints included various complications of myocardial infarction.

Results: At 30 days, 488 (5.9%) of patients in the reteplase group had died, compared with 468 (5.6%) in the combined reteplase and abciximab group (odds ratio 0.95 [95% CI 0.83-1.08], p=0.43).

There were fewer deaths or non-fatal reinfarctions with the combination than with reteplase alone, and there was less need for urgent revascularization and fewer major non-fatal ischemic complications of acute myocardial infarction. On the other hand, there were more non-intracranial bleeding complications in the combination group. The rates of intracranial hemorrhage and non-fatal disabling stroke were similar.

Interpretation: Although combined reteplase and abciximab was not superior to standard reteplase, the 0.3% absolute (5% relative) decrease in 30 day mortality fulfilled the criteria of non-inferiority.

GUSTO V Trial cont.

Lancet 2001; 357: 1905-14