European Heart Journal (2008) **29**, 2972–2980
doi:10.1093/eurheartj/ehn467

Randomized comparison between tirofiban and abciximab to promote complete ST-resolution in primary angioplasty: results of the facilitated angioplasty with tirofiban or abciximab (FATA) in ST-elevation myocardial infarction trial

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Received 9 June 2008; revised 4 September 2008; accepted 29 September 2008; online publish-ahead-of-print 21 October 2008

Aims To test the equivalence of high-dose bolus (HDB) tirofiban vs. abciximab during primary percutaneous coronary intervention (PPCI) in terms of ST-segment resolution (STR).

Methods and results The FATA trial (Facilitated Angioplasty with Tirofiban or Abciximab) was a prospective, multicentre, open-label trial that enrolled 692 patients with ST-segment elevation myocardial infarction (STEMI) undergoing PPCI. Patients were randomized 1:1 to receive abciximab ($n = 341$) or HDB tirofiban ($n = 351$). Primary endpoint was the rate of complete ($\geq$70%) STR 90 min after first balloon inflation. Thirty-day incidence of major bleedings, death, re-infarction and new revascularizations was also evaluated. Baseline characteristics of the two groups were well-balanced, with the exception of previous MI rates (tirofiban 6% vs. abciximab 2.6%, $P = 0.03$). The procedure was successful in 96.7% of the abciximab and in 96.6% of the tirofiban cohort ($P = 0.94$). Complete STR was obtained in 67.05% of the tirofiban and 70.45% of the abciximab group (Δ −3.4%, 95% confidence interval −10.35 to +3.56), which falls beyond the predefined $\Delta \pm$ 10% equivalence boundaries. Rates of secondary endpoints were similar between the two groups.

Conclusion This study failed to show the equivalence of HBD of tirofiban and abciximab as adjunctive therapy to PPCI.

Keywords Angioplasty • Acute myocardial infarction • Reperfusion • Glycoprotein IIb/IIIa inhibitors • ST-resolution

Introduction

Primary percutaneous coronary intervention (PPCI) with stenting by providing high rate of early and adequate revascularization of the infarct-related artery (IRA), is the treatment of choice for ST-elevation myocardial infarction (STEMI).[1–3] However, despite the optimal recanalization of the epicardial artery, microvascular damage may occur.[4–6] It has been consistently shown that

ClinicalTrials.gov Identifier: NCT00383136

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microvascular impairment is associated with an adverse prognosis, even if good epicardial flow has been restored. Several invasive and non-invasive diagnostic tools have been proposed to evaluate the microvascular effects of recanalization of the IRA, though the simplest indirect method remains to be the criterion of ST-segment resolution (STR) on surface electrocardiogram. STR is a reliable marker of effective myocardial reperfusion and its analysis yields prognostic information distinct from that provided by coronary angiography.[7–10]

In order to improve myocardial tissue reperfusion, powerful platelet inhibition with glycoprotein (Gp) IIb/IIIa inhibitors has been proposed as adjunctive therapy to mechanical reperfusion during PPCI. Abciximab, a monoclonal antibody fragment Gp IIb/IIIa inhibitor, ameliorates myocardial perfusion and left ventricular (LV) recovery after pPCI,[11,12] thus improving both early and late clinical outcomes.[13–16]

Tirofiban, a small-molecule Gp IIb/IIIa inhibitor, has been largely investigated in the setting of acute coronary syndromes without ST-elevation.[17,18] In patients undergoing PCI, tirofiban reduces the incidence of early adverse ischaemic events.[19] Importantly however, in a head-to-head comparison with abciximab, tirofiban was associated with a higher rate of the composite endpoint of death, non-fatal myocardial infarction (MI) and urgent target vessel revascularization (TVR) at 30 days.[20] This unfavourable result was ascribed to the suboptimal platelet inhibition obtained with the standard low-dose bolus (10 μg/kg) regimen of tirofiban.[21] Subsequent dose-ranging studies showed that a HBD (25 μg/kg) of tirofiban can achieve >90% platelet aggregation inhibition 10 min after infusion,[22] which is comparable or even better than obtained with the standard dose of abciximab.[23]

The present study was designed to evaluate whether the HDB regimen of tirofiban has an equivalent effect to the standard dose of abciximab for patients undergoing PPCI in terms of effective myocardial tissue reperfusion, as measured by STR.

Methods

Study design and population

The Facilitated Angioplasty with Tirofiban or Abciximab (FATA) study is a randomized controlled multicenter open-label trial in patients with STEMI undergoing PPCI. Patients were enrolled from November 2004 through August 2007. They were eligible for the study if all the following criteria were met: age >18 years, chest pain persisting more than 20 min associated with ST-segment elevation of at least 0.1 mV in two or more contiguous echocardiogram (ECG) leads, admission within 6 h from symptom-onset, release of written informed consent. Exclusion criteria were: complete left bundle branch block (LBBB), previous MI in the same territory, bleeding diathesis, administration of fibrinolytic agents for the current episode, postanoxic coma, known thrombocytopenia or leucopenia, severe hepatic dysfunction, known severe renal failure (serum creatinine >3 mg/dL), known contraindication to aspirin, thienopyridines, or heparin, a limited life-expectancy (<1 year), child-bearing potential, recent major surgery (within 3 months), uncontrolled hypertension, history of stroke within the previous 30 days, history of intracranial disease (aneurysm, arterovenous malformation), major trauma within the previous six weeks, oral anticoagulant therapy, participation in other studies in progress. There were no angiographic selection criteria. The study protocol complies with the Declaration of Helsinki and was approved by the ethics committees of all participant centres.

Study protocol and randomization

All patients who met inclusion criteria received aspirin (250 mg i.v.) and a bolus of heparin (70 IU/kg) before the procedure and were randomly assigned 1:1 to treatment with either abciximab or tirofiban. Randomization was performed using a centralized computerized automatic system using short messaging service messages sent through ordinary mobile phones. Randomization schedule was generated by a standard automatic algorithm, without stratification, in blocks of 10 per centre. Study medication was administered as soon as possible after randomization either in the emergency ambulance, in the emergency room, or in the catheterization laboratory. Enrolment of a patient and randomization in the ambulance or in the emergency room had to be performed by a study investigator following a telephone conversation with the physician on-site, and after the diagnosis of STEMI had been confirmed by a cardiologist in the coronary care unit (with ECG transmission and telephone consultation). In all cases, study medication had to be administered before coronary angiography. Patients received either abciximab as a bolus of 0.25 mg/kg of body weight, followed by 12 h infusion of 0.125 μg/kg/min, or tirofiban as bolus of 25 μg/kg of body weight, followed by 18 h infusion of 0.15 μg/kg/min. In the event of coronary obstruction or stenosis >50% at angiography, PPCI was performed and stent implantation was recommended. Revascularization of the IRA with PCI and stenting was always attempted, even when there was left main involvement and severe three-vessel disease. Decision to proceed with further revascularization procedures (either PCI or coronary artery bypass grafting) was demanded for subsequent evaluation. Cardiogenic shock at admission was defined as persistent systolic blood pressure <90 mmHg, or the need of inotropes or intra-aortic balloon pumping required to maintain blood pressure >90 mmHg. The procedure was considered successful when a final residual stenosis <30% and TIMI flow 2 or 3 were achieved.

In case of stent placement, a bolus of clopidogrel 300 mg was administered orally during or immediately after the procedure, followed by 75 mg/day for at least 30 days, or ticlopidine 500 mg orally during or immediately after the procedure, followed by 250 mg twice a day for at least 30 days. All patients were advised to continue aspirin lifelong. Beta-blockers and angiotensin-converting enzyme-inhibitors were administered according to current guidelines, unless contraindicated.

In all patients, a 12-lead ECG was recorded at the time of the first medical contact and 90 min after the PCI. A standard two-dimensional echocardiogram was performed within 48 h in all patients. Creatine kinase (CK) and CKMB isoform values were assessed 8, 16, 24, and 48 h after the PCI procedure.

Follow-up data were prospectively collected from hospital records, and during outpatient clinic visits or telephone interviews performed at 30-day.

Endpoints and definitions

The primary endpoint was the rate of complete STR 90 min after first balloon inflation. The absolute level of ST-elevation was measured 20 ms after the end of QRS complex with the PR segment as reference baseline. Summed STE was calculated as follows: for anterior MI, the sum of ST-elevation in V1–V6, I, aVL; for inferior MI the sum of STE in leads II, III, aVF. STR was calculated as summed STR (∑STR), i.e. the percentage reduction in the summed ST-elevation score between the pre- and the postprocedure ECG. STR was considered complete when ≥70%. Patients with incomplete STR were further

divided in two subgroups: absent STR (<30%), and partial STR (30–70%). All ECG assessments were done in a core laboratory by two skilled readers blinded to the treatment. In addition, as primary safety endpoint, we assessed the in-hospital incidence of major and minor bleedings. Major bleedings were defined by a combination of the Thrombolysis In Myocardial Infarction (TIMI) and Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) definitions:[24] requiring transfusion or surgery, reduction in haemoglobin of more than 5 g/dL, and intracranial haemorrhage. Minor bleedings were defined as local haematoma and any other clinically relevant bleeding that did not meet criteria for severity.

The clinical secondary endpoints comprised the incidence of death, re-infarction, and TVR at 30 days. Angiographic secondary endpoints were pre- and postprocedural TIMI flow 3 rates, and postprocedure myocardial blush grade,[25] and they were also assessed in a core laboratory by clinicians blinded to study treatment. Re-infarction was defined as the recurrence of typical clinical symptoms and new ECG changes with a new elevation of the CKMB levels >2 times the upper limit of normal. TVR was defined any revascularization, either surgical or percutaneous, to treat the IRA. TVR was defined 'urgent' when performed within 24 h from the index procedure.

Statistical analysis

The primary hypothesis was that tirofiban would be equivalent to abciximab in achieving complete STR. Before starting the trial, we performed a pilot study on 100 unselected STEMI patients undergoing PPCI with abciximab, and we observed a 71% complete STR according to our criterion of ≥70% STR at 90 min. On the basis of a 50% expected rate of complete STR in patients treated with PPCI without Gp IIb/IIIa inhibitors (51% in the Zwolle experience),[9] the margin of clinical equivalence between the two drugs was fixed at Δ (difference between rates of patients with STR) ±10%. In fact, in order to meet the definition of equivalence, the boundaries of the 95% confidence interval (CI) for the comparison of tirofiban with abciximab had to be within ±10%, consistent with the preservation of a difference of at least 50% of the effect of abciximab as compared with that of placebo.[20] Using the method described by Jones *et al.*[26] and assuming that the same proportion of patients with complete STR in both the study groups, 660 patients were required to have 80% power and $\alpha = 0.05$. Primary analysis was performed on an intention-to-treat basis, with the exclusion of patients in which the primary endpoint was not assessable (*Figure 1*). To account for possible cross-over, a per treatment analysis was also performed, following the indications of the International Conference on Harmonisation E9 (Statistical Principles for Clinical Trials), which stated that in equivalence study, both analyses play an equal role.[27]

Continuous variables are presented as means ± SD and compared with Student's *t*-test. Categorical variables were expressed as counts and percentages, and χ^2 test was used for comparison. Time delays and ∑ST-elevation are presented as medians and compared with Mann–Whitney *U* test. To identify independent predictors of the primary endpoint we performed a multivariable logistic regression, using the following variables: age, gender, diabetes mellitus, hypertension, anterior location, pain onset-to-balloon, TIMI flow >0 at first

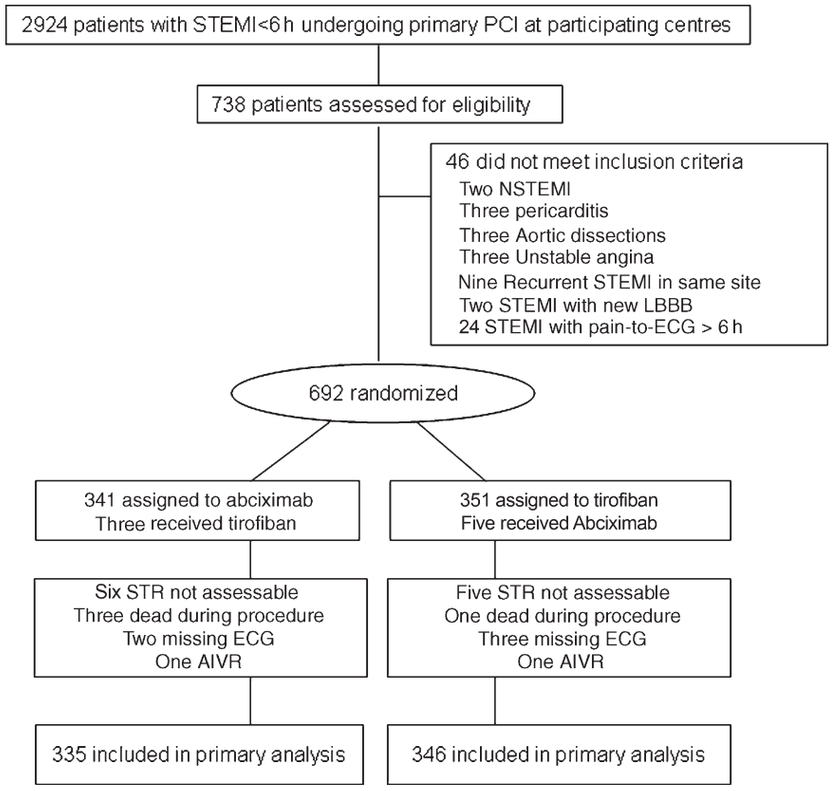

Figure 1 Study flow. NSTEMI, non-ST-elevation acute myocardial infarction; LBBB, left bundle branch block; AIVT, accelerated idioventricular tachycardia.

angiography, study drug, previous MI, number of vessel disease, smoking status. All statistical tests were two-sided. A *P*-value<0.05 was considered significant. All analyses were performed with the SPSS 15.0 software (SPSS Inc., Chicago, IL, USA).

Results

During the study period, 738 patients were assessed for eligibility. Among them, 46 did not meet inclusion criteria and were therefore excluded, and 692 were randomized to study treatment (abciximab, $n = 341$; tirofiban, $n = 351$). Percentage of patients enrolled vs. overall number of STEMI patients undergoing PPCI within 6 h from symptom-onset at participating centres during the study period was 23.7% (range 7.1–42.6%). The flow of the study is shown in *Figure 1*. Baseline clinical, angiographic, and procedural characteristics are summarized in *Table 1*. As a result of randomization, only minor differences between study groups were observed. Specifically, the incidence of previous MI was higher in the tirofiban cohort (6% vs. 2.6%, $P = 0.03$). Importantly, age, rates of diabetes mellitus, presentation with cardiogenic shock, anterior location, and multivessel disease were comparable between the abciximab and the tirofiban groups, as well as time-to-Gp IIb/IIIa inhibitor administration, time from administration of the drug-to-balloon, and overall ischaemic time (pain-to-balloon). TIMI 3 flow rate at first angiography was slightly higher, although not significantly, in tirofiban-treated patients (16.5% tirofiban vs. 13.5% abciximab). The procedure was successful in 96.7% of the abciximab and in 96.6% of the tirofiban cohort ($P = 0.94$). Postprocedural LV ejection fraction was on average around 50% and similar in both the groups.

STR between baseline and 90 min ECG was evaluated in 681 patients (98.4%) (*Figure 1*). Overall, 67.05% of the patients treated with tirofiban met the primary endpoint of complete STR at 90 min when compared with 70.45% of the patients treated with abciximab (Δ −3.4%, 95% CI −10.35 to +3.56), which is beyond the predefined equivalence threshold (*Figures 2* and *3*). A few patients did not receive the drug resulted from randomization and crossed-over to the other treatment group (three in the abciximab and five in the tirofiban group). Therefore, we also performed a *per treatment* analysis, which confirmed the results of the intention-to-treat analysis for 90 min complete STR (tirofiban 67.15%, abciximab 70.33%, Δ −3.18%, 95% CI −10.13 to +3.78). In a *post hoc* confirmatory analysis, we assessed the rates of $>50\%$ STR, which is an alternative criterion used by some authors to define effective microvascular reperfusion. With this threshold, the difference between the two study drugs appeared to be increased and statistically significant in favour of abciximab (tirofiban 76.59%, abciximab 84.78%, Δ −8.19, 95% CI −14.08 to −2.30).

The clinical outcome is reported in *Table 2*. The primary safety endpoint was similar in both the groups (major bleeding 1.8% abciximab vs. 1.4% tirofiban, $P = 0.73$). No significant differences were detected in terms of mortality, re-infarction, need for urgent or any revascularization both in-hospital and at 30-day follow-up.

At multivariable analysis (*Table 3*), the factors independently associated with complete STR were anterior MI, pain-to-balloon, baseline TIMI flow >0, and hypertension.

Discussion

This study failed to show the equivalence of HDB tirofiban when compared with standard abciximab to achieve complete STR in the setting of PPCI.

PPCI with stent implantation is considered the preferred reperfusion strategy for STEMI because it is associated with higher rates of successful IRA recanalization, a reduction of the progression of ischaemic myocardial damage and, most importantly, a reduction of mortality.[1,2] Administration of abciximab during PPCI is recommended by current guidelines (class IIa),[1,2] based on the results of several studies showing enhanced microvascular protection and improved early and late clinical outcomes.[11–16] Tirofiban is a highly specific competitive inhibitor of the Gp IIb/IIIa complex with rapidly reversible pharmacodynamics and short plasma half-lives which has been proposed as a possible alternative to abciximab in STEMI patients undergoing PPCI.[28] Preliminary studies using a HBD of tirofiban demonstrated early platelet inhibition similar or even higher than abciximab.[22,23] Promising clinical results have also been reported to support this hypothesis,[29] together with preliminary evidence of similar efficacy of HDB tirofiban compared with abciximab on LV recovery[22] and clinical outcomes.[28] Tirofiban and eptifibatide, another small molecule and competitive inhibitor of the Gp IIb/IIIa, are mentioned in the American College of Cardiology/American Heart Association guidelines as possibly useful therapy to support PPCI for STEMI (Class IIb recommendation).[2] The promising results of observational studies[22,30] have provided the background for an increasing utilization of these two molecules during PPCI. In addition, the high cost of abciximab might have a substantial impact on financial resources, and alternative and less expensive treatment are certainly appealing for the medical community and the health-care administrators. In fact, at current market prices, treatment with tirofiban and eptifibatide would cost around one-third of treatment with abciximab. Unfortunately, the results of our study do not allow drawing definitive conclusions. Several randomized trials and observational studies have consistently shown a strong relationship between STR, LV recovery, and short- and long-term mortality.[6,7,9,10,31,32] However, the absolute difference in rates of complete STR observed between abciximab and tirofiban in the FATA trial was indeed quite small (3.4%), and the question whether this could translate into a different clinical benefit is legitimate. Indeed, residual ST-segment elevation, another important predictor of outcome, as a continuous variable was not different between the groups. A further note of caution should be raised after the recent publication of the results of the Multicentre Evaluation of Single High-Dose Bolus Tirofiban vs. Abciximab With Sirolimus-Eluting Stent or Bare Metal Stent in Acute Myocardial Infarction Study (MULTISTRATEGY).[33] In a very similar group of patients, this study showed that HDB tirofiban compared with abciximab was associated with non-inferior STR ($\geq 50\%$) at 90 min following coronary intervention (83.6% abciximab vs. 85.3% tirofiban; RR 1.020, 95% CI 0.958–1.086). On the other hand, the equivalence boundaries of our study were broad enough ($\pm 10\%$) to allow good likelihood of proving the primary hypothesis to be true. Besides, the difference between the study drugs was enhanced by considering 50% STR as cut-off value for

Table 1 Clinical, angiographic, and procedural characteristics

	Abciximab (n = 341)	Tirofiban (n = 351)	P
Age (years) (Mean ± SD)	63.4 (12.5)	65.0 (12.7)	0.49
Male gender	269 (78.9)	252 (71.8)	0.03
Risk factors			
Hypertension	180 (52.8)	204 (58.1)	0.16
Diabetes	59 (17.3)	66 (18.8)	0.61
Hypercholesterolaemia	154 (45.2)	173 (49.3)	0.28
Smoking status			
Current	147 (43.1)	127 (36.2)	0.09
Previous (>1 month)	81 (23.8)	81 (23.1)	
Never smoked	113 (33.1)	143 (40.7)	
Family history of CAD	105 (30.8)	99 (28.2)	0.45
Prior myocardial infarction	9 (2.6)	21 (6.0)	0.03
Prior coronary artery bypass graft	1 (0.3)	4 (1.1)	0.19
Prior percutaneous coronary intervention	13 (3.8)	18 (5.1)	0.40
Anterior acute myocardial infarction	158 (46.3)	163 (46.4)	0.99
Cardiogenic shock	14 (4.1)	14 (4.0)	0.94
Killip class			
I	289 (84.7)	294 (83.8)	0.49
II	30 (8.8)	39 (11.1)	
III	8 (2.3)	4 (1.1)	
IV	14 (4.1)	14 (4.0)	
Infarct-related artery			
No obstructive lesions	7 (2.1)	5 (1.4)	0.80
Right	132 (38.5)	143 (40.7)	
Left circumflex	43 (12.6)	42 (12.0)	
Left anterior descending	157 (46.0)	158 (45.0)	
Left main	1 (0.3)	3 (0.9)	
Multivessel disease			
2	124 (36.4)	130 (37.0)	0.72
3	59 (17.3)	70 (19.9)	
Left main disease	4 (1.2)	4 (1.1)	0.97
Time intervals (min)*			
Pain-to-ECG	80 (45–125)	74 (46–130)	0.8
Pain-to-study drug	125 (90–190)	121 (86–190)	0.99
Pain-to-balloon	160 (115–220)	153 (118–226)	0.98
ECG-to-study drug	40 (24.5–63)	40 (23–61)	0.90
ECG-to-balloon	71 (53–97)	70 (53–93)	0.97
Study drug-to-angiography	13 (4–35)	12 (4–32)	0.68
Study drug-to-balloon	25 (12.5–45)	25 (12–45)	0.71
Radial access	76 (22.3)	83 (23.6)	0.67
Infarct-related artery stenting	308 (90.3)	307 (87.5)	0.23
No percutaneous coronary intervention	12 (3.5)	8 (2.3)	0.19
Preprocedure TIMI flow grade			
0	206 (60.4)	212 (60.4)	0.47
1	38 (11.1)	29 (8.3)	
2	51 (15.0)	52 (14.8)	
3	46 (13.5)	58 (16.5)	

Continued

Table 1 *Continued*

	Abciximab (n = 341)	Tirofiban (n = 351)	P
Postprocedure TIMI flow grade			
0	4 (1.2)	8 (2.3)	0.42
1	7 (2.1)	4 (1.1)	
2	26 (7.6)	21 (6)	
3	304 (89.1)	318 (90.6)	
Peak CK-MB, IU ± SD	220 ± 206	226 ± 219	0.7
Left ventricular ejection fraction (%), ± SD	50.3 ± 10.4	49.7 ± 10.3	0.72
MBG, no. (%)†			
0	50 (19.9)	58 (21.9)	0.39
1	26 (10.3)	29 (10.9)	
2	61 (24.3)	47 (17.7)	
3	114 (45.4)	131 (49.4)	
Preprocedure ∑ST-elevation (mm)*	8.5 (5.5–12.5)	8.0 (5.0–13.6)	0.31
Postprocedure, ∑ST-elevation (mm)*	1.5 (0.0–3.5)	1.5 (0.0–4.5)	0.93

Data are expressed as n (%) unless otherwise indicated.
*Median (IQR).
†MBG not assessable in 176 patients (90 in the abciximab and 86 in the tirofiban group, P = ns).

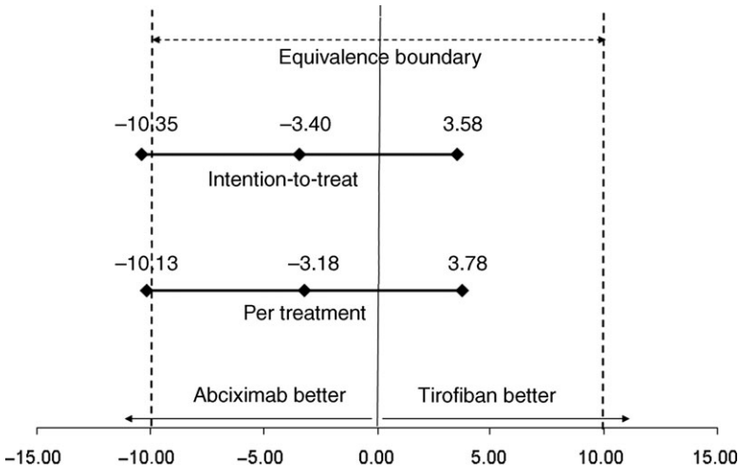

Figure 2 Primary endpoint: absolute difference and 95% confidence interval in the rates of complete ST-segment resolution between abciximab and tirofiban at the intention-to-treat analysis. Result of the *per-treatment* analysis is also illustrated. The prespecified equivalence boundary is reported on top of the figure.

good reperfusion. The reason for these conflicting results is unclear, and this highlights once again that clinical trials with surrogate endpoints can be very important to generate hypothesis, but they cannot replace clinical trials powered to detect clinical differences between different therapeutic options.

Limitations

In the FATA trial, administration of study drug was not blind. However, it is extremely unlikely that the subsequent in-lab treatment of patients differed as a result of knowledge of the assigned drug, and evaluation of the primary endpoint was performed blindly in a core laboratory. Secondly, although patients were assigned on a randomized basis, some imbalance in the distribution of the characteristics such as proportion of patients with prior MI, smoking status, and female gender may have influenced the results, considering a narrow difference in the primary endpoint. However, results of the multivariable analysis did not show these factors to be among the independent predictors of the primary endpoint in our study, thus corroborating the

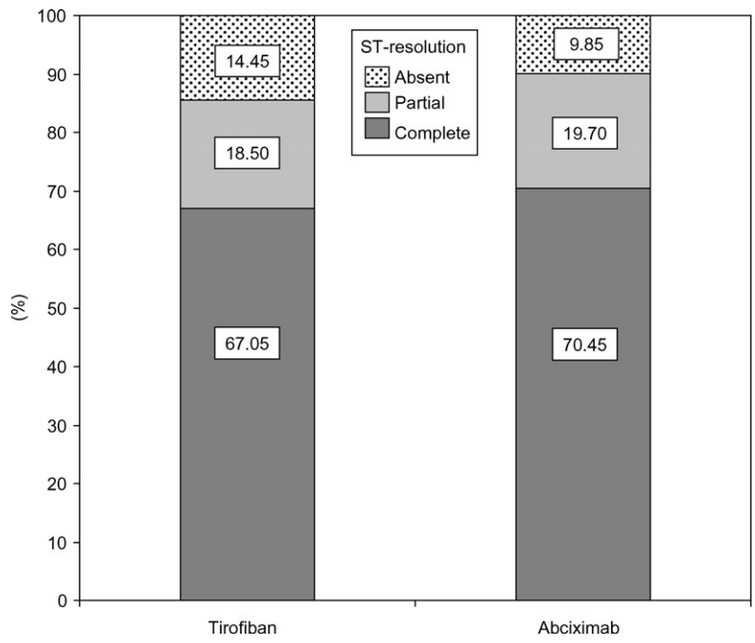

Figure 3 Rates of complete (≥70%), partial (30–70%), and absent (<30%) ST-segment resolution 90 min after primary angioplasty in both the study groups.

Table 2 Clinical outcomes

	Abciximab (*n* = 341)	Tirofiban (*n* = 351)	*P*
In-hospital events	6 (1.8)	8 (2.3)	0.63
Death	5 (1.5)	4 (1.1)	0.70
Re-infarction	1 (0.3)	2 (0.6)	0.58
Urgent target vessel revascularization	0	1 (0.3)	0.32
In-hospital major bleeding	6 (1.8)	5 (1.4)	0.73
Intra-cranial haemorrhage	0	0	
Local, no.	2 (0.6)	1 (0.3)	
Other, no.	4 (1.2)	4 (1.1)	
In-hospital minor bleeding	4 (1.2)	1 (0.3)	0.17
30-day events	6 (1.8)	10 (2.8)	0.34
Death	5 (1.5)	7 (2.0)	0.60
Re-infarction	1 (0.3)	2 (0.6)	0.58
Target vessel revascularization	0	3 (0.8)	0.09

Data are expressed as *n* (%) unless otherwise indicated.

Table 3 Logistic regression: predictors of complete ST-segment resolution

	OR	95% CI	*P*-value
Anterior myocardial infarction	0.371	0.260–0.529	<0.0001
Pain-to-balloon (each increment minute)	0.998	0.996–1.000	0.040
Preprocedural TIMI grade flow >0	1.643	1.139–2.369	0.008
Hypertension	0.618	0.42–0.897	0.011
Age (each increment year)	0.999	0.982–1.015	0.870
Male gender	0.904	0.583–1.403	0.652
Diabetes	1.210	0.764–1.917	0.416
Abciximab	1.145	0.807–1.624	0.449
Current smokers	1.384	0.923–2.075	0.116
Prior myocardial infarction	0.793	0.346–1.818	0.583
Number of vessel diseased	0.996	0.782–1.268	0.971

reliability of our findings. Finally, rates of short-term mortality and bleeding complications were quite low when compared with most of those reported in the medical literature. Noteworthily, radial approach was used in a good proportion of patients. Low-mortality rates could be ascribed to an evident, though not planned, patient selection. Despite the broad inclusion criteria, in fact, it remains quite difficult to collect written informed consent in an emergency scenario. Besides, some operators could be less willing to screen and enrol very seriously ill patients in clinical trials. Perhaps, most importantly, routine administration of abciximab in the ambulance had previously been implemented in all participating centres, and several patients had already received abciximab before being evaluated for eligibility. The number of patients who were not

even screened confirmed the former hypotheses (*Figure 1*). However, it should be highlighted that all participating centres are high-volume catheterization laboratories with good territorial networks for STEMI, as showed by the relatively short total ischaemic time (<3 h) in both groups (*Table 1*). This is reflected also in a very short time from study drug to angiography (13 min), suggesting that in most of the cases administration was done in the catheterization laboratory or in ambulances enabled to ECG transmission and direct transportation of the patient in the catheterization laboratory (bypassing the emergency room and the coronary care unit).[34] In this perspective, the FATA cannot be considered a study on facilitation of PCI.

Conclusion

This trial failed to demonstrate the equivalence of HBD tirofiban and abciximab as adjunctive therapy to primary PCI for achieving effective microvascular reperfusion as measured by the incidence of complete STR. Further investigation is necessary to assess whether the small difference of STR observed between the two study drugs could have a sizeable impact on LV recovery and clinical outcomes, although it seems quite unlikely.

Acknowledgements

We are indebted to Anna Schembari for monitoring data quality. Schembari received a research grant from the Institute of Cardiology, University of Bologna.

Funding

The FATA trial was a spontaneous, non-company promoted study almost entirely funded by each participating centre and from the Fondazione Fanti-Melloni, a charitable institution linked to the University of Bologna. The study was partially supported by a research grant from Merck & Co. Inc. The company had no role in the study design, analysis, and interpretation of the data, or the drafting or revision of the final manuscript.

Conflict of interest: none declared.

Appendix

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