### **CLINICAL RESEARCH**

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Interventional Cardiology

# Randomized Comparison of Eptifibatide Versus Abciximab in Primary Percutaneous Coronary Intervention in Patients With Acute ST-Segment Elevation Myocardial Infarction

Results of the EVA-AMI Trial

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<b>Objectives</b>	The aim of this study was to compare eptifibatide and abciximab as adjuncts to primary percutaneous coronary intervention (PCI).
Background	The glycoprotein (GP) IIb/IIIa receptor inhibitor abciximab as adjunct to primary PCI in patients with ST-segment elevation myocardial infarctions has been shown to reduce ischemic complications and improve clinical out- comes. So far, no trial has been performed to compare the efficacy of another GP IIb/IIIa receptor inhibitor, eptifibatide, and abciximab in primary PCI.
Methods	A total of 427 patients with ST-segment elevation myocardial infarctions $<12$ h and planned primary PCI were randomized to double-bolus eptifibatide (n = 226) followed by a 24-h infusion or single-bolus abciximab (n = 201) followed by a 12-h infusion. In this noninferiority trial, the primary end point was the incidence of complete ( $\geq$ 70%) ST-segment resolution (STR) 60 min after PCI, a measure of myocardial reperfusion. The assumption was a 60% complete STR rate in the abciximab group. The noninferiority margin was set to 15%.
Results	The incidence of complete STR at 60 min after PCl in the intention-to-treat analysis was 62.6% after eptifibatide and 56.3% after abciximab (adjusted difference: 7.1%; 95% confidence interval: 2.7% to 17.0%). All-cause mor- tality 6.2% versus 4.5% ( $p = 0.50$ ); reinfarction 0.4% versus 3.5% ( $p = 0.03$ ); target vessel revascularization 4.4% versus 6.5% ( $p = 0.40$ ); the combined end point of death, nonfatal reinfarction, and target vessel revascu- larization 10.6% versus 10.9% ( $p = 0.90$ ); stroke 0.5% versus 0.5% ( $p = 1.00$ ) after 6 months; and Thromboly- sis In Myocardial Infarction major bleeding complications 4.0% versus 2.0% ( $p = 0.20$ ) after 30 days were ob- served after eptifibatide and abciximab, respectively.
Conclusions	Eptifibatide as an adjunct to primary PCI is equally as effective as abciximab with respect to STR. (Efficacy of Eptifibatide Compared to Abciximab in Primary Percutaneous Coronary Intervention [PCI] for Acute ST Elevation Myocardial Infarction [STEMI]; NCT00426751) (J Am Coll Cardiol 2010;56:463–9) © 2010 by the American College of Cardiology Foundation

Primary percutaneous coronary intervention (PCI), if performed in a timely fashion by experienced operators, has emerged as the preferred reperfusion strategy in patients with ST-segment elevation myocardial infarction (STEMI) (1,2). In primary PCI, the additional stent implantation does not improve early myocardial reperfusion but decreases the incidence of reintervention (3). Distal embolization and impairment of microvascular flow have been

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Abbreviations and Acronyms
ASA = acetylsalicylic acid ECG = electrocardiogram GP = glycoprotein PCI = percutaneous coronary intervention
STEMI = ST-segment elevation myocardial infarction
STR = ST-segment resolution
<b>TIMI</b> = Thrombolysis In Myocardial Infarction

well recognized as major problems in primary PCI (4,5). In several randomized trials and a recent meta-analysis, abciximab plus heparin have been shown to improve the clinical courses of patients with primary PCI by improving myocardial reperfusion, left ventricular function, and clinical outcomes compared with heparin alone (3,6-9). These studies have been mainly performed without the upstream administration of thienopyridines. Therefore, the current PCI guidelines of the European

Society of Cardiology recommend abciximab in primary PCI (Class IIa, Level of Evidence: A) (10). The recently

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published ON-TIME2 (Ongoing Tirofiban in Myocardial Infarction Evaluation 2) trial showed that high-bolus dose tirofiban improved myocardial reperfusion and clinical outcomes after primary PCI compared with placebo with provisional tirofiban in 29% during PCI (11). This positive result supports the use of glycoprotein (GP) IIb/IIIa inhibitors, in addition to a loading dose of clopidogrel, for patients with STEMI. Abciximab and eptifibatide reduced the rate of thrombotic complications in patients with nonurgent stent implantation (12,13). Eptifibatide, a synthetic specific GP IIb/IIIa inhibitor, is less expensive than abciximab and induces a reversible receptor occupation. Platelet function is normalized 4 to 6 h after termination of infusion, which is desirable in patients with unplanned urgent coronary bypass grafting (14). In 2 randomized trials, eptifibatide was associated with an improvement in Thrombolysis In Myocardial Infarction (TIMI) flow grade 3 patency before primary PCI (15,16). This advantage was in the same magnitude as observed in trials using abciximab (17,18). According to a recent report, eptifibatide is the most commonly used GP IIb/IIIa inhibitor in primary PCI in the U.S. (19). Therefore, we sought to compare the efficacy and safety of eptifibatide and abciximab in primary PCI in adjunction to the standard pharmacological treatment including clopidogrel.

### **Methods**

Study design and patients. The EVA-AMI (Eptifibatide Versus Abciximab in Primary PCI for Acute Myocardial Infarction) trial was an international, multicenter, randomized, prospective, open parallel group comparison of eptifibatide, clopidogrel, acetylsalicylic acid (ASA), and heparin or enoxaparin versus abciximab, clopidogrel, ASA, and

heparin or enoxaparin in patients with STEMI <12 h undergoing primary PCI.

The primary objective of the trial was to demonstrate the noninferiority of eptifibatide compared with abciximab as an adjunct in patients undergoing primary PCI for STEMI.

The study population consisted of patients age >18 years with STEMI <12 h and planned primary PCI. They were eligible for randomization if they had experienced angina or equivalent symptoms of more than 20 min and ST-segment elevation in  $\geq 2$  contiguous leads ( $\geq 2$  mm precordial lead,  $\geq 1$  mm limb lead) and had given written informed dated consent to participate in the study. Exclusion criteria were the following: left bundle branch block, thrombolytic therapy within 24 h before randomization, oral anticoagulation with international normalized ratio >2, known platelets <100,000/µl or known hemorrhagic diathesis, stroke or transient ischemic attack within 30 days in the past 6 months or any permanent residual neurological defect, evidence of an active gastrointestinal or urogenital bleeding, major surgery within 6 weeks, history of allergic reaction to abciximab or eptifibatide or any component used in the study (including contrast media), known severe renal (creatinine clearance <30 ml/min) or hepatic insufficiency, severe concomitant disease with life expectancy <1 year, participation in any study using an investigational drug or device within 30 days or within 5 half-lives of the investigational drug (whichever was longer) of entry into this study, and inaccessibility due to geographic or social factors during treatment or follow-up.

The study was approved by all local ethics committees involved. Randomization was stratified by infarct location (anterior vs. nonanterior) and done using sealed and opaque envelopes.

**Procedures.** Patients randomized to eptifibatide received a double bolus of 180  $\mu$ g/kg (10-min interval) followed by an infusion of 2.0  $\mu$ g/kg/min over 24 h as early as possible. Patients randomized to abciximab received a bolus of 0.25 mg/kg followed by an infusion of 0.125  $\mu$ g/kg/min over 12 h.

Angiographic catheter evaluation of the anatomy of the coronary arteries and PCI, possibly with stent implantation, were done according to the local guidelines as early as possible but at least within 2 h after randomization. PCI and stenting if feasible of the infarct-related coronary artery were performed. The use of thrombectomy devices and the intracoronary use of medications such as adenosine, verapamil, or other calcium-channel blockers were left to the discretion of the investigator. In case of multivessel disease, PCI of the nonculprit lesions should be postponed if possible for at least 1 week.

End points. The primary end point was the incidence of successful myocardial reperfusion as measured by complete ST-segment resolution (STR) ( $\geq$ 70%) 60 min (range 45 to 75 min) after PCI as assessed by a blinded core electrocardiographic (ECG) laboratory (20,21). ST-segment elevation was analyzed by a single investigator (R.S.) with lens-intensified calipers to the nearest 0.025 mV 20 ms after the end of the QRS complex, with the PR segment as the reference baseline, from leads I, aVL, and V1 to V6 for anterior infarction and leads II, III, aVF, V<sub>5</sub>, and V<sub>6</sub> for inferior infarction. ST-segment depression from leads with  $\geq 0.1$ -mV depression were measured in leads II, III, and aVF for anterior and leads  $V_1$  to  $V_4$  for inferior infarction. Sum STR was measured by the sum of ST-segment elevation from all ECG leads related to infarct location. Single-lead STR was measured by the ST-segment deviation on the single lead that showed maximum deviation at baseline and at 60 min, irrespective of the ECG lead in which ST-segment deviation was measured at baseline. STR was expressed as percent from baseline and graded as complete ( $\geq$ 70%), partial (<70% to 30%), or none (<30%). Electrocardiograms were obtained before randomization, directly before angiography, and 60 min after the completion of PCI.

Secondary end points included other ECG measures of myocardial reperfusion and angiographic assessments of the patency of the infarct-related artery (TIMI flow grade 3 and TIMI flow grade 2/3 patency before the procedure, TIMI flow grade 3 patency after the procedure as assessed by a core angiographic laboratory [22], corrected TIMI frame count, and myocardial blush grade before and after PCI). In addition, individual and combined clinical end points of death, reinfarction, urgent target vessel revascularization, stroke, and bleeding complications as assessed by the TIMI scale (22) until day 30 were reported. Clinical follow-up was done until 6 months, looking for the occurrence of death, reinfarction, and urgent target vessel revascularization. A blinded clinical end point committee adjudicated all clinical end points.

**Patient populations.** The safety population comprised all subjects who received at least 1 dose of study medication. The intention-to-treat population comprised all randomized subjects who received at least 1 dose of study medication and fulfilled the ECG inclusion criteria.

Statistical analysis. The null hypothesis tested was that eptifibatide is inferior to abciximab in terms of the rate of complete STR 60 min after PCI. The alternative hypothesis was the noninferiority of eptifibatide compared with abciximab in this primary efficacy end point. This hypothesis was tested via the lower limit of the 1-sided 95% confidence interval of the difference of the STR rate if under eptifibatide minus the one under abciximab. The a priori assumption was that both treatments were able to demonstrate a 60% rate of complete STR within 60 min after PCI. The noninferiority margin was set to 15%. Under these assumptions, the study would have needed 181 patients per group available for the primary efficacy analysis to guarantee 90% power. Assuming a rate of 10% of unevaluable patients for the per protocol analysis, it was planned to randomize approximately 400 subjects to achieve at least 352 (176 per group) evaluable subjects.

A generalized model (under binomial probability distribution) stratified and adjusted by center was used to assess treatment differences in the primary efficacy end point (complete sum STR). Results are presented in the form of differences of the response rates between the treatment groups with the associated lower limit of the 1-sided 95% confidence interval. The latter statistical estimate was used for the decision on the inferiority null hypothesis. Analyses of clinical outcomes and bleeding were based on the safety population. Descriptive statistics were generated for baseline and clinical demographics, treatment variables, and outcomes. The continuous variables were assessed using the Wilcoxon rank sum test, and values are presented as medians and quartiles. Comparisons between the groups were done using Fisher exact tests. A p value <0.05 was considered significant. The analysis was performed using SAS version 8.2 (SAS Institute Inc., Cary, North Carolina).

## Results

Between November 2006 and May 2007, a total of 427 patients (226 randomized to eptifibatide and 201 to abciximab) were enrolled at 22 centers (11 in France and 11 in Germany). The randomization and the initiation of study medication were done before angiography in 75%, during angiography in 21% and after angiography in 4% of the patients.

The 2 groups were well balanced with respect to baseline variables (Table 1). The time between the onset of symptoms and study medication was  $3.9 \pm 3.2$  h in the eptifibatide group and  $3.8 \pm 3.8$  h in the abciximab group. The interval between initial electrocardiography and the administration of study drug was  $54 \pm 38$  min in the eptifibatide and  $57 \pm 48$  min in the abciximab group. The time interval between the start of study drug and angiography was  $28 \pm 33$  min in the eptifibatide group and  $30 \pm 32$  min in the abciximab group.

### Table 1 Baseline Variables of the Patients

Variable	Eptifibatide (n = 226)	Abciximab (n = 201)	p Value
Age (yrs)	$\textbf{61.3} \pm \textbf{12.4}$	$\textbf{60.5} \pm \textbf{12.7}$	0.49
Women	54 (23.9%)	40 (19.9%)	0.35
Current smokers	101 (44.7%)	96 (47.8%)	0.56
Diabetes	33 (14.6%)	35 (17.4%)	0.43
Hypertension	117 (51.8%)	95 (47.3%)	0.38
Hypercholesterolemia	91 (40.3%)	89 (44.3%)	0.43
Family history of MI	70 (31.0%)	60 (29.9%)	0.83
Previous MI	19 (8.4%)	17 (8.5%)	1.00
Previous PCI	16 (7.1%)	17 (8.5%)	0.72
Previous CABG	7 (3.1%)	2 (1.0%)	0.18
Killip class >1	22 (9.8%)	20 (10.0%)	1.00
Heart rate (beats/min)	$\textbf{77.3} \pm \textbf{17.7}$	$\textbf{77.2} \pm \textbf{17.6}$	0.96
Systolic blood pressure (mm Hg)	$\textbf{136.0} \pm \textbf{24.7}$	$\textbf{135.8} \pm \textbf{20.9}$	0.94
Diastolic blood pressure (mm Hg)	$\textbf{80.2} \pm \textbf{15.4}$	$\textbf{80.6} \pm \textbf{13.9}$	0.80
Time between symptom onset and start of study medication (min)	234.1 ± 177.6	221.3 ± 203.1	0.58

Data are expressed as mean  $\pm$  SD or as n (%).

CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Coronary angiography was performed and available for central analysis in 424 patients. The angiographic results and PCI procedures are shown in Table 2 and did not differ between the groups. Radial access was used in 27% versus 30% of the patients with eptifibatide versus abciximab, respectively. Study drug was infused for 22.6  $\pm$  54.8 h in the eptifibatide group and 14.0  $\pm$  5.1 h in the abciximab group. The concomitant medication consisted of ASA, clopidogrel, heparin or enoxaparin, statins, beta-blockers, and renin-angiotensin system inhibitors in a high percentage of patients in both groups (Table 3). Clopidogrel was initiated >30 min before angiography in 52.0%, 30 to 1 min before angiography in 7%, and after angiography in 20%, and the timing was unknown in 21% of the patients.

Table 2         Angiographic and Procedural Findings				
	Variable	Eptifibatide (n = 224)	Abciximab (n = 200)	p Value
Infarct-related artery				
RCA		100 (44.6%)	90 (45.2%)	1.00
RCX		20 (8.9%)	21 (10.6%)	0.62
LAD		98 (43.8%)	86 (43.2%)	0.92
Left main	I	0	1 (0.5%)	0.47
Graft		6 (2.7%)	1 (0.5%)	0.13
Findings bet	fore PCI			
TIMI flow	grade			
Not det	ermined	22	10	
0/1		117 (57.9%)	123 (64.7%)	1.00
2		11 (5.5%)	8 (4.2%)	0.39
3		74 (36.6%)	59 (31.0)	
Corrected	TIMI frame count	$\textbf{44.5} \pm \textbf{41.4}$	$\textbf{43.7} \pm \textbf{32.2}$	0.89
Myocardia	al blush grade			
Not det	ermined	40	30	
0/1		126 (68.5%)	138 (82.2%)	
2		1 (0.5%)	0	0.01
3		57 (31.0%)	32 (18.8%)	
PCI perform	ed	215 (95.1%)	191 (95.0%)	1.00
Stent impla	nted	204 (94.9%)	181 (94.8%)	1.00
BMS		171 (83.8%)	145 (80.6%)	0.35
DES		30 (14.9%)	33 (18.4%)	0.41
Direct stent	ing	67.6%	59.3%	
Thrombecto	my	40 (18.6%)	32 (16.8%)	0.70
Urgent CAB	G	2 (0.9%)	3 (1.5%)	0.67
Elective CAE	3G	5 (2.2%)	6 (3.0%)	0.76
Findings aft	er PCI			
TIMI flow	grade			
Not det	ermined	38	28	
0/1		10 (5.6%)	11 (6.7%)	
2		22 (12.4%)	15 (9.2%)	0.60
3		145 (82.0%)	137 (84.0%)	
Median corrected TIMI frame count		$\textbf{25.3} \pm \textbf{21.0}$	$\textbf{23.6} \pm \textbf{17.6}$	0.42
Myocardia	al blush grade			
0/1		111 (52.1%)	107 (54.8%)	
2		1 (0.5%)	0	0.65
3		64 (30.0%)	54 (27.7%)	

Data are expressed as mean  $\pm$  SD or as n (%).

BMS = bare-metal stent(s); DES = drug-eluting stent(s); LAD = left anterior descending coronary artery; RCA = right coronary artery; RCX = right circumflex coronary artery; TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

Table 3	Table 3         Concomitant Medication			
,	Variable	Eptifibatide $(n = 226)$	Abciximab (n = 201)	p Value
ASA		218 (96.5%)	189 (94.0%)	0.26
Clopidogrel		224 (99.2%)	197 (98.0%)	0.43
Unfractionated heparin		136 (60.2%)	129 (64.2%)	0.42
Low-molecular weight heparin		157 (69.5%)	143 (71.1%)	0.75
Beta-blocker		202 (89.4%)	181 (90.0%)	0.87
ACE inhibitor/ARB		184 (81.4%)	157 (78.1%)	0.40
Statins		205 (90.7%)	174 (86.6%)	0.22

 $\label{eq:ACE} \mbox{ACE} = \mbox{angiotensin-converting enzyme; } \mbox{ARB} = \mbox{angiotensin receptor blocker; } \mbox{ASA} = \mbox{acetylsalicylic acid.}$ 

The number of patients fulfilling the inclusion criteria undergoing PCI and with electrocardiograms available for the central evaluation of STR was 381. In the intention-totreat analysis, the median time between PCI and the 60-min ECG study was 75  $\pm$  72 min in the eptifibatide group and  $68 \pm 41$  min in the abciximab group (p = 0.60). The incidence of complete STR in the intention-to-treat population did not differ between the 2 groups and was 62.6% and 56.3% (adjusted difference: 7.1%; 95% confidence interval: 2.7% to 17.0%) in the eptifibatide and abciximab groups, respectively. The incidence of the primary end point of complete (>70%) STR at 60 min after PCI in the per protocol analysis (including only patients with 60-min electrocardiograms in a window of 45 to 75 min after PCI) was 62.8% after eptifibatide and 58.6% after abciximab (adjusted difference: 2.1%; 95% confidence interval: -8.5% to 12.8%). Thus, the pre-specified margin for noninferiority was met. Additional measures of STR are given in Table 4. The clinical events occurring during the 6-months follow-up period are listed in Table 5 and

# ST-Segment Deviation Analysis in the Intention-to-Treat-Analysis

Variable	Eptifibatide (n = 198)	Abciximab (n = 183)	p Value
Sum ST-segment deviation at baseline (mm)	$\textbf{10.2} \pm \textbf{7.0}$	$\textbf{11.3} \pm \textbf{7.8}$	0.14
Findings before PCI			
Sum STR (%)	$\textbf{25.9} \pm \textbf{32.0}$	$\textbf{21.2} \pm \textbf{29.0}$	0.21
Complete STR	19 (13.1%)	12 (10.0%)	0.34
Partial STR	30 (20.7%)	23 (19.2%)	0.31
No STR	96 (66.2%)	85 (70.8%)	0.32
Single-lead complete STR	12 (9.7%)	7 (6.3%)	0.75
Sum ST-segment deviation before PCI (mm)	$\textbf{9.3} \pm \textbf{9.5}$	$\textbf{10.5} \pm \textbf{7.9}$	0.26
Findings 60 min after PCI			
Sum STR (%)	$\textbf{71.6} \pm \textbf{27.2}$	$\textbf{66.3} \pm \textbf{31.1}$	0.08
Complete STR	124 (62.6%)	103 (56.3%)	0.16
Partial STR	56 (28.3%)	51 (27.9%)	0.99
No STR	18 (9.1%)	29 (15.8%)	0.04
Single-lead complete STR	105 (59.7%)	82 (49.1%)	0.06
Sum ST-segment deviation (mm)	$\textbf{2.9} \pm \textbf{3.6}$	$\textbf{3.9} \pm \textbf{4.4}$	0.01

Data are expressed as mean  $\pm$  SD or as n (%).

PCI = percutaneous coronary intervention; STR = ST-segment resolution.

Table 5         Cumulative Clinical Outcomes at Different Time Points					
Variable		Eptifibatide (n = 226)	Abciximab (n = 201)	p Value	
Until day 7	or discharge				
Death/re	current MI/TVR	12 (5.3%)	14 (7.0%)	0.55	
Death		8 (3.5%)	7 (3.5%)	1.00	
Recurrent	t MI	0	3 (1.5%)	0.10	
TVR		5 (2.2%)	8 (4.0%)	0.40	
Until day 30	)				
Death/re	current MI/TVR	17 (7.5%)	17 (8.5%)	0.72	
Death		13 (5.8%)	7 (3.5%)	0.36	
Recurren	t MI	0	5 (2.5%)	0.02	
TVR		5 (2.2%)	10 (5.0%)	0.19	
Until 180 da	ays				
Death/re	current MI/TVR	24 (10.6%)	23 (10.9%)	0.88	
Death		14 (6.2%)	9 (4.5%)	0.52	
Recurren	t MI	1 (0.4%)	7 (3.5%)	0.03	
TVR		10 (4.4%)	13 (6.5%)	0.39	

MI = myocardial infarction; TVR = target vessel revascularization.

revealed no significant differences between the 2 groups (Fig. 1), except for reinfarction, which occurred less often after eptifibatide (0.4% vs. 3.5%, p = 0.03). Major bleeding events according to the TIMI classification were rare and occurred more often with eptifibatide, but this difference was statistically not significant (Table 6).

#### Discussion

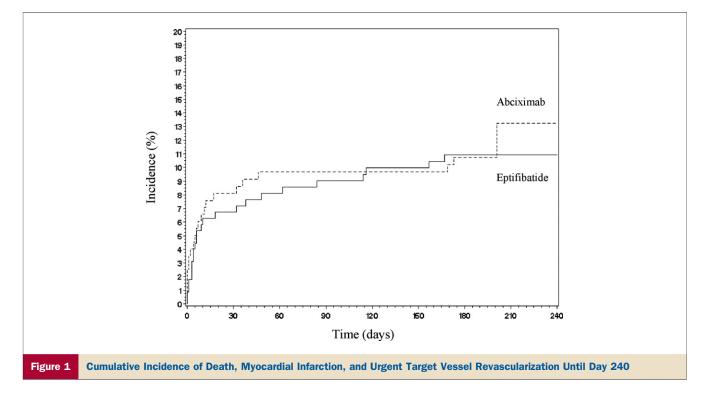
Platelets play a major role in the pathogenesis of acute coronary syndromes (4,5). Therefore, platelet inhibition is a cornerstone of therapy in patients with STEMI (2). This is

Table 6	Safety Events Until Day 30				
	Variable	Eptifibatide (n = 226)	Abciximab (n = 201)	p Value	
TIMI major bleeding		9 (4.0%)	4 (2.0%)	0.27	
TIMI minor bleeding		28 (12.4%)	18 (9.0%)	0.28	
Stroke		1 (0.4%)	1 (0.5%)	1.00	
Moderate thrombocytopenia (in hospital) ${<}100{,}000~\text{cells/mm}^3$		5 (2.2%)	7 (3.5%)	0.56	
Severe thrombocytopenia (in hospital) <50,000 cells/mm <sup>3</sup>		1 (0.4%)	0	1.00	

TIMI = Thrombolysis In Myocardial Infarction.

the first randomized trial comparing abciximab and eptifibatide as adjuncts to primary PCI in patients with acute STEMI. By far the best studied GP IIb/IIIa inhibitor in patients with primary PCI is abciximab. In a meta-analysis, it was shown to reduce death and myocardial infarction (9). In the most recent trial of abciximab versus placebo in patients undergoing primary PCI, STR was significantly improved with abciximab, indicating improved myocardial reperfusion, and this advantage was associated with reduced mortality after 12 months (8).

There are no randomized controlled trials available comparing eptifibatide with placebo in patients undergoing primary PCI for acute STEMI. Similar to abciximab, eptifibatide inhibits platelet aggregation through GP IIb/ IIIa receptor blockade. In contrast to abciximab, eptifibatide induces a competitive and rapidly reversible antagonism, which might be desirable in patients with bleeding events or the need for urgent coronary bypass grafting. However, the effect of abciximab can be readily reversed by platelet transfusions, which might not have the same efficacy in



patients treated with the small molecules. Kereiakes et al. (23) compared ex vivo platelet function at the time of PCI in patients with unstable angina who were treated with 1 of the 3 GP IIb/IIIa antagonists eptifibatide, abciximab, or tirofiban. In this study, the consistency of the level of platelet inhibition with abciximab was more diverse and less uniform compared with that with eptifibatide. Platelet activation in patients with STEMI and primary PCI is much higher than in those with elective PCI, so a randomized trial is necessary to compare these 2 compounds in primary PCI. Our study was powered on the basis of the preservation of a difference of at least 25% in the effect of abciximab on the recovery of ST-segment deviation versus placebo. From previous experience, we estimated a rate of 60% complete STR in the abciximab group. This aim was nearly achieved with a complete STR rate of 56.3% in the intention-to-treat analysis. We observed no significant difference in complete STR between abciximab and eptifibatide, and the criteria for noninferiority were met. The lower 95% confidence interval indicated that at least 75% of the benefit of abciximab over placebo was preserved. STR has been shown to be closely related to myocardial perfusion and mortality in STEMI (20,21,24,25), so this is an excellent surrogate end point for comparative trials (26,27) and has been widely used.

Our study was not powered to detect any differences in the rate of clinical events. However the rate of the combined end point of death, nonfatal reinfarction, and target vessel revascularization was identical after 6 months. Although there were fewer reinfarctions with eptifibatide, we observed more major bleeding complications with eptifibatide. The reason might be the different durations of the infusions, which were 14 h with abciximab and 22 h with eptifibatide. **Study limitations.** This was an open study, leaving some bias for the investigators. However, the STR end points and angiographic evaluations were done centrally by blinded and highly experienced core laboratories.

Our results are confirmed by a nonrandomized comparison of abciximab and eptifibatide in patients undergoing primary PCI (19). In the propensity score analysis, the investigators found no difference in hospital mortality or bleeding complications. In 2 recent randomized trials, an accelerated infusion regimen of tirofiban was as effective and as safe as abciximab in primary PCI (26,27), suggesting that if the small molecule GP IIb/IIIa inhibitors eptifibatide and tirofiban are given in dose regimens ensuring a rapid and effective initial platelet inhibition their effects seem comparable with those of the gold standard abciximab.

### Conclusions

Our results suggest that eptifibatide as an adjunct to primary PCI in STEMI is equally effective to abciximab with respect to complete STR, a measure of myocardial reperfusion. Reprint requests and correspondence: Prof. Dr. Uwe Zeymer, Herzzentrum Ludwigshafen, Bremserstrasse 79, D-67063 Ludwigshafen, Germany. E-mail: uwe.zeymer@t-online.de.

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**Key Words:** primary percutaneous coronary intervention • glycoprotein IIb/IIIa inhibitors • randomized trial • abciximab • eptifibatide.

### APPENDIX

For a list of EVA-AMI investigators, please see the online version of this article.