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**EVA-AMI**

## **Presenter disclosure information**

**Uwe Zeymer, MD**

**Eptifibatide versus Abciximab in primary PCI for  
acute ST elevation myocardial infarction.**

**EVA-AMI Trial.**

**Disclosure Information:**

**Research grants and speakers honoraria  
from Glaxo Smith Kline and Eli Lilly**

# **Eptifibatide Versus Abciximab in primary PCI for Acute ST elevation Myocardial Infarction**

## **EVA-AMI Trial**

**Uwe Zeymer**

**on behalf of the EVA-AMI Investigators  
Herzzentrum Ludwigshafen, Germany**



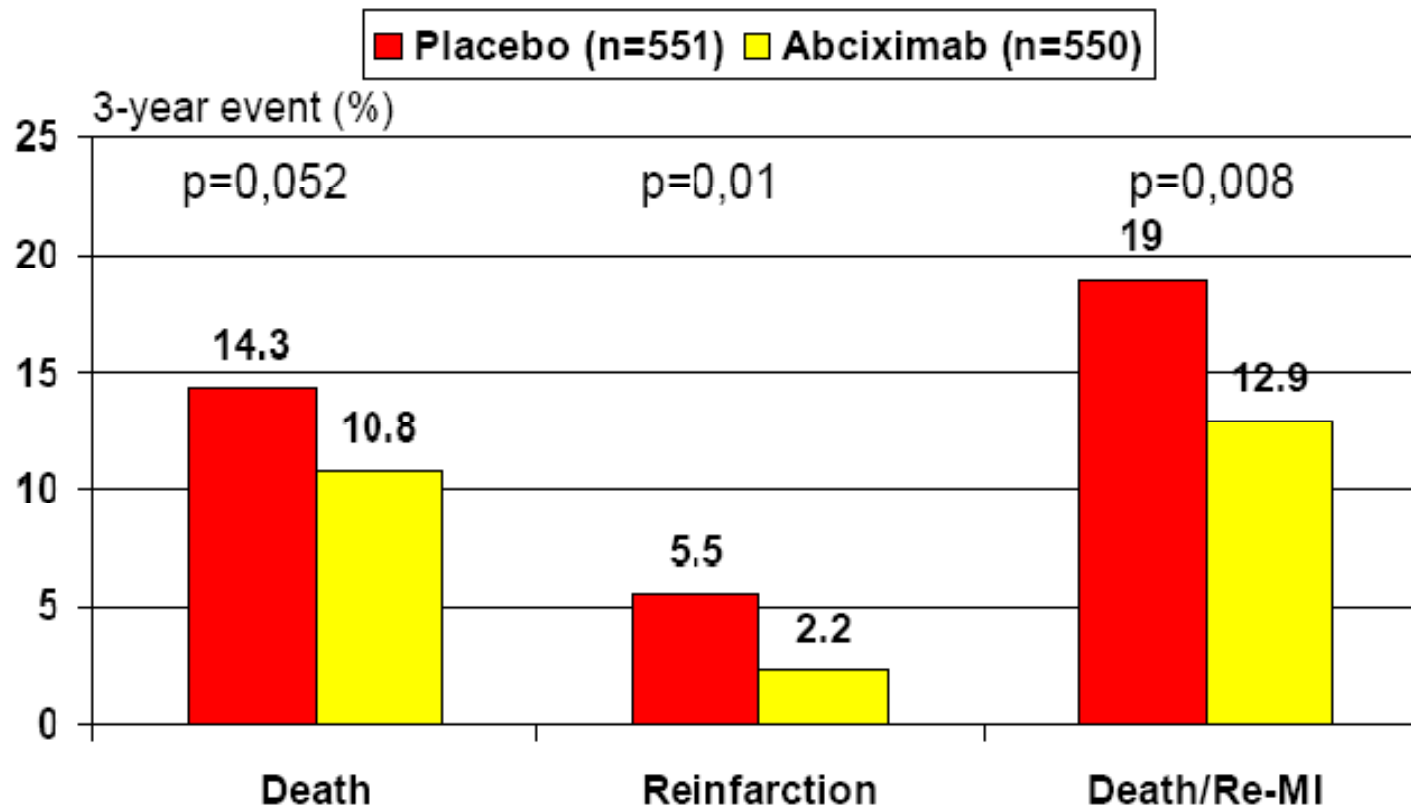
Institut für Herzinfarktforschung Ludwigshafen  
an der Universität Heidelberg

2007 Scientific Sessions of the AHA, Late-breaking Clinical Trials 1  
Orlando, FL, November 4th, 2007

- Abciximab has been shown to reduce ischemic complications in patients undergoing primary PCI in a number of randomized placebo controlled trials
- Eptifibatide reduced events in patients with elective PCI comparable to abciximab
- So far no head-to-head comparison of two GP IIb/IIIa inhibitors in primary PCI

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## Long-term efficacy of abciximab Meta-analysis of 3 RCTs



Montalescot et al, Eur Heart J 2007

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## **Objective**

To demonstrate non-inferiority  
of eptifibatide compared to abciximab  
as adjunctive treatment in patients  
undergoing primary PCI

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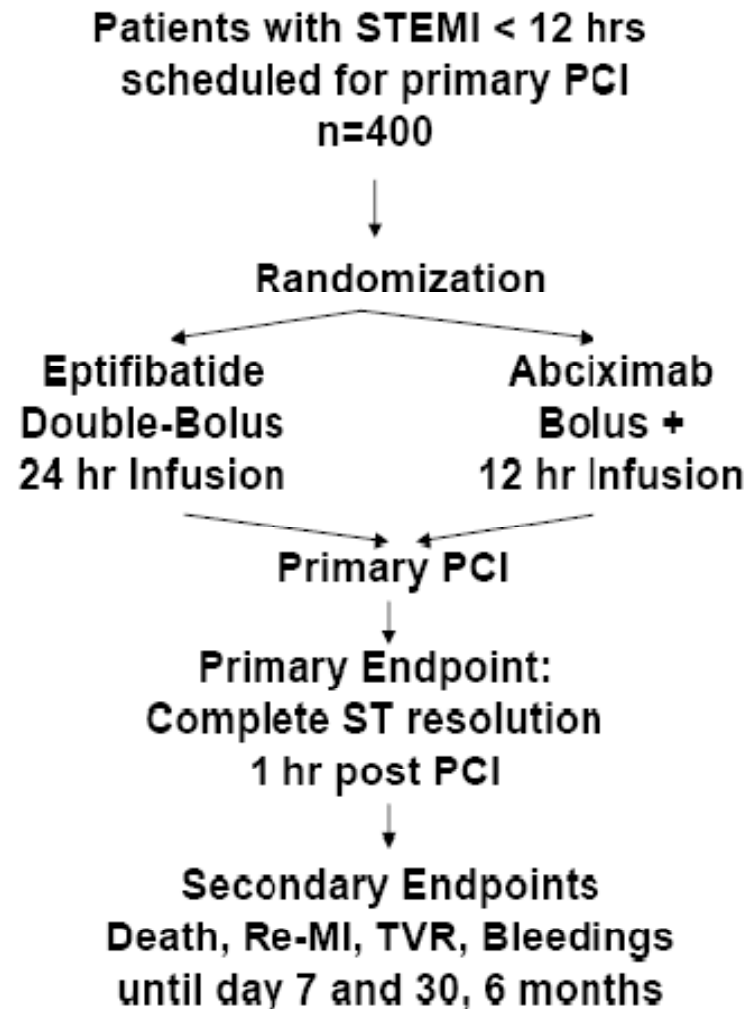
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## **Study design**

International, multicentre, randomised,  
open, parallel group comparison of  
eptifibatide and abciximab in patients with  
STEMI < 12 h treated with  
aspirin, clopidogrel and UFH or enoxaparin  
scheduled for primary PCI

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# Study Design



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## **Study organisation**

- Study chairmen:  
Uwe Zeymer, Germany, Emmanuel Teiger, France
- ECG Core laboratory  
Rolf Schröder, Berlin
- Angiographic Core laboratory  
Gilles Montalescot, Paris
- Statistical Analysis  
Norbert Banik, GlaxoSmithKline, Munich
- Clinical event committee  
Hans-Jürgen Rupprecht, Philip-Gabriel Steg
- Sponsor: GlaxoSmithKline, Europe  
Stefan Kropff, Munich, Ryad Bourkaib, Paris

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# Centres and Enrollment

**France**

<b>Investigator / City</b>	<b>Pts</b>
Teiger, Margenet / Créteil	61
Moulichon, Garcia / Perpignan	32
Delarche / Pau	26
Thicoïpe, Coste / Bordeaux, Pessac	23
Arzalier / Toulon	16
Aptecar, Le Tarnec / Melun	16
Goldstein, Lablanche / Lille	12
Chouihed, Angioi / Nancy	9
Barragan / Ollioules	5
Sans / Toulon	3
Henry, Grollier / Alençon	1
<b>Total France</b>	<b>208</b>

**Germany**

<b>Investigator / City</b>	<b>Pts</b>
Zeymer, Senges / Ludwigshafen	49
Haude / Neuss	38
Bode / Freiburg	32
Heuer / Dortmund	28
Buerke / Halle	17
vom Dahl / Mönchengladbach	17
Girth / Offenbach	10
Hoffmann / Aachen	9
Katus / Heidelberg	8
Voelker / Wuerzburg	8
Boehm / Homburg	5
<b>Total Germany</b>	<b>221</b>

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### **Current status of study and data processing**

- **ECG-Data (primary endpoint) is completely cleaned and consistent with clinical documentation**
- **CRF-pages are complete and cleaned incl. day 7 / hospital discharge**
- **CEC has not assessed clinical events / sAE's**
- **6-month Follow-Up complete by end Nov-07**
- **So far no information about concomitant medication**
- **Disposition of patients in PP-collective may slightly change once conmed will be assessed**

- Acute ST elevation myocardial infarction within 12 hours after symptom onset defined as:
  - chest pain > 20 min
  - and
  - ST elevations in 2 contiguous leads  
( $\geq 2$  mm in precordial, > 1 mm in limb lead)
- Planned primary PCI
- Informed consent
- Age > 18 years

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## **Exclusion criteria**

- Left bundle branch block
- Fibrinolytic therapy within 24 hours
- Oral anticoagulation INR > 2
- Known platelets < 100.000 or hemorrhagic diathesis
- Evidence of active GI or urogenital bleeding
- Major surgery < 6 weeks
- History of allergic reaction to any of the study compounds
- Known severe renal (CCR < 30) or hepatic insufficiency
- Severe concomitant disease
- Study participation in another trial < 30 days
- Inaccessible to follow up due to social or geographic factors

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## **Primary endpoint**

Incidence of complete sum ST resolution (> 70 %) at 60 (45-75) minutes after PCI compared to the baseline ECG assessed by a blinded core ECG-laboratory

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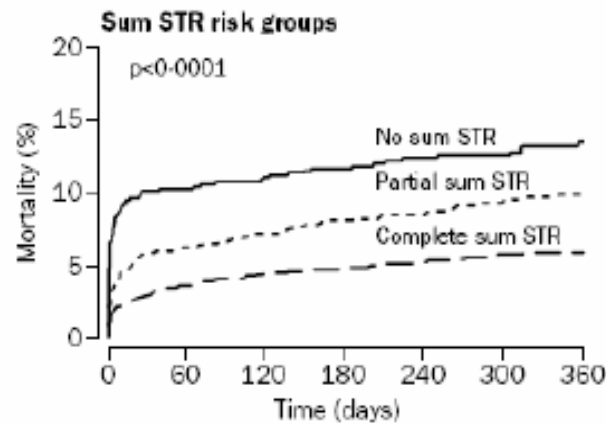
## **ST resolution**

- ST resolution is a marker of myocardial reperfusion
- Closely linked to short- and long-term mortality after STEMI
- Ideal surrogate endpoint to compare reperfusion therapies

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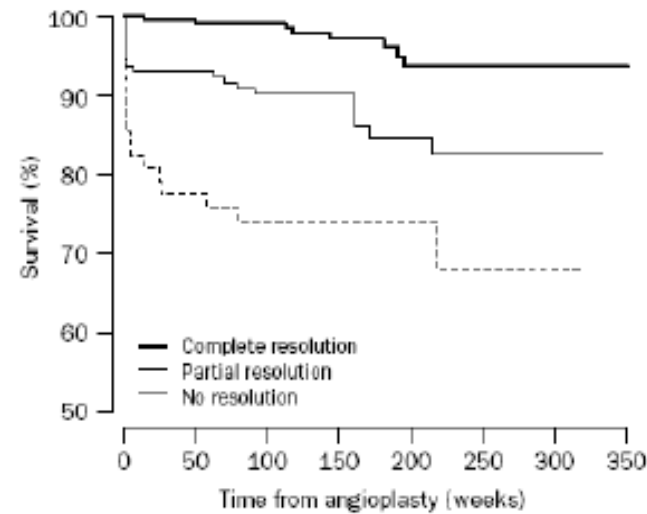
## ST resolution as a predictor of mortality after STEMI

### Fibrinolysis



Number at risk	0	60	120	180	240	300	360
No sum STR	660	569	563	558	474	424	363
Partial sum STR	968	871	862	581	721	656	569
Complete sum STR	1091	1012	1000	992	815	752	677

### Primary PCI



Kaplan-Meier survival curve for 398 patients who underwent successful primary angioplasty

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# Statistical assumptions

- The assumption was that both treatments will achieve a 60% rate of complete ST resolution at 60 mins after PCI.
- The non-inferiority margin was set to 15%.
- To guarantee 90% power 181 patients per group would be necessary. To account for a drop-out rate of 10% 200 patients per group should be included.

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# Secondary endpoints

- Complete or partial ST resolution ( $\geq 30\%$ ) before and after the procedure
- TIMI 2/3 patency prior to procedure, as assessed by a core angiographic laboratory
- TIMI 3 patency following procedure
- cTIMI Frame counts following procedure
- Myocardial blush grade following PCI (TMPG)
- Combined endpoint of death, re-MI and urgent target vessel revascularization until day 7 or hospital discharge and day 30
- Death, re-MI and urgent target vessel revascularization (individually counted) until day 7 or hospital discharge and day 30
- Stroke (hemorrhagic, non-hemorrhagic), major and minor bleeding complications until day 7 or hospital discharge and day 30
- Death, Re-MI and TVR until 6 months

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## Baseline characteristics

429 pts. enrolled between  
11/2006 and 05/2007

	Abciximab (n=203)	Eptifibatide (n=226)	p-value
Age(yrs)	60.5	61.3	n.s.
Male	80.1 %	76.1 %	n.s.
Prior MI	8.5 %	8.4 %	n.s.
HX of CHF	3.5 %	2.2 %	n.s.
Diabetes	17.4 %	14.6 %	n.s.
Killip > 1	10.0 %	9.7 %	n.s.
Anterior infarct	45.3 %	43.4 %	n.s.

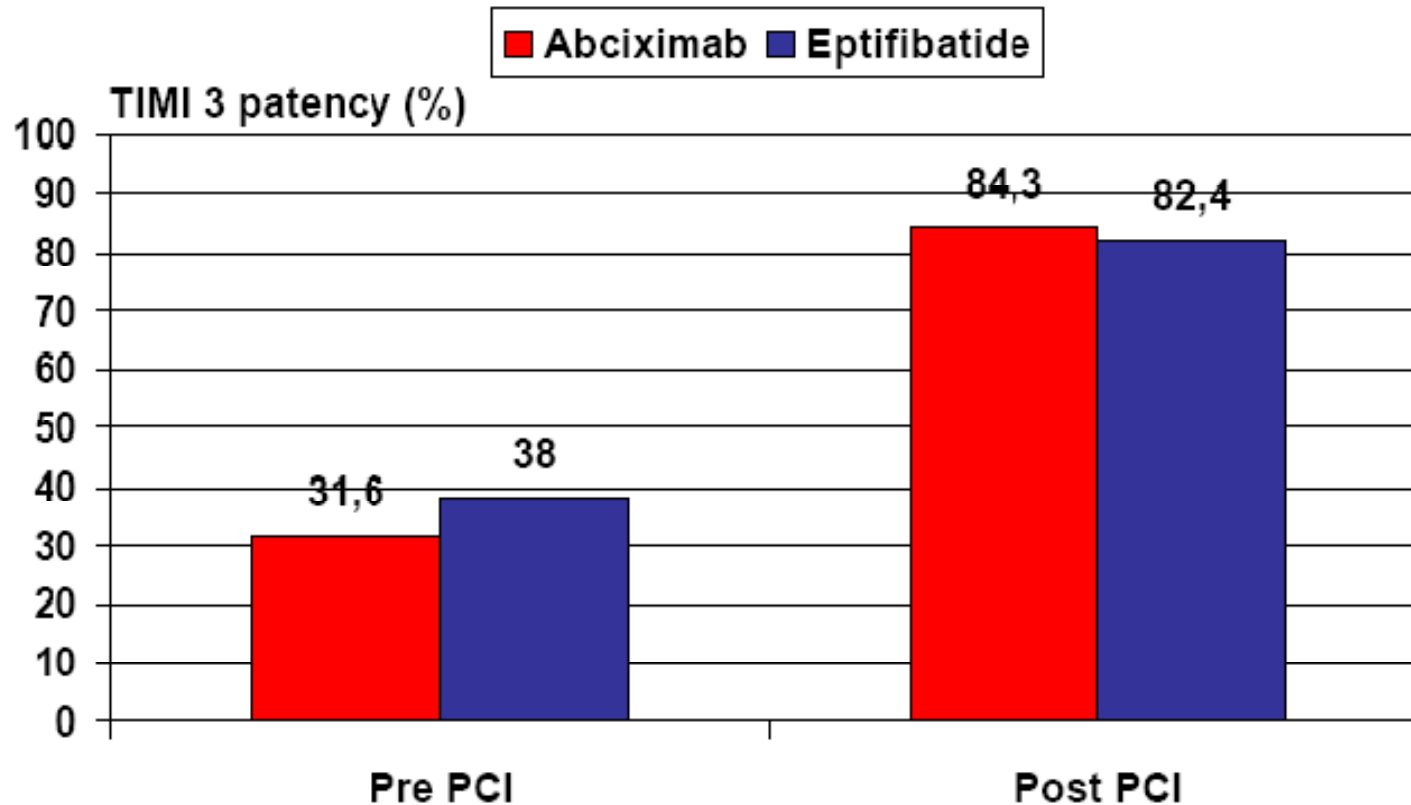
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## Time intervals and PCI

	Abciximab (n=203)	Eptifibatide (n=226)
Onset of symptoms – Study medication	224 mins	234 mins
Study medication – Angiography	30 mins	29 mins
No PCI performed	10 (5%)	9 (4%)

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## TIMI 3 patency before and after PCI (Core lab, ITT)



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**Sum ST resolution 60 mins after PCI  
Per-protocol-analysis**

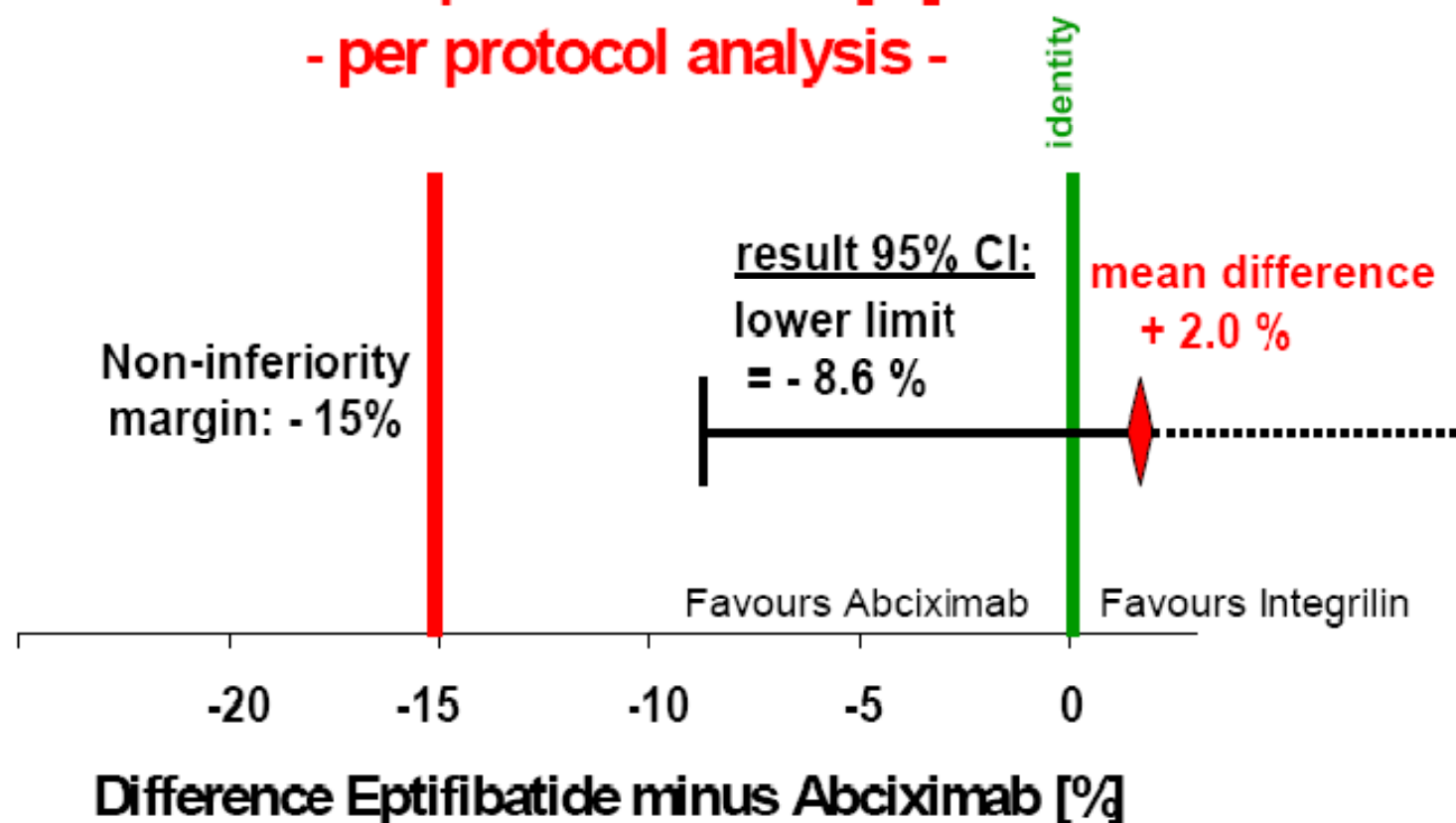
	Abciximab (n=109)	Eptifibatide (n=111)	p-value
<b>Complete</b>	<b>59.6 %</b>	<b>63.1 %</b>	<b>n.s.</b>
Partial	25.7 %	31.5 %	n.s.
No	14.7 %	5.4 %	p = 0.021
Single lead complete	51.4 %	55.9 %	n.s.

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# Primary Endpoint

adjusted by centre and infarct location

Complete sum STR [%]  
- per protocol analysis -



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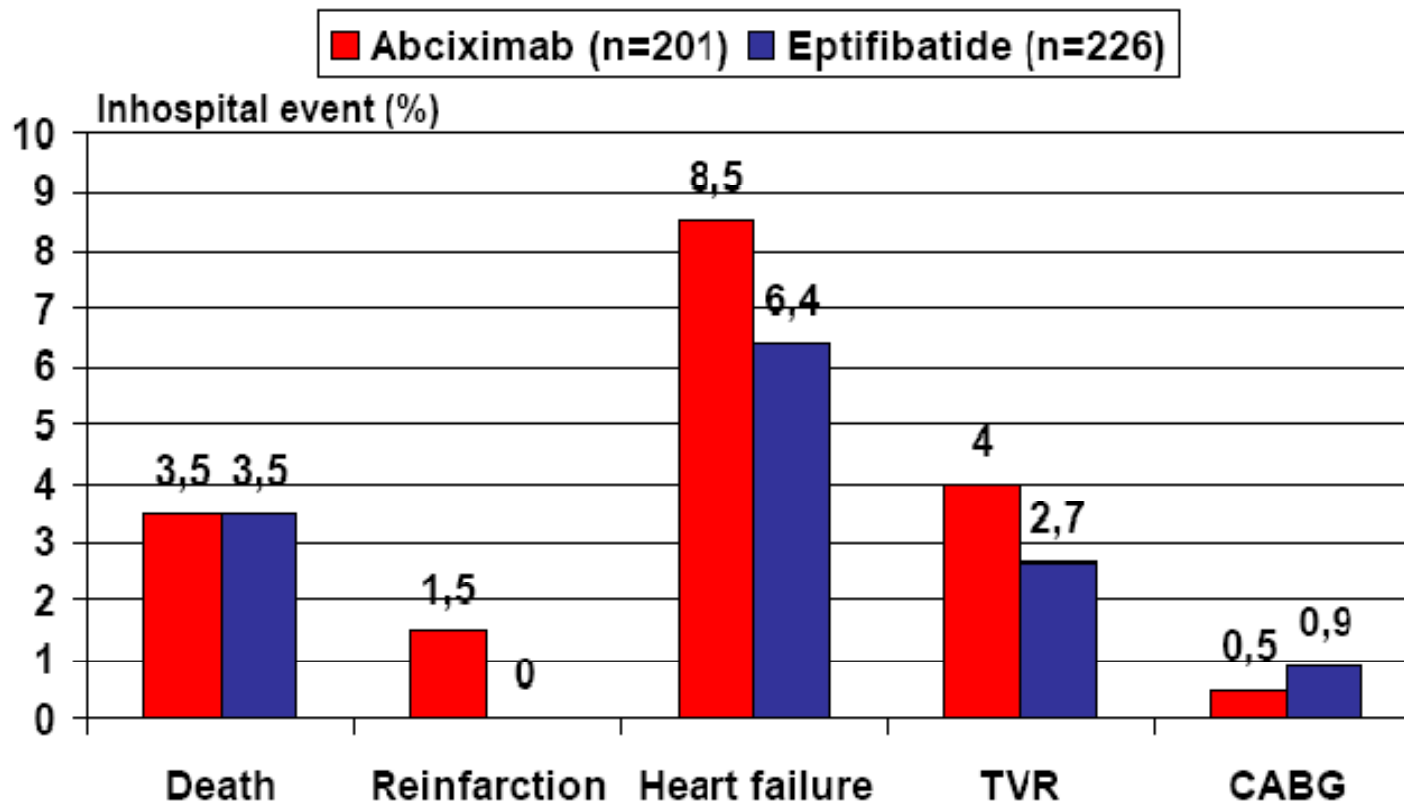
**Sum ST resolution 60 mins after PCI  
Intention-to-treat-analysis**

	Abciximab (n=200)	Eptifibatide (n=225)	p-value
<b>Complete</b>	<b>47.5 %</b>	<b>50.2 %</b>	<b>n.s.</b>
Partial	24.5 %	22.2 %	n.s.
No	28.0 %	27.6 %	n.s.
Single lead complete	41.0 %	46.2 %	n.s.

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# Inhospital events

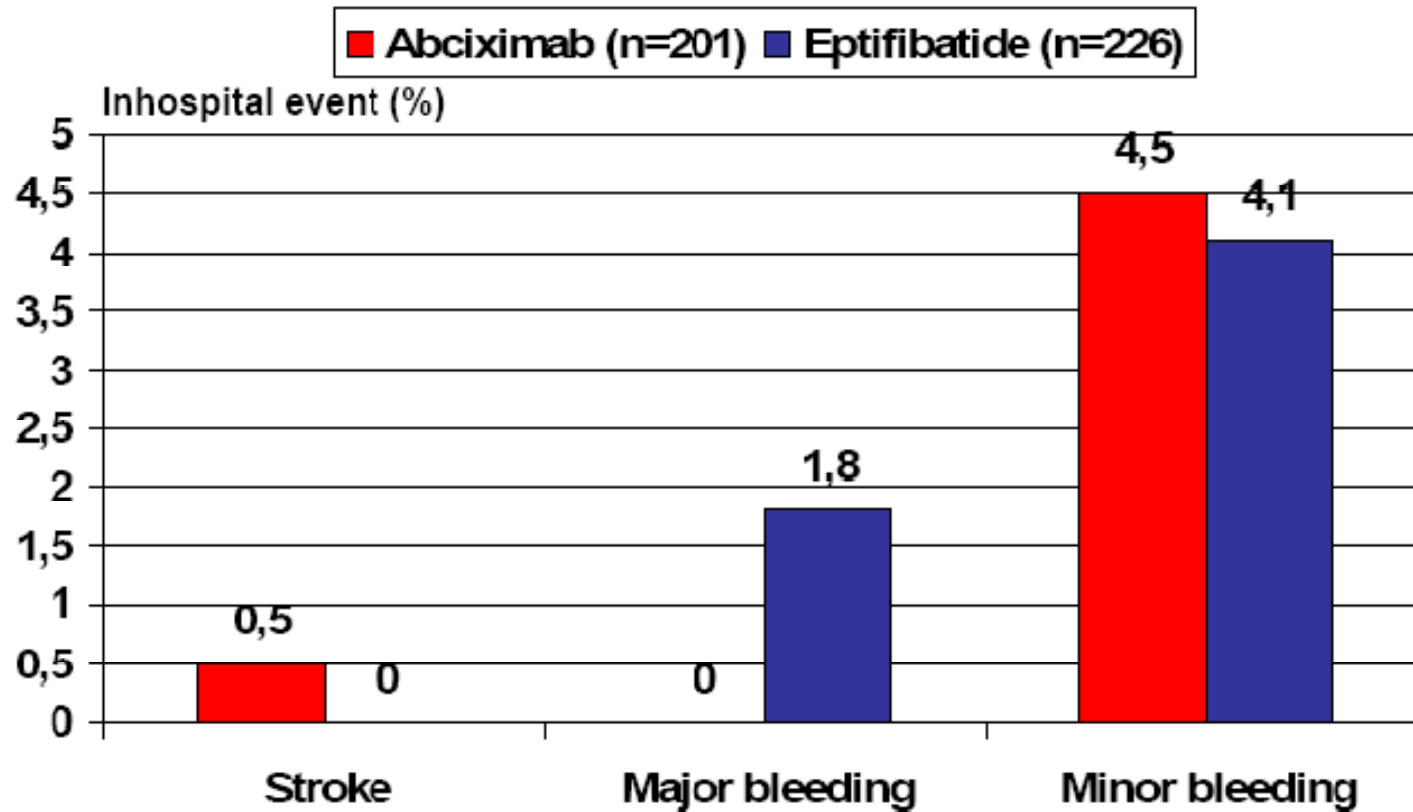
## Preliminary unadjudicated results



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# Inhospital events

Preliminary unadjudicated results

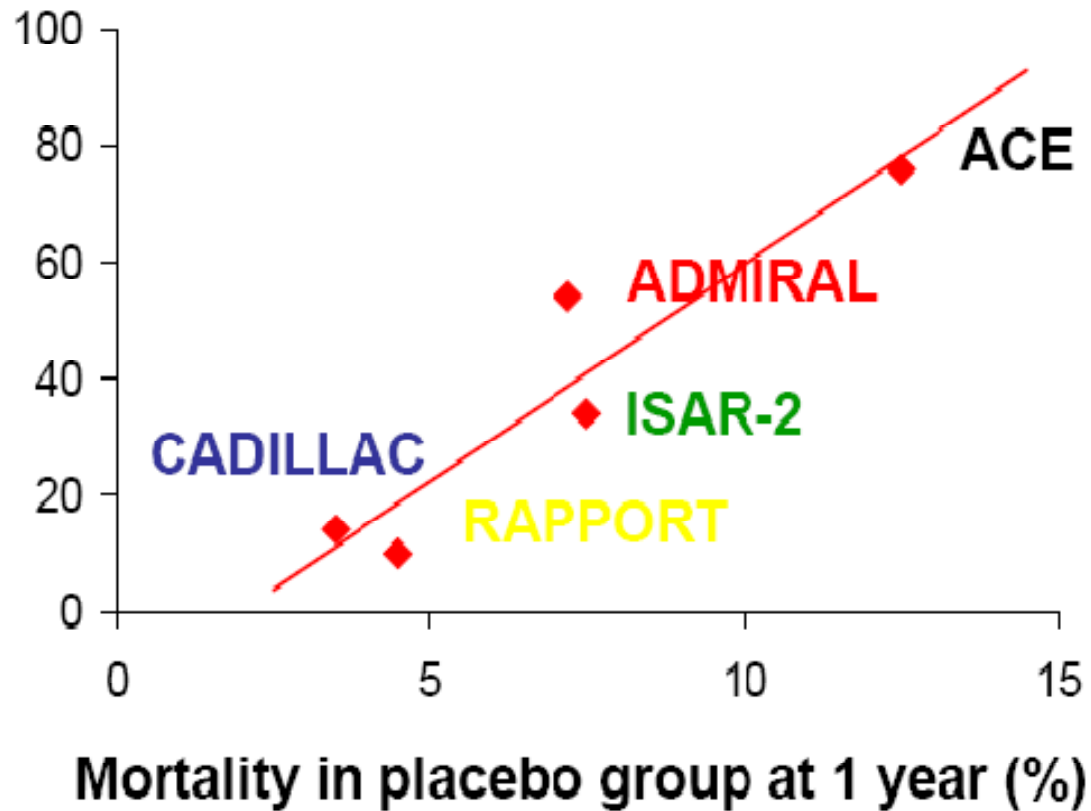


- ✓ Eptifibatide given as a double-bolus is equally effective as abciximab as adjunct to primary PCI with respect to myocardial reperfusion
- ✓ The preliminary clinical events did not show any differences between the two compounds
- ✓ Therefore eptifibatide seems an alternative to abciximab in patients with STEMI undergoing primary PCI

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## Abciximab for PCI in STEMI More Benefit in Higher Risk Cohorts

Mortality reduction  
in abciximab group (%)



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## Summary of protocol violations leading to exclusion from PP analysis

Remark: Multiple violations per patient possible

	Treatment group		
	Eptifibatide N	Abciximab N	TOTAL N
No Intake of Study drug <sup>§</sup>	-	2	2
Exclusion criterium: Left bundle branch block	-	1	1
Thrombolytic therapy within 24 hours before randomisation	1	-	1
Missing ECG I	5	6	11
Missing ECG III	9	7	15
Missing PCI End time	2	1	3
Randomisation failure: Study drug not according to randomis.	-	1	1
Start of study medication intake before ECG I	2	1	3
ECG III not 45-75 minutes after procedures	76	63	139
Uncertain Infarct localisation (via ECG evaluation)	37	24	61
<b>TOTAL</b>	<b>141</b>	<b>116</b>	<b>257</b>
<b>Number of patients excluded from PP analysis set</b>	<b>115</b>	<b>102</b>	<b>207</b>

§ "No Intake of Study drug" leads to exclusion from Safety, ITT and PP analysis set,