

# Tirofiban vs. Abciximab during primary PCI in STEMI



**MULTISTRATEGY**

ClinicalTrials.gov number, NCT00229515

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On behalf of Multistrategy  
Investigators**

# Disclosures

- Speaker's bureau: Iroko, Merck, Medicure
- Research grant: Iroko, Eli Lilly
- Advisory Board: Iroko, Eli Lilly, Medicine company

# Background

- **There is limited data on the comparison between Abciximab vs. Tirofiban at high bolus dose (HDB: 25  $\mu$ g/kg over 3 min)**
  - 4 RCTs have so far contrasted these two drugs in 719 pts undergoing PCI of whom less than 300 were recruited in the setting of STEMI <sup>1,2</sup>

# Trial Design

## Aspirin

160-325 mg orally or 250 mg intravenously  
mg or 25

300

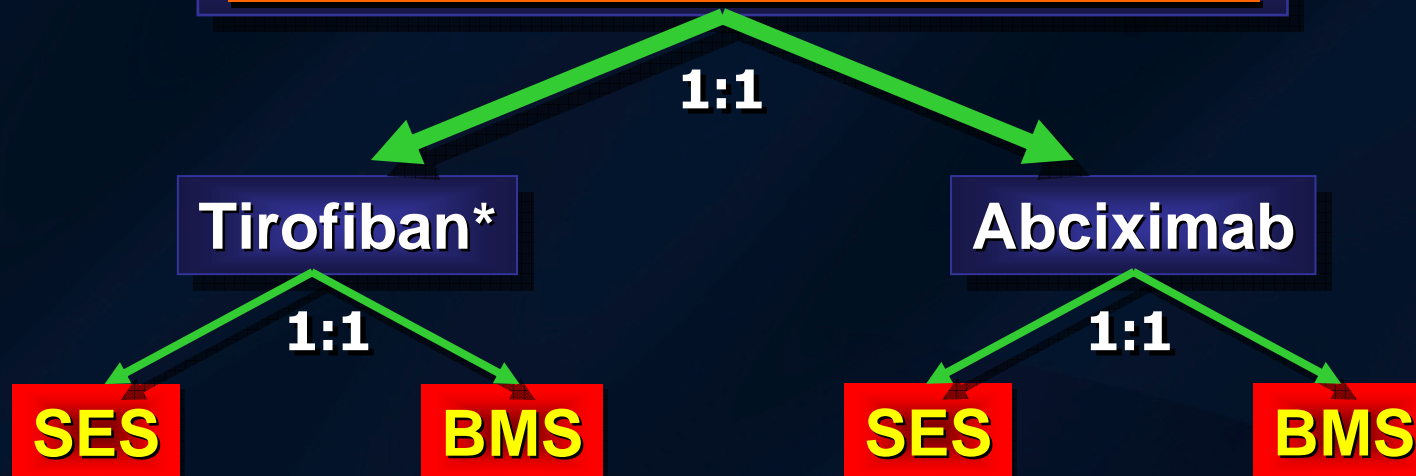
### No exclusion criteria based on:

- *Haemodynamic Status*
- *Angiographic Findings*

protein  
a inhibitors

# Trial Design

**STEMI all-comer Patients**  
**Aspirin + Clopidogrel + UFH**  
**Before Arterial Sheath Insertion**



**Coronary Angiography ± PCI**  
Stenting was the default strategy in pts  
with a RVD  $\geq$  2.5 mm at visual estimation

\*: given as a bolus of 25  $\mu\text{g}/\text{kg}$ , followed by an 18-24 hour infusion at 0.15  $\mu\text{g}/\text{kg}/\text{min}$

# Study Primary Endpoints

## Pharmacology Arm

**Non-inferiority basis**

**$\geq 50\%$   $\Sigma$  ST segment elevation resolution within 90' after last balloon inflation @ tt-EKG**

## Stent Arm

**Superiority basis**

**Cumulative rate of MACE, defined as overall death, Reinfarction or TVR within 8 months**

# Study Primary Endpoints Power Analysis

With 600 pts randomized and type I error set @2.5%

Assumed event rates

Endpoint	Test	Abciximab	Tirofiban	SES	BMS	$\delta$	Power
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$\geq \Sigma 50\%$ >85%	N-Inf.	85%	85%	—	—	9%*	
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STR

MACE 80%	Sup.	—	—	16%	27%	—	
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\*: ~50% of previously reported  $\Delta \geq \Sigma 50\%$  STR between Abciximab vs. placebo in the ACE trial (Antoniucci et al. J Am Coll Cardiol 2003)



# Study Organization

## Sponsor:

University of Ferrara, *Italy*

## Data Management:

Medical Trial Analysis, *Switzerland*

## Site and data monitoring:

Medical Trial Analysis, *Italy*; Sermes  
C.R.O., *Spain*

## Clinical Events Committee:

P. Agostoni (Chair), *Belgium*, E.  
Meliga, *The Netherlands*.

## ECG core lab:

MTA, C. Arcozzi (Chair)

## Angiographic core lab:

MTA, P. Malagutti (Chair)

## DSMB:

P. Vranckx, (Chair), *Belgium*



# MULTISTRATEGY P.I.s and Sites

**G Campo** Ferrara



**R Moreno** Madrid



**G Percoco** Lagosanto



**T Piva** Ancona



**M Anselmi** Verona



**I Sheiban** Torino



**L Bolognese** Arezzo



**G Paschetto** Mirano



**S Colangelo** Torino



**F Prati** Rome



**N de Cesare** Zingonia



**M Nazzaro** Rome



**A Rodriguez** B. Aires



**J Fernández** Huelva



**M Ferrario** Pavia



**J Mieres** B Aires



**1030 Patients Assessed  
for Eligibility**

**72%**

**745 Randomized**

**285 Excluded**

- 153 Not Meeting Inclusion Criteria
- 132 Refused to Participate

1:1:1:1

**Abciximab and  
Uncoated Stent  
(n=186)**

**Abciximab and  
Sirolimus-Stent  
(n=187)**

**Tirofiban and  
Uncoated Stent  
(n=186)**

**Tirofiban and  
Sirolimus-Stent  
(n=186)**

99% received Abciximab  
**97% received PCI**  
90% received Abc+BMS  
99% qualified as STEMI  
3% non-interpretable ECG

100% received Abciximab  
**99% received PCI**  
87% received Abc+BMS  
100% qualified as STEMI  
2% non-interpretable ECG

100% received Tirofiban  
**98% received PCI**  
95% received Tir+BMS  
99% qualified as STEMI  
1% non-interpretable ECG

100% received Tirofiban  
**98% received PCI**  
89% received Abc+BMS  
99.5% qualified as STEMI  
4% non-interpretable ECG

**97%**

**N=179**

**N=182**

**N=184**

**N=177**

**ST Segment Resolution Study**

**100%**

**N=186**

**N=186**

**N=186**

**N=186**

**8 month Follow-up Study**

# ST Segment Resolution

## Rationale for choosing this endpoint in STEMI

- ST segment resolution correlates with infarct size and infarct transmuralty as assessed at MRI or SPECT

Circulation 2004;110(21):e506-10.

Jama 2005;293(9):1063-72.

Eur Heart J. 2007 Jun;28(12):1433-9.

- ST segment resolution has strong and independent prognostic implications in terms of both death or the composite of death or MI

Lancet 1997;350(9078):615-9

- Interventions in STEMI which improve ST segment resolution have a consistent effect on outcomes and viceversa

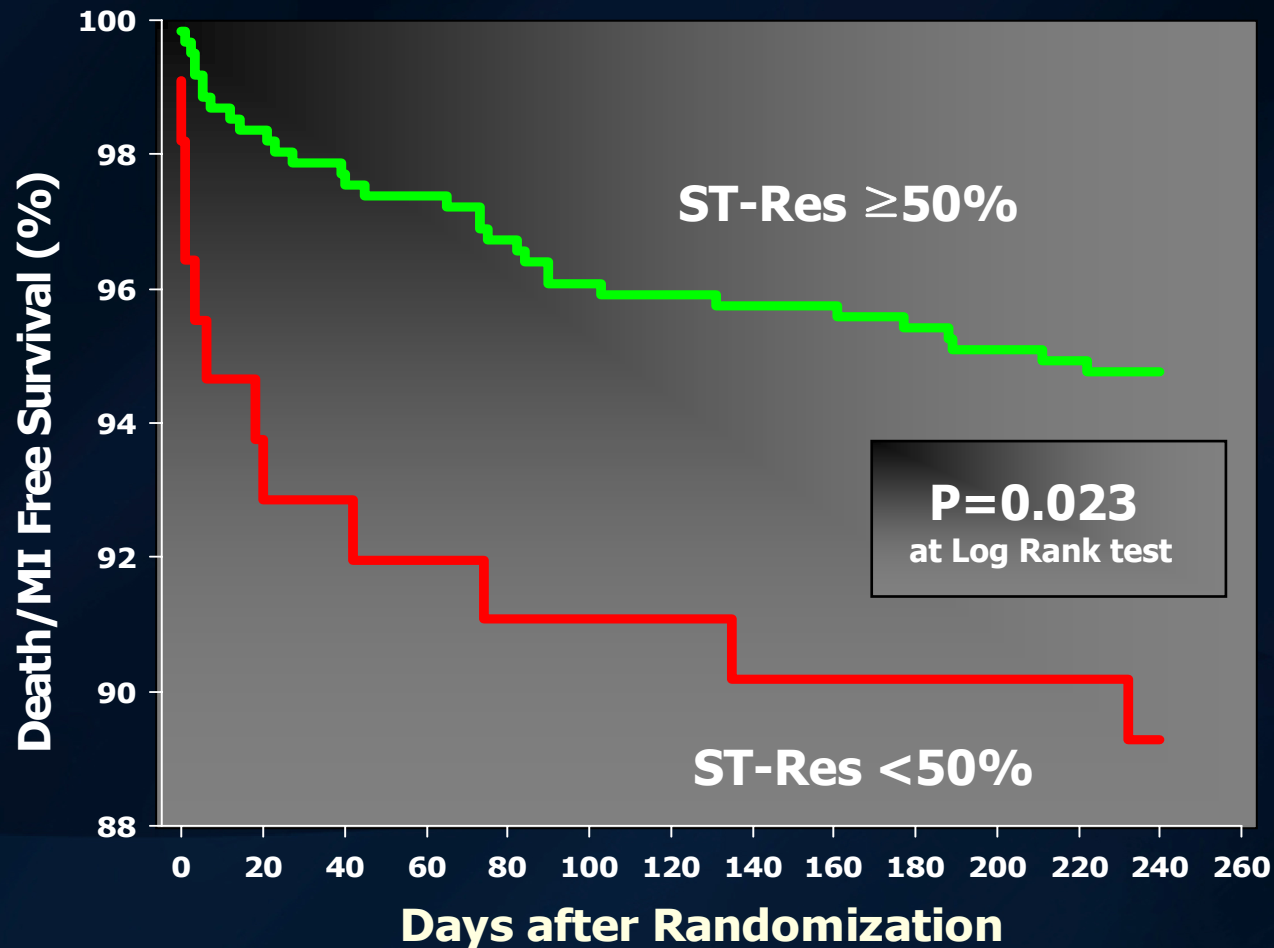
N Engl J Med. 2008 Feb 7;358(6):557-67

J Am Coll Cardiol 2003;42(11):1879-85

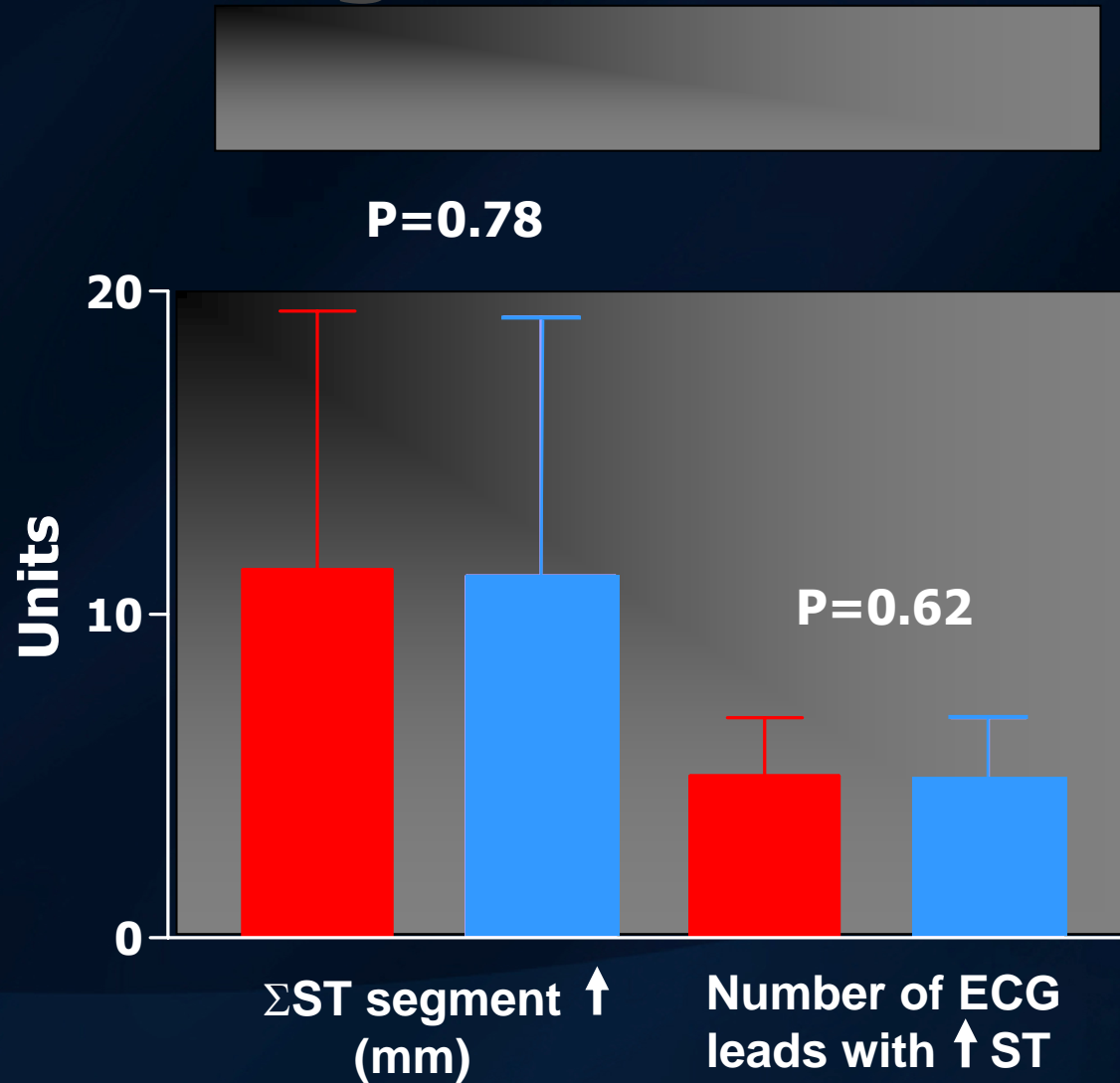
Jama 2005;293(9):1063-72.

# ST Segment Resolution

## Internal Validity Assessment of the Chosen 1° Endpoint

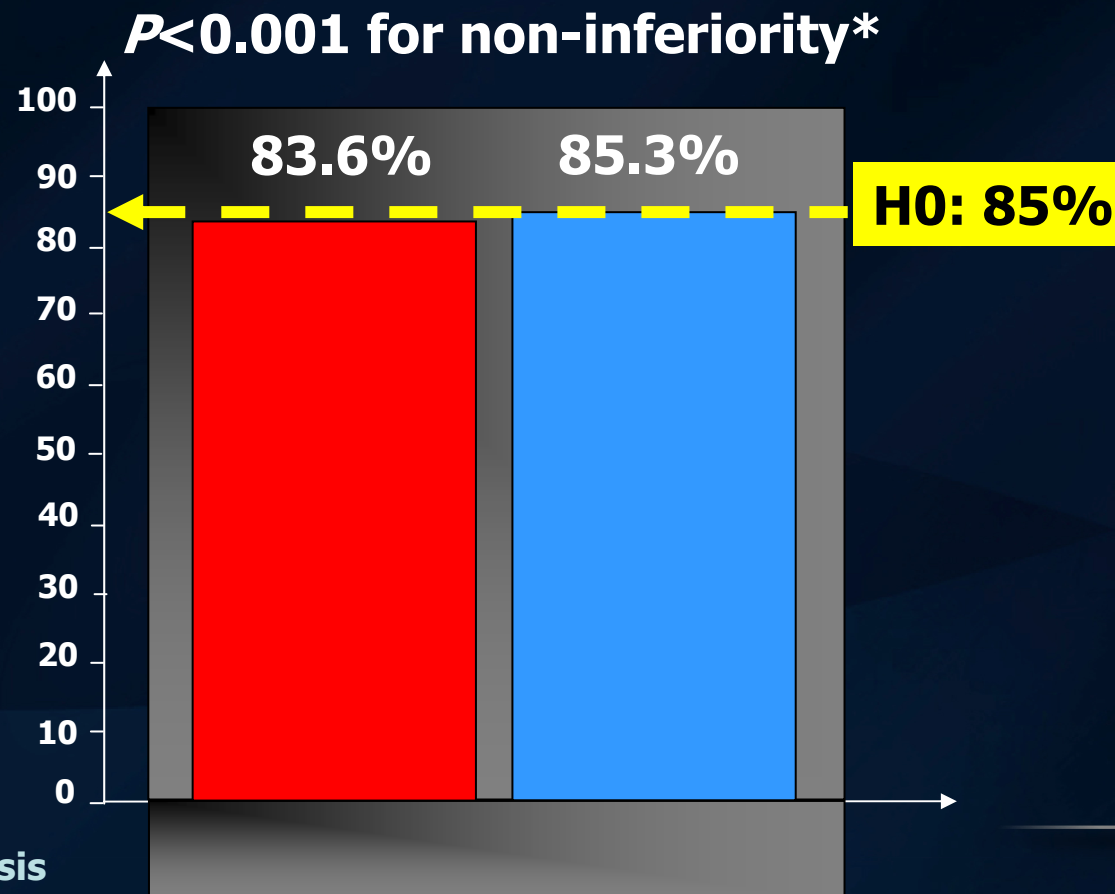


# ST Segment Elevation



# Primary Endpoint

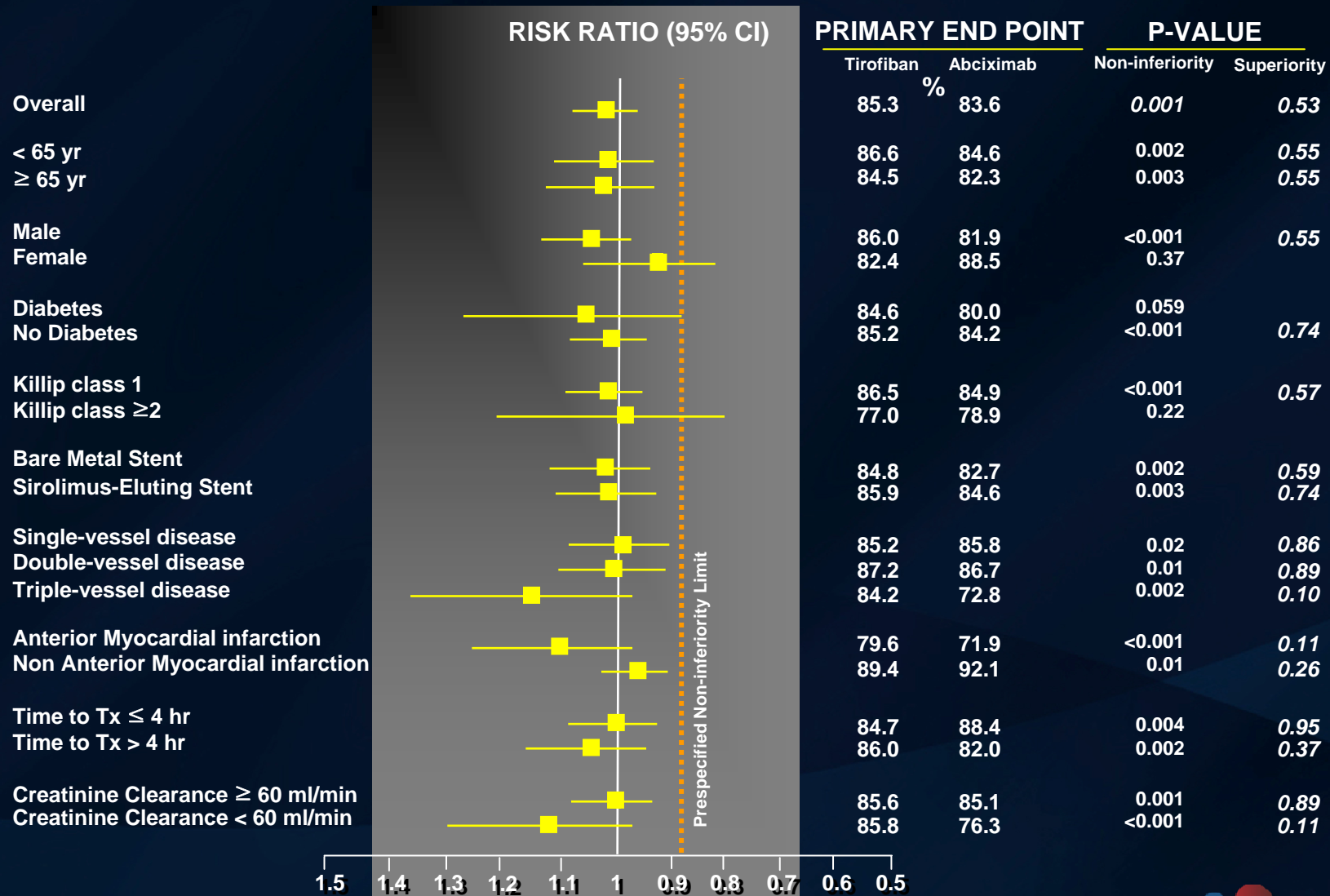
## $\geq 50\% \Sigma$ ST segment resolution



\*: at *ITT* and *PP* Analysis

# 1° Endpoint: $\geq 50\%$ ST segment resolution

## Subgroup Analysis



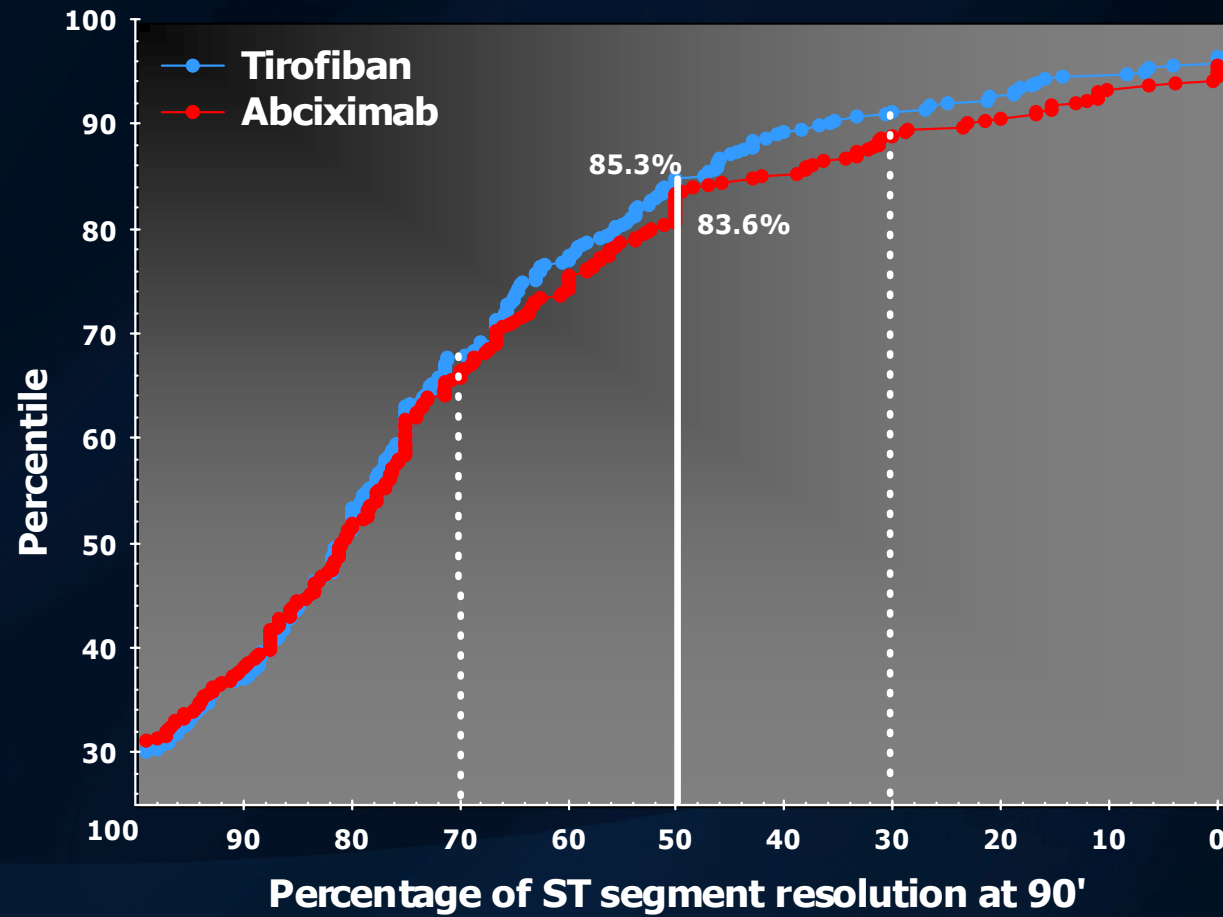
Tirofiban Better

Abciximab Better



# ECG Analysis Core Lab Evaluation

N=722

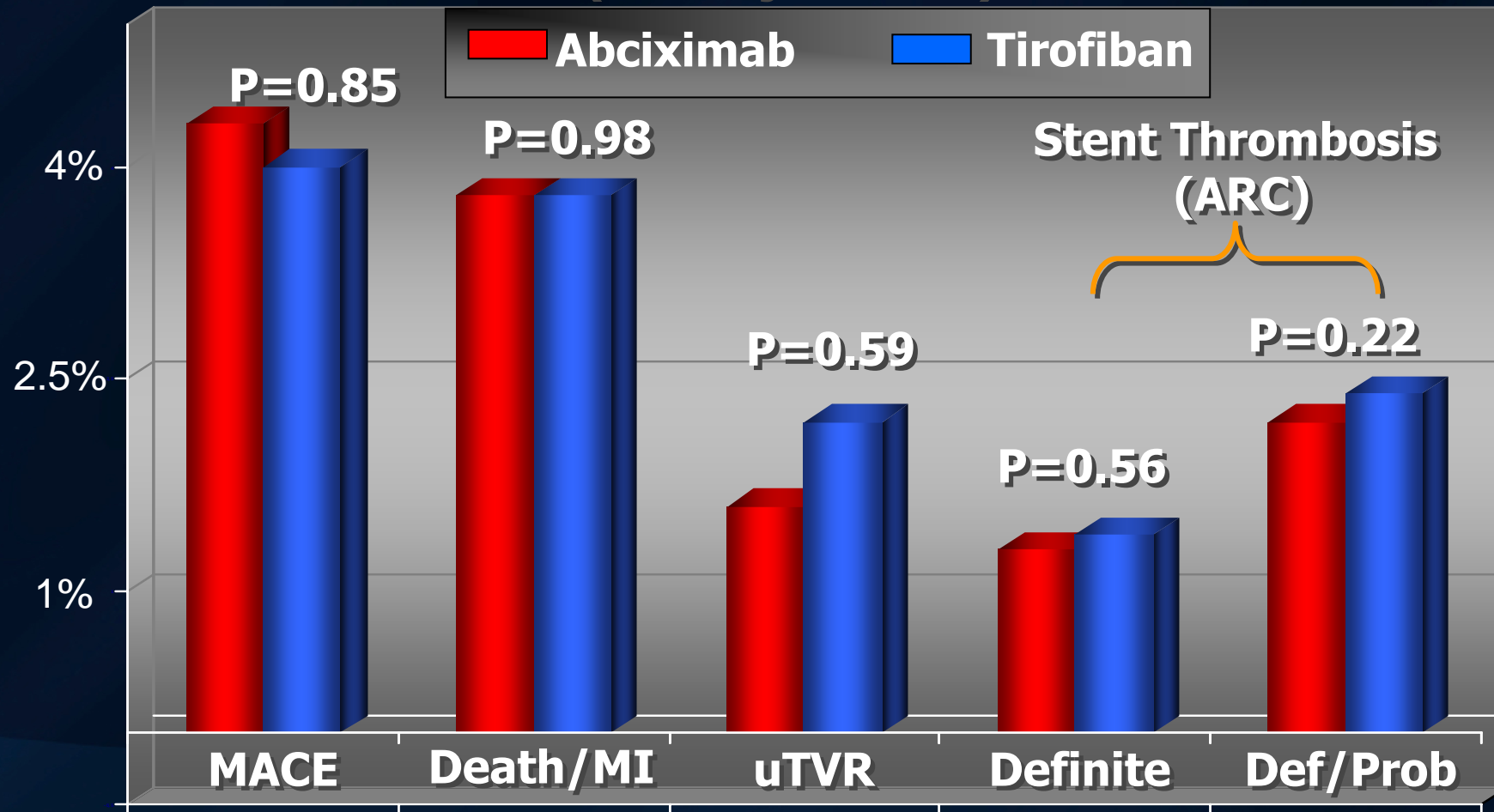




# 30-Day Outcomes

## Efficacy Endpoints

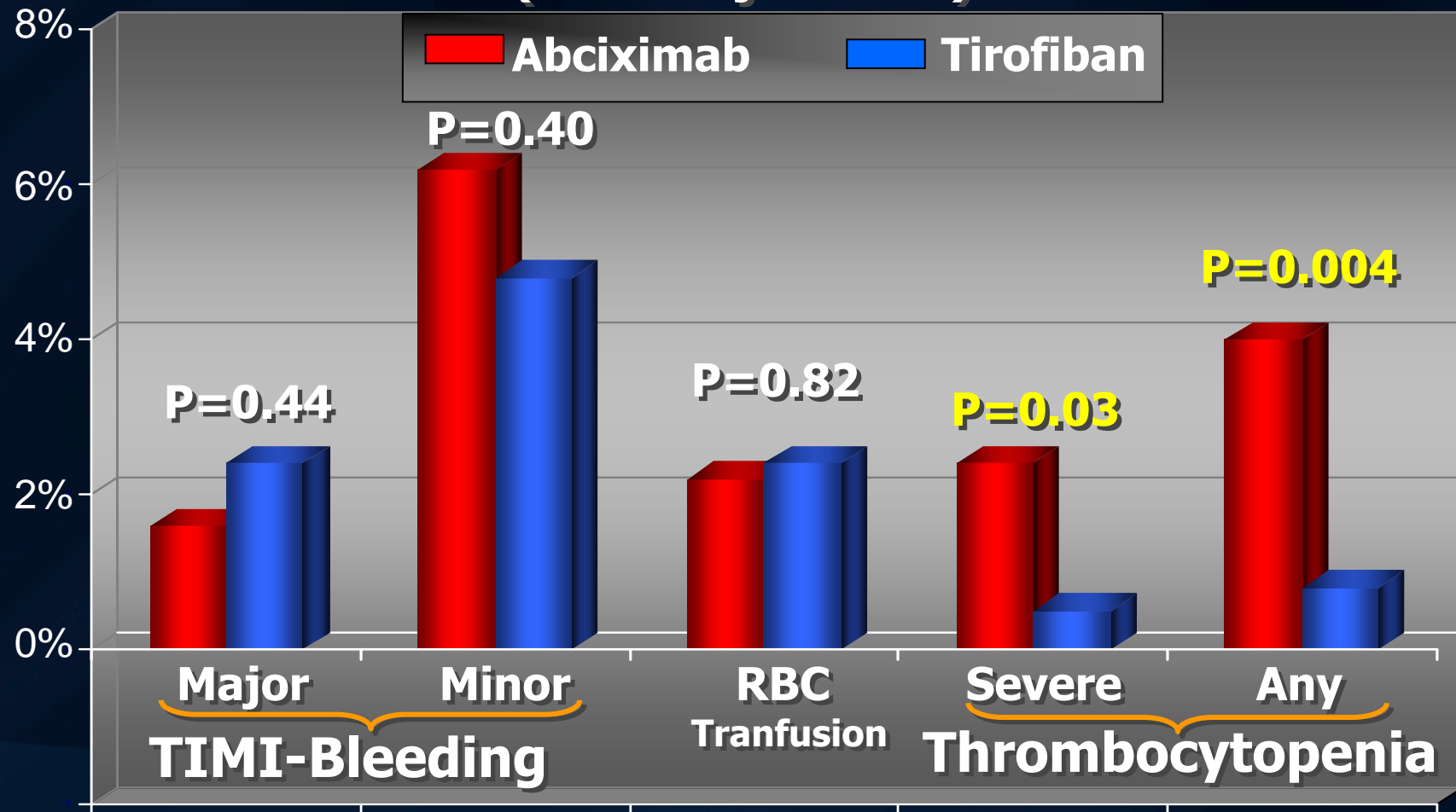
(CEC adjudicated)



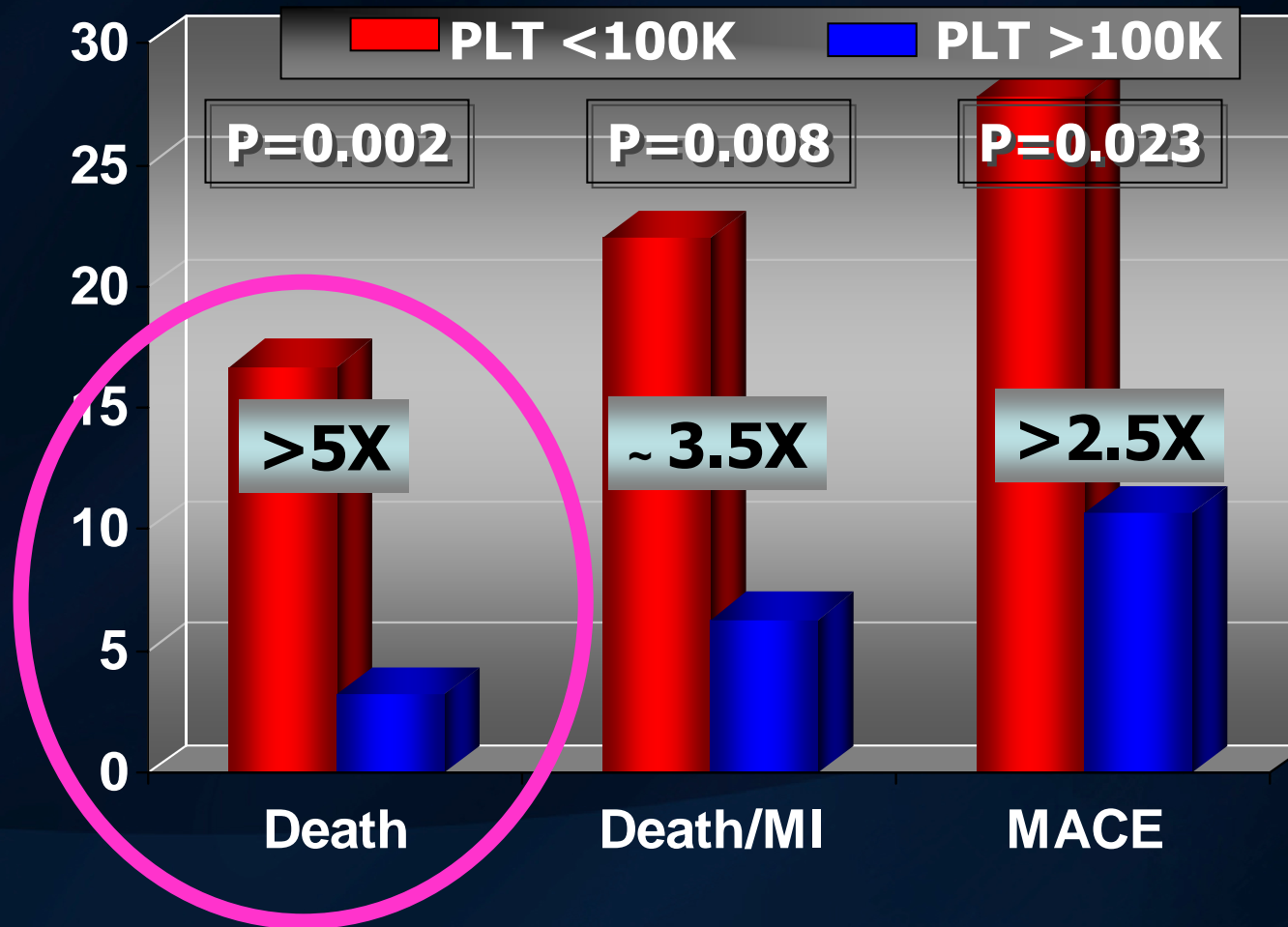
# 30-Day Outcomes

## Safety Endpoints

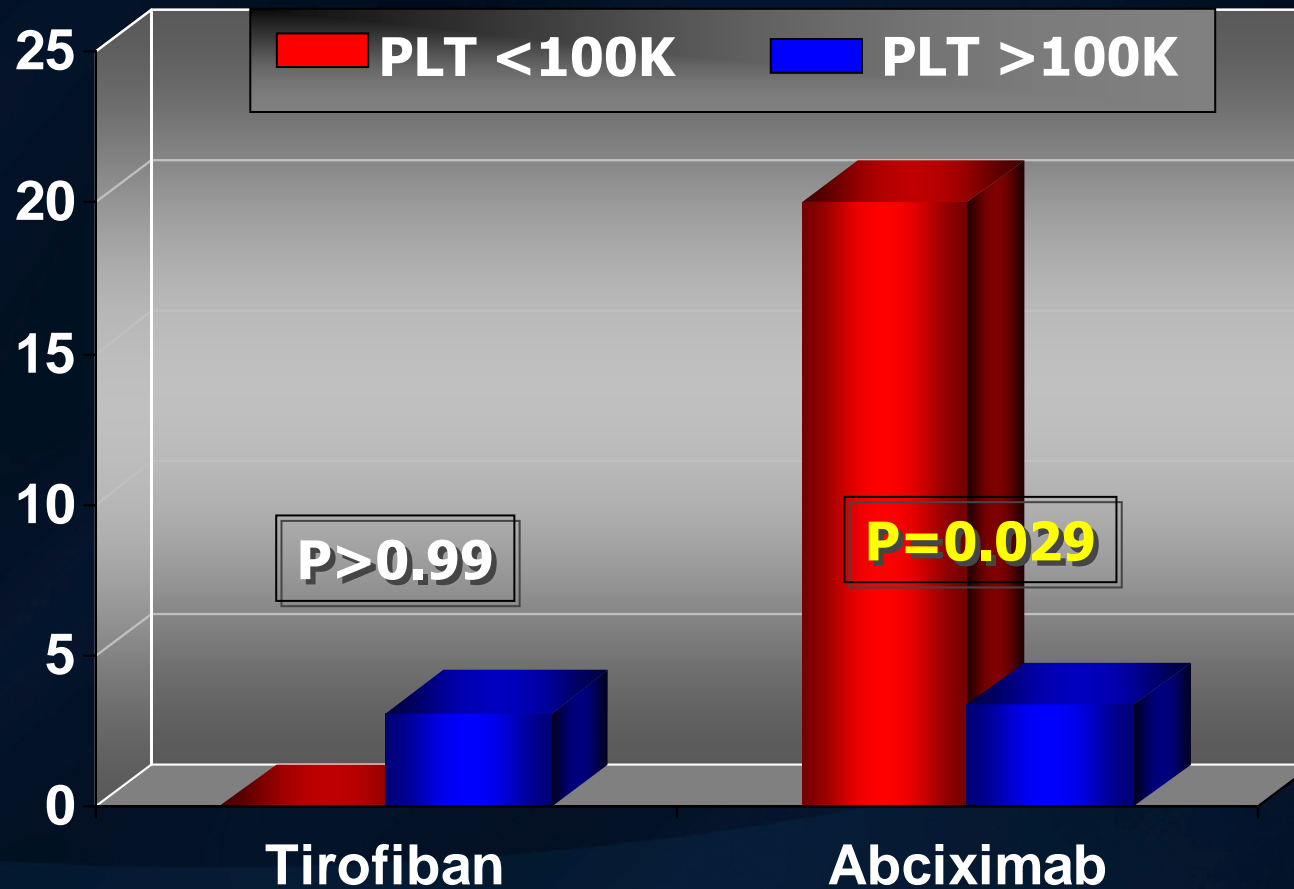
(DSMB adjudicated)



# Does Thrombocytopenia impact on patient outcome ?



# Differential impact of Thrombocytopenia on mortality

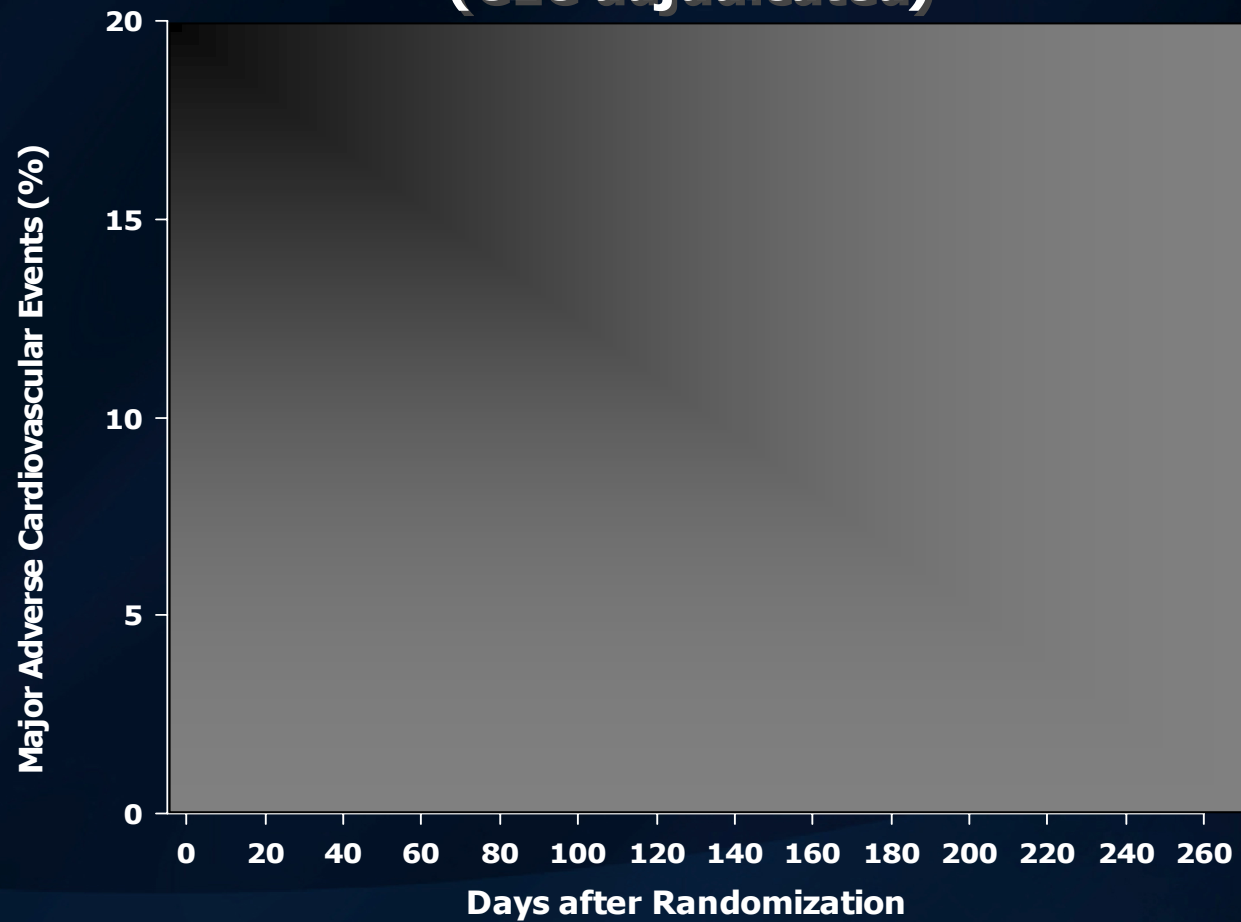


Rate of thrombocytopenia was 0.8% in tirofiban vs. 4.0% in abciximab group,  $p=0.004$

# 8 Month Outcomes

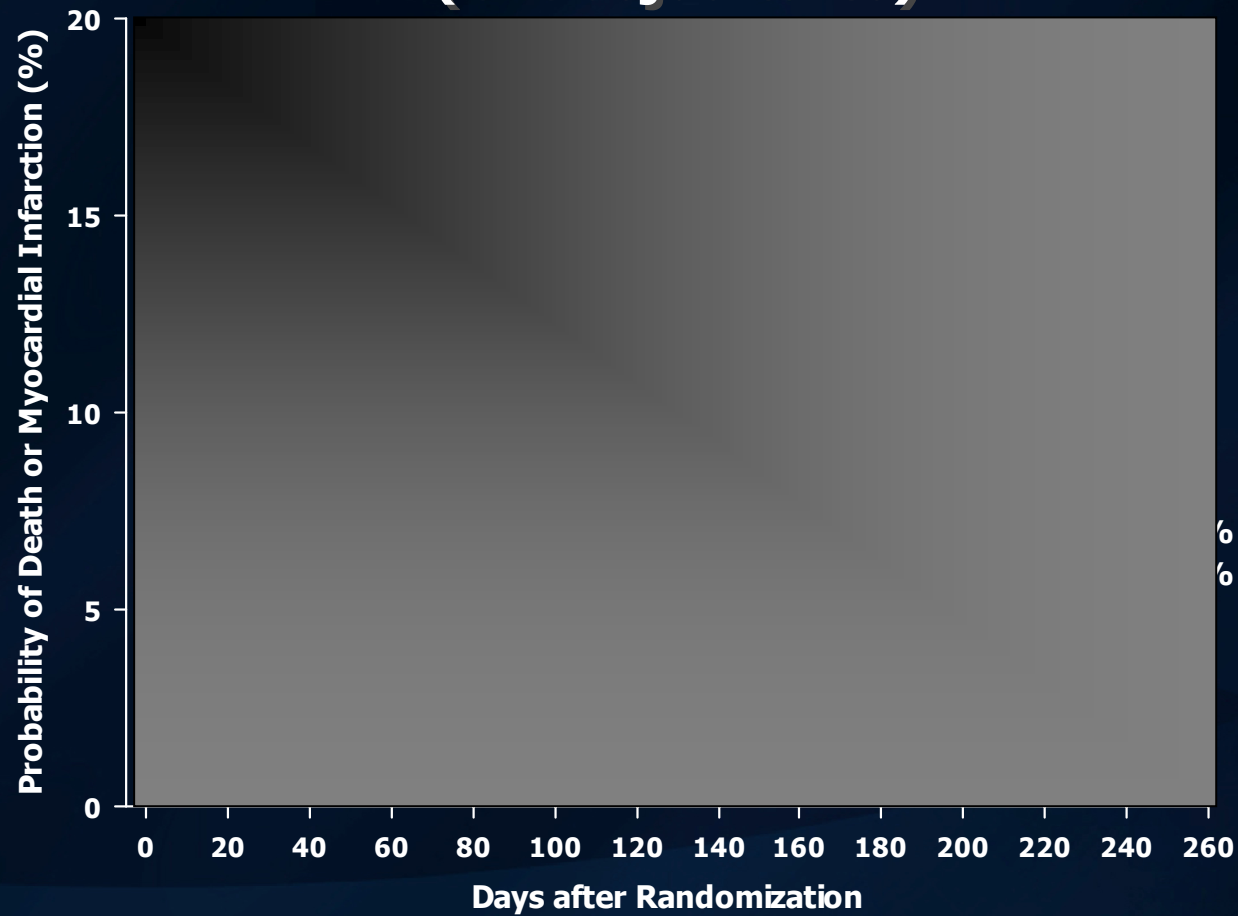
## MACE

(CEC adjudicated)



# 8 Month Outcomes

## Death/MI (CEC adjudicated)

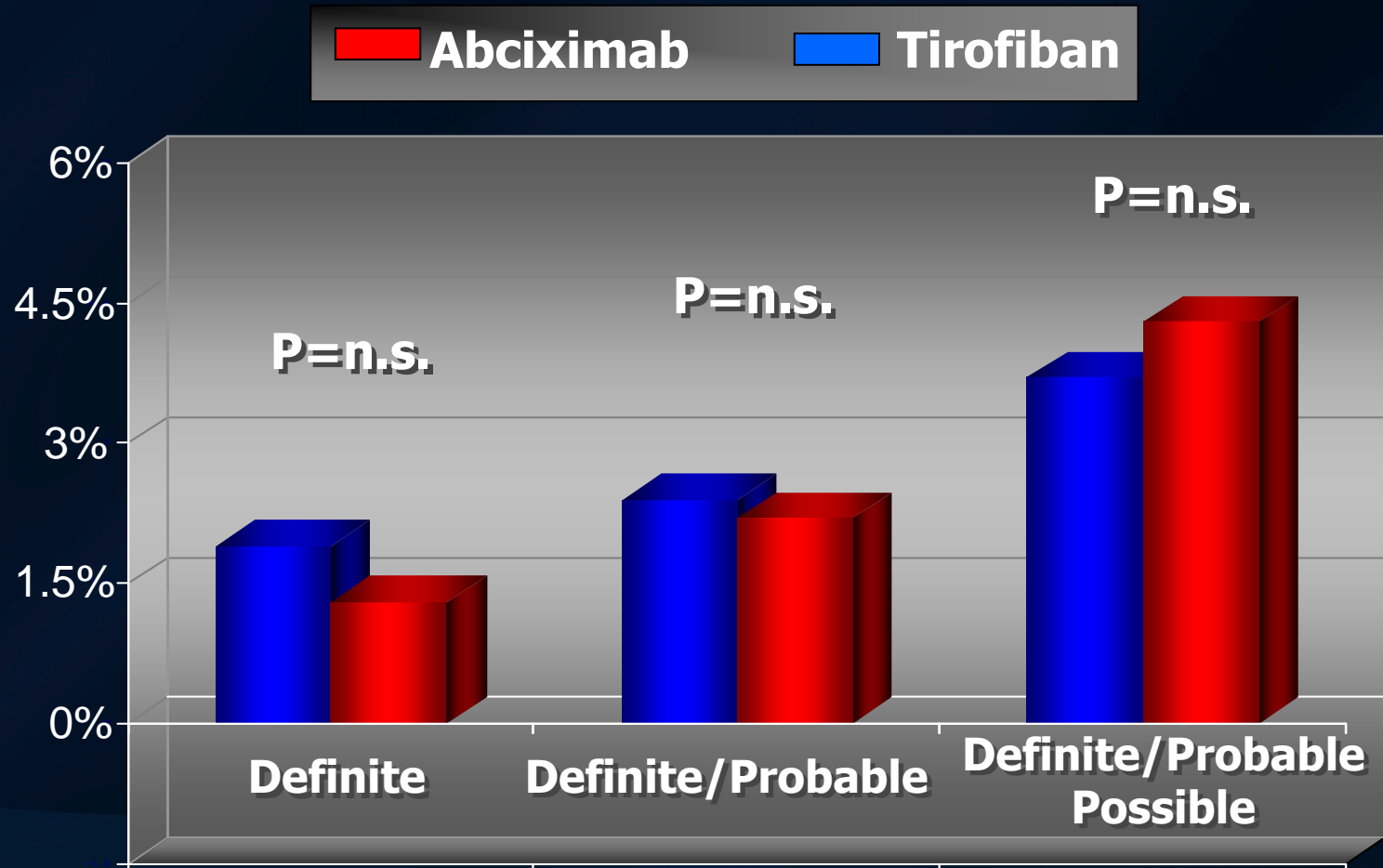


Valgimigli et al, JAMA 2008



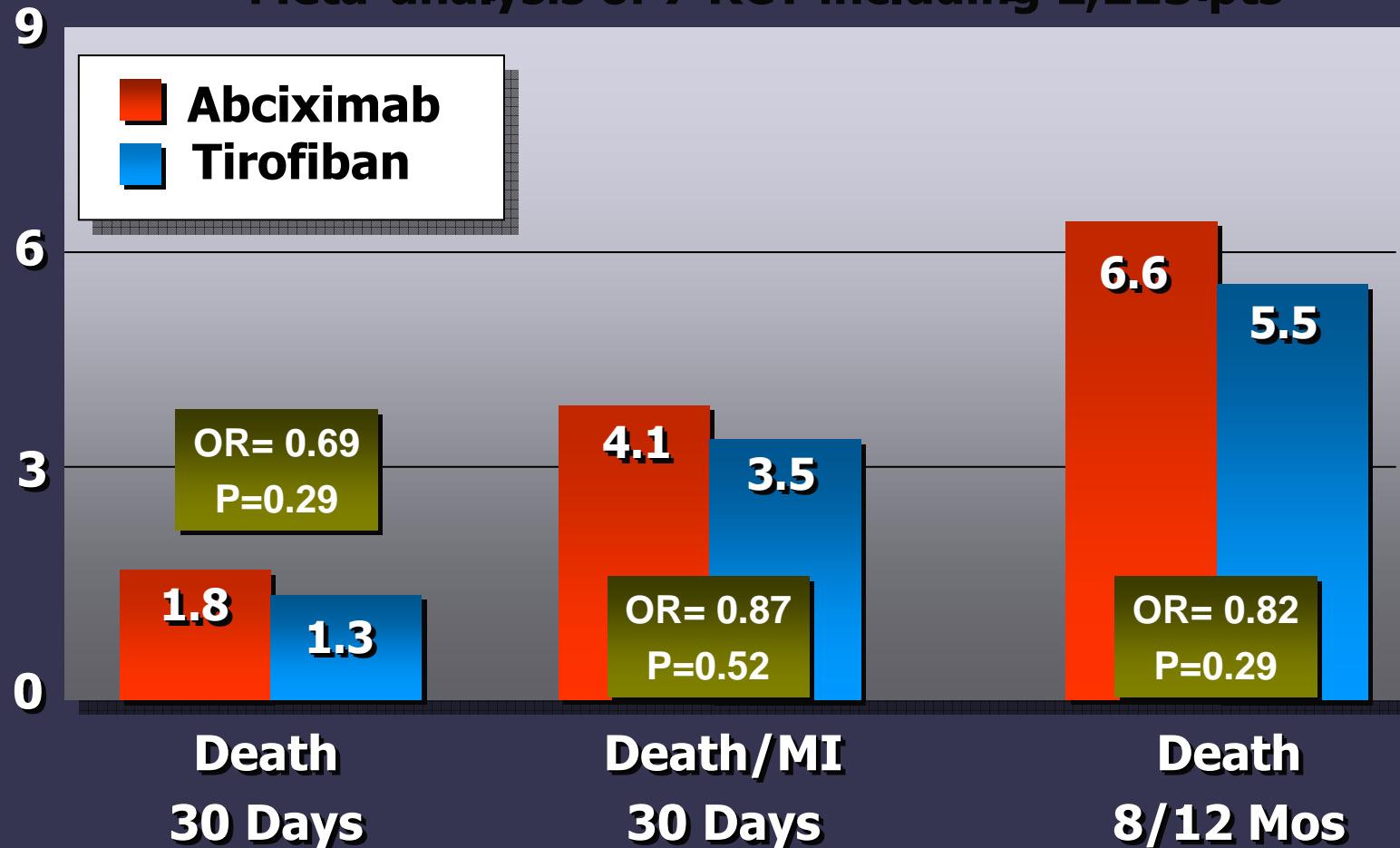
# ARC Stent Thrombosis

(CEC adjudicated)



# Similar Short and long-term anti-ischemic effect

Meta-analysis of 7 RCT including 2,213 pts

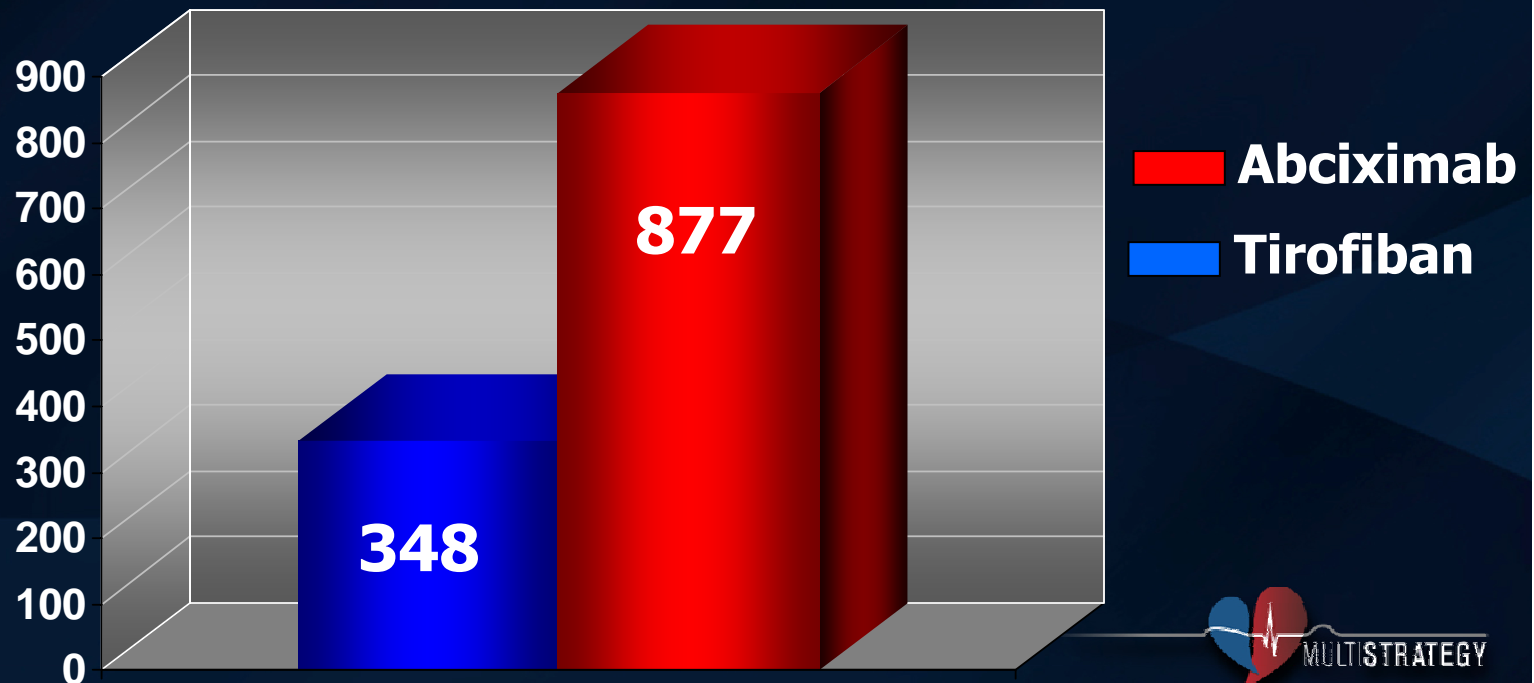




# Pharmaco-economic Analysis

- Drug utilization and major procedural resources between groups were similar;
- Duration of HDB tirofiban infusion was longer 19.97h v. 11.44h ( $p < 0.0001$ ) whereas, amount of Glycoprotein inhibitor and number of required vials of drug was higher for Abciximab

**Δ: 530/patient; 100,000 every 188 treated pt**



# Summary

*Our study provides evidence that in a broad population of largely unselected patients undergoing angioplasty for ST-elevation myocardial infarction:*

- **Tirofiban enables non-inferior STR within 90' after intervention and similar outcomes at 8 months than Abciximab**
- **The safety profile favoured the use of tirofiban for a lower incidence of thrombocytopenia which has prognostic implications**
- **Tirofiban appeared a more cost-efficient drug than abciximab**