

# **Upstream Use of GP IIb/IIIa Inhibitors:** ***Indication, Efficacy and Safety***

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**Milan- Italy**

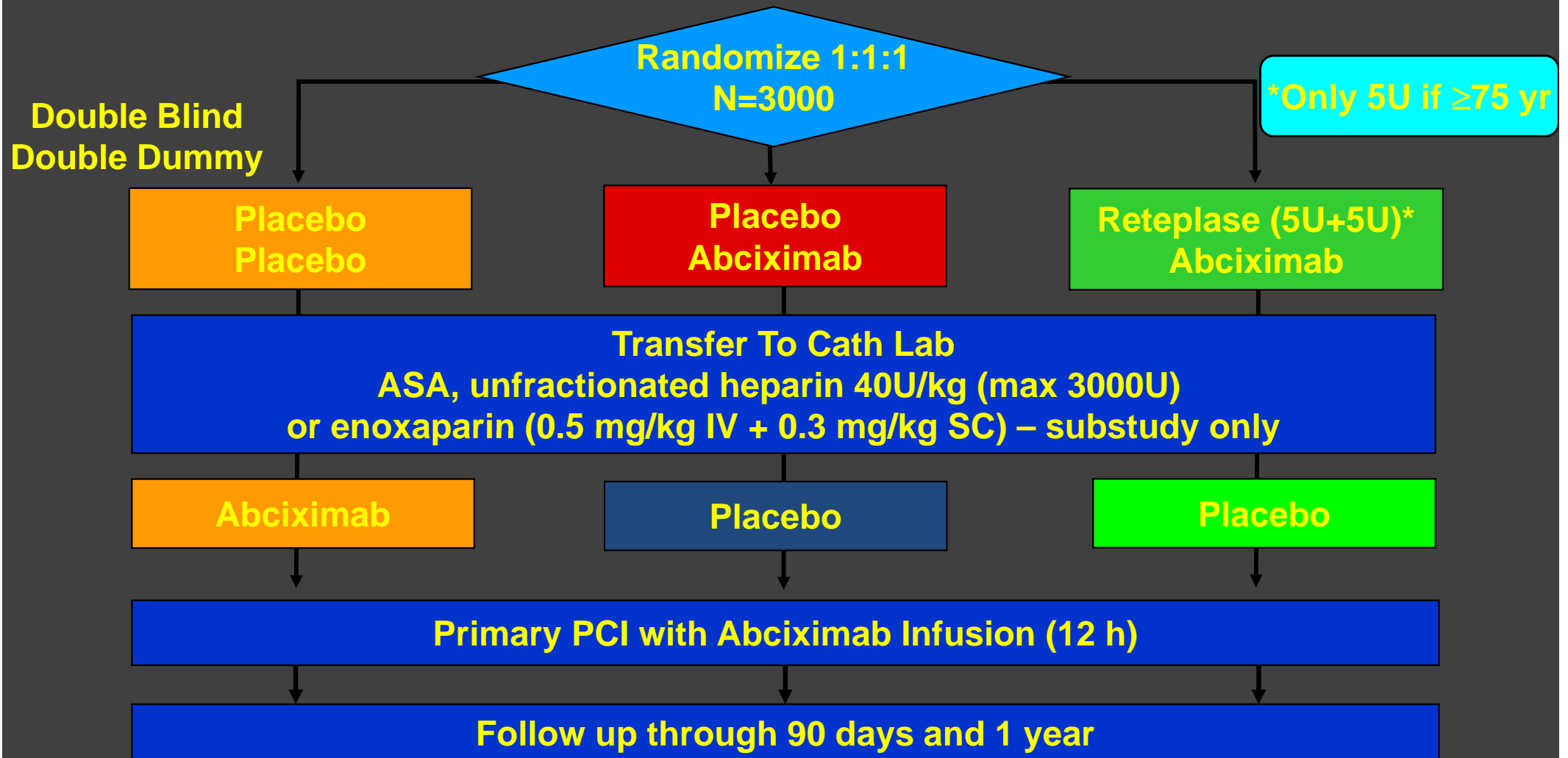
# Periprocedural anti thrombotic medication in primary PCI, *con't*

Recommendations	Class	Level
GP IIb/IIIa inhibitors should be considered for bailout therapy if there is angiographic evidence of massive thrombus, slow or no-reflow or a thrombotic complication.	IIa	C
Routine use of a GP IIb/IIIa inhibitor as an adjunct to primary PCI performed with unfractionated heparin may be considered in patients without contraindications.	IIb	B
Upstream use of a GP IIb/IIIa inhibitor (vs. in-lab use) may be considered in high-risk patients undergoing transfer for primary PCI.	IIb	B
Options for GP IIb/IIIa inhibitors are (with LoE for each agent):		
• Abciximab		A
• Eptifibatide (with double bolus)		B
• Tirofiban (with a high bolus dose)		B

GP = glycoprotein; i.v. = intravenous; lab = catheterization laboratory.

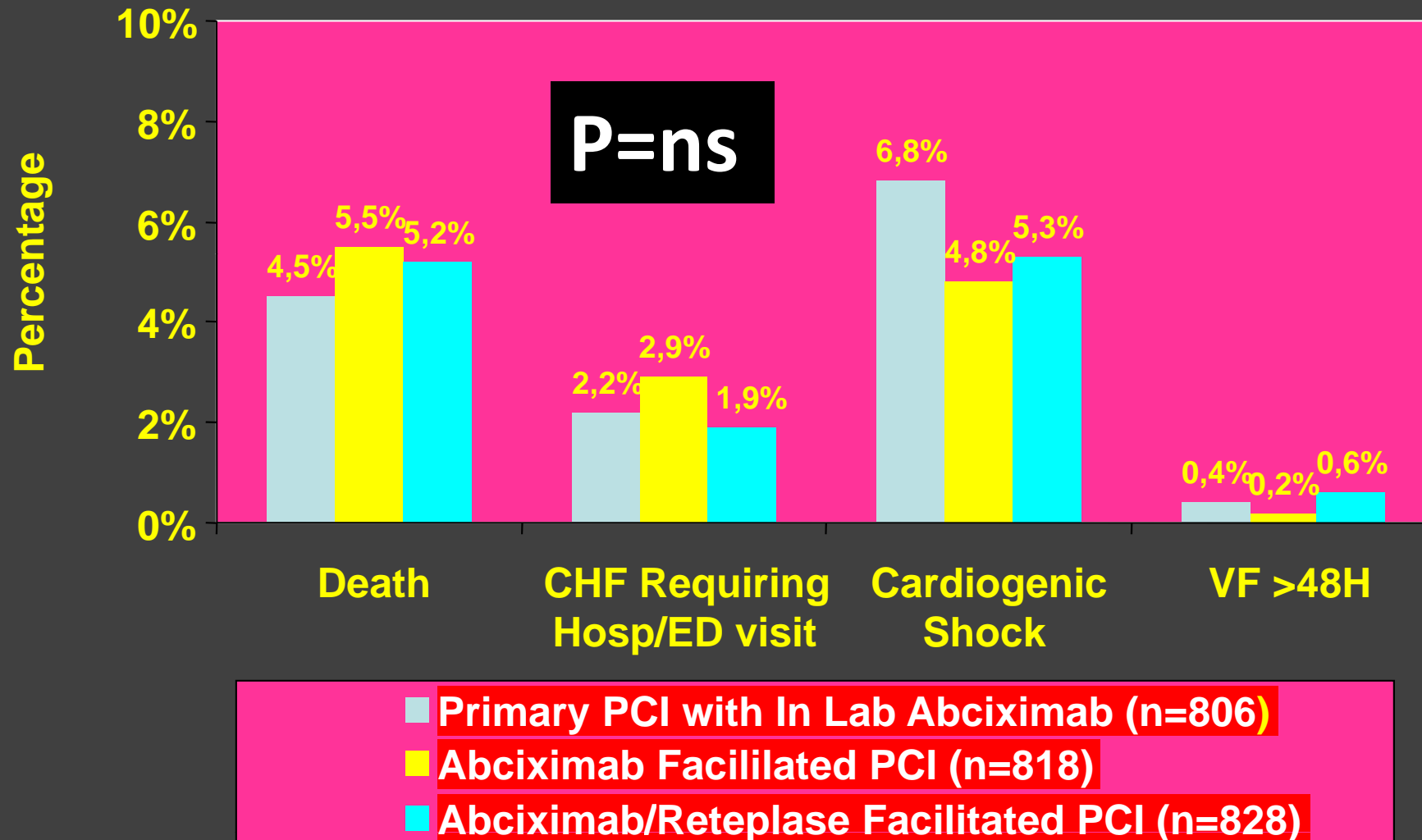
# FINESSE: Study Design

Acute ST Elevation MI (or New LBBB) within 6h pain onset  
Presenting at Hub or Spoke with estimated time to Cath between 1 and 4 hours



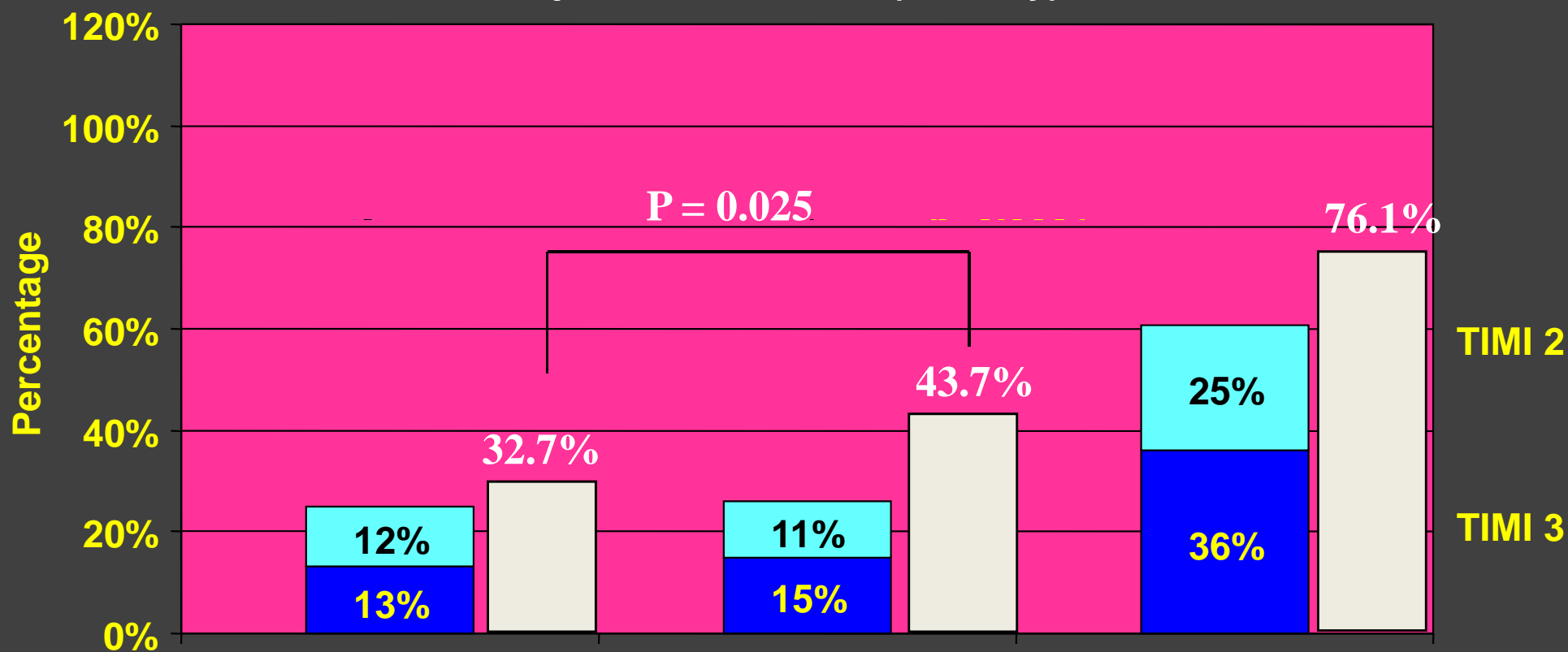
# Primary Endpoint by Components

% Subjects with Event through Day 90



# TIMI Flow in IRA Pre-PCI

% Subjects with TIMI 2/3 (Patency) Pre-PCI



FINESSE-ANGIO.  
Prati F, JACC Interv  
2011

Primary PCI (in lab  
Abciximab) (n=790)

Abciximab Facilitated  
PCI (n=809)

Reteplase/Abciximab  
Facilitated PCI (n=815)

Ave Time from First Abciximab Bolus  
to Angiogram In Facilitated Groups:

74min

76min

Modified ITT Population with Index PCI: ITT, PCI and any dose of study drug (active or placebo); Investigator assessment

# **LIMITATIONS**

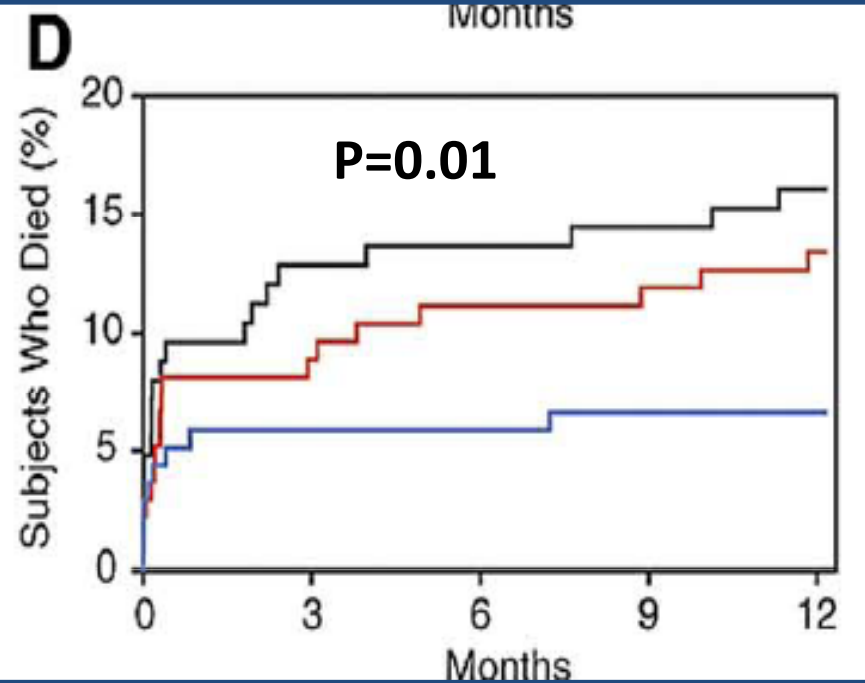
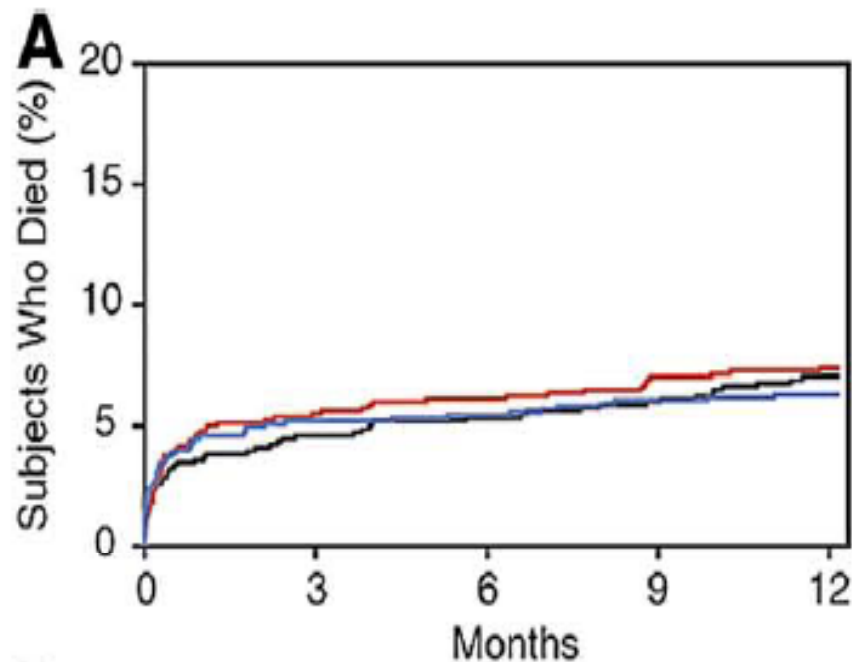
1. About half of the patients enrolled at primary PCI centers
2. Low enrollment rate (around 10 pts/center/year)
3. Probably, too late administration

# FINESSE TRIAL: 1-YEAR SURVIVAL

— Primary PCI  
— Abciximab - Facilitated PCI  
— Reteplase/Abciximab - Facilitated PCI

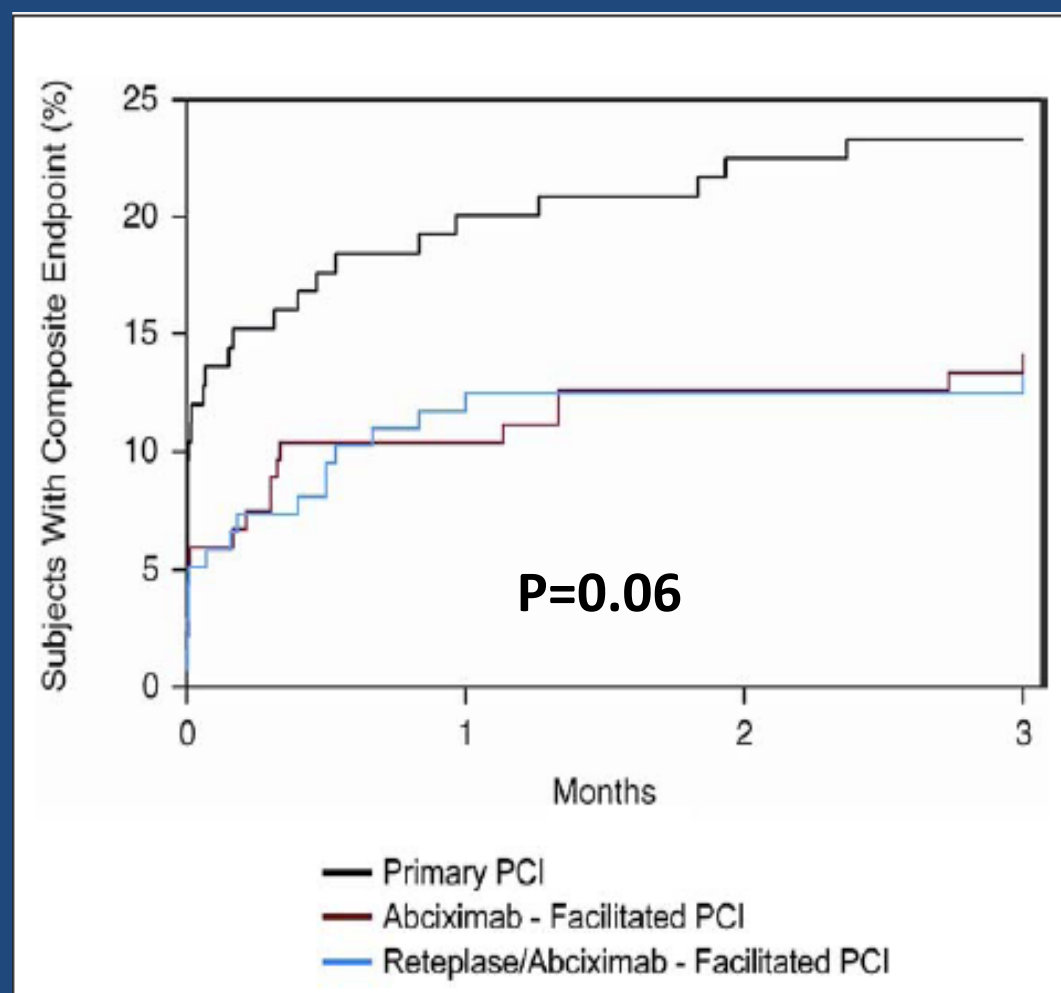
All patients (n = 2452)

Timi Risk Score  $\geq 3$  and spoke  
site randomization, and TTT <  
4h (n = 397)



# FINESSE TRIAL: 1-YEAR FOLLOW-UP

Timi Risk Score  $\geq 3$  and spoke site randomization, and TTT  $< 4$ h (n =397)



# **Upstream Use of GP IIb/IIIa Inhibitors During Primary PCI**

**“There is a wrong perception that GP IIb/IIIa Inhibitors are not beneficial as an adjunctive therapy during PPCI”**

# BRAVE-3: Abciximab on top of 600 mg Clopidogrel

% LV

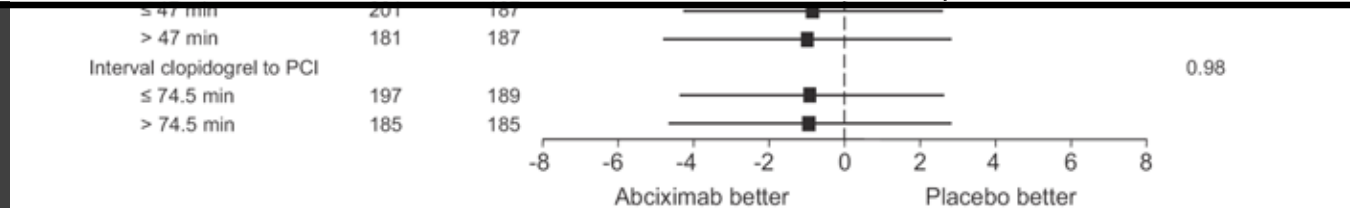
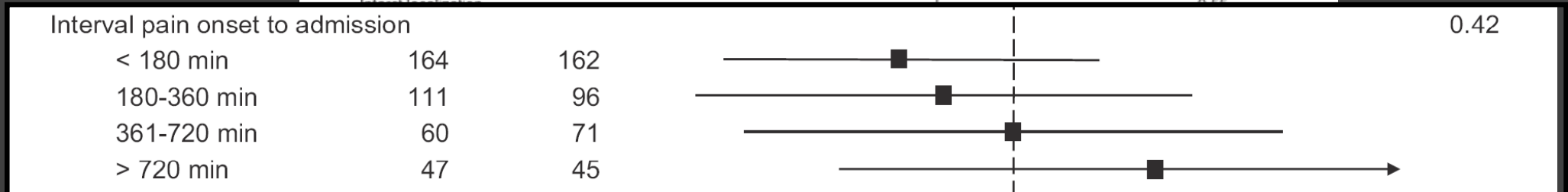
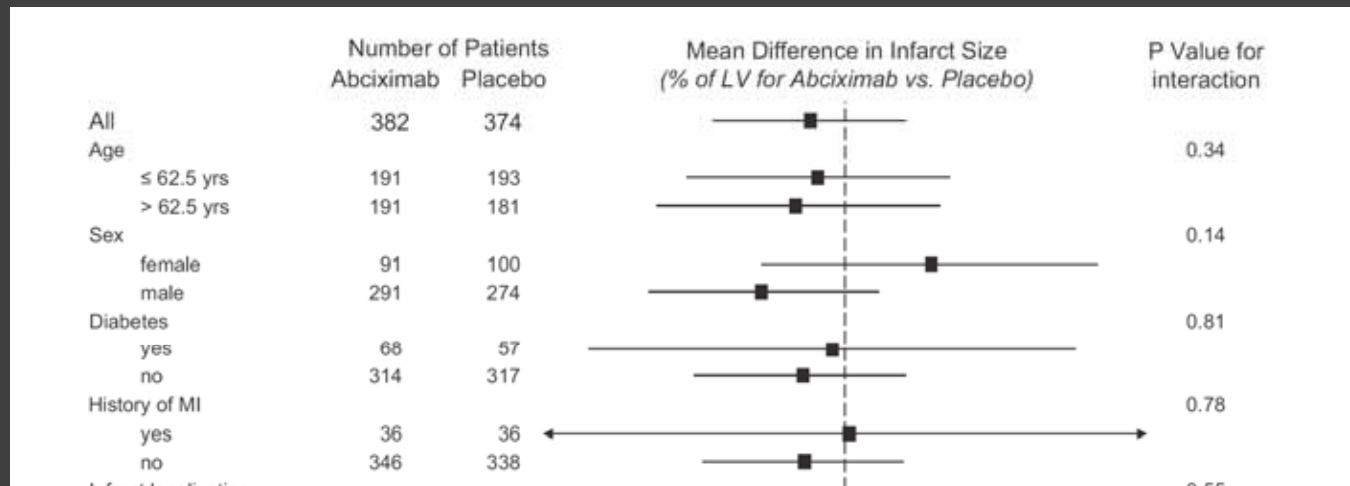
	Median (Interquartile Range), min	
Time Intervals*	Abciximab (n=401)	Placebo (n=399)
Symptom onset to hospital admission	210 (110–420)	216 (110–468)
Symptom onset to study drug	255 (140–465)	260 (135–515)
Symptom onset to PPCI	302 (190–540)	315 (189–585)
Hospital admission to PPCI	78 (59–110)	80 (58–110)
Clopidogrel loading to PPCI	73 (54–104)	75 (53–105)
Clopidogrel loading to study drug	23 (13–41)	21 (12–38)

**>50% pts received drug >4 hour delay**

**>50% pts received PPCI >5 hour delay**

# BRAVE-3: Abciximab on top of 600 mg Clopidogrel

## TIME Matters even in Munich !!

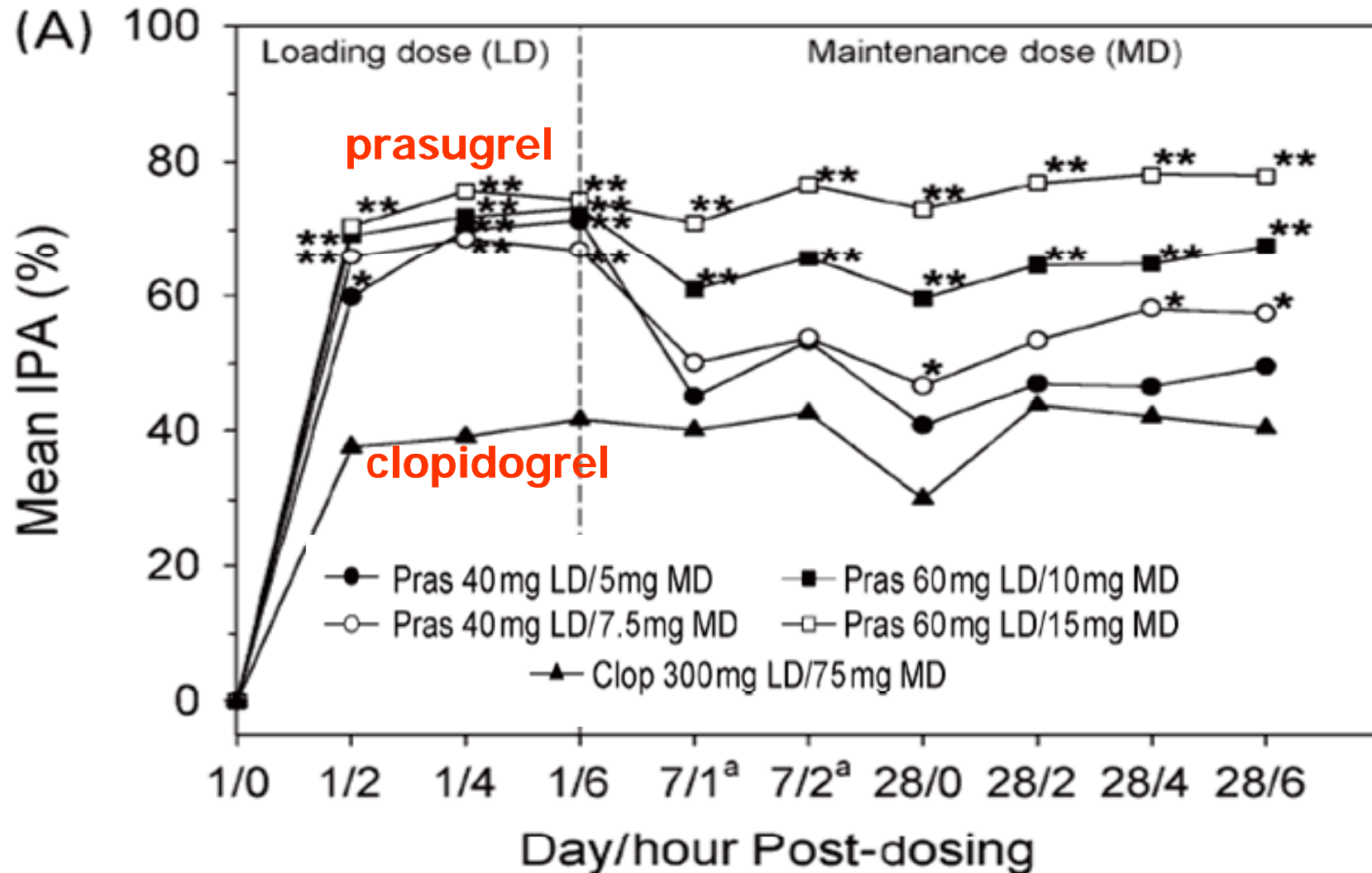


# Periprocedural anti thrombotic medication in primary PCI

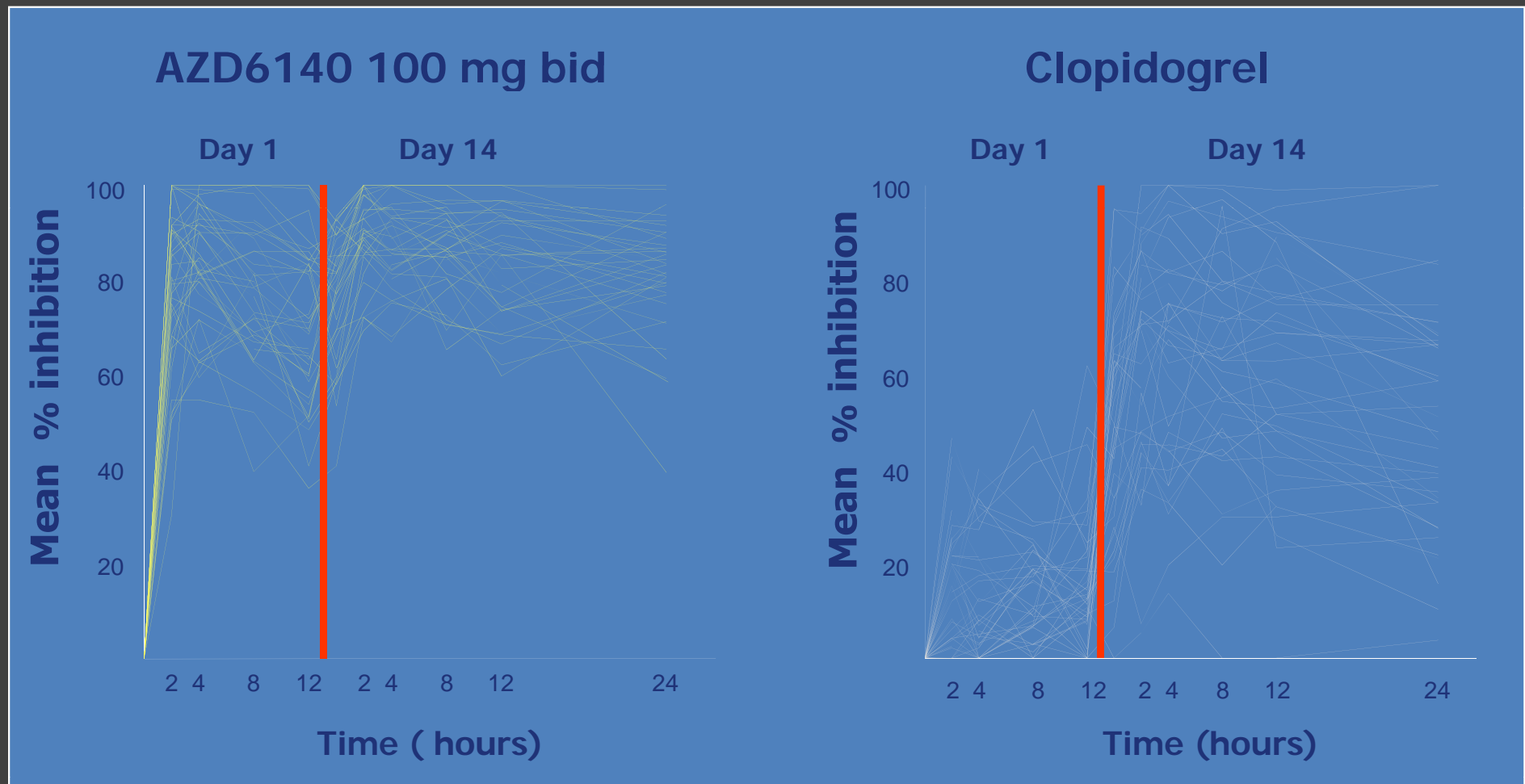
Recommendations	Class	Level
<b>Antiplatelet therapy</b>		
Aspirin oral or i.v. (if unable to swallow) is recommended	I	B
An ADP-receptor blocker is recommended in addition to aspirin. Options are:	I	A
<ul style="list-style-type: none"><li>• Prasugrel in clopidogrel-naïve patients, if no history of prior stroke/TIA, age &lt; 75 years.</li></ul>	I	B
<ul style="list-style-type: none"><li>• Ticagrelor.</li></ul>	I	B
<ul style="list-style-type: none"><li>• Clopidogrel, preferably when prasugrel or ticagrelor are either not available or contraindicated.</li></ul>	I	C

ADP = adenosine diphosphate.

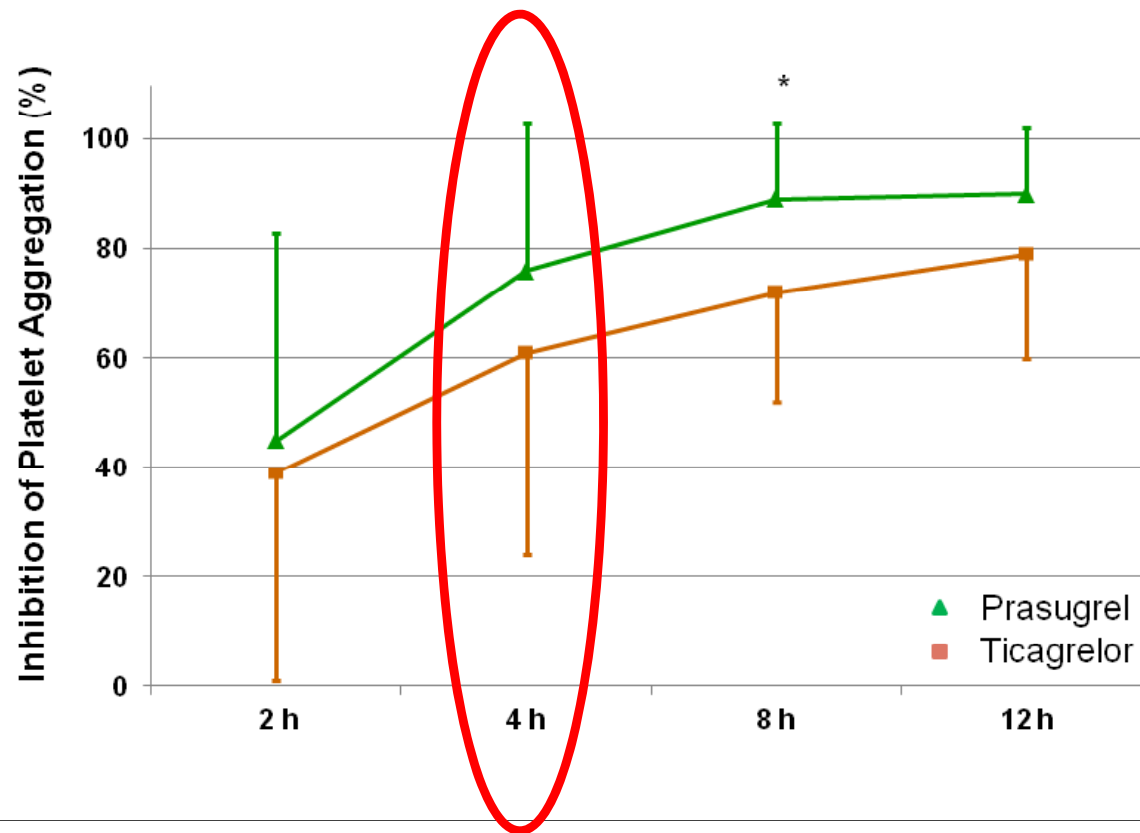
# Prasugrel: faster and more powerful



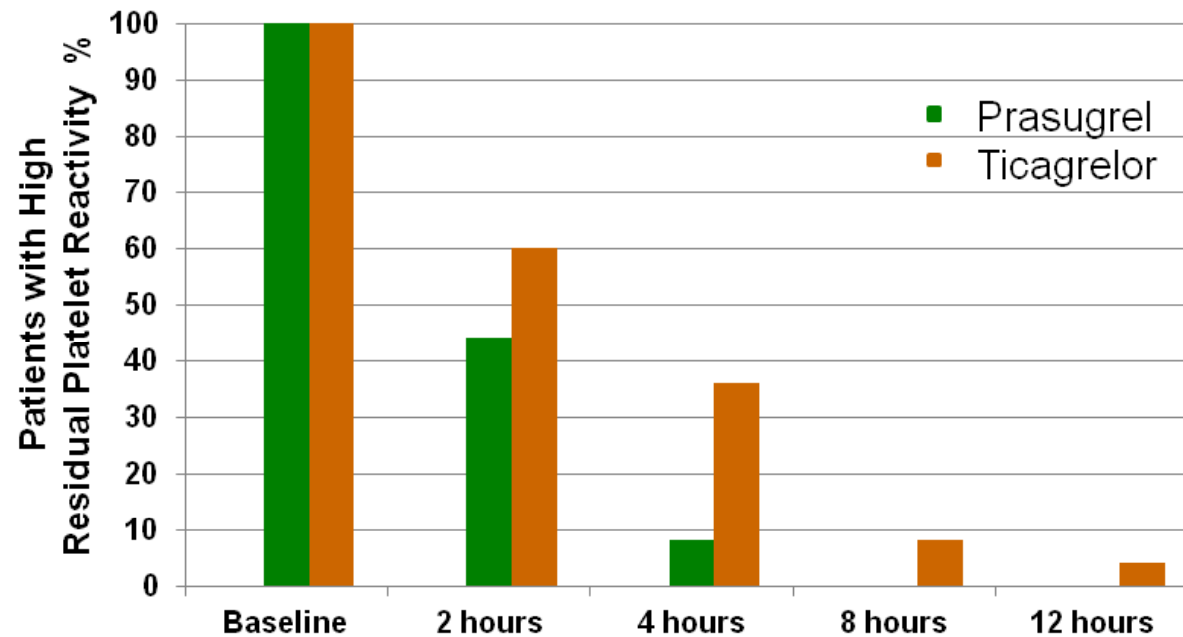
# Ticagrelor: DISPERSE trial



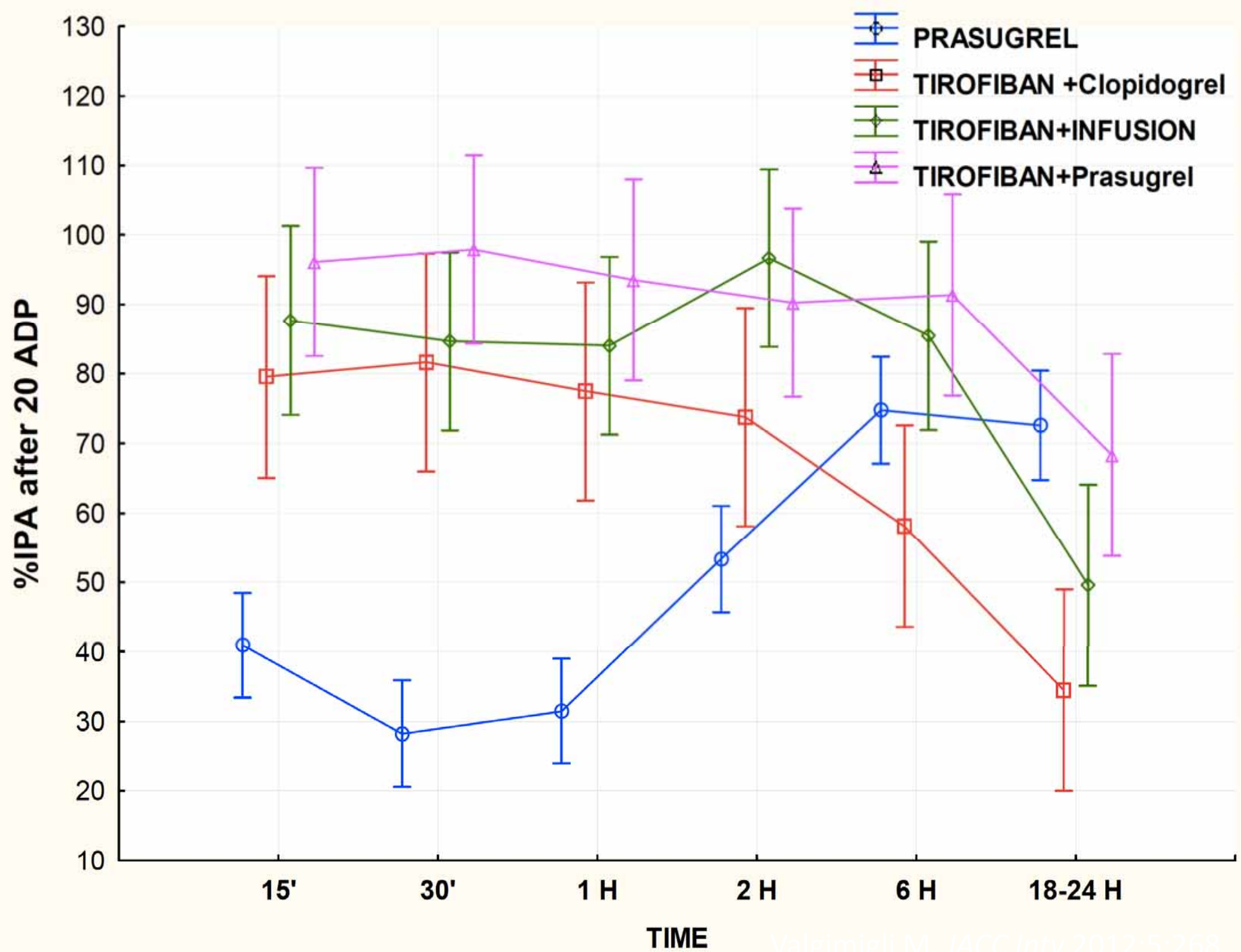
# Inhibition of Platelet Aggregation over Time



# % of Patients with HRPR



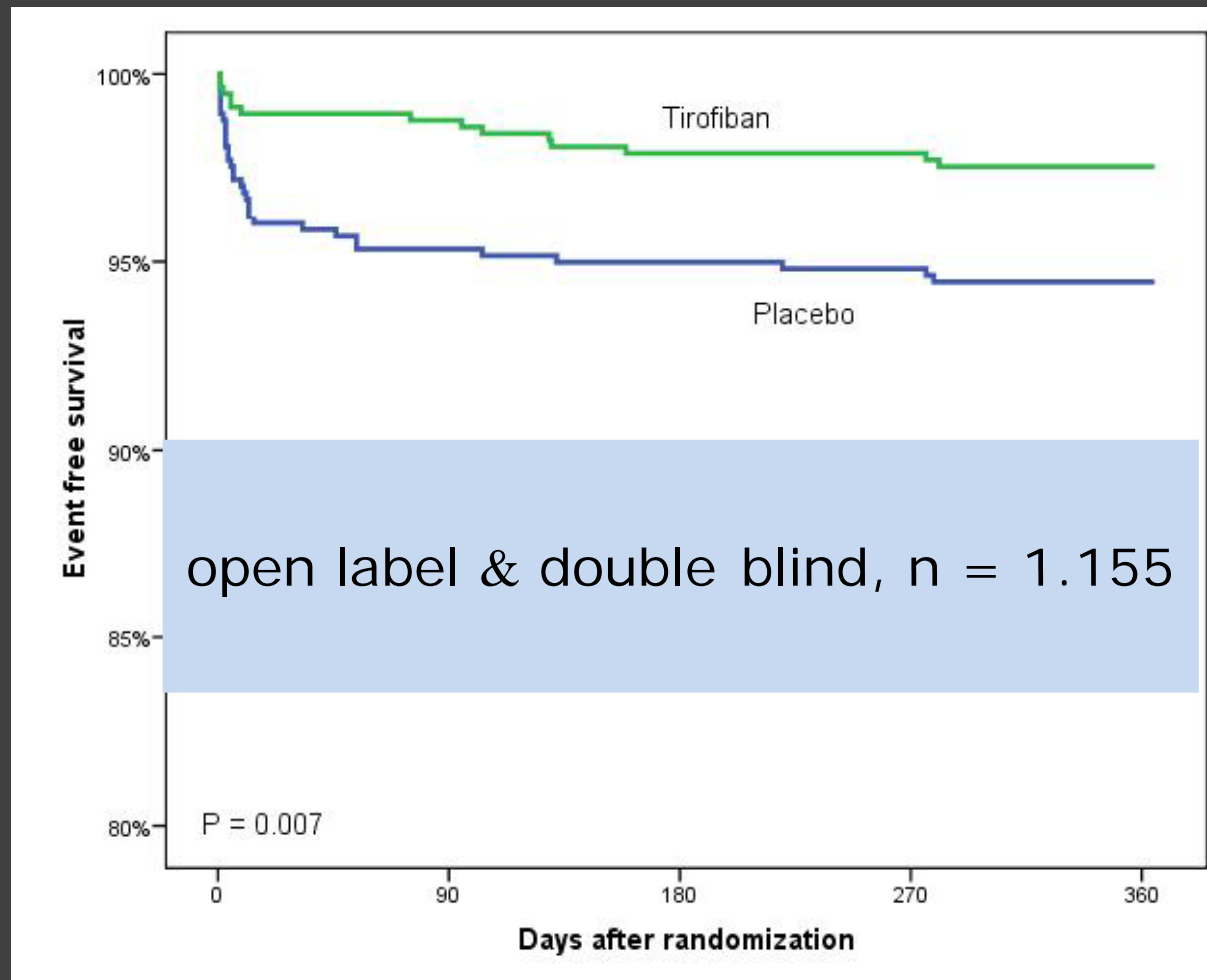
Parodi G, *JACC* 2013 in press



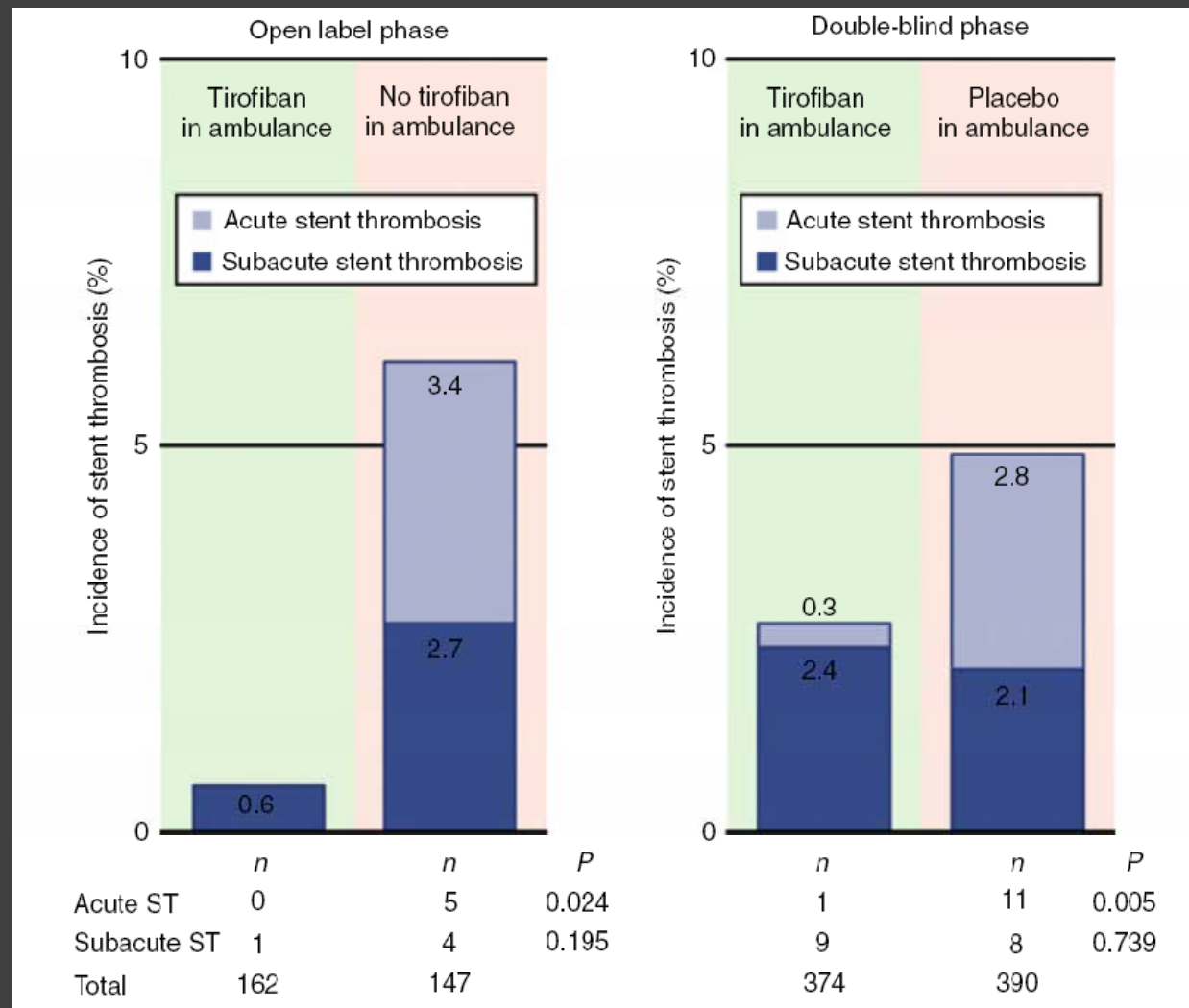
# On-TIME 2

## Pre Hospital Initiation of Tirofiban on top of Clopidogrel

1-year Survival in Patients with Primary PCI



# Reduction of early stent thrombosis with pre-Hospital high-dose tirofiban in STEMI



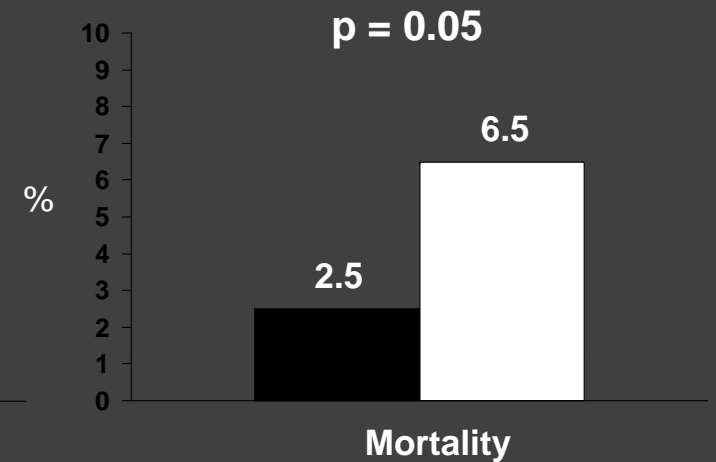
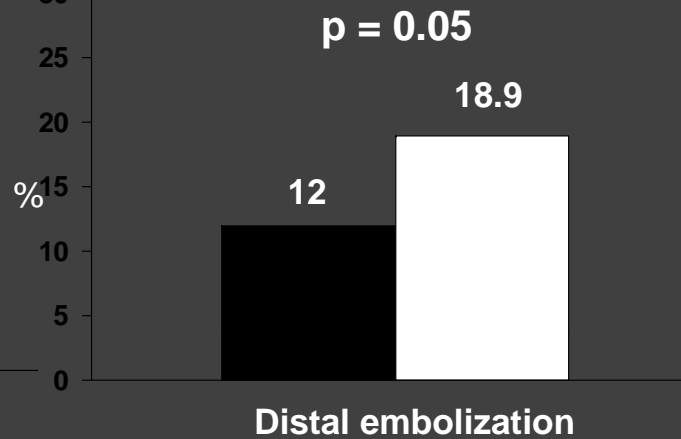
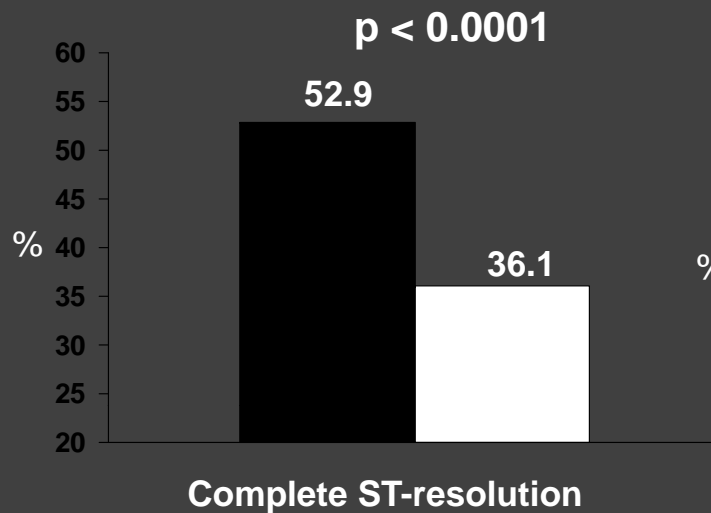
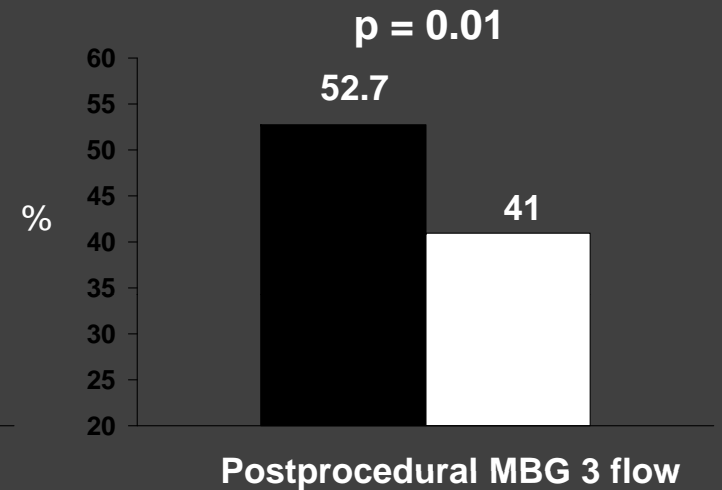
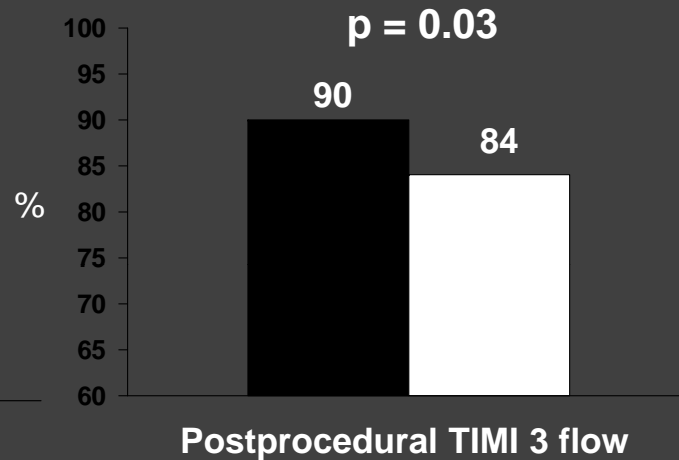
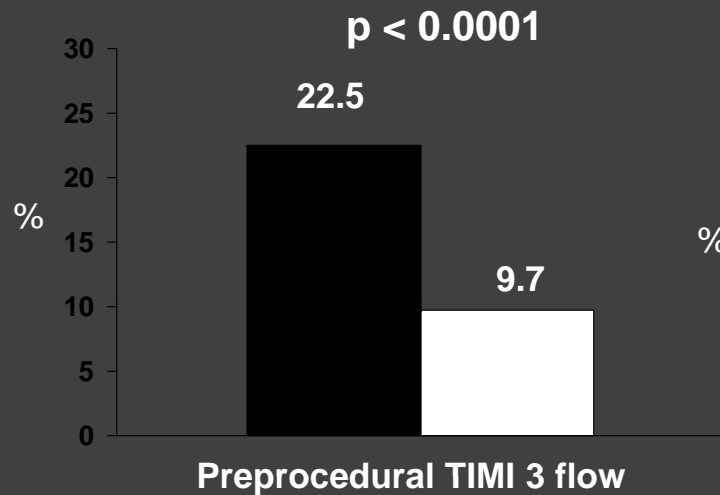
# EGYPT - ALT



Early abciximab

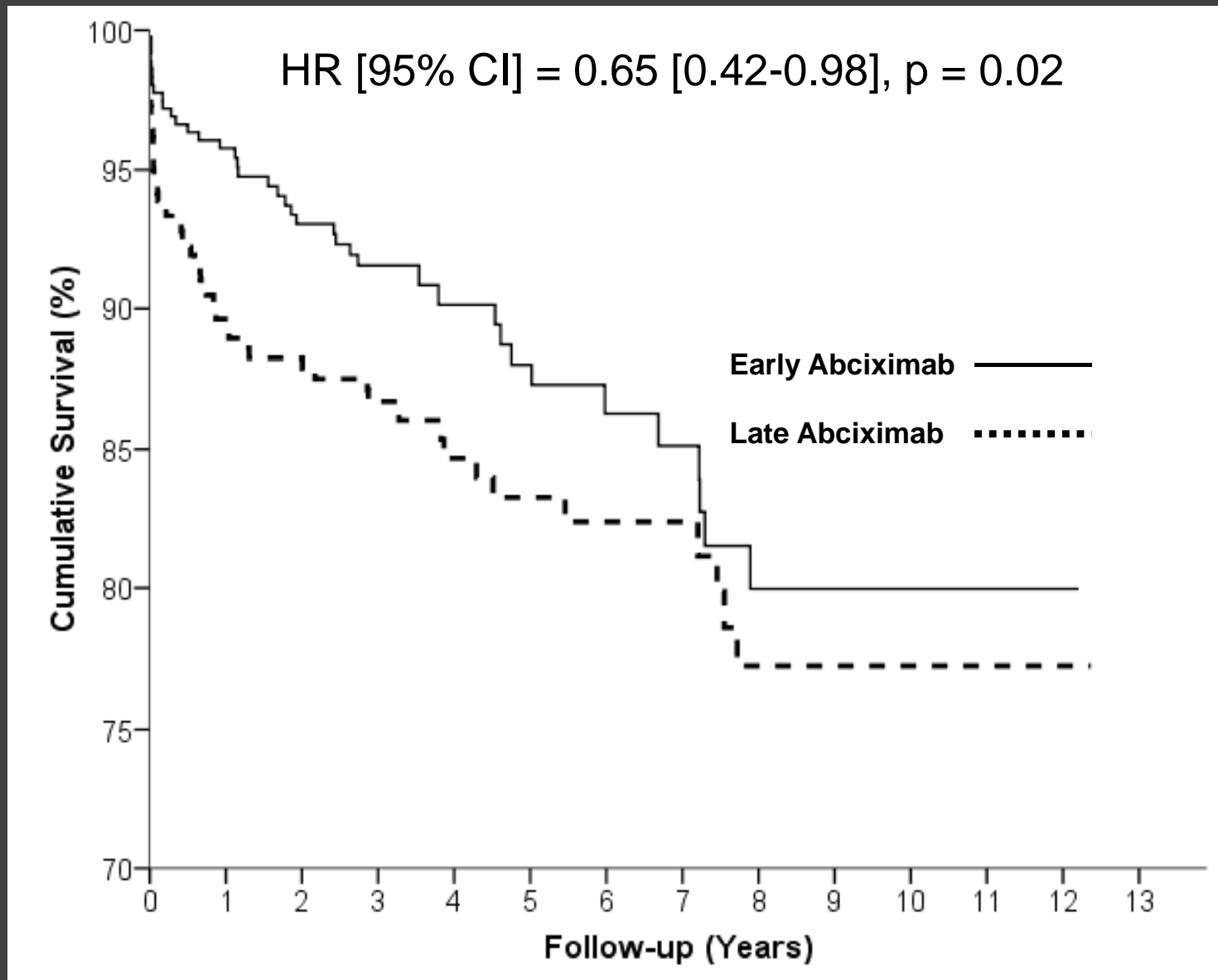


Late abciximab



# EGYPT-ALT

## Survival at Follow-Up



# Upstream Use of GP IIb/IIIa Inhibitors *in Patients with STEMI*

**Who benefit the most?**

# Emilia Romagna REGISTRY



European Heart Journal (2009) 30, 33–43  
doi:10.1093/eurheartj/ehn480

## CLINICAL RESEARCH

*Interventional cardiology and angiology*

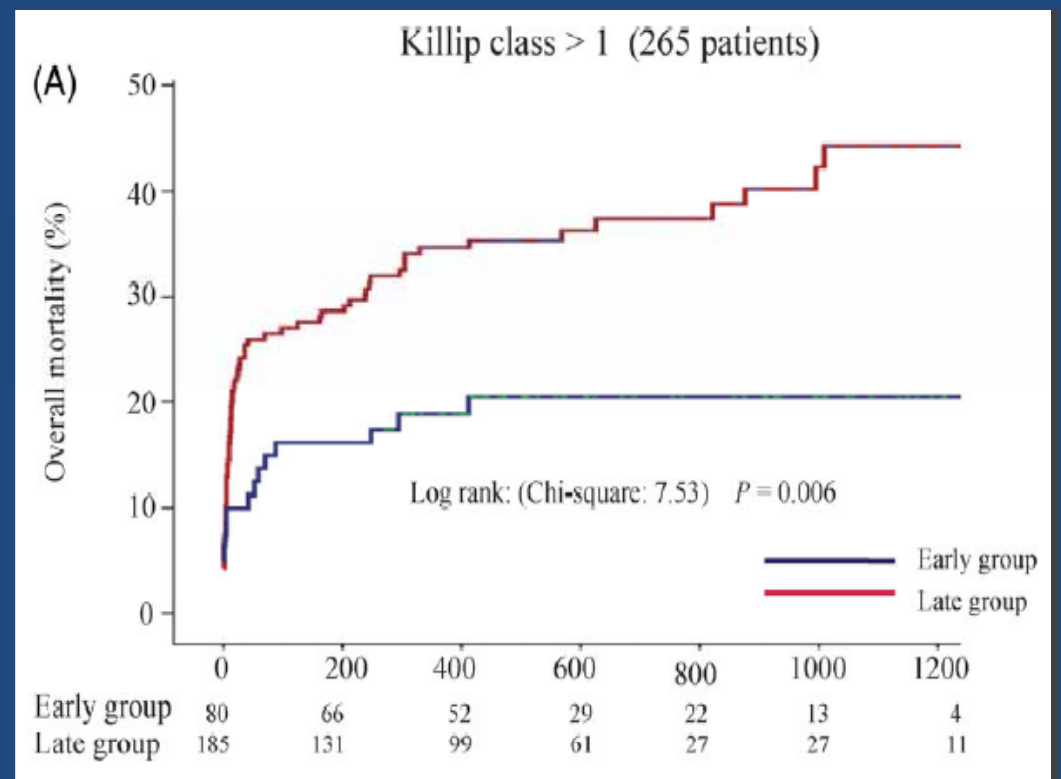
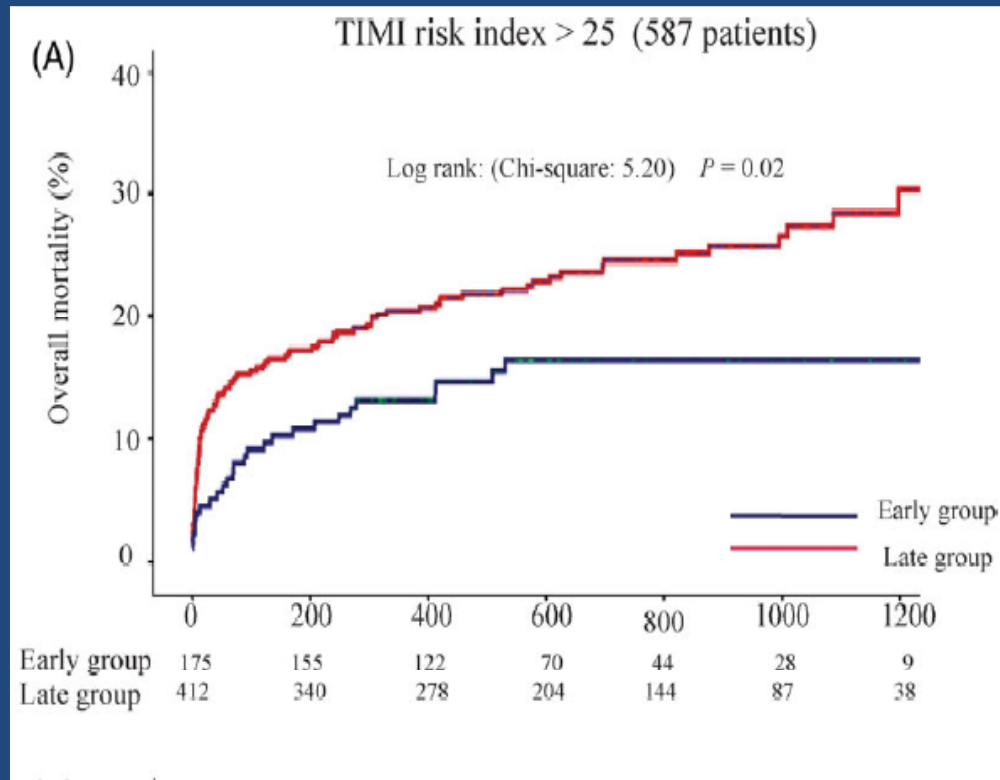
### Long-term effectiveness of early administration of glycoprotein IIb/IIIa agents to real-world patients undergoing primary percutaneous interventions: results of a registry study in an ST-elevation myocardial infarction network

Paolo Ortolani<sup>1\*</sup>, Antonio Marzocchi<sup>1</sup>, Cinzia Marrozzini<sup>1</sup>, Tullio Palmerini<sup>1</sup>, Francesco Saia<sup>1</sup>, Nevio Taglieri<sup>1</sup>, Federica Baldazzi<sup>1</sup>, Gianni Dall'Ara<sup>1</sup>, Paola Nardini<sup>1</sup>, Silvia Gianstefani<sup>1</sup>, Paolo Guastaroba<sup>2</sup>, Roberto Grilli<sup>2</sup>, and Angelo Branzi<sup>1</sup>

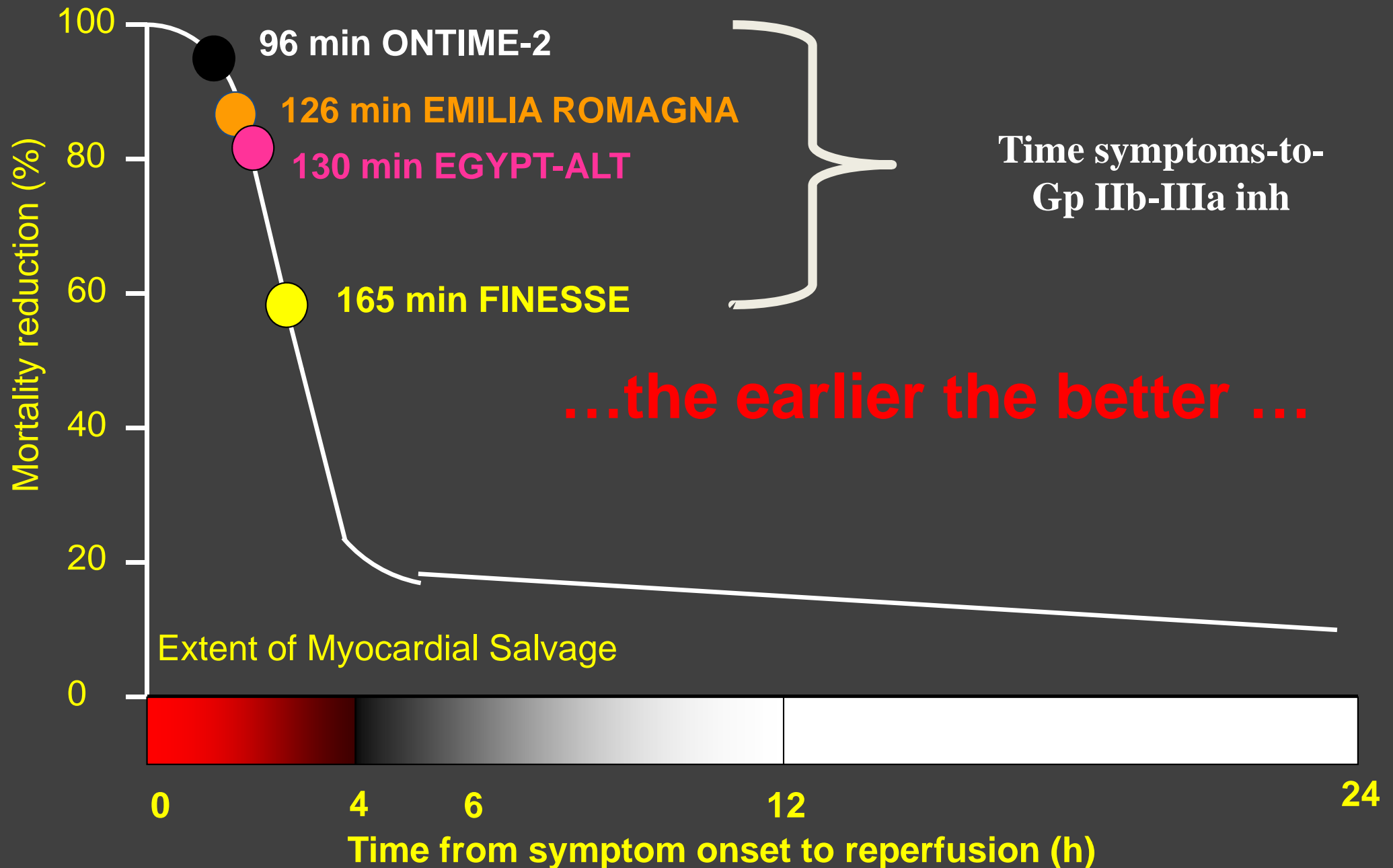
#### In-hospital clinical adverse events according to IIb/IIIa treatment strategy

	Early Group (n = 380)	Late Group (n = 744)	OR	95% CI	P-value
All-cause mortality [n (%)]	16 (4)	53 (7)	0.57	0.32–1.02	0.07
Recurrent myocardial infarction [n (%)]	5 (1)	3 (0.4)	1.81	0.78–13.85	0.18
Target vessel revascularization, [n (%)]	7 (2)	5 (0.7)	2.77	0.87–8.79	0.13
Stroke [n (%)]	0	5 (0.7)	NA	NA	0.26
Major bleeding <sup>a</sup> [n (%)]	4 (1)	17 (2)	0.45	0.15–1.36	0.23
In-hospital events <sup>b</sup> [n (%)]	26 (7)	72 (10)	0.68	0.43–1.09	0.14

# Emilia Romagna REGISTRY

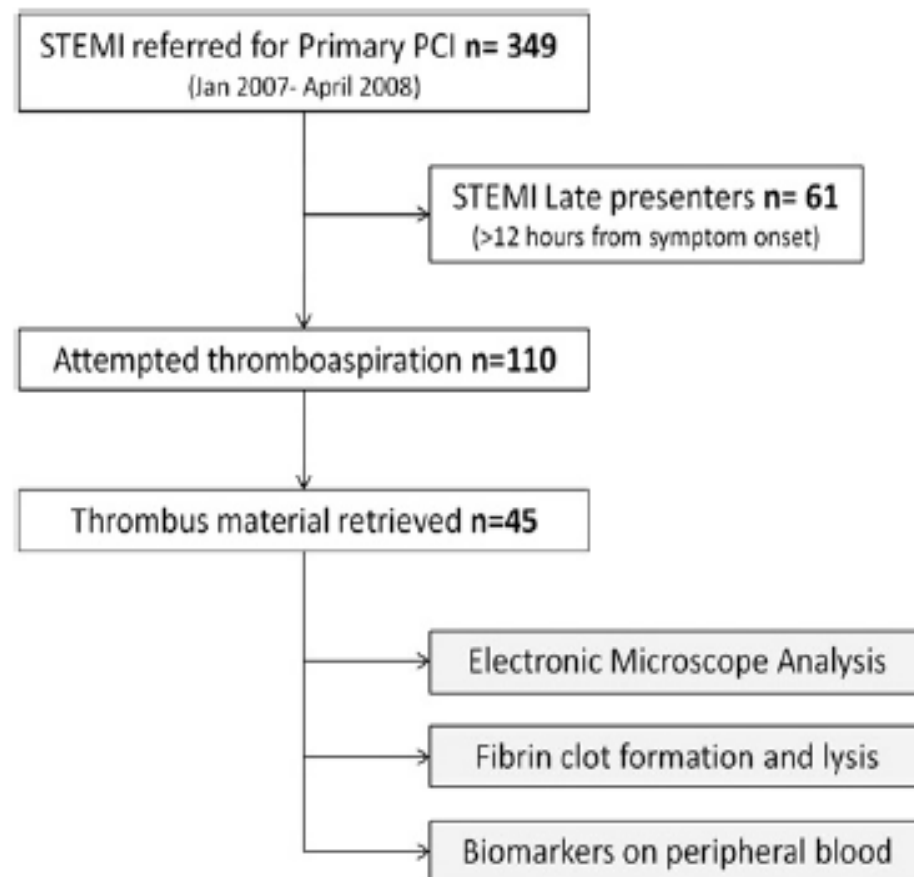


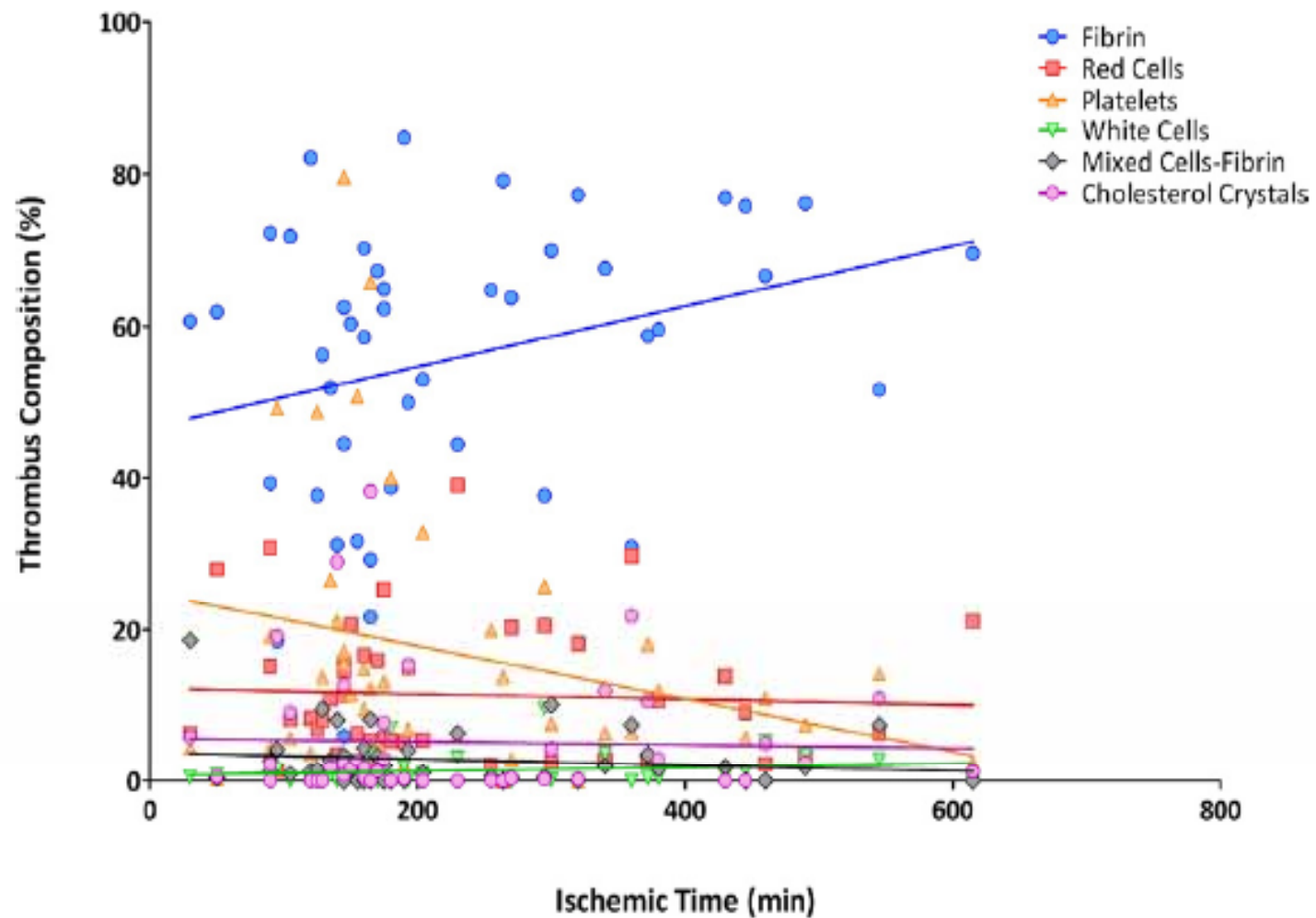
# Time-to-treatment and myocardial salvage



# Composition of Coronary Thrombus in Acute Myocardial Infarction

Johanne Silvain, MD, PhD,\* Jean-Philippe Collet, MD, PhD,\* Chandrasekaran Nagaswami, MD,†  
Farzin Beygui, MD, PhD,\* Kathryn E. Edmondson, PhD,† Anne Bellemain-Appaix, MD,\*  
Guillaume Cayla, MD,\* Ana Pena, PhD,\* Delphine Brugier, PhD,\* Olivier Barthelemy, MD,\*  
Gilles Montalescot, MD, PhD,\* John W. Weisel, PhD†





Evolution of the Percentage Thrombus Composition for Each Component

# CONCLUSIONS

Even in the era of new oral antiplatelet therapies, the rapid onset of action and high power in platelet aggregation inhibition of Gp IIb-IIIa inhibitors make an early administration of these drugs **a key point** in mechanical reperfusion for STEMI, especially when administrated in the early phase of STEMI, among high risk patients and those undergoing transfer