Pre-hospital antiplatelet and anticoagulant regimes for STEMI

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DISCLOSURE

Dr. Bueno reports having received research grants from Astra-Zeneca and consulting/speaking fees from Astra-Zeneca, Bayer Healthcare, Daichii-Sankyo, Eli-Lilly, and Novartis.

Contemporary pre-hospital management of ACS patients
Results from the EPICOR study

Table 2. Pre-hospital therapies (% patients)

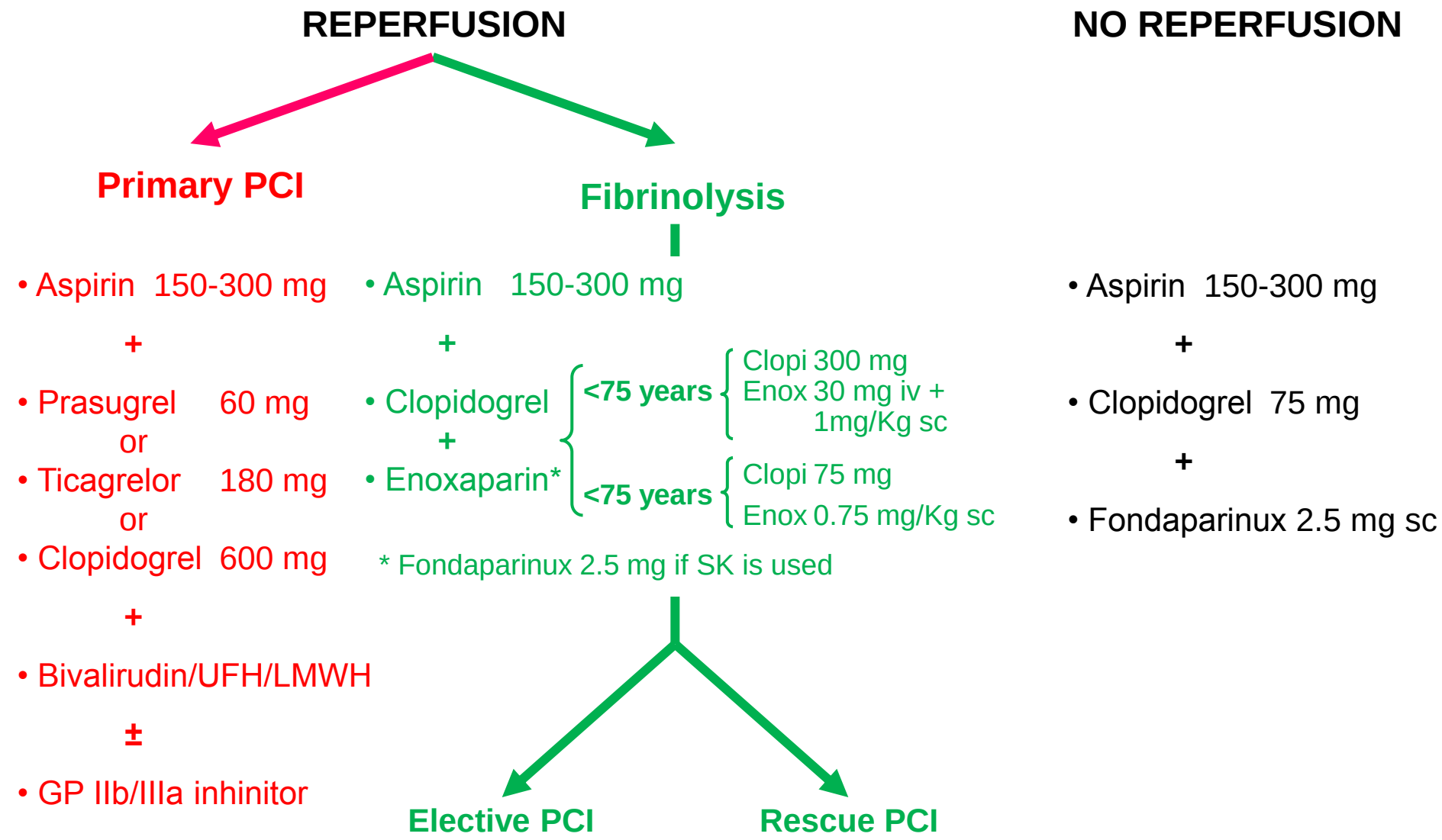
	All (N=10,568)	STEMI (N=4943)	NSTE ACS (N=5625)
Thrombolytic	1.1	2.2	0.1
Aspirin	20	26	14
Clopidogrel	8	13	4
Prasugrel	0.4	0.8	0.1
Glycoprotein IIb/IIIa inhibitor	0.3	0.5	0.1
Unfractionated heparin	6	10	3
Low molecular weight heparin	2.7	3.8	1.6
Bivalirudin	0	0	0

Table 4. Therapies per pre-hospital ECG (% patients)

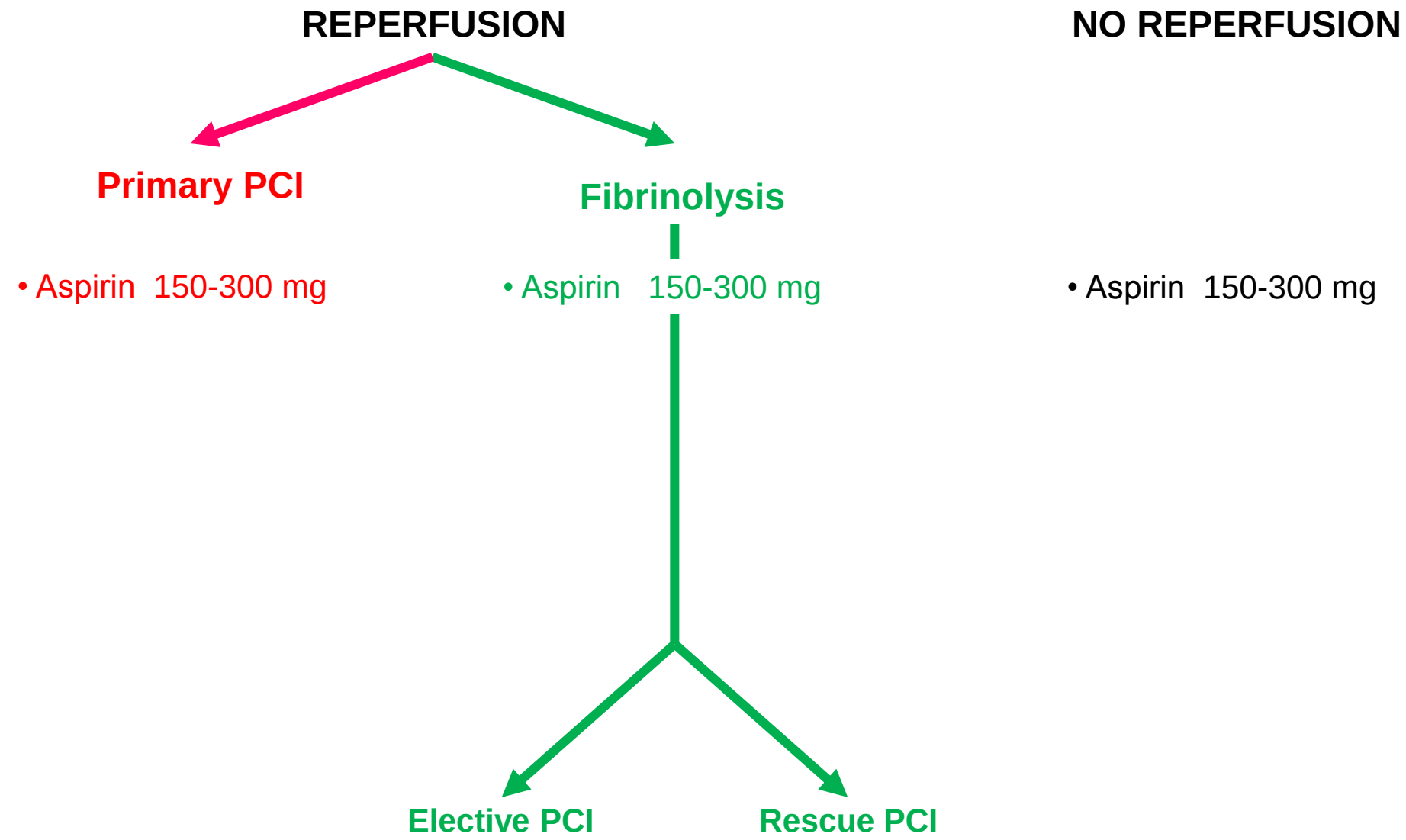
	All (N=10,568)	STEMI (N=4943)	NSTE ACS (N=5625)
Patients with pre-hospital ECG (%)	40	45	36
Aspirin pre-hospital (% of pts with pre-hospital ECG)	38	48	27
Clopidogrel	17	26	8
Prasugrel	0.9	1.5	0.3
Abciximab	0.4	0.8	0.0
Patients without pre-hospital ECG	60	55	64
Aspirin pre-hospital (% of pts without pre-hospital ECG)	7	8	7
Clopidogrel	2	3	1
Prasugrel	0.1	0.3	0.0
Abciximab	0.0	0.0	0.0

Sinnaeve PR. ESC 2012

Initial antithrombotic therapy in patients with STEMI



Pre-hospital antithrombotic therapy in patients with STEMI



Pre-hospital antithrombotic therapy in patients with STEMI

REPERFUSION

NO REPERFUSION

- Aspirin 150-300 mg

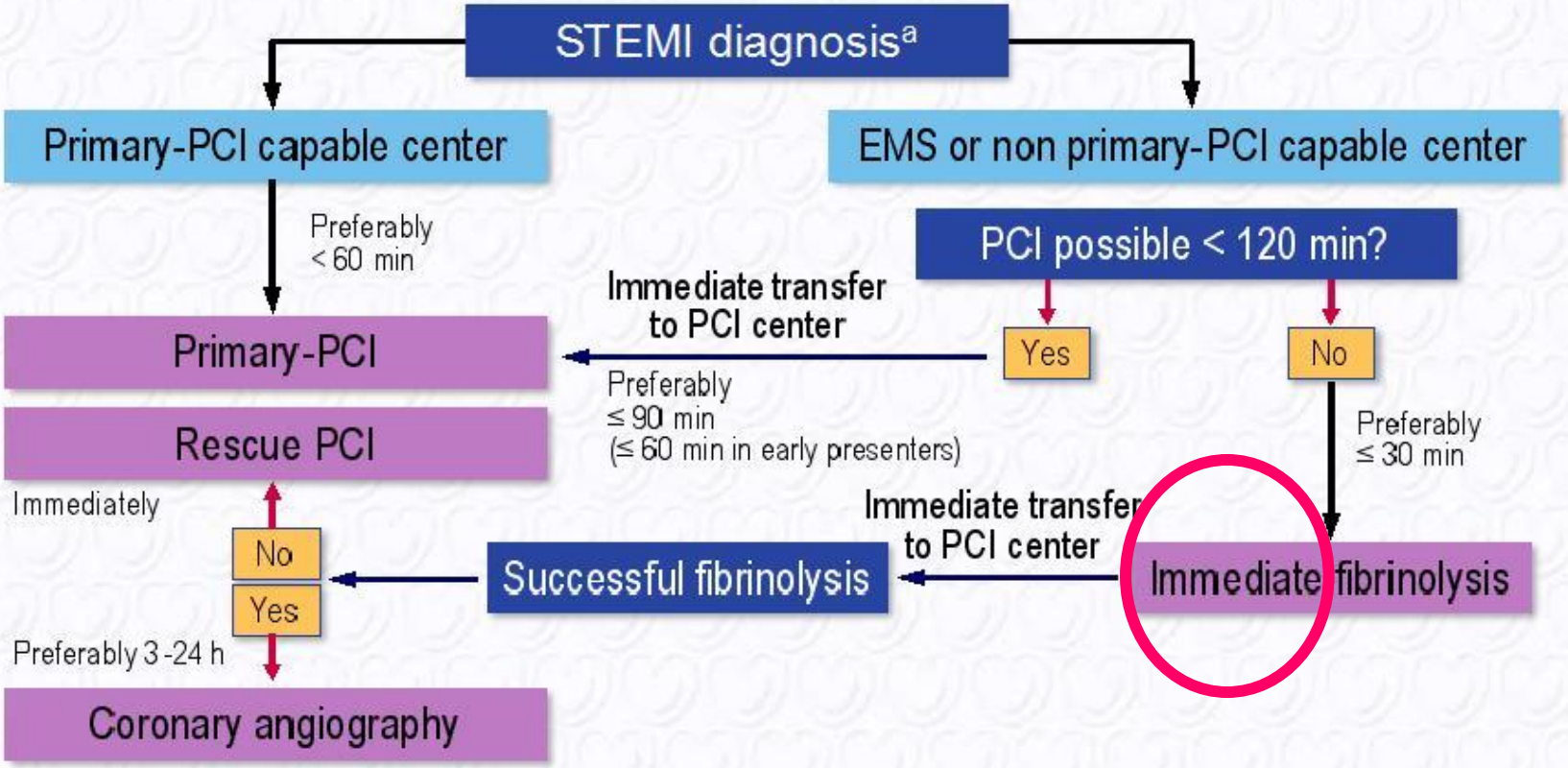
+

- Clopidogrel 75 mg

+

- Fondaparinux 2.5 mg sc

Prehospital and in-hospital management, and reperfusion strategies within 24 h of FMC



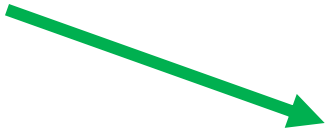
[a] The time point the diagnosis is confirmed with patient history and ECG ideally within 10 min from the first medical contact (FMC). All delays are related to FMC (first medical contact).

Cath = catheterization laboratory; EMS = emergency medical system; FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

European Heart Journal (2012) 33, 2569–2619
doi:10.1093/eurheartj/ehs215

Pre-hospital antithrombotic therapy in patients with STEMI

REPERFUSION



Fibrinolysis

- Aspirin 150-300 mg

+

- Clopidogrel
  - **<75 years**: Clopi 300 mg; Enox 30 mg iv + 1mg/Kg sc

+

- Enoxaparin*
  - **<75 years**: Clopi 75 mg; Enox 0.75 mg/Kg sc

* Fondaparinux 2.5 mg if SK is used

Pre-hospital antithrombotic therapy in patients with STEMI

REPERFUSION

Primary PCI

- Aspirin 150-300 mg

+

- Prasugrel 60 mg

or

- Ticagrelor 180 mg

or

- Clopidogrel 600 mg

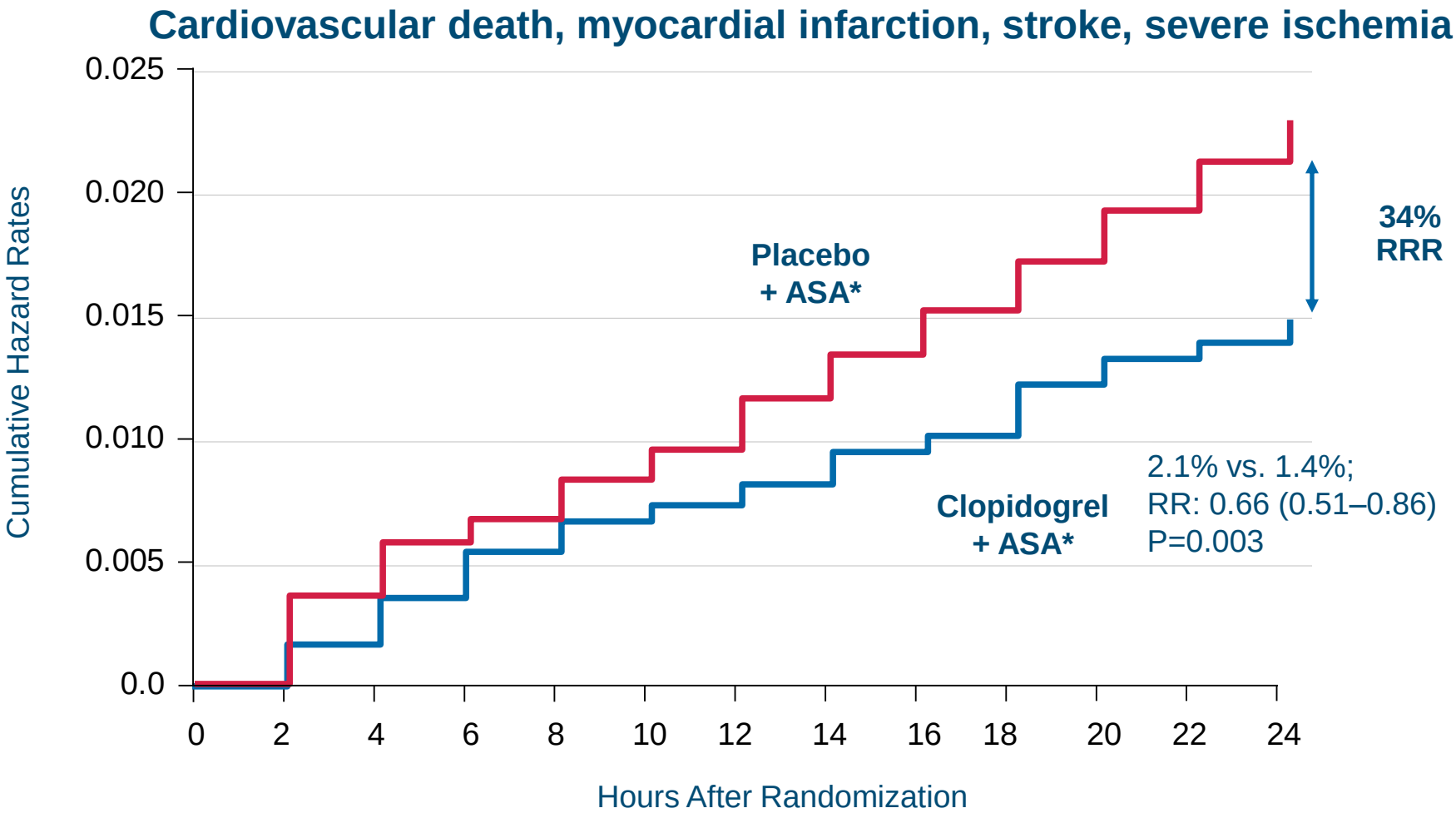
+

- Bivalirudin/UFH/LMWH

±

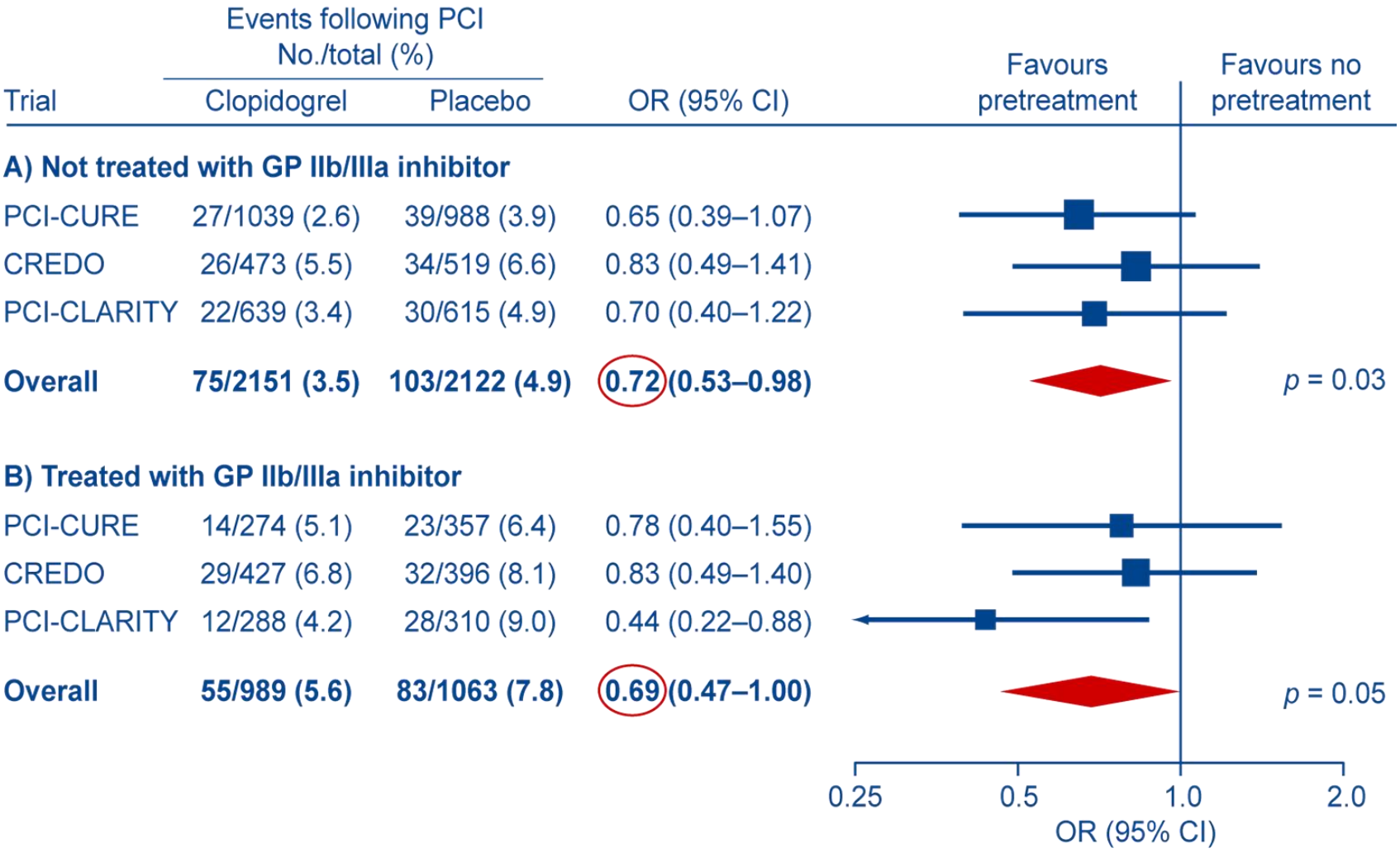
- GP IIb/IIIa inhinitor

CURE: Early effects of clopidogrel on NSTEACS event reduction



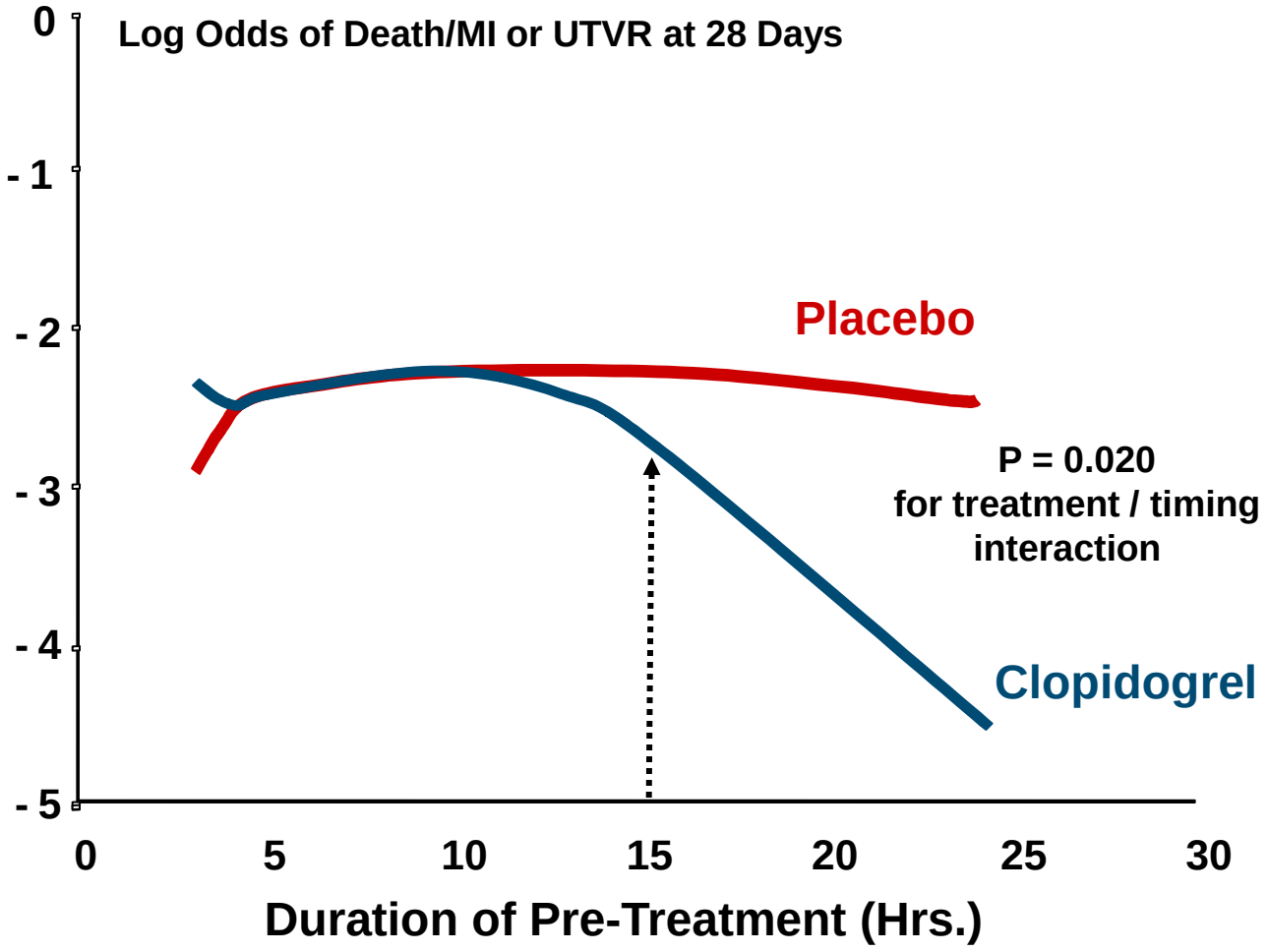
Yusuf S. *Circulation* 2003;107:966–72.

Meta-analysis of Clopidogrel Pretreatment in PCI:
Effect on CV death, MI, or stroke after PCI



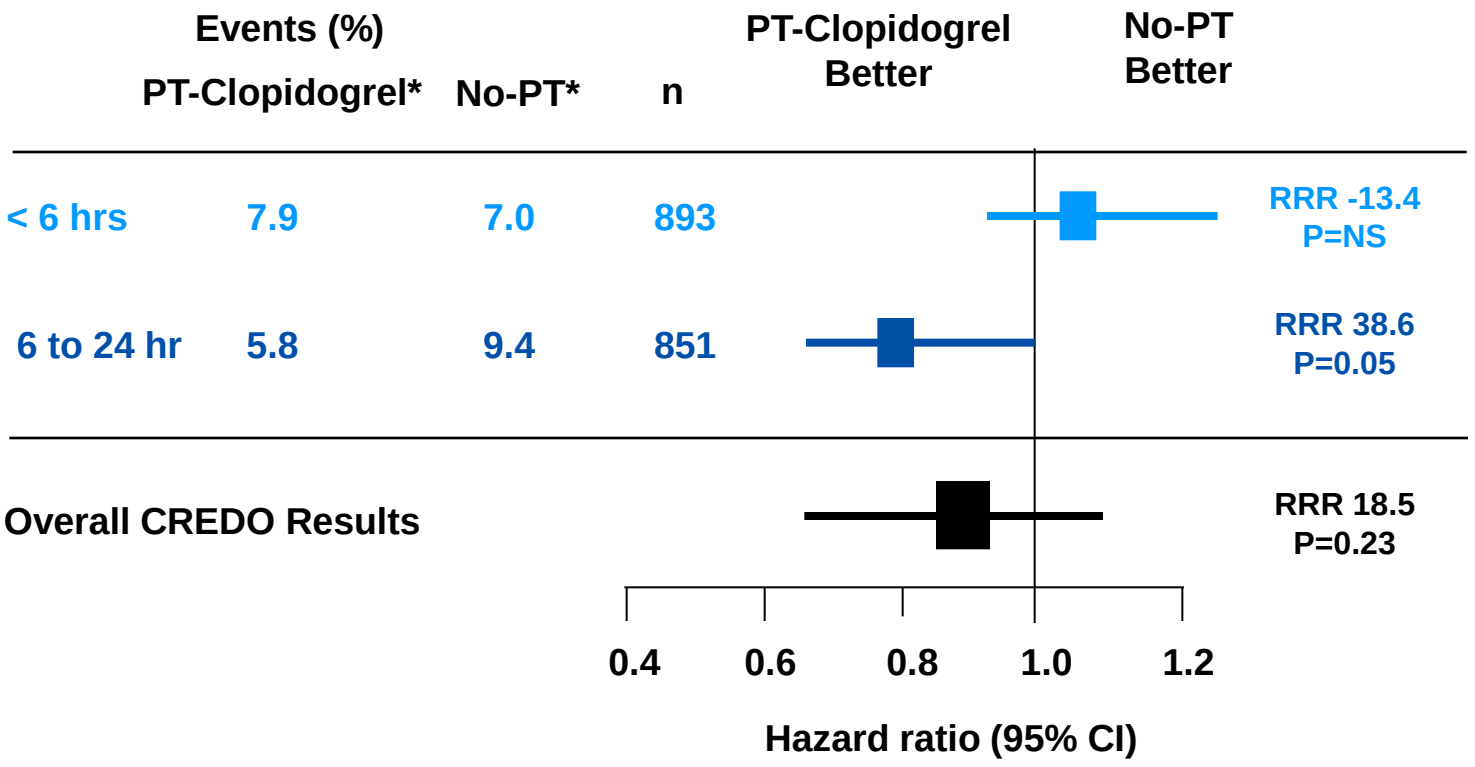
Sabatine MS. *Am Heart J* 2008;155:910–917

CREDO: Effects of loading dose timing of clopidogrel pretreatment on PCI outcomes



Steinhubl SR. *J Am Coll Cardiol*. 2006;4:939-43.

CREDO: Effects of earlier pretreatment with clopidogrel on PCI



Steinhubl SR. *JAMA* 2002;288: 2411–20.

Impact of Pretreatment With Clopidogrel on Initial Patency and Outcome in STEMI Patients Treated With Primary PCI

Table 4 Association of clopidogrel pre-treatment and covariates with in-hospital mortality after primary PCI in multiple logistic regression analyses

Variable	Basic model			Extended model			GP IIb/IIIa co-treatment, yes			GP IIb/IIIa co-treatment, no		
	OR	95% CI	*P*-value	OR	95% CI	*P*-value	OR	95% CI	*P*-value	OR	95% CI	*P*-value
Clopidogrel pre-treatment (yes vs. no)	0.58	0.34–0.96	0.04	0.60	0.35–0.99	0.048	0.40	0.19–0.83	0.01	0.88	0.39–1.95	0.75

Table 3. Effect of Pretreatment With Clopidogrel on Early Reperfusion and Adverse Event Rates in Univariate-Weighted Logistic Regression Analysis

	Unadjusted Treatment Effect		
	OR	95% CI	*P*
TIMI grade 2/3 flow	1.53	1.39–1.68	<0.0001
Mortality	0.52	0.41–0.67	<0.0001
Death/reinfarction	0.50	0.40–0.62	<0.0001

OR is for the occurrence of TIMI grade 2/3 flow, mortality, and death/reinfarction for pretreatment with clopidogrel.

Dörler J. Eur Heart J 2011; 32(23):2954-61.

Vlaar PJ. *Circulation* 2008;118:1828–36.

Impact of Pre-hospital treatment with Clopidogrel on Initial Patency in STEMI Patients Treated With Primary PCI (CIPAMI Trial)

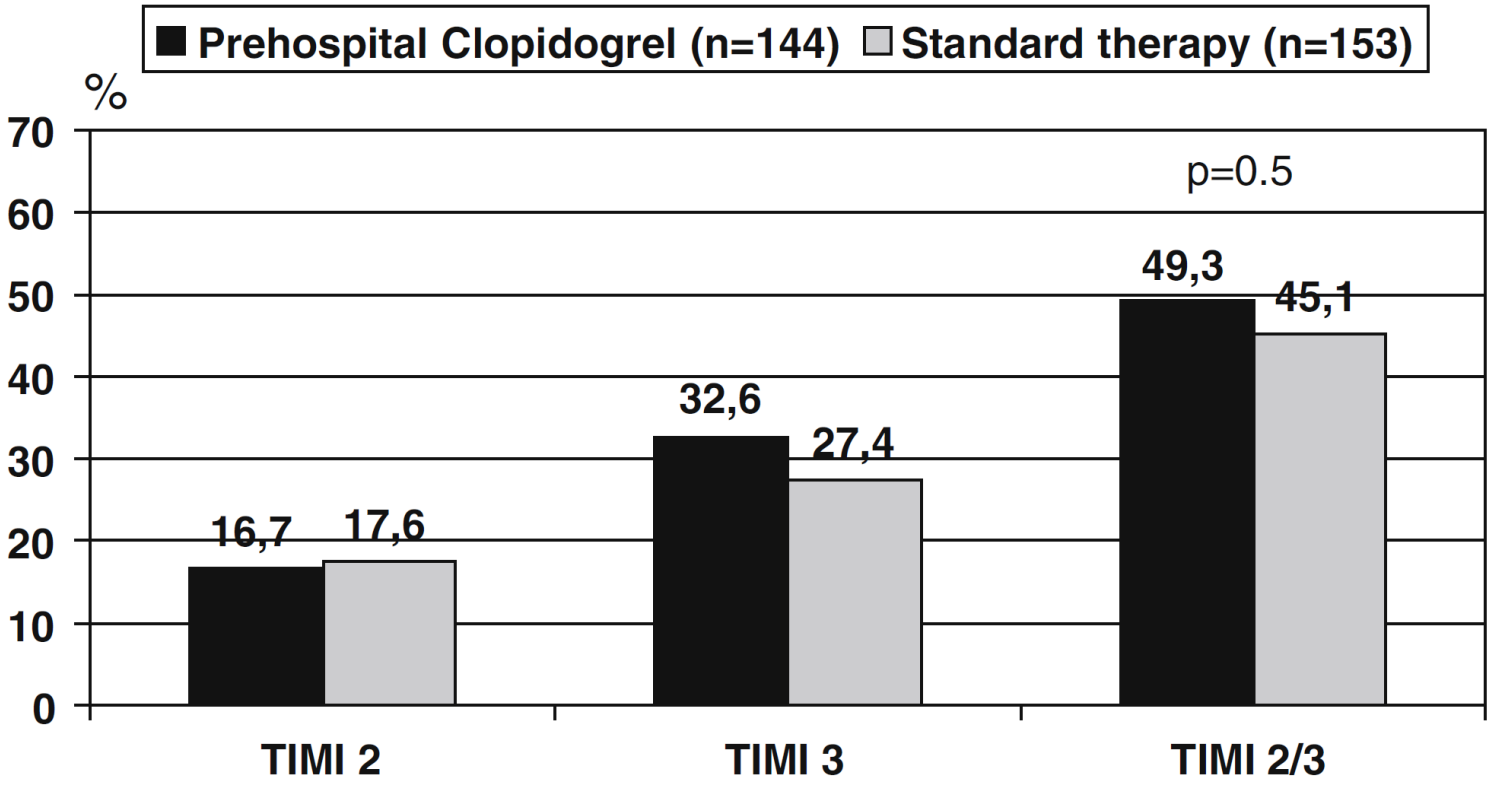


Fig. 2 TIMI patency of the infarct related artery before PCI as assessed by the angiographic core laboratory

Zeymer U. *Clin Res Cardiol* 2012;101:305-312.

Comparison of rapid antiplatelet effect between prasugrel and ticagrelor

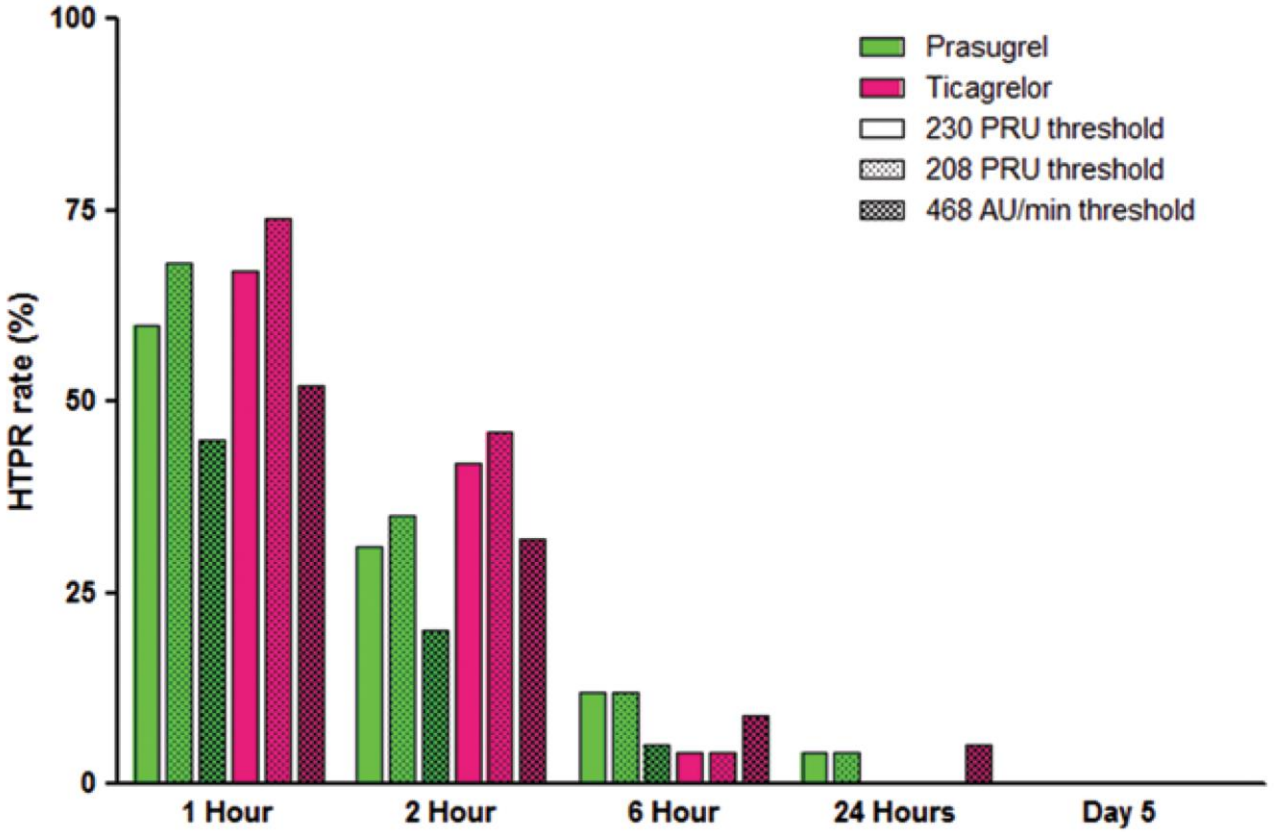
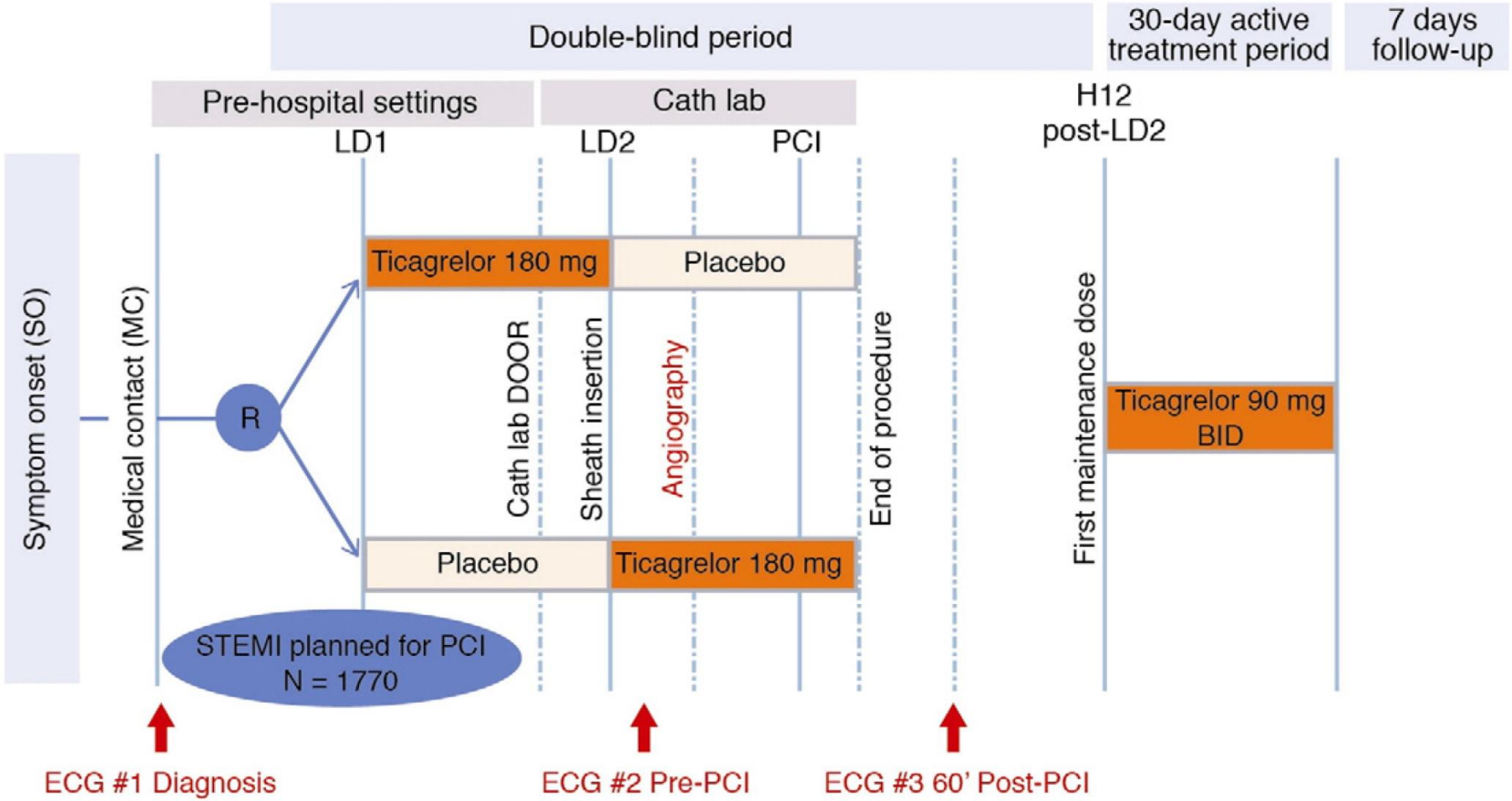


Figure 3. High on-treatment platelet reactivity (HTPR) rates at the different time points of the study in ticagrelor and prasugrel-treated patients according to the method and threshold used. AU indicates aggregation units; PRU, P2Y12 reaction units.

Alexopoulos D. *Circ Cardiovasc Interv* 2012;5;797-804

ATLANTIC Trial

A 30 Day Study to Evaluate Efficacy and Safety of Pre-hospital vs. in-hospital Initiation of Ticagrelor Therapy in STEMI Patients Planned for PCI



ATLANTIC study protocol. H, hour; LD, loading dose; R, randomization.

Montalescot G. *Am Heart J* 2013;165:515-22.

TIROFIBAN BEFORE PRIMARY PCI
(On-time 2 Trial)

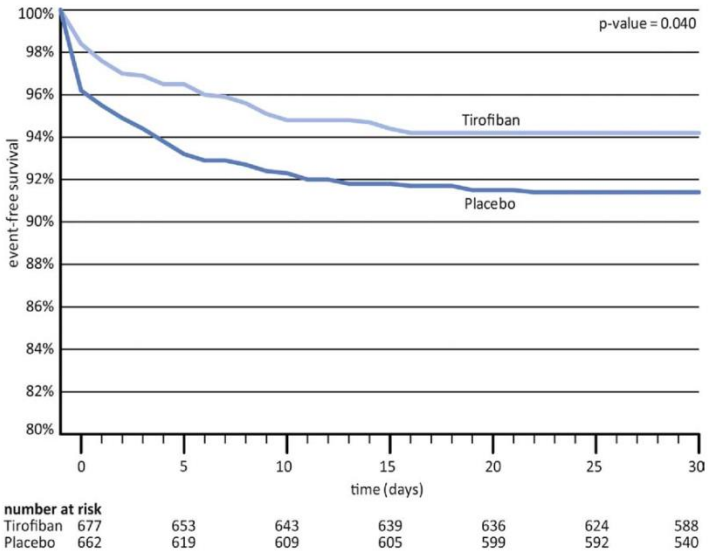


Figure 3 Kaplan-Meier Survival Curves Free From Major Adverse Cardiac Events in the Group of 1,339 Patients From the Open-Label and Blinded Study Phases Who Had 30-Day Follow-Up

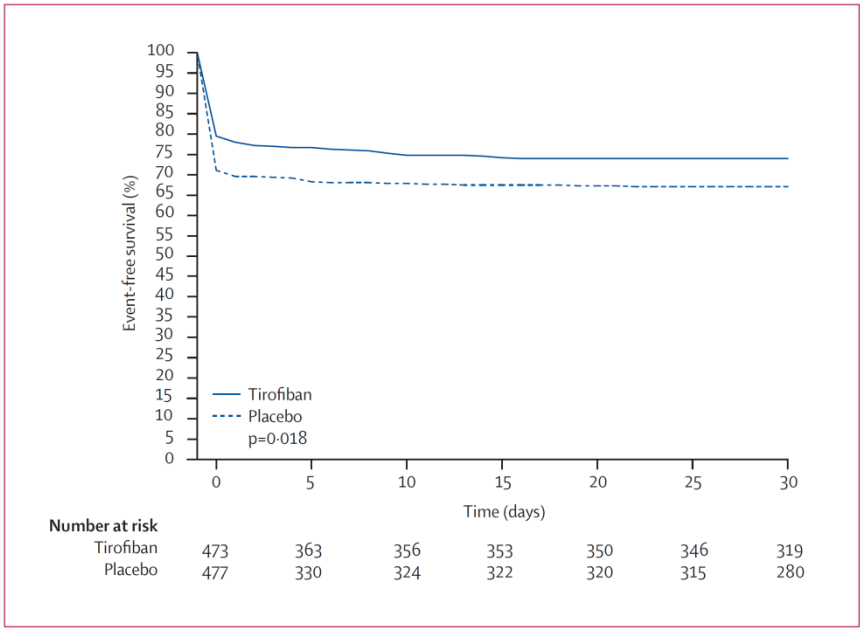
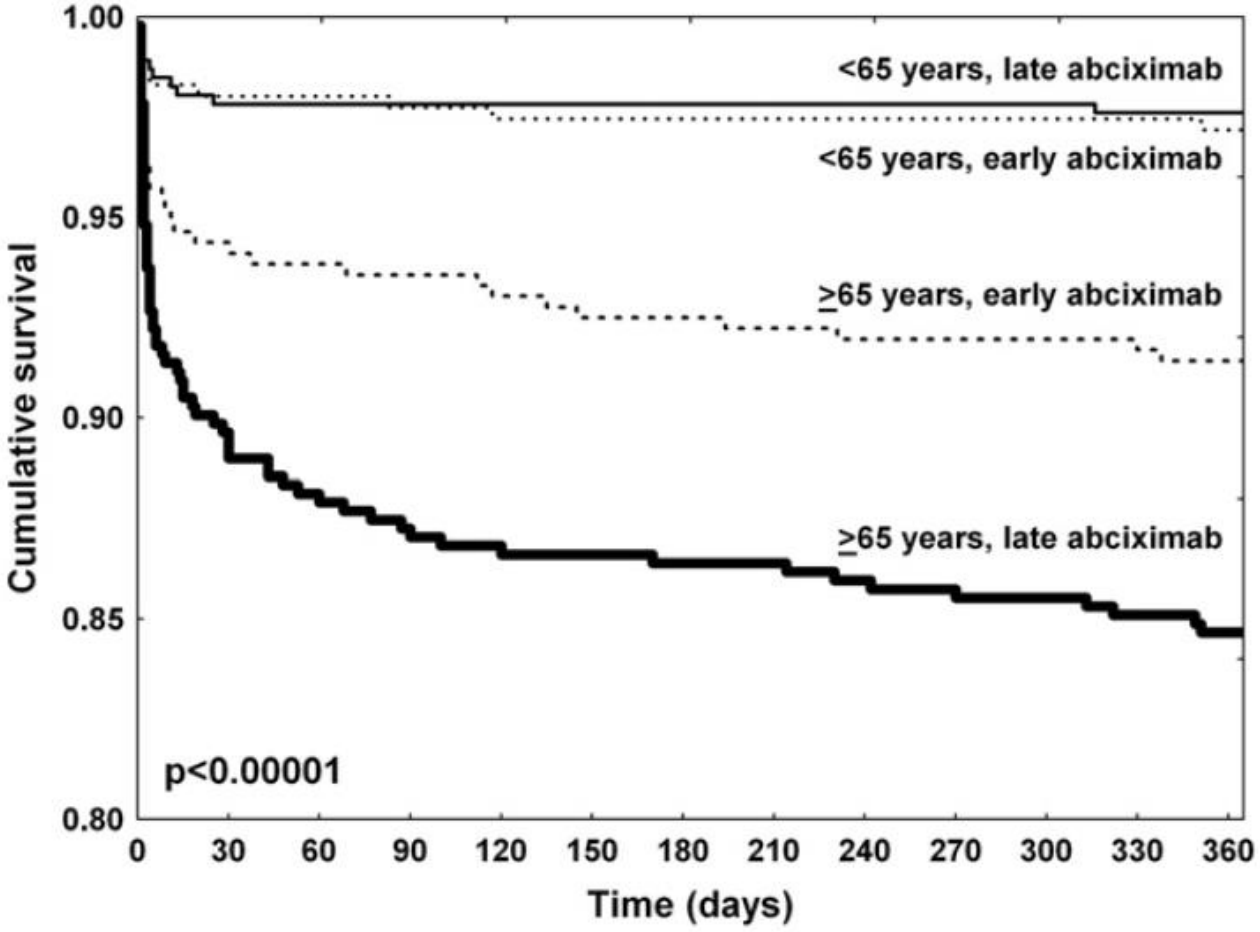


Figure 4: Kaplan-Meier event-free survival showing survival free from death, recurrent myocardial infarction, urgent target vessel revascularisation, or blinded bail-out use of study drug

Timmer JR. EuroIntervention 2010;6:336-42.

van't Hof AWJ. Lancet 2008; 372: 537–46

ABCIXIMAB BEFORE PCI
(EUROTRANFER)



Dziewierz A. *Int J Cardiol* 2010;143;147–53.

Prehospital treatment of patients with acute myocardial infarction with bivalirudin

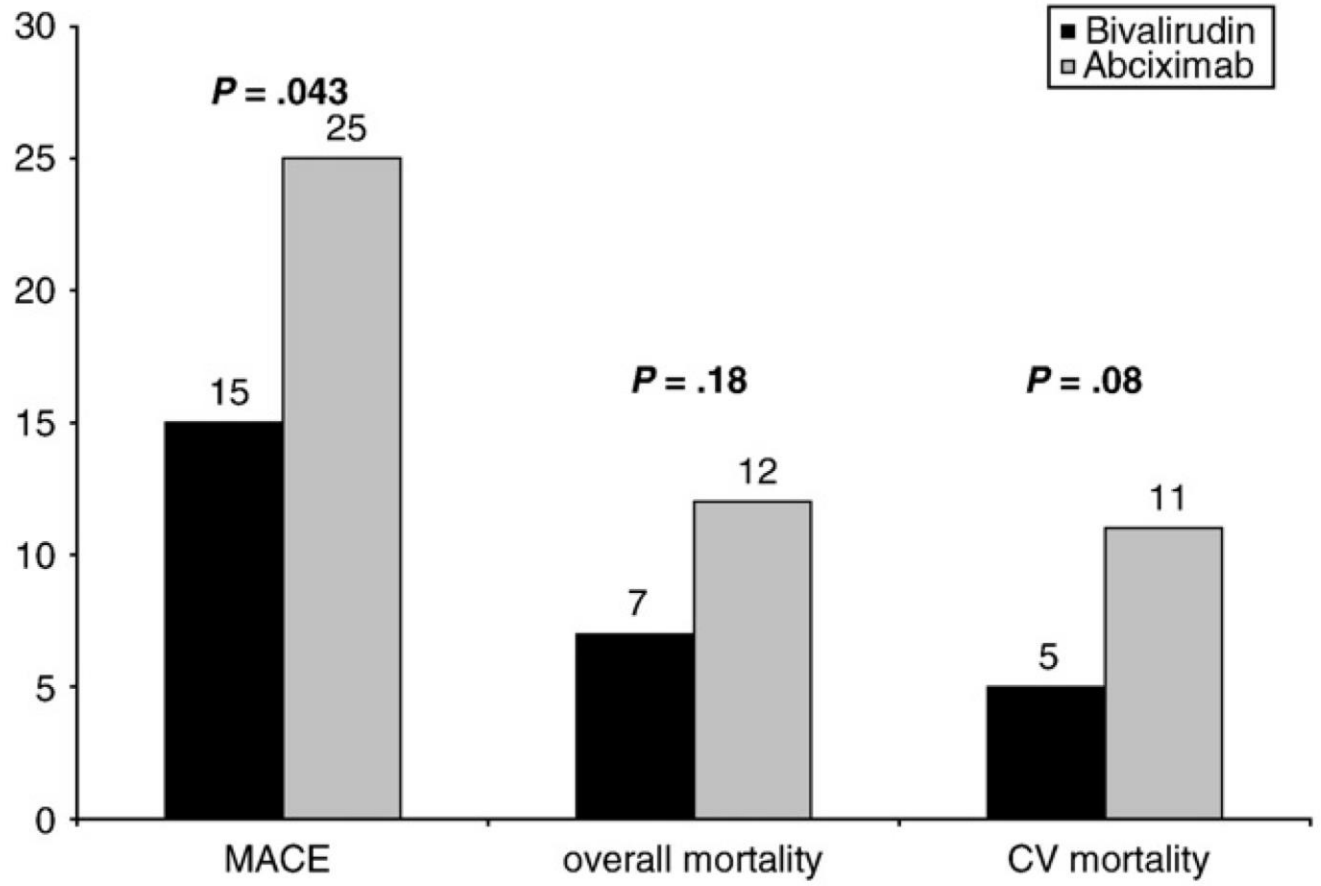


Fig. 1 Frequency of MACE and cardiovascular death in both groups.

Hirschl MM. *Am J Emerg Med* 2012;30:12–17.

Table 12 **Periprocedural antithrombotic medication in primary percutaneous coronary intervention**

Recommendations	Class [a]	Level [b]	Ref [c]
Antiplatelet therapy			
Aspirin oral or i.v. (if unable to swallow) is recommended	I	B	133, 134
An ADP-receptor blocker is recommended in addition to aspirin. Options are:	I	A	135, 136
• Prasugrel in clopidogrel-naive patients, if no history of prior stroke/TIA, age <75 years.	I	B	109
• Ticagrelor.	I	B	110
• Clopidogrel, preferably when prasugrel or ticagrelor are either not available or contraindicated.	I	C	-
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	137–141
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	127, 128, 137, 142
Options for GP IIb/IIIa inhibitors are (with LoE for each agent):			
• Abciximab		A	137
• Eptifibatide (with double bolus)		B	138, 139
• Tirofiban (with a high bolus dose)		B	140, 141
Anticoagulants			
An injectable anticoagulant must be used in primary PCI.	I	C	-
Bivalirudin (with use of GP IIb/IIIa blocker restricted to bailout) is recommended over unfractionated heparin and a GP IIb/IIIa blocker.	I	B	124
Enoxaparin (with or without routine GP IIb/IIIa blocker) may be preferred over unfractionated heparin.	IIb	B	122
Unfractionated heparin with or without routine GP IIb/IIIa blocker must be used in patients not receiving bivalirudin or enoxaparin.	I	C	1
Fondaparinux is not recommended for primary PCI.	III	B	118
The use of fibrinolysis before planned primary PCI is not recommended.	III	A	127, 143

Pre-hospital antiplatelet and anticoagulant regimes for STEMI

Conclusions

- Pre-hospital fibrinolysis is well proven and should be given with all coadjuvant therapy.
- Although pre-hospital initiation of antithrombotic therapy intuitevely makes sense and is used widely for primary , there is no solid evidence supporting its clinical advantages, particularly for pre-hospital anticoagulation.
- Whether the theoretical advatages overcome potential risks needs still to be proven.