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Pretreatment With Oral P2Y12 Inhibitors in NSTE-ACS and STEMI-Against

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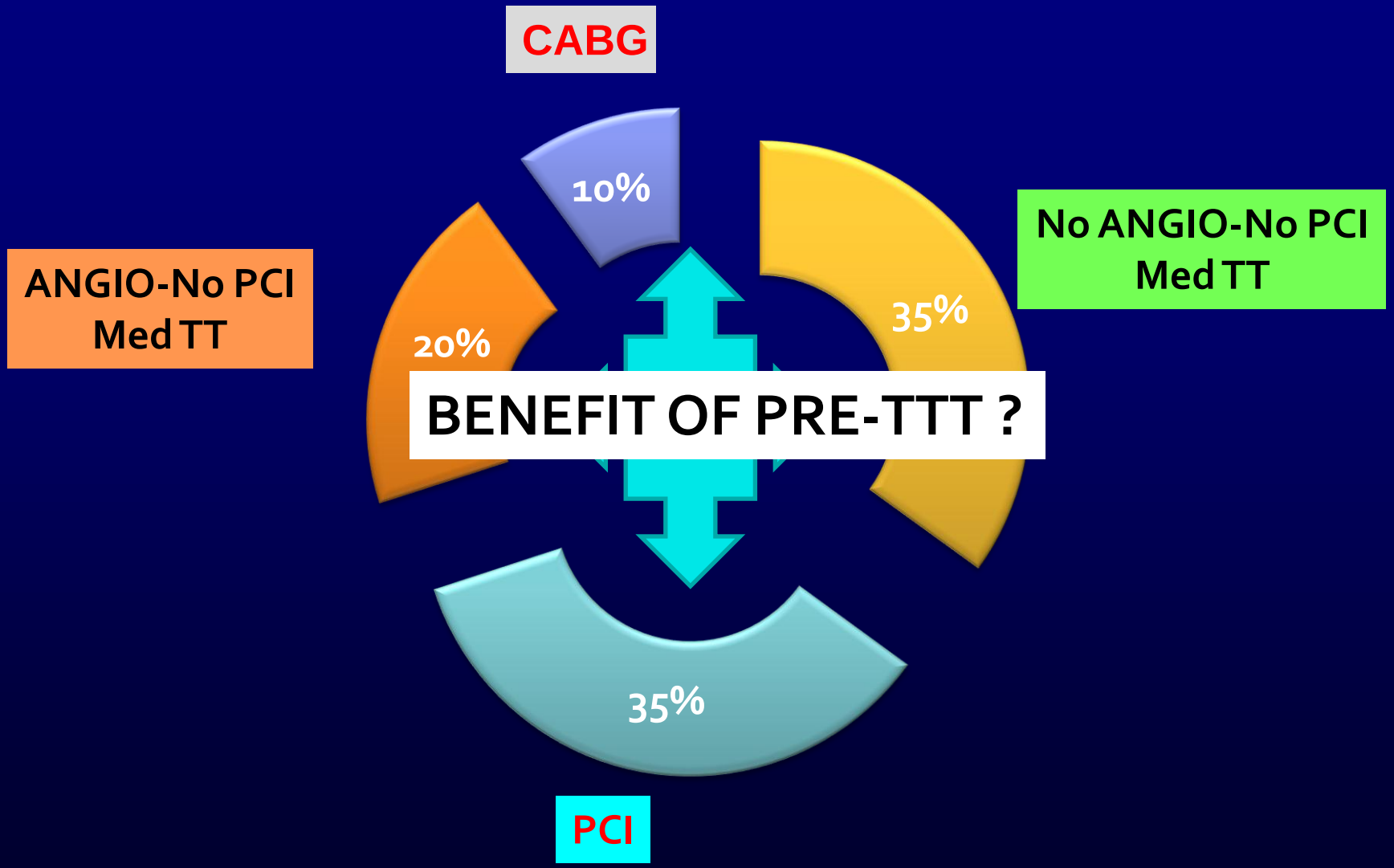
COI DISCLOSURE FOR DR. COLLET are available @ http://www.action-coeur.org

Definition

Pre-treatment in ACS : a treatment given before the coronary angiogram when an invasive strategy is used

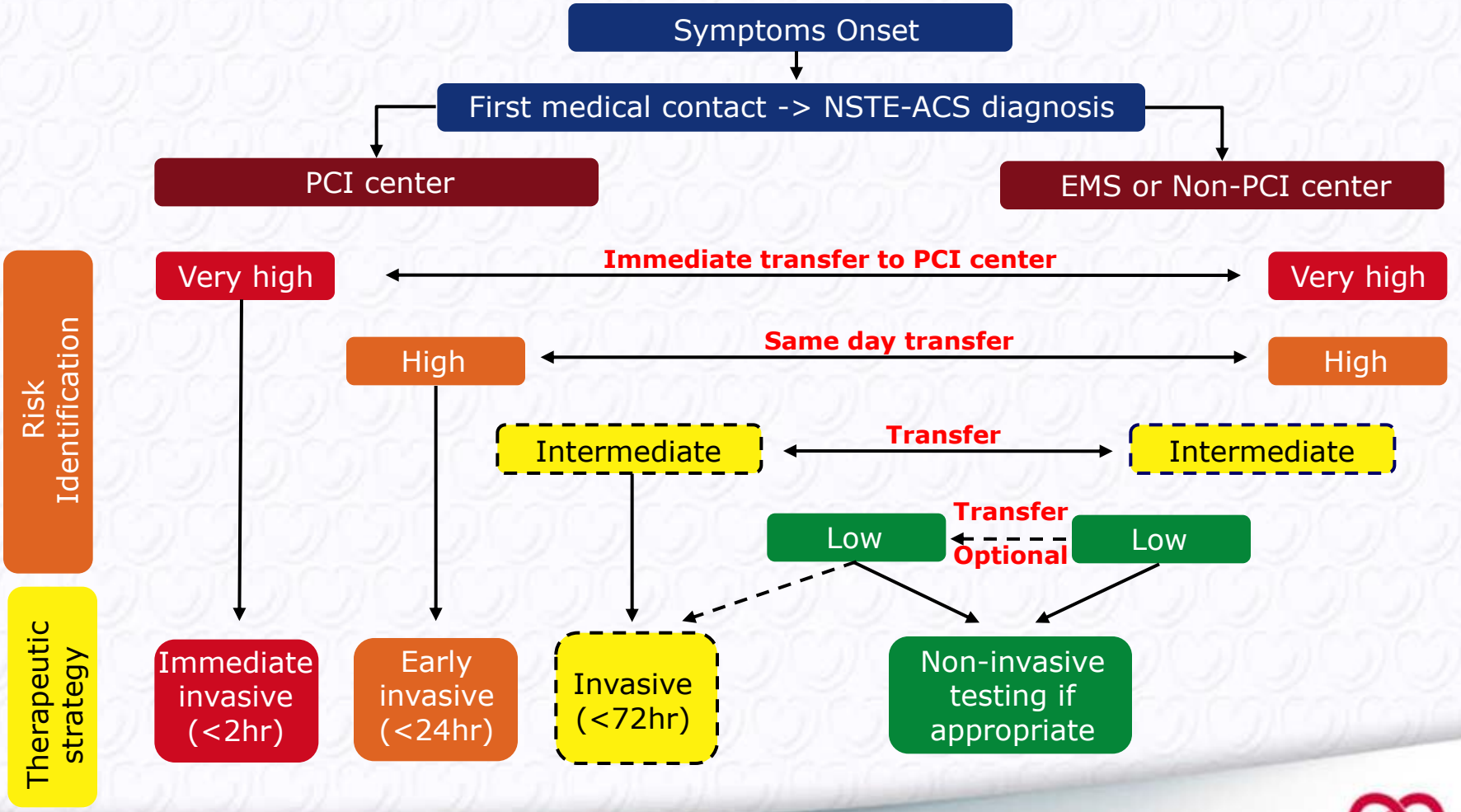
Pretreatment in NSTE-ACS

NSTE-ACS in the Real World of All-comers



Mandelzweig et al., *Eur Heart J. 2006;27:2285-2293*
O' Donoghue et al; *JAMA* 2008; **300:** 71–80.
Patel et al; *Am Heart J* 2006; **152:** 641–47.

Selection of NSTE-ACS treatment strategy



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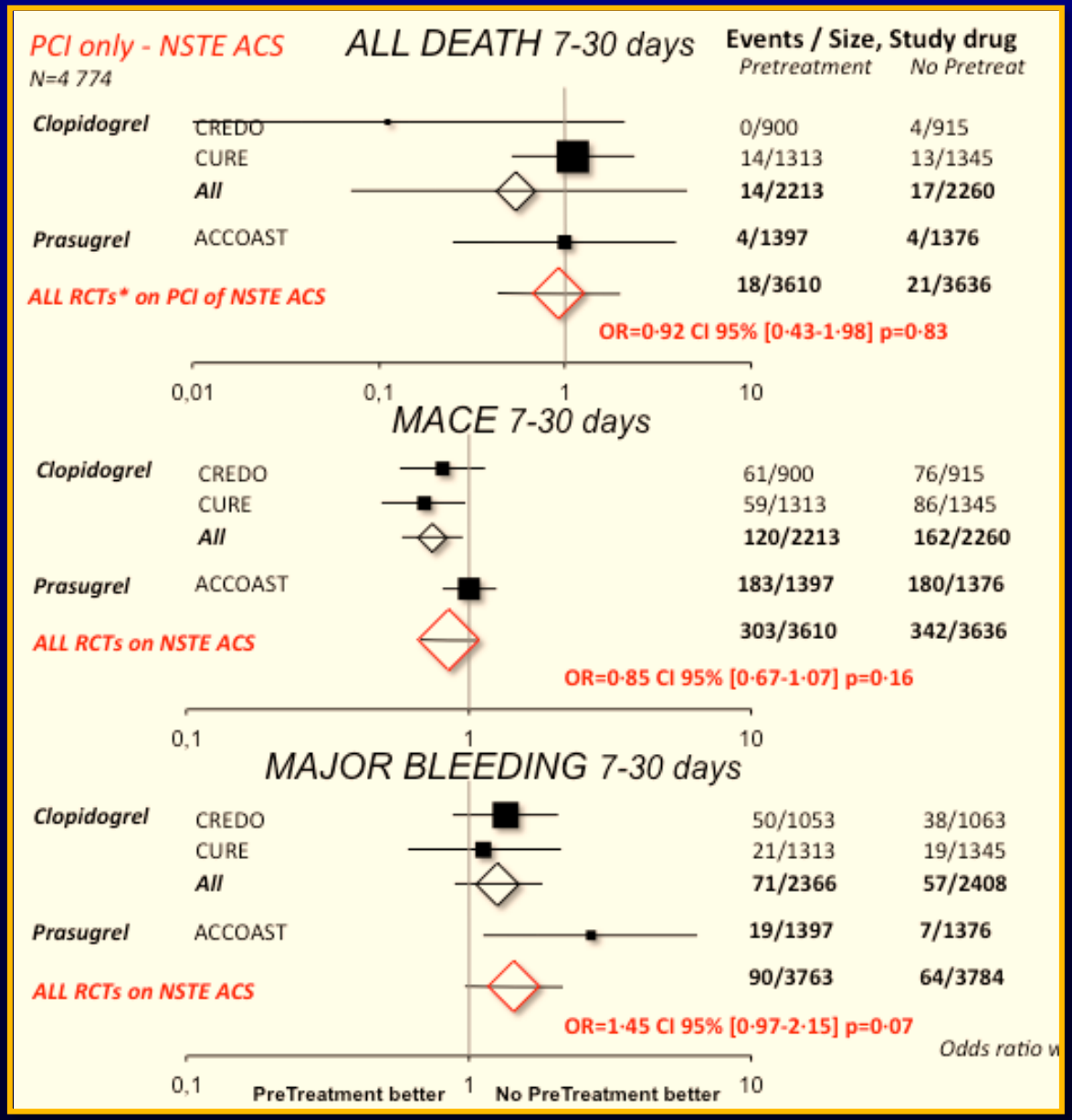
Oral Antiplatelet Therapy in NSTE-ACS

Recommendations Antiplatelet therapy	Class[a]	Level[b]
Oral Antiplatelet Therapy		
A $P2Y_{12}$ inhibitor is recommended, in addition to aspirin, for 12 months unless there are contra-indications*	I	A
It is not recommended to administer prasugrel in patients in whom coronary anatomy is not known.	**III**	**B**

Recommendations Antiplatelet therapy in patients **in need for OAC**	Class[a]	Level[b]
Oral Antiplatelet Therapy		
Itnitial DAPT with aspirin plus a P2Y12 inhibitor in addition to OAC before coronary angiography is not recommended	**III**	**C**

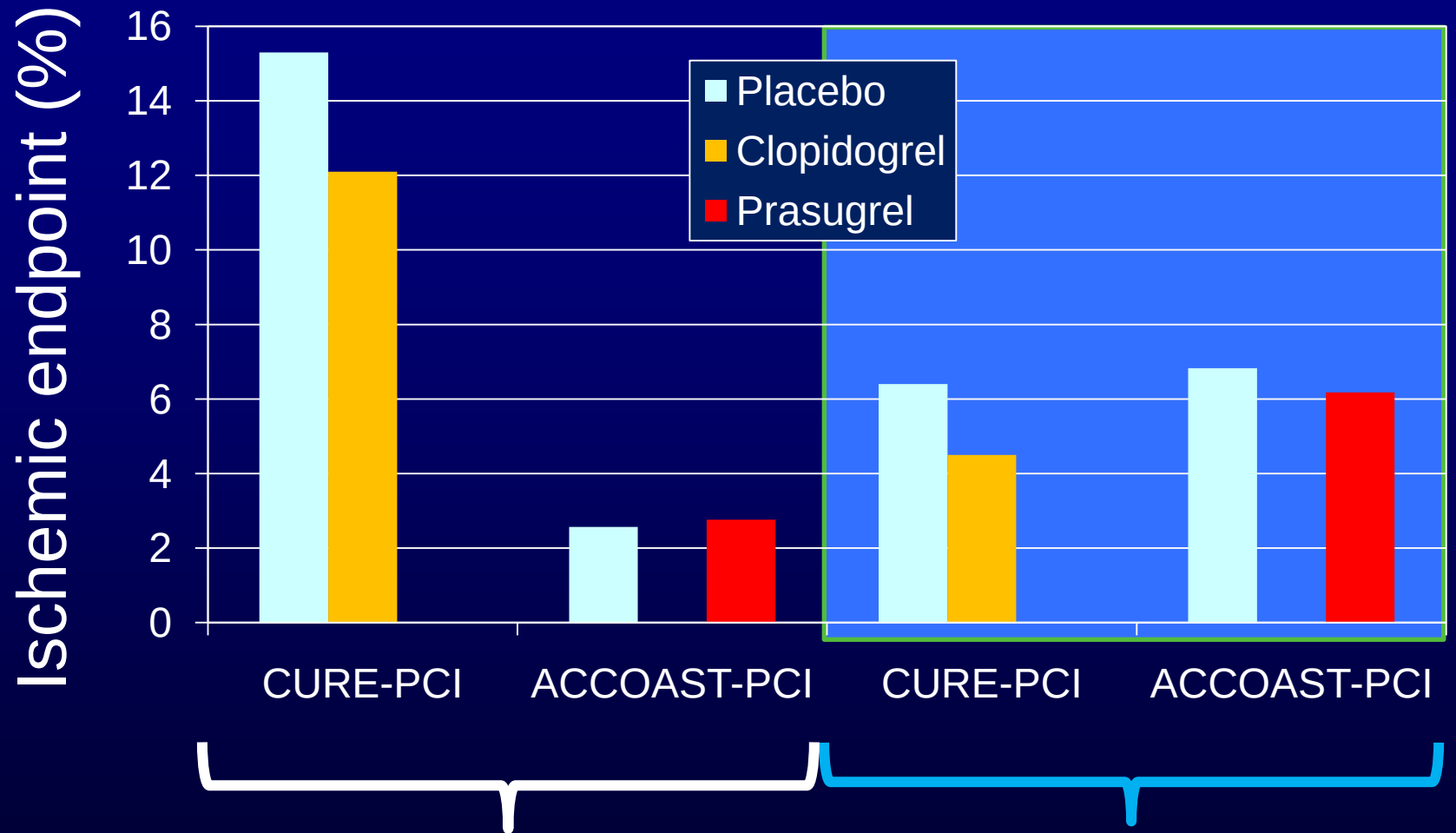
*Contra-indications for ticagrelor: previous intracranial haemorrhage or ongoing bleeds. Contra-indications for prasugrel: previous intracranial haemorrhage, previous stroke or transient ischaemic attack, or ongoing bleeds; prasugrel is generally not recommended for patients aged 75 years or more or with body weight <60 kg.

Pre-treatment in NSTE-ACS + PCI (Rx trials)



Bellemain-Appaix A, BMJ. 2014 Oct 24;349:g626

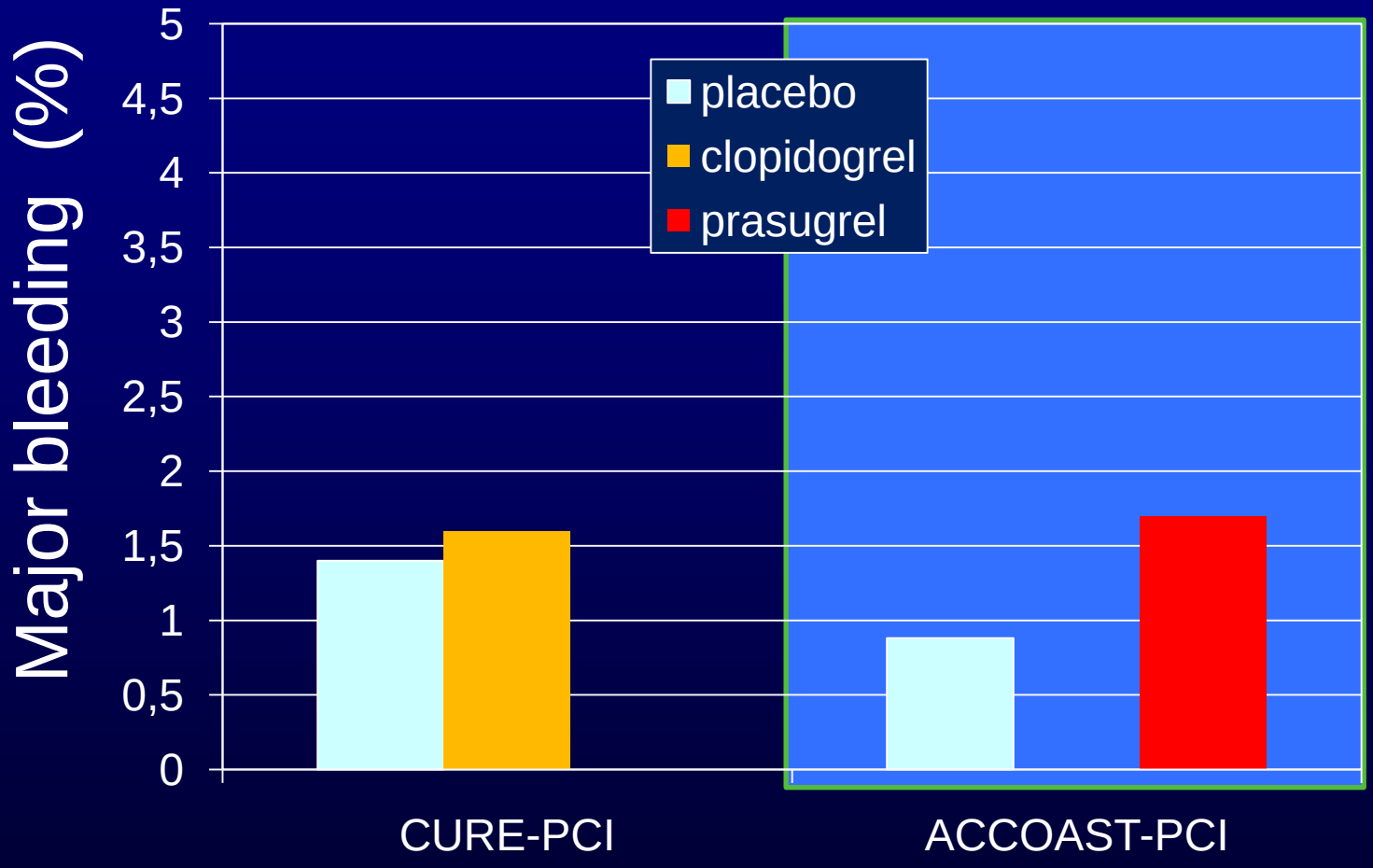
CURE vs. ACCOAST according to PCI



Mehta SR et al. *Lancet* 2001;358:527-533

Montalescot G et al. N Engl J Med.2013;369:999-1010

CURE vs. ACCOAST according to PCI



Mehta SR et al. *Lancet* 2001;358:527-533

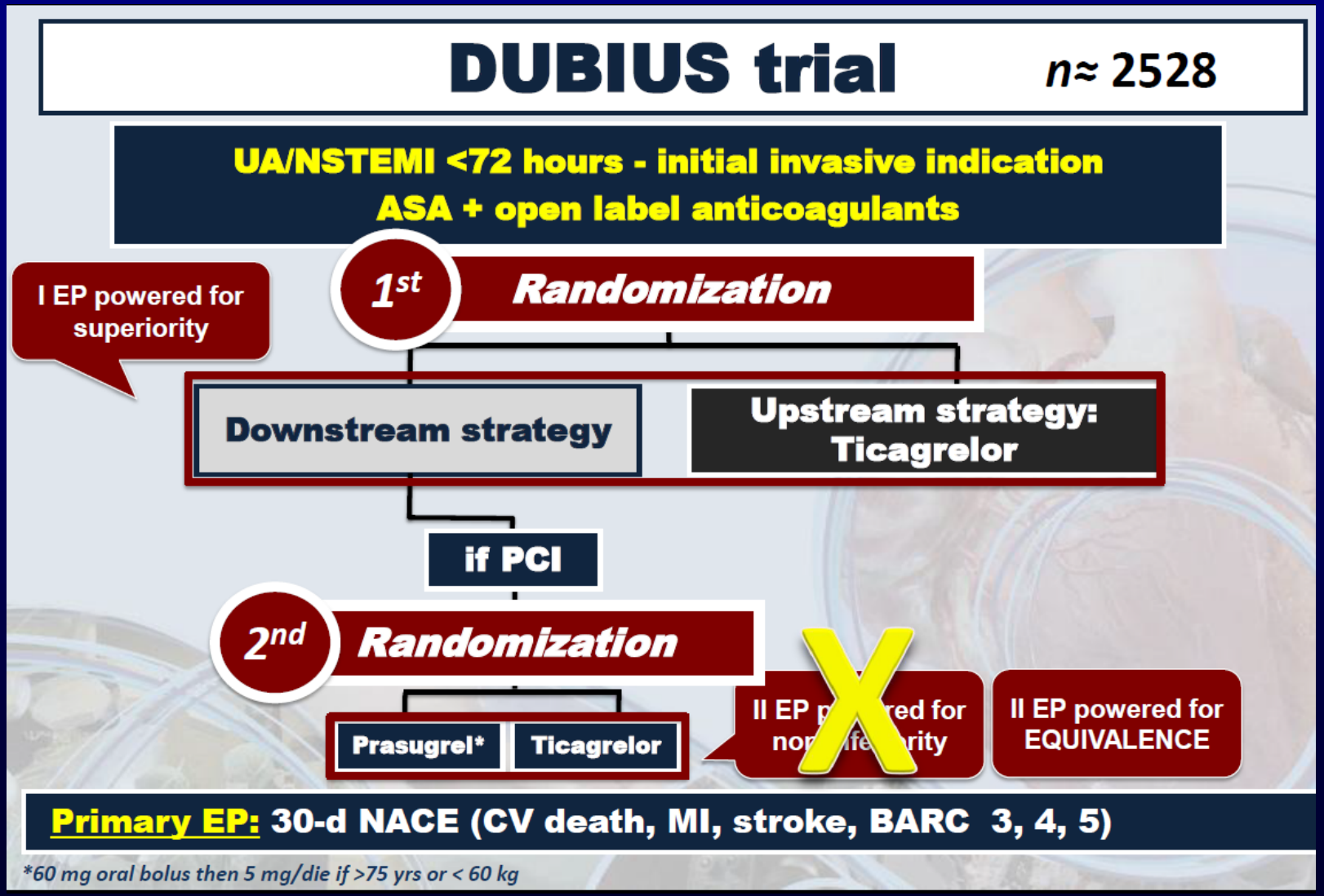
Montalescot G et al. N Engl J Med.2013;369:999-1010

Ticagrelor data

- No dedicated study exists assessing early (i.e. before coronary angiography) vs. delayed (i.e. after coronary angiography) ticagrelor

- A drug approach instead of a Strategy

The only dedicated study for ticagrelo is ongoing : Dubius study



Pretreatment in STEMI

Antiplatelet therapy for STEMI undergoing PCI

Recommendations	Class[a]	Level[b]
Antiplatelet therapy		
$P2Y_{12}$ inhibitors should be given at time of first medical contact.	I	B

CLOPIDOGREL – *Metanalysis*

DEATH

				I^2, p value
CIPAMI	1/164	4/171	0·26 [0·03-2·32]	8·7%
CLARITY PCI	13/933	24/930	0·53 [0·27-1·05]	91·3%
All	14/1097	28/1101	0·50 [0·26-0·96]	100%
Observational studies				

0%, p=0.53

OR=0·50 CI 95% [0·26-0·96] p=0·04

Table 4. Effect of Pretreatment With Clopidogrel on Early Reperfusion and Adverse Event Rates In Multivariate-Weighted and Propensity Score–Adjusted Logistic Regression Analysis

	Multivariate-Adjusted Treatment Effect*			Jackknife Estimation*			Propensity Score–Adjusted Treatment Effect		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
TIMI grade 2/3 flow	1.51	1.31–1.74	<0.0001	1.51	1.31–1.74	<0.0001	1.53	1.39–1.68	<0.0001
Mortality	0.57	0.38–0.85	0.0055	0.57	0.40–0.81	0.0019	0.52	0.41–0.67	<0.0001
Death/reinfarction	0.54	0.38–0.75	0.0003	0.54	0.39–0.73	0.0001	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.

*Adjusted for age, gender, history of diabetes mellitus, history of hypertension, heparin dose (high vs low dose), symptom duration, smoking, and year of publication.

Méta-analyse pPCI STEMI *Vlaar et al. Circulation 2008, 118:1828-1836*

MACE

RCT*				
CIPAMI	5/164	12/171	0·42 [0·14-1·21]	14·2%
CLARITY PCI	34/933	58/930	0·57 [0·37-0·88]	85·8%
All	39/1097	70/1101	0·54 [0·36-0·81]	100%
Observational studies				
Dorler et al.	480/4879	173/1076	0·57 [0·47-0·69]	85·5%
Fefer et al.	47/217	56/166	0·54 [0·34-0·86]	14·5%
All	527/5096	229/1242	0·57 [0·48-0·67]	100%

0%, p=0.003

OR=0·54 CI 95% [0·36-0·81] p=0·003

0%, p<0.00001

OR=0·57 CI 95% [0·48-0·67] p<0·00001

0 0,5 1 1,5 2 2,5 3 3,5 4

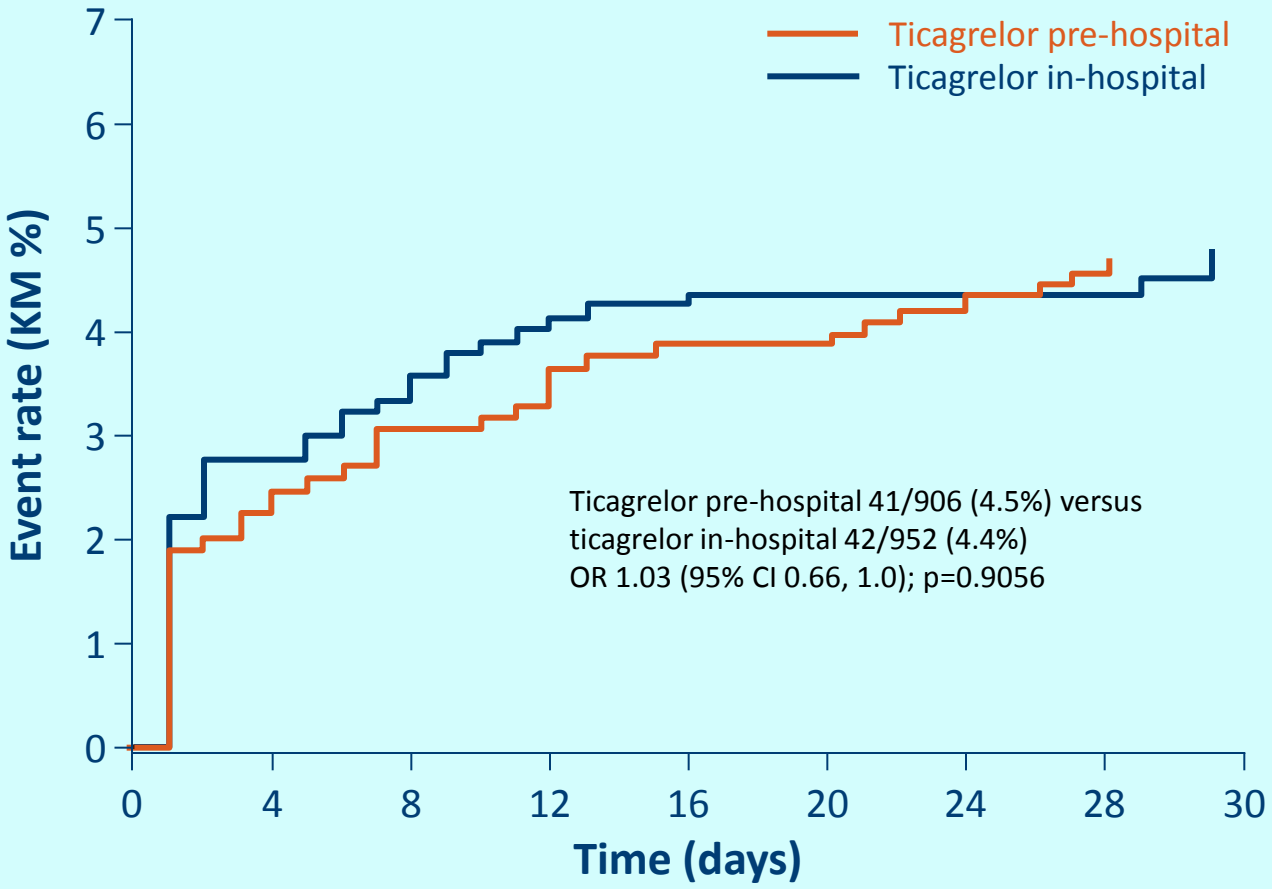
PreTreatment better — No PreTreatment better

CLOPIDOGREL

** RCT=Randomized Controlled Trials*

A. Bellemain-Appaix et al.,JAMA2012;308(23):2507-2517

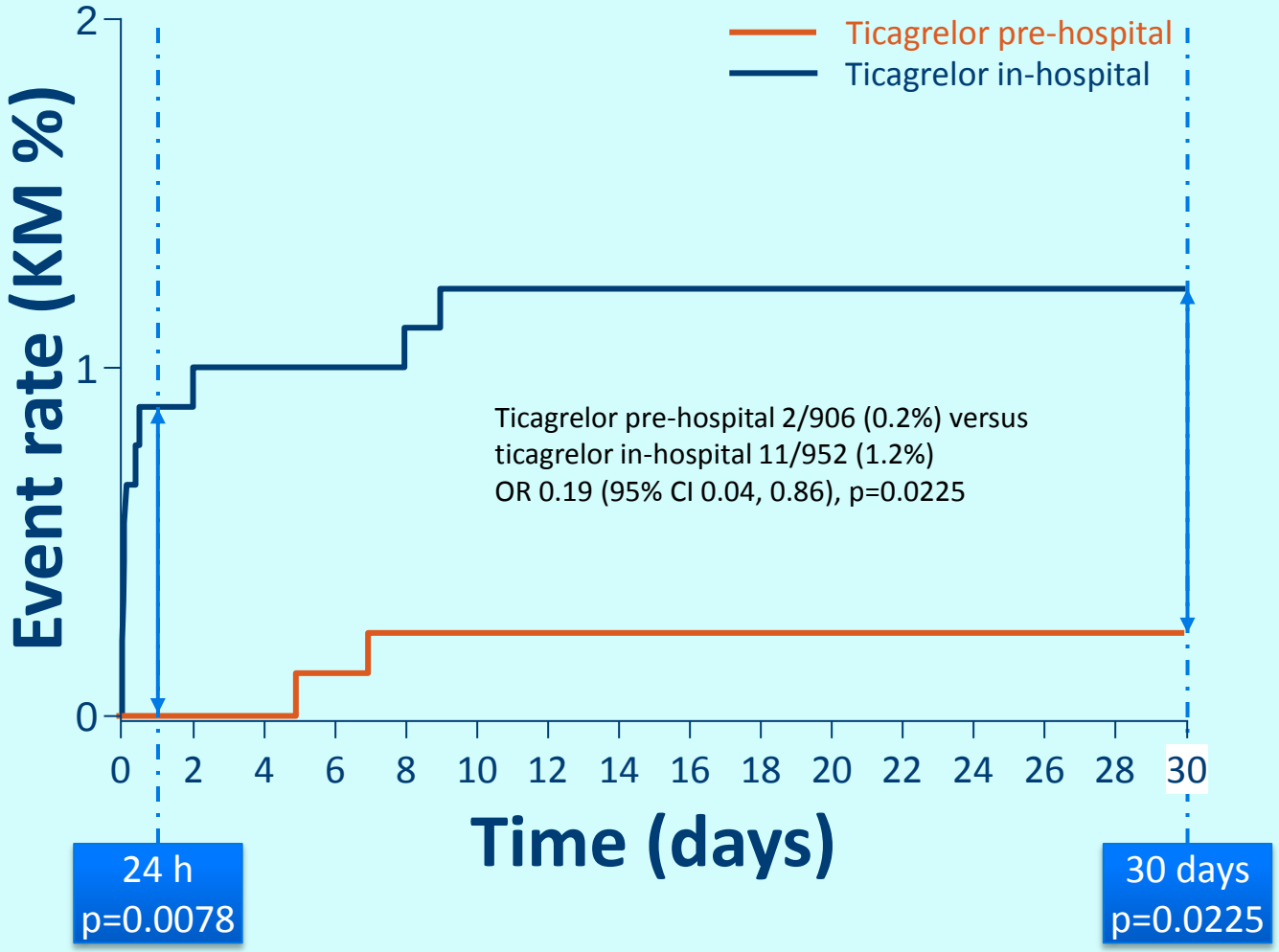
Major adverse CV events up to 30 days: Kaplan–Meier curves



Major adverse CV events: death, myocardial infarction, stroke or urgent revascularisation

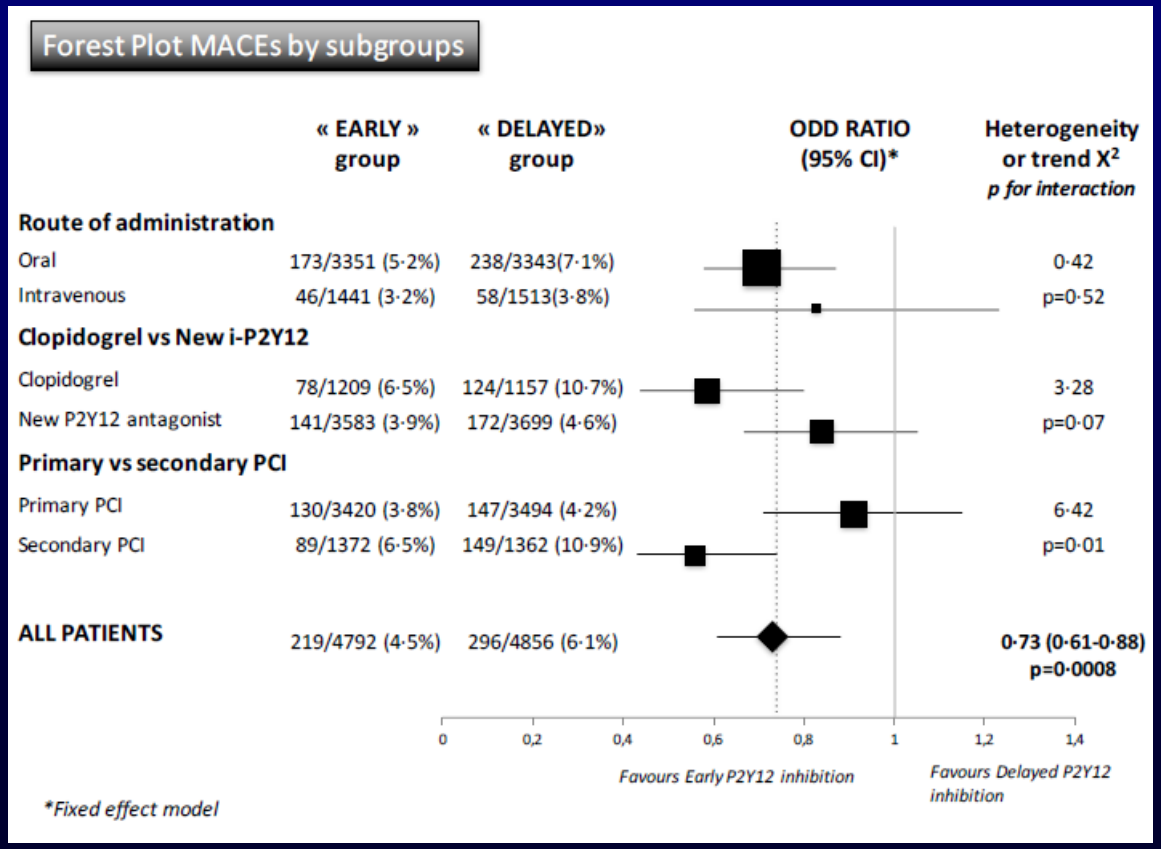
2014 nejm

Definite acute stent thrombosis up to 30 days: Kaplan–Meier curves



Biases of interpretation

- Most of the benefit derives from secondary PCI
- Most of the benefit derives from old clopidogrel data



Bellemain-appaix et al. JACC Int (submitted)

CONCLUSIONS

- Outdated, Ineffective, Harmful in **NSTE-ACS**
  - No access to a cath lab/need to wait several days for a cath → Apply CURE/PLATO and be ready for the safety consequences.
  - Treating after the angiogram → flexibility, avoids over-treatment & select the right treatment for the right patient.

- Recommended in **STEMI** when there is no doubt with respect to the diagnosis