

ISAR-REACT 5, comment

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DOI public at www.action-coeur.org



	Prasugrel	Ticagrelor
ACS invasive	 TRITON TIMI-38	
ACS conservative	 TRILOGY ACS	PLATO 
Timing in STEMI		 ATLANTIC
Timing in NSTEMI	 ACCOAST	

Wiviott SD et al. NEJM 2007;357:2001-15

Roe MT et al. NEJM 2012;367:1297-309

Montalescot G et al. NEJM 2013;369:999-1010

Wallentin L et al. NEJM 2009;361:1045-57

Montalescot G et al. NEJM 2014;371:1016-27

ISAR-REACT 5

STEMI

Randomization

Ticagrelor
180 mg loading

Prasugrel
60 mg loading

Angiography + PCI

Ticagrelor
90 mg 1-0-1

Prasugrel
10 mg 1-0-0[#]

NSTE-ACS

Randomization

Ticagrelor
180 mg loading

Prasugrel
60 mg loading*

Angiography

Prasugrel
60 mg loading

PCI

Ticagrelor
90 mg 1-0-1

Prasugrel
10 mg 1-0-0[#]

ACS

time

drug

Primary Endpoint:
Composite of Death, Myocardial infarction or Stroke
at 12 Months After Randomization

$$x + 3y - 4z = ?$$

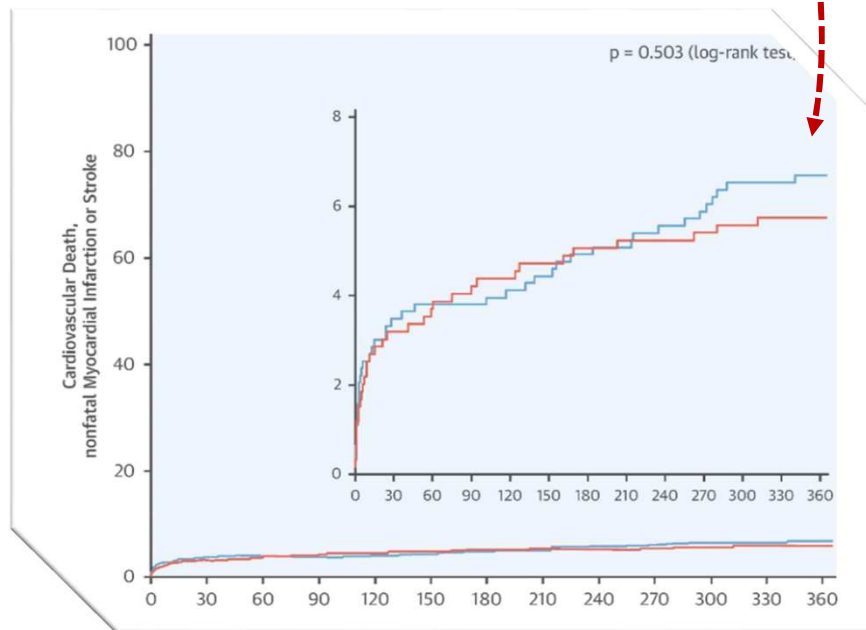


Randomization by envelopes
Open label
Not a drug trial
84% PCI
Superiority hypothesis for Tica



Academic study
Randomized
Stratification by ACS type
Pragmatic
CEC and core labs

13% event rate with prasugrel and RRR 22.5%



Motovska Z et al. *Circulation* 2016; 134:1603-1612
Motovska Z et al. *J Am Coll Cardiol* 2018; 71:371-81
Schulz et al, *J Cardiovasc Transl Research* 2014;7:91-100

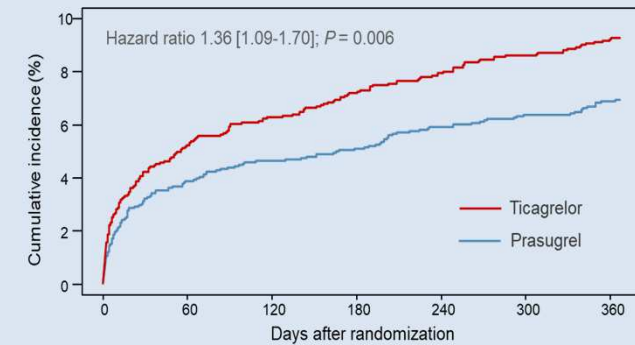


1st thoughts



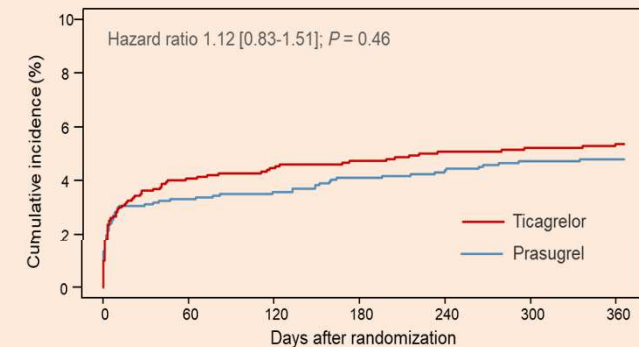
Negative trial?

→ Informative trial!



Similar safety?

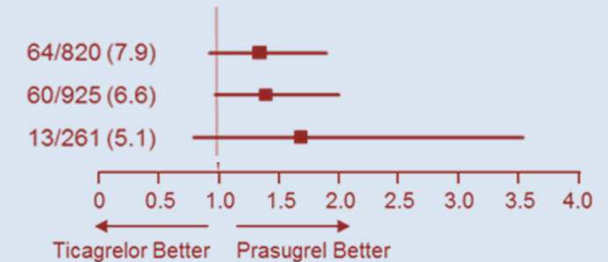
→ superior timing strategy in NSTEMI!?



Consistency?

→ Clinical Presentation

STEMI	83/833 (10.1)
NSTEMI	81/930 (8.8)
Unstable Angina	20/249 (8.2)



2nd thoughts

One-size fits all strategy (tica) < Individualized strategy (prasu)



Excellent **PCI** drug (TRITON)



PCI	162/1676 (9.8)	120/1701 (7.1)
conservative	17/285 (6.1)	12/268 (4.6)
CABG	5/47 (10.6)	5/36 (13.9)



1.41 (1.11-1.78)
1.29 (0.62-2.70)
0.66 (0.19-2.30)



HBR → adjust the **dose** down (TRILOGY)



Prasugrel 5 mg in patients ≥ 75 years of age or weight < 60 kg

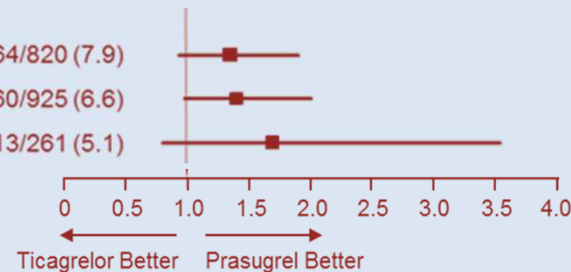


In NSTEMI, **do not pre-treat** (ACCOAST)



Clinical Presentation

STEMI	83/833 (10.1)	64/820 (7.9)
NSTEMI	81/930 (8.8)	60/925 (6.6)
Unstable Angina	20/249 (8.2)	13/261 (5.1)



ISAR-REACT 5?

A landmark study!

Slides available at **www.action-coeur.org**

