

# ISAR-REACT 5, comment

***G. Montalescot***





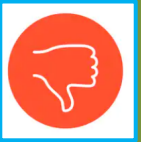




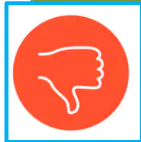

*Institute of Cardiology,  
Pitié-Salpêtrière Hospital, Paris, France*

*DOI public at [www.action-coeur.org](http://www.action-coeur.org)*



# Declaration of interest

- Consulting/Royalties/Owner/ Stockholder of a healthcare company (public at [www.action-coeur.org](http://www.action-coeur.org))
- Research contracts (public at [www.action-coeur.org](http://www.action-coeur.org))

|                  | Prasugrel  | Ticagrelor  |
|------------------|--|---|
| ACS invasive     |     |   |
| ACS conservative |     |    |
| Timing in STEMI  |  |   |
| Timing in NSTEMI |   |   |

*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<sup>#</sup>

## 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<sup>#</sup>

ACS

time

drug

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

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

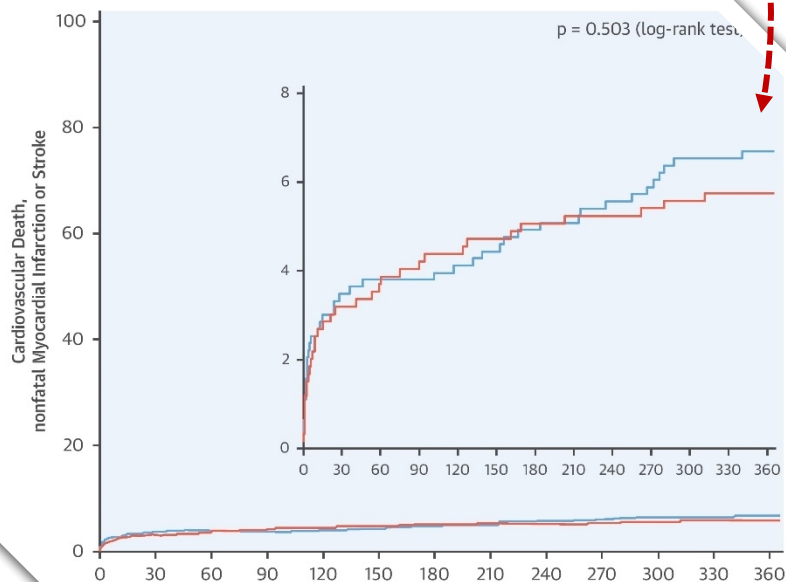
Randomization by envelopes  
Open label  
Not a drug trial  
84% PCI  
Superiority hypothesis for Tica

STRENGTH →

← WEAKNESS

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

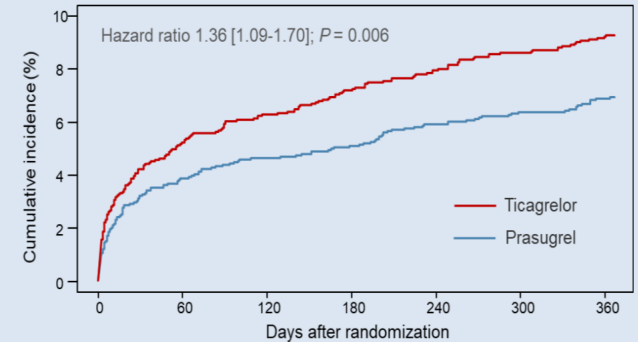


# 1<sup>st</sup> thoughts



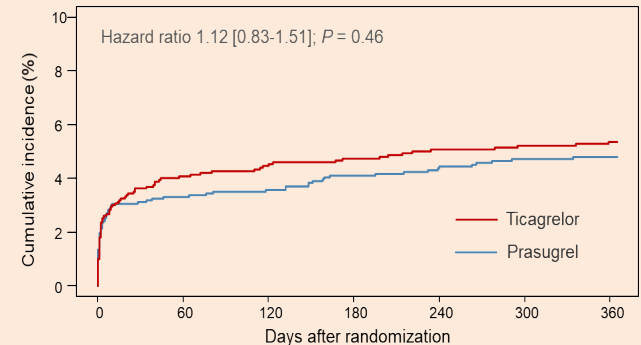
## Negative trial?

→ Informative trial!



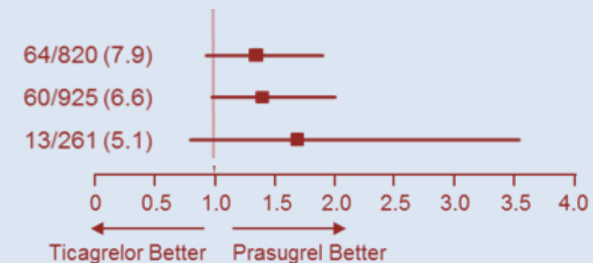
## Similar safety?

→ timing of administration in NSTEMI!?



## Consistency?

| Clinical Presentation |               |
|-----------------------|---------------|
| → STEMI               | 83/833 (10.1) |
| NSTEMI                | 81/930 (8.8)  |
| Unstable Angina       | 20/249 (8.2)  |



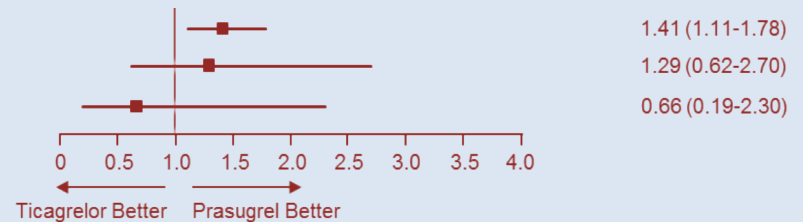
# 2<sup>nd</sup> thoughts

**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)    |



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

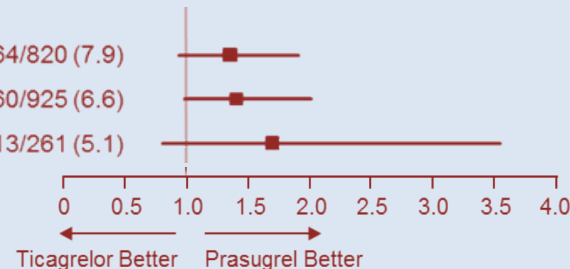


*Prasugrel 5 mg in patients  $\geq 75$  years of age or weight  $< 60$  kg*

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



| Clinical Presentation | Ticagrelor (n/N, %) | Prasugrel (n/N, %) |
|-----------------------|---------------------|--------------------|
| 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](http://www.action-coeur.org)**

