



Switching between anti-platelet ADP receptor inhibitors

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Case #1

- 62 y/o male admitted with anterior wall STEMI
- Chest pain for 3 hours prior to arrival
- Risk factors: HTN, dyslipidemia
- In the ER receives aspirin, heparin and clopidogrel 600 mg
- Successful PCI performed with aspiration and DES implantation



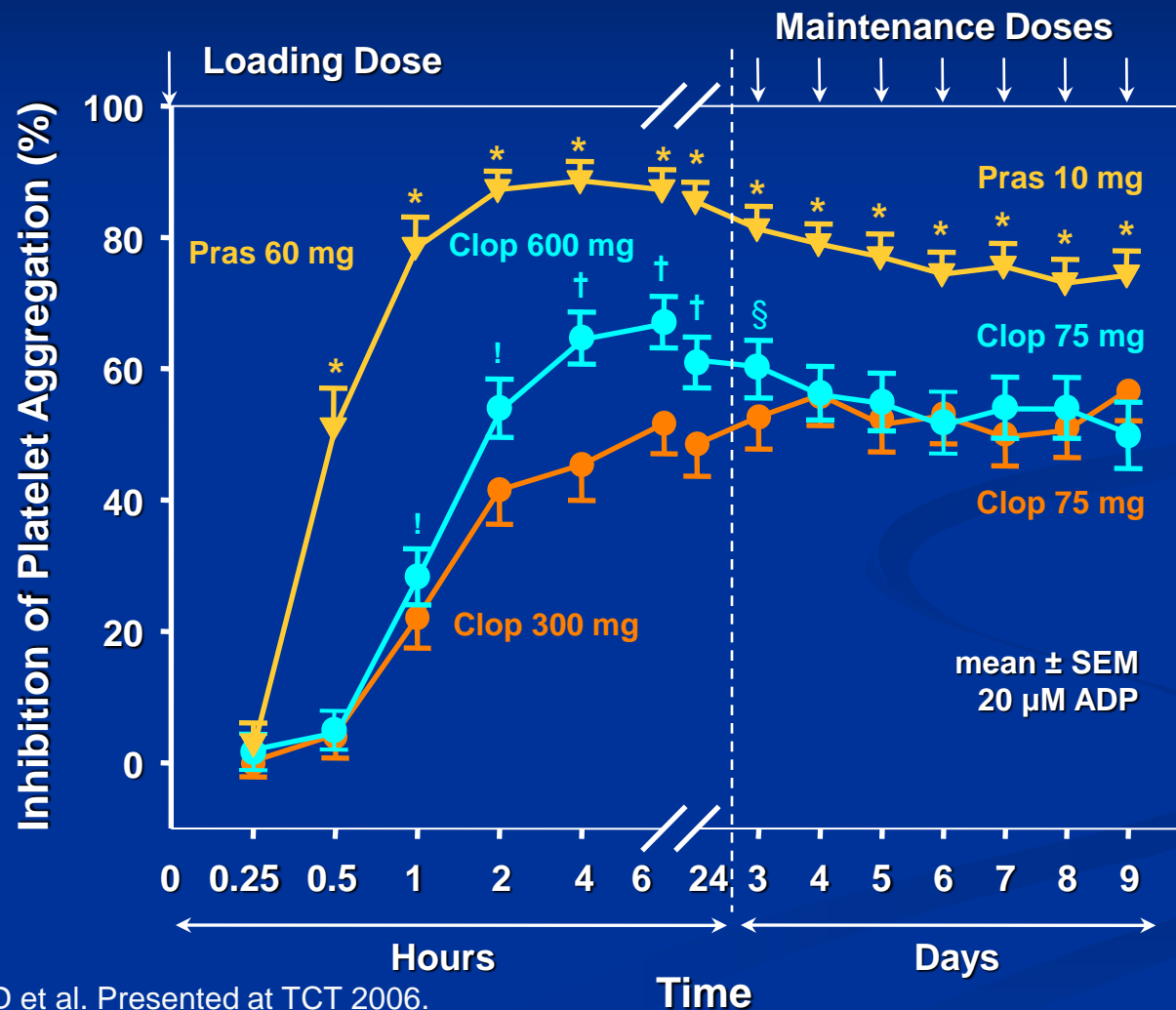
Questions

- The following day the patient should be treated with:
 1. Clopidogrel 75 mg a day
 2. Clopidogrel 150 mg a day for a week followed by 75 mg a day
 3. Prasugrel 10 mg a day (without any loading)
 4. Prasugrel 30 mg loading followed by 10 mg a day
 5. Prasugrel 60 mg loading followed by 10 mg a day
 6. Ticagrelor 180 mg loading followed by 90 mg bid
 7. Ticagrelor 90 mg bid (without loading)

SWITCHING TO PRASUGREL

- Safe switch from clopidogrel LD (600-900 mg) → prasugrel MD (ACAPULCO, Thromb Haemost 2010).
- Safe switch from clopidogrel MD → prasugrel LD or MD. Switching to the LD provides faster onset of platelet inhibition (SWAP).
- No published data on clopidogrel LD → prasugrel LD switch; however, TRIPLET study partly addresses this question

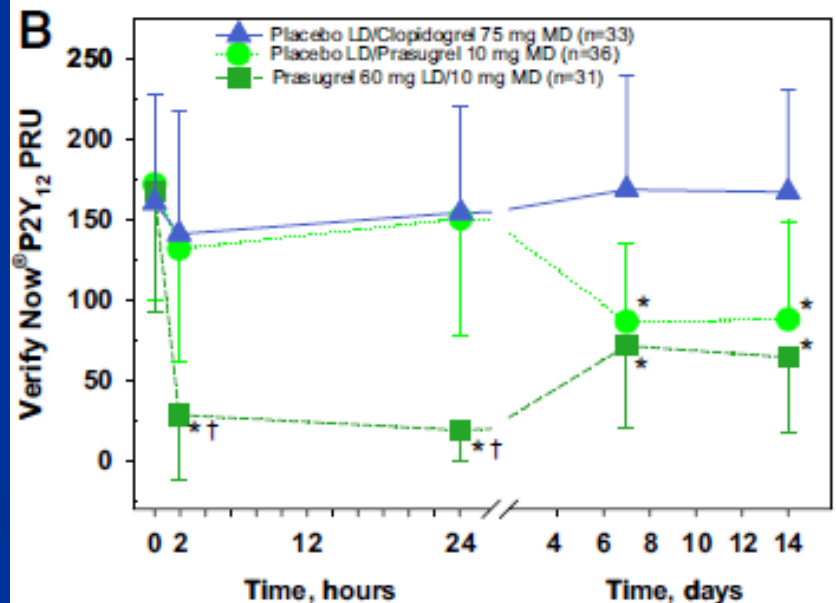
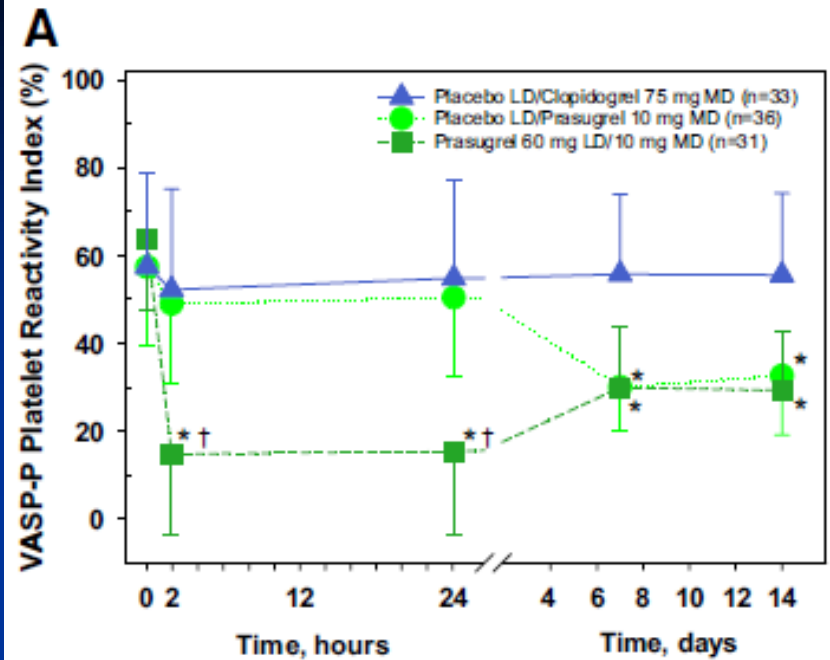
Prasugrel 10 mg MD vs. Clopidogrel 75 mg MD: Higher IPA During Maintenance Dosing



The SWAP study

Switching from maintenance clopidogrel to prasugrel in 100 patients with ACS

Angiolillo et al, JACC 2010



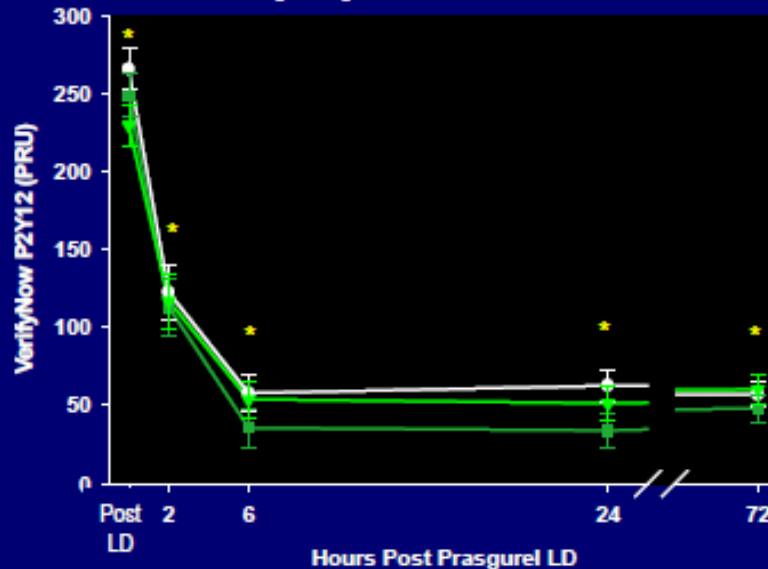
TRIPLET – Switching from clopidogrel loading to prasugrel

TRIPLET
Study

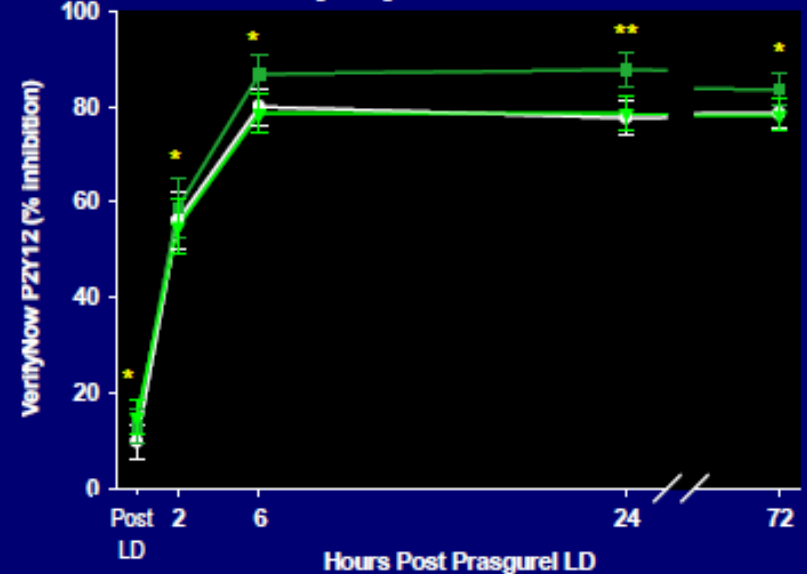
Time Course: Pharmacodynamic Population

Presented at EUROPCR 2012

PRU (LS mean), PD population



% Inhibition (LS mean), PD population



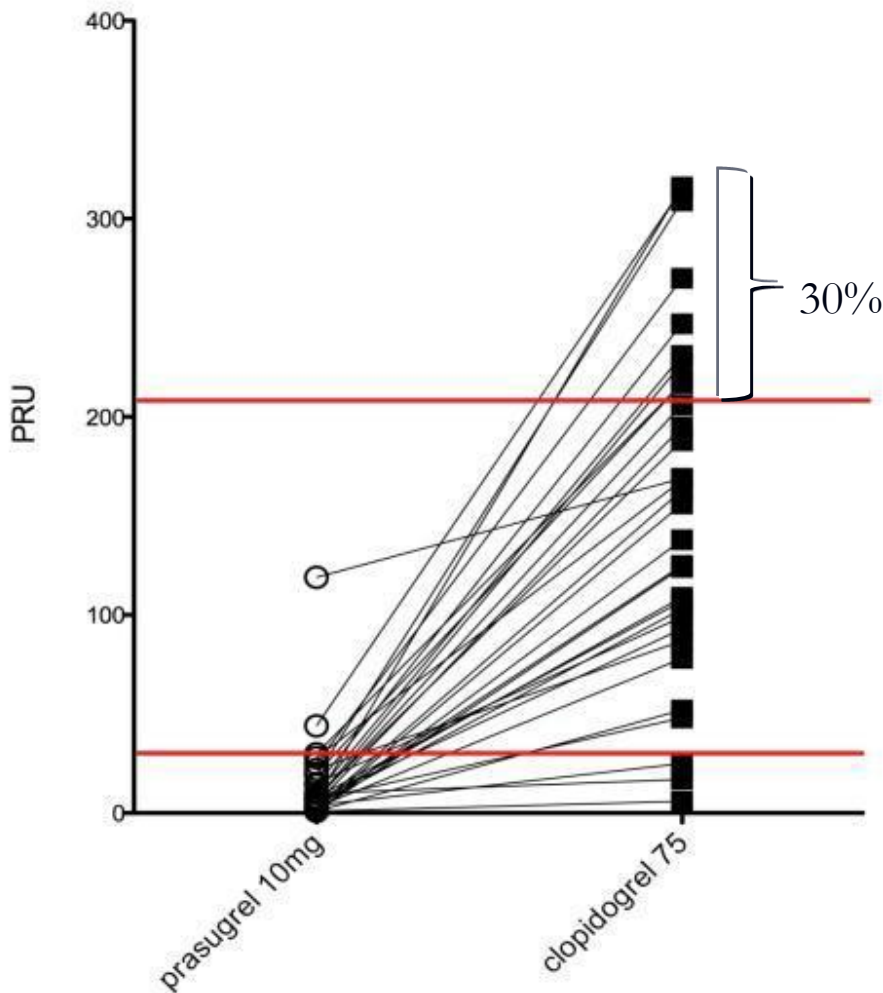
ACS PCI patients

- Placebo and Prasugrel 60 mg/10 mg
- Clopidogrel 600 mg and Prasugrel 60 mg/10 mg
- ▼ Clopidogrel 600 mg and Prasugrel 30 mg/10 mg

*P=NS at each time point vs. placebo/prasugrel 60 mg, **P=0.049 between the placebo/prasugrel 60 mg group and the clopidogrel 600 mg/prasugrel 60 mg group
Euro PCR. 2012

LD=Loading Dose, LS=Least Square, PD=Pharmacodynamic, PRU= P2Y12 Reaction Units

Switching from prasugrel to clopidogrel



- ACS pts treated with prasugrel 10 mg for 2 wks
- Pts displaying low on-treatment platelet reactivity (by VerifyNow) or at high risk of bleeding were considered for switch to clopidogrel 75 mg

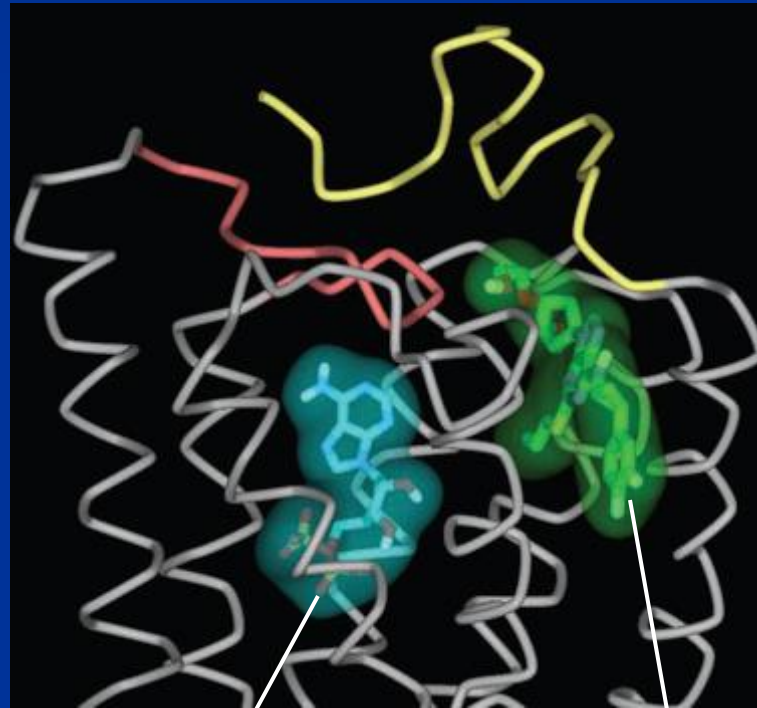
Switching drugs

- Switching from maintenance clopidogrel to prasugrel → more efficient and rapid platelet inhibition achieved by adding prasugrel loading dose
- Switching after clopidogrel loading dose may also require additional prasugrel loading of 30-60 mg

Ticagrelor – mode of action

P2Y₁₂ receptor model

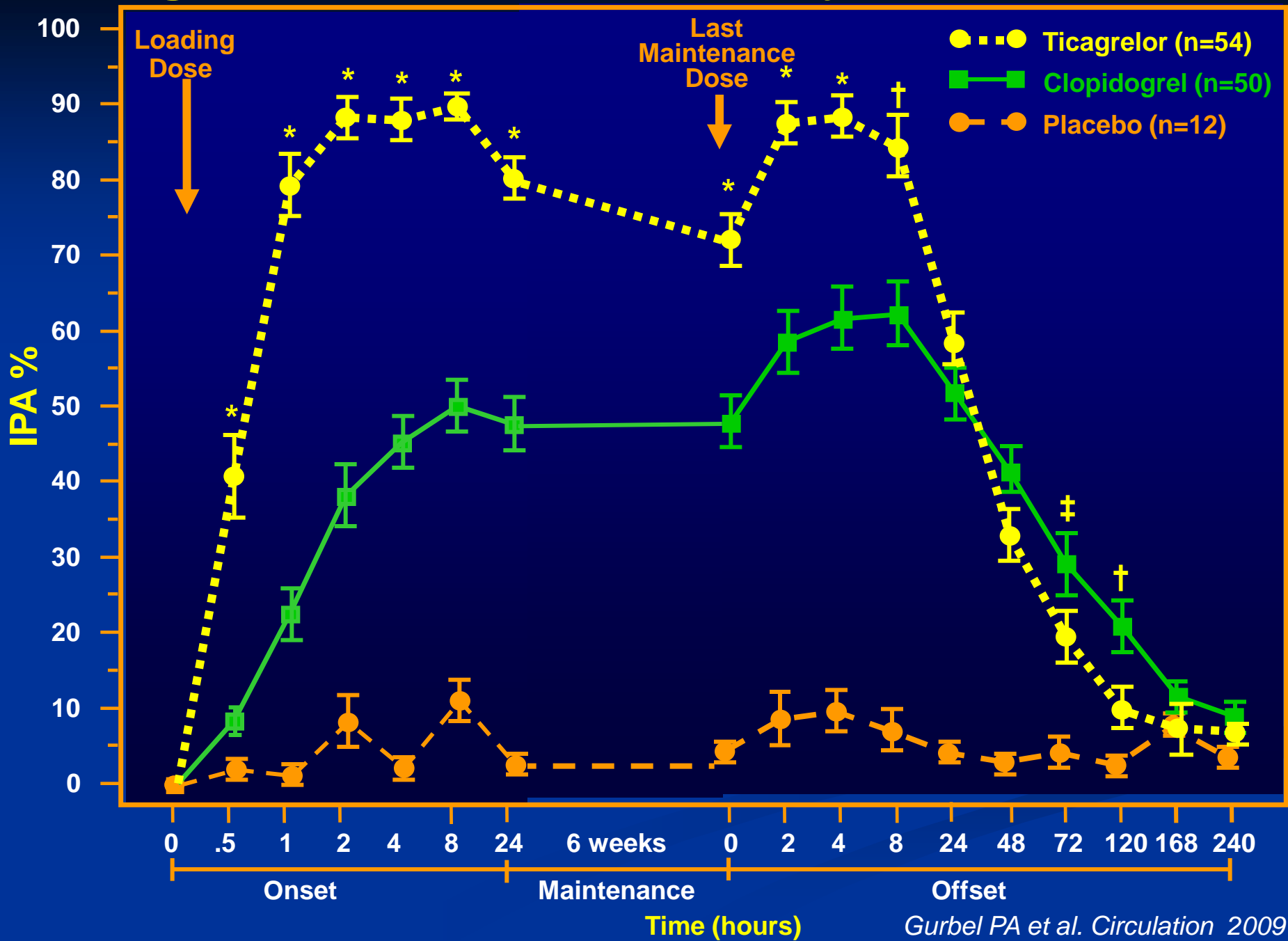
(Giezen et al, JTH 2009)



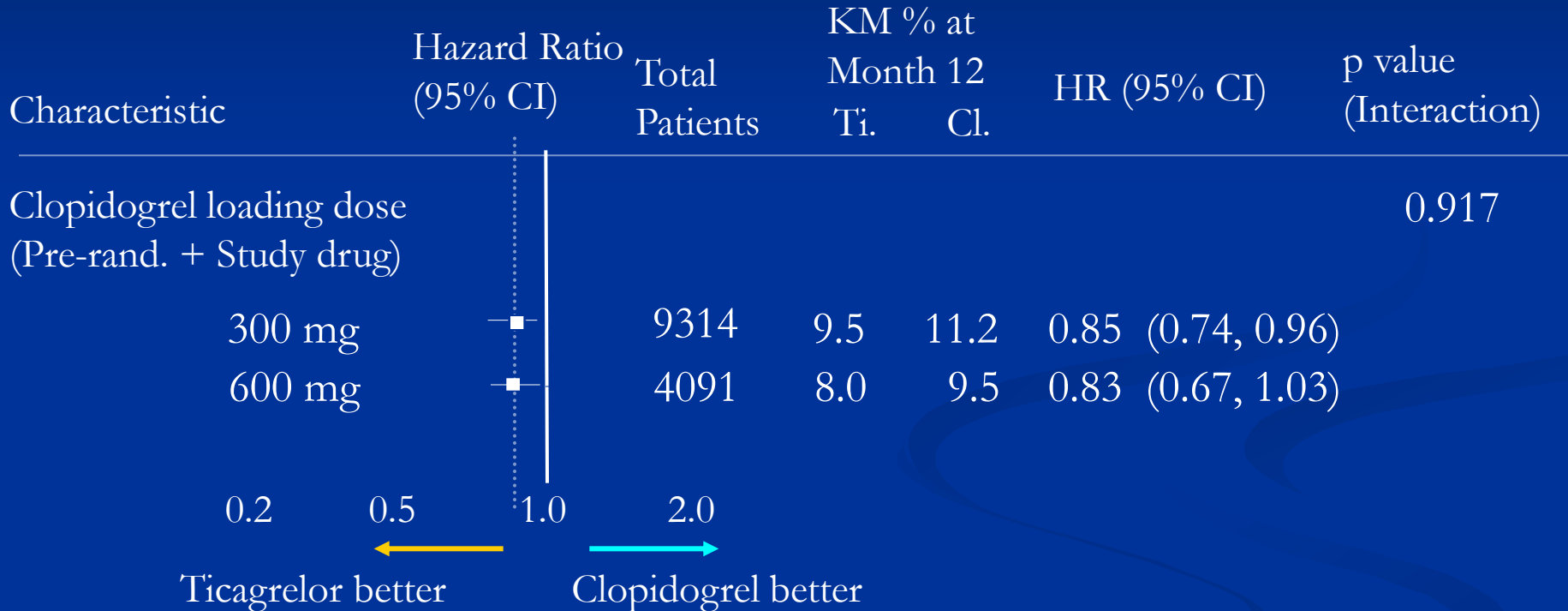
ADP
binding site

Ticagrelor
binding site

Ticagrelor - Onset / Offset Study, IPA to 5uM ADP



Primary efficacy endpoint by clopidogrel loading dose

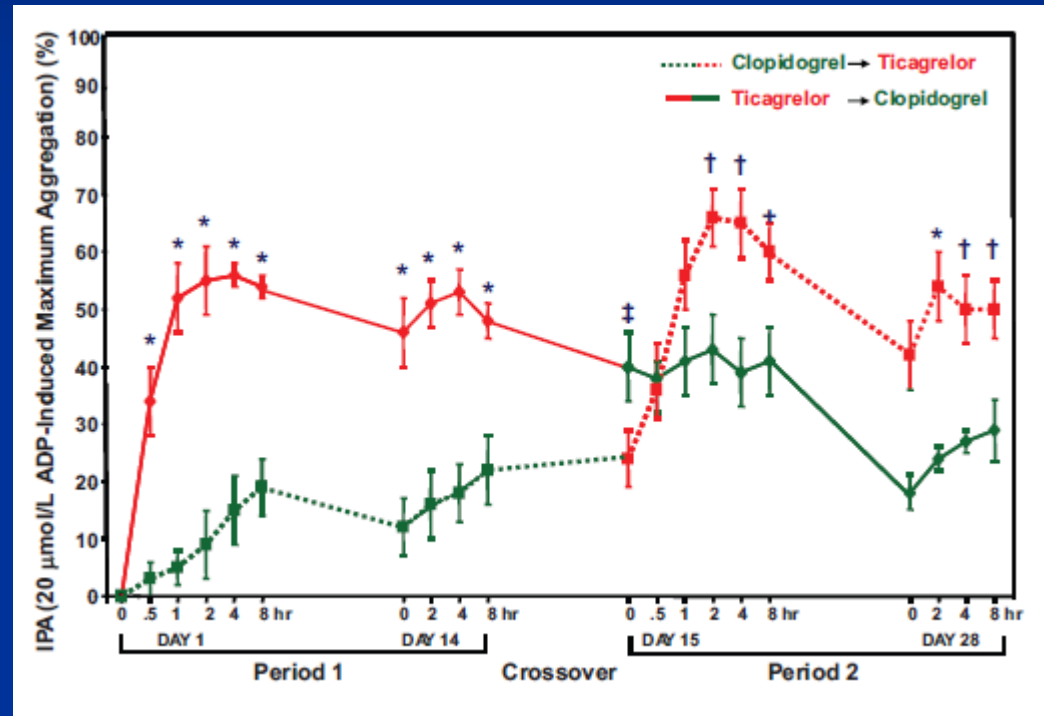


Medication	Ticagrelor (n=9,333)	Clopidogrel (n=9,291)
Clopidogrel start-up, %		
Clopidogrel in hospital before randomisation	46.0	46.1

Switching drugs in the RESPOND study

Patients treated with ticagrelor in period 1 received a 600-mg clopidogrel load followed by 75-mg daily maint. therapy

Patients treated with clopidogrel in period 1 received a 180-mg ticagrelor load followed by 90-mg twice daily maint. therapy.



41 patients non-responsive to clopidogrel

Gurbel et al, Circulation 2010

Switching drugs

- Switching from clopidogrel (loading or maintenance) to ticagrelor requires ticagrelor loading
- Switching from ticagrelor to clopidogrel probably also requires loading because of differences in compounds and active sites

THANK YOU

