NSTEMI:
C'è ancora spazio per il pre-trattamento?

ASL Biella
Azienda Sanitaria Locale di Biella

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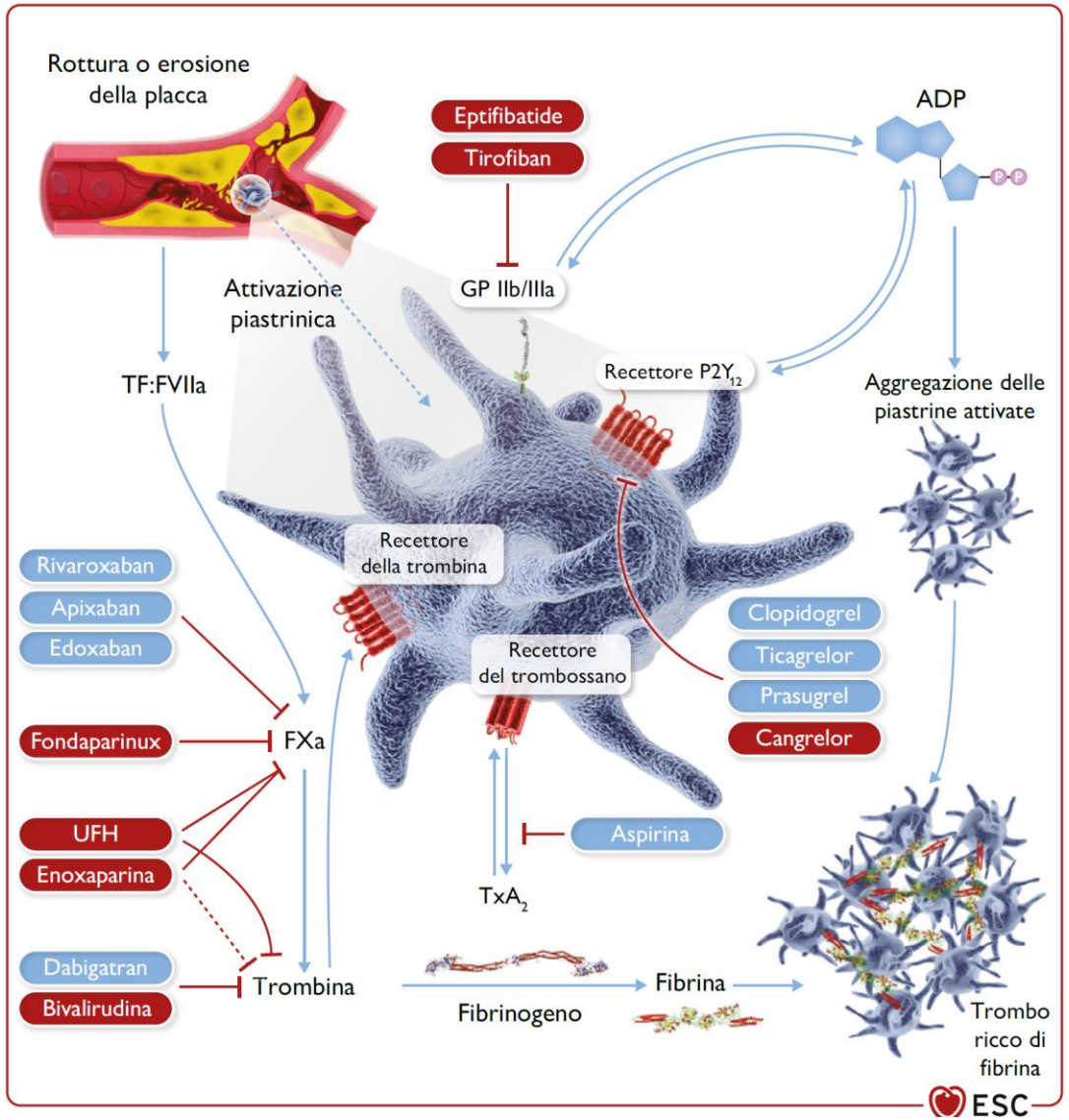


ESC guidelines on ACS, European Heart Journal 2023

Come rispondiamo alla domanda sul pretrattamento?

…cerchiamo risposta nelle linee guida!

Antiplatelet treatment		
Aspirin is recommended for all patients without contraindications at an initial oral LD of 150–300 mg (or 75–250 mg i.v.), and at a MD of 75–100 mg o.d. for long-term treatment.[179–181]	I	A
A $P2Y_{12}$ receptor inhibitor is recommended in addition to aspirin, and maintained over 12 months unless there are contraindications or an excessive risk of bleeding.[170,171,182] Options are:	I	A
• Prasugrel in $P2Y_{12}$ receptor inhibitor-naïve patients proceeding to PCI (60 mg LD, 10 mg/d as standard dose, 5 mg/d for patients aged ≥75 years or with a body weight <60 kg).[171]	I	B
• Ticagrelor irrespective of the planned treatment strategy (invasive or conservative) (180 mg LD, 90 mg b.i.d.).[170]	I	B
• Clopidogrel (300–600 mg LD, 75 mg daily dose), only when prasugrel or ticagrelor are not available, cannot be tolerated, or are contraindicated.[182,183]	I	C
Prasugrel should be considered in preference to ticagrelor for NSTE-ACS patients who proceed to PCI.[174]	IIa	B
GP IIb/IIIa antagonists should be considered for bail-out if there is evidence of no-reflow or a thrombotic complication.	IIa	C
Cangrelor may be considered in $P2Y_{12}$ receptor inhibitor-naïve patients undergoing PCI.[184–187]	IIb	A
Pre-treatment with a $P2Y_{12}$ receptor inhibitor may be considered in patients with NSTE-ACS who are not planned to undergo an early invasive strategy and do not have an HBR.	IIb	C
Treatment with GP IIb/IIIa antagonists in patients in whom coronary anatomy is not known is not recommended.[188,189]	III	A
It is not recommended to administer routine pre-treatment with a $P2Y_{12}$ receptor inhibitor in patients in whom coronary anatomy is not known and an early invasive management is planned.[174,177,178,190,191]	III	A

Raccomandazioni	Classe[a]	Livello[b]
Il pretrattamento con un inibitore del recettore $P2Y_{12}$ può essere preso in considerazione nei pazienti che devono essere sottoposti ad una strategia di PPCI[244,245].	IIb	B
Il pretrattamento con un inibitore del recettore $P2Y_{12}$ può essere preso in considerazione nei pazienti con NSTE-ACS che non si ritiene debbano essere sottoposti ad una strategia invasiva precoce (<24 h) e che non presentano un HBR[c 263].	IIb	C
Il pretrattamento con antagonisti del recettore GP IIb/IIIa non è raccomandato[292].	III	A
Il pretrattamento di routine con inibitori del recettore $P2Y_{12}$ non è raccomandato nei pazienti con NSTE-ACS senza anatomia coronarica nota candidati a strategia invasiva precoce (<24 h)[244,247,248,293-295].	III	A

ESC guidelines on NSTEMI, European Heart Journal 2021
ESC guidelines on ACS, European Heart Journal 2023

Ottimo abbiamo una risposta

C'è ancora spazio per il pretrattamento?

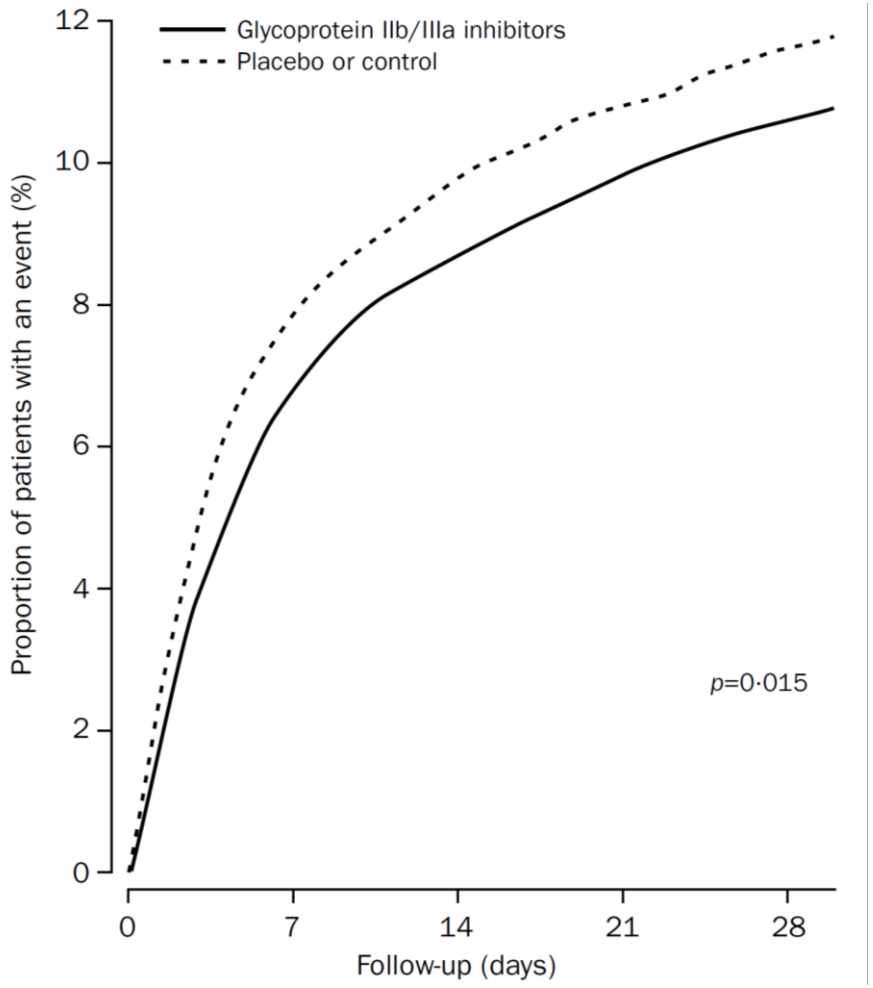
NO!

Ma è veramente così semplice?

Da dove derivano queste indicazioni?

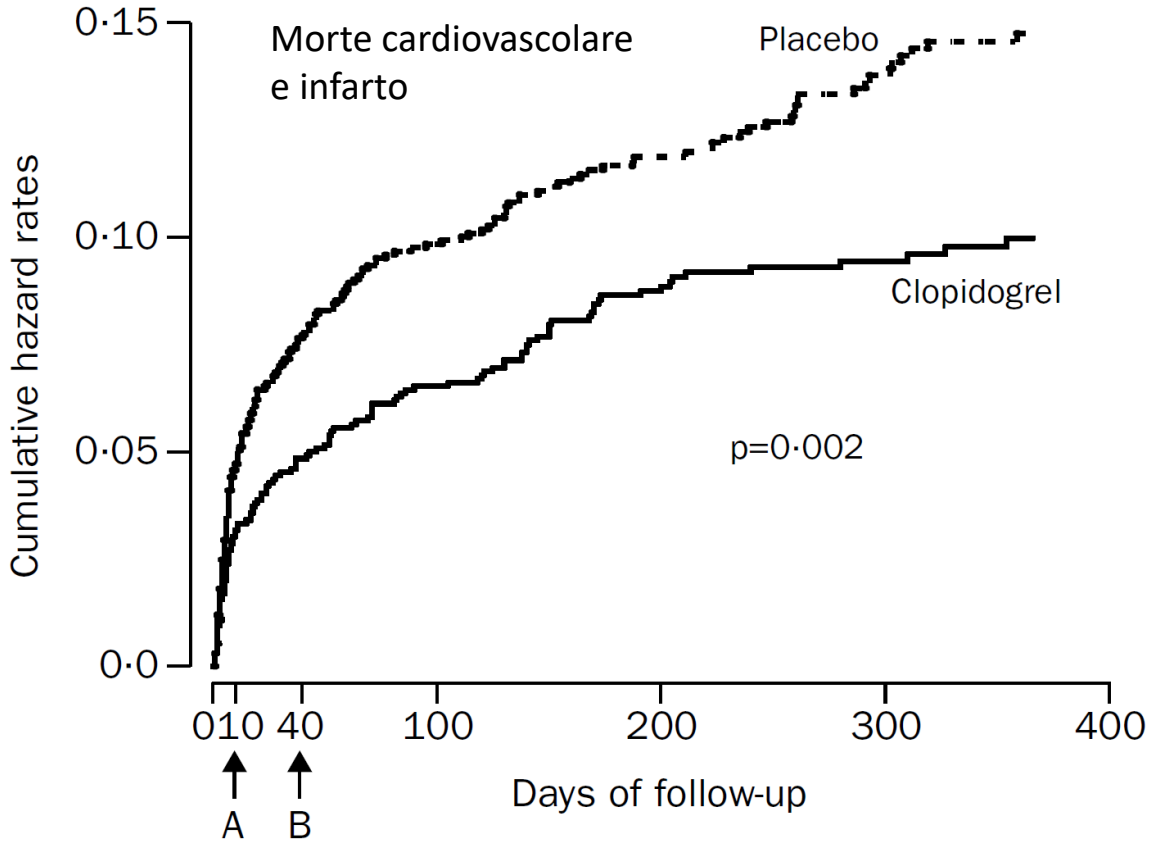
Ci sono delle eccezioni?

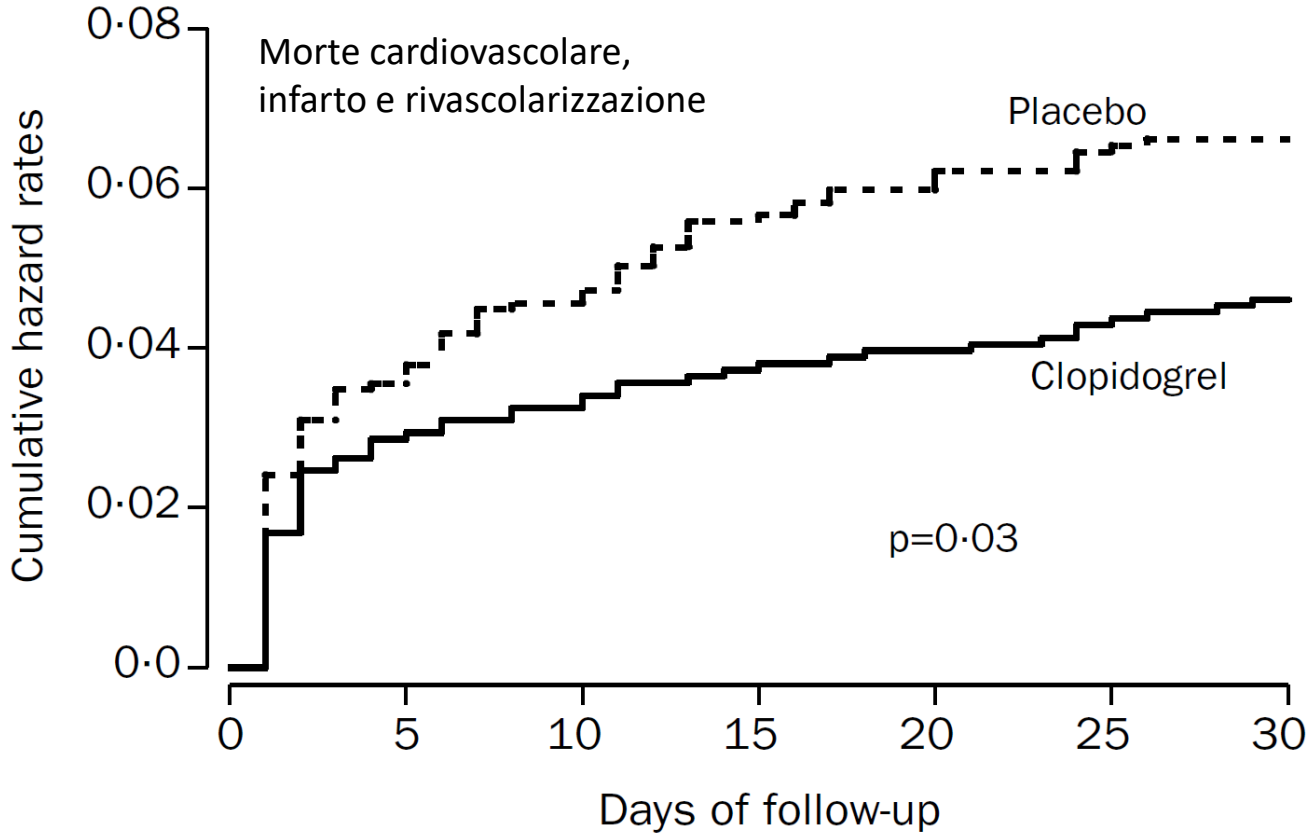
Inibitori della Glicoprotenia IIb/IIIa



Boersma et al, Lancet 2002

PCI-CURE : Clopidogrel pre-treatment

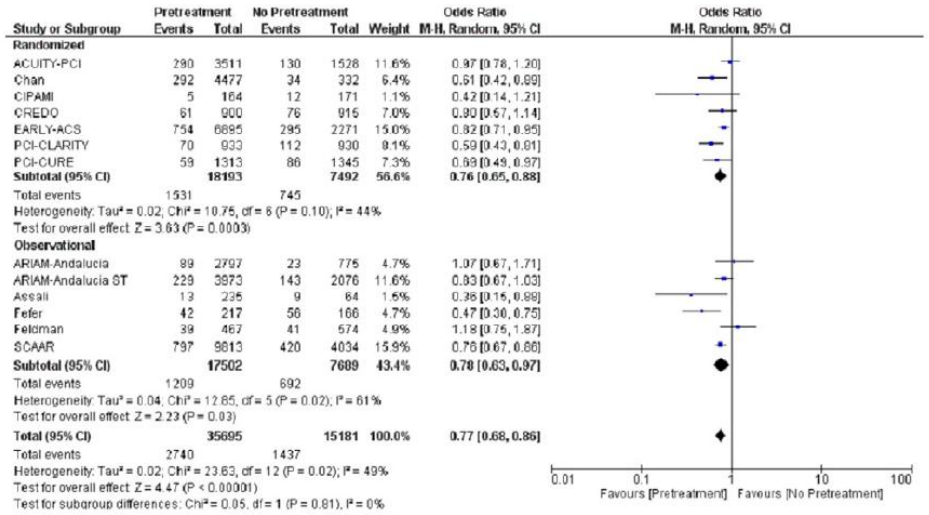




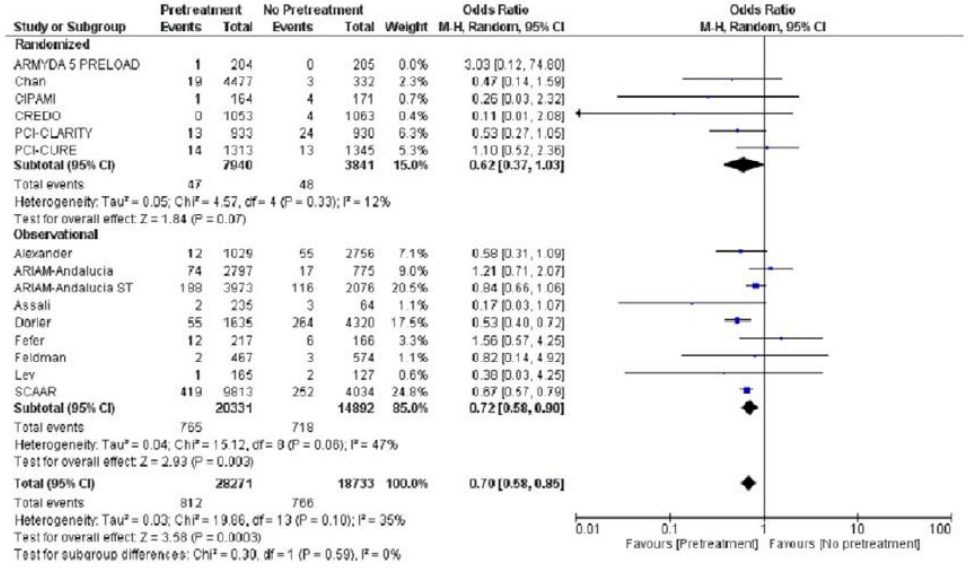
Mehta et al, Lancet 2001

Metanalisi su 61517 pazienti : Clopidogrel pre-treatment

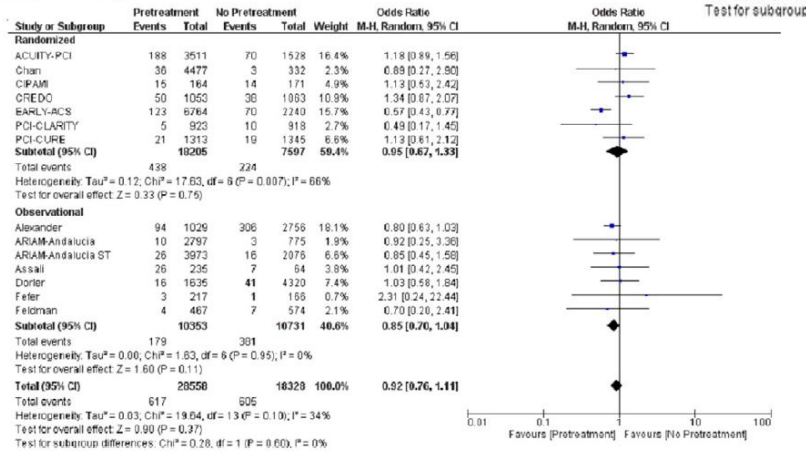
MACE



Mortality

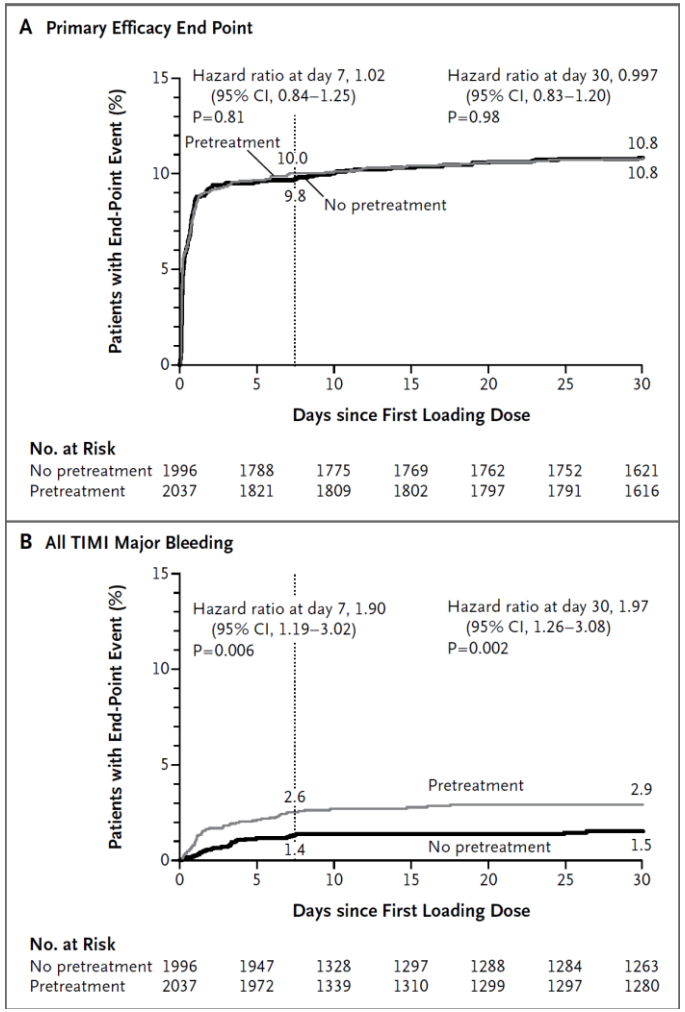


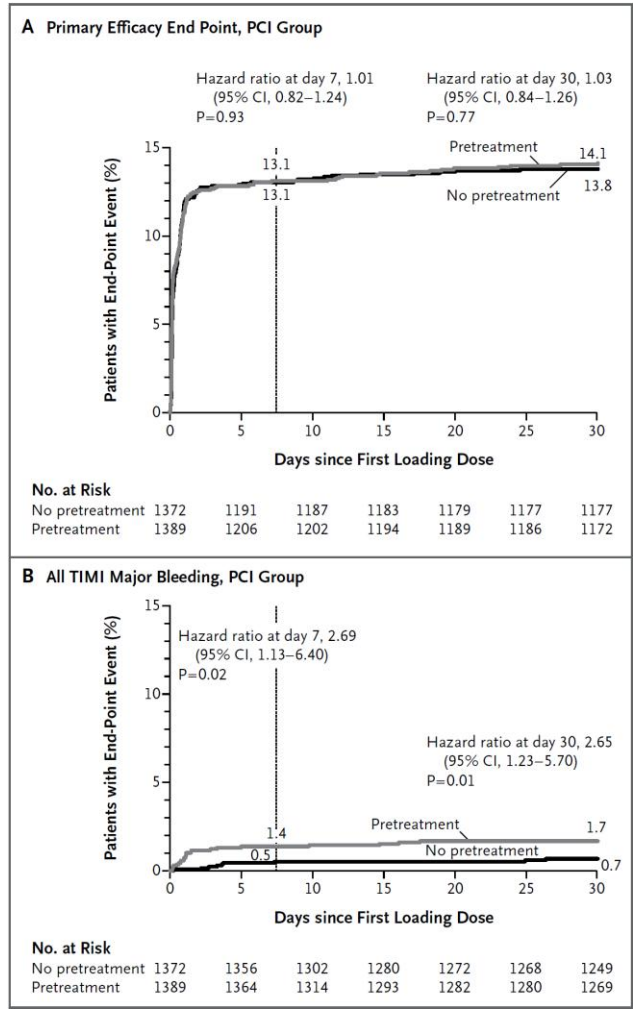
Major bleeding



Nairooz et al, International Journal of Cardiology 2017

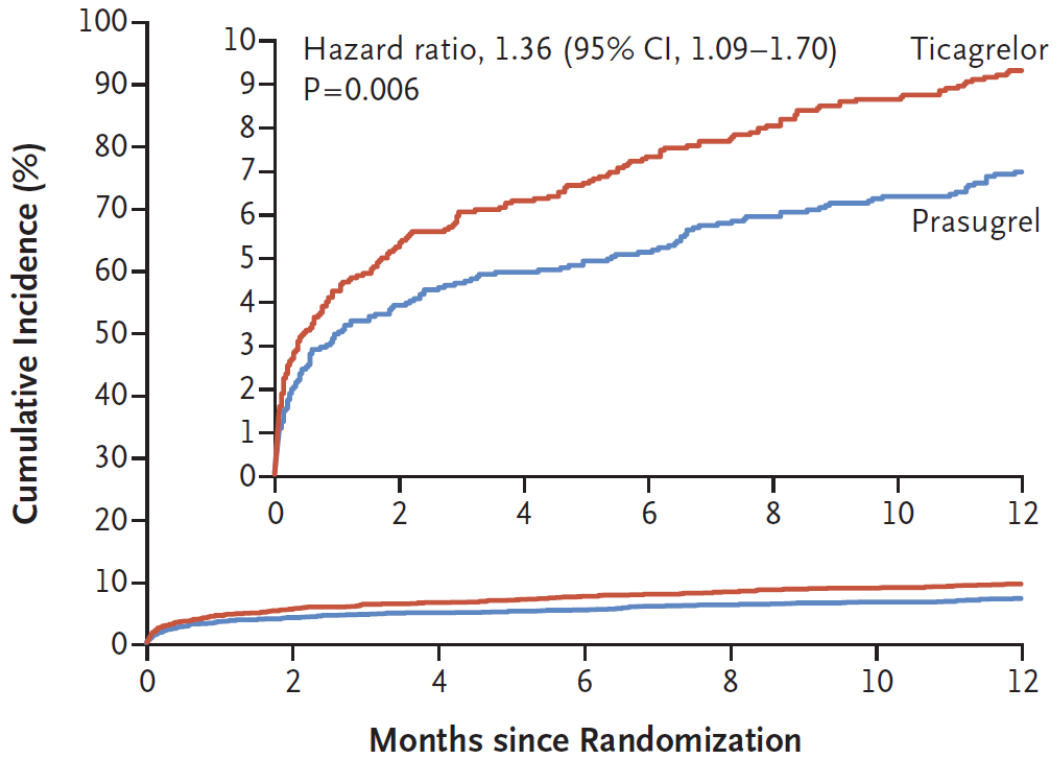
ACCOST: Prasugrel pre-treatment





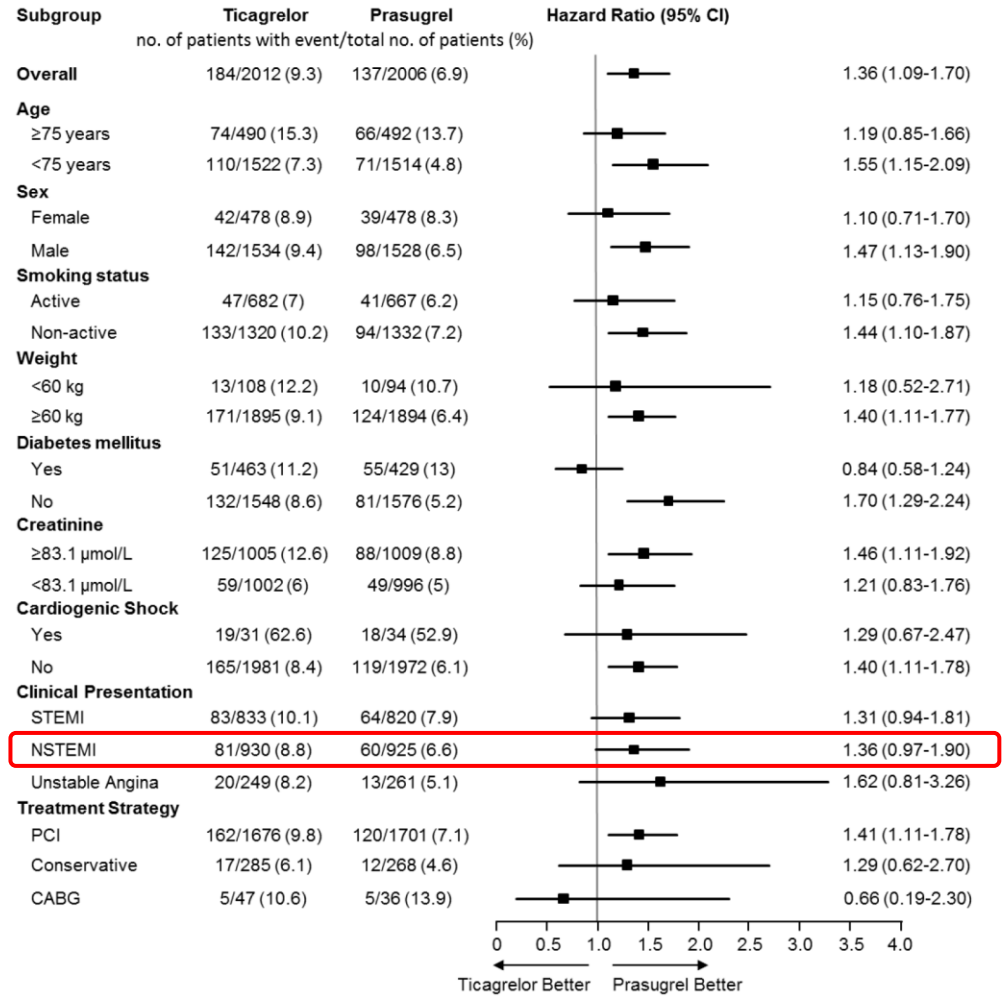
Montalescot et al, N Engl J Med 2013

ISAR-REACT-5: Ticagrelor vs. Prasugrel



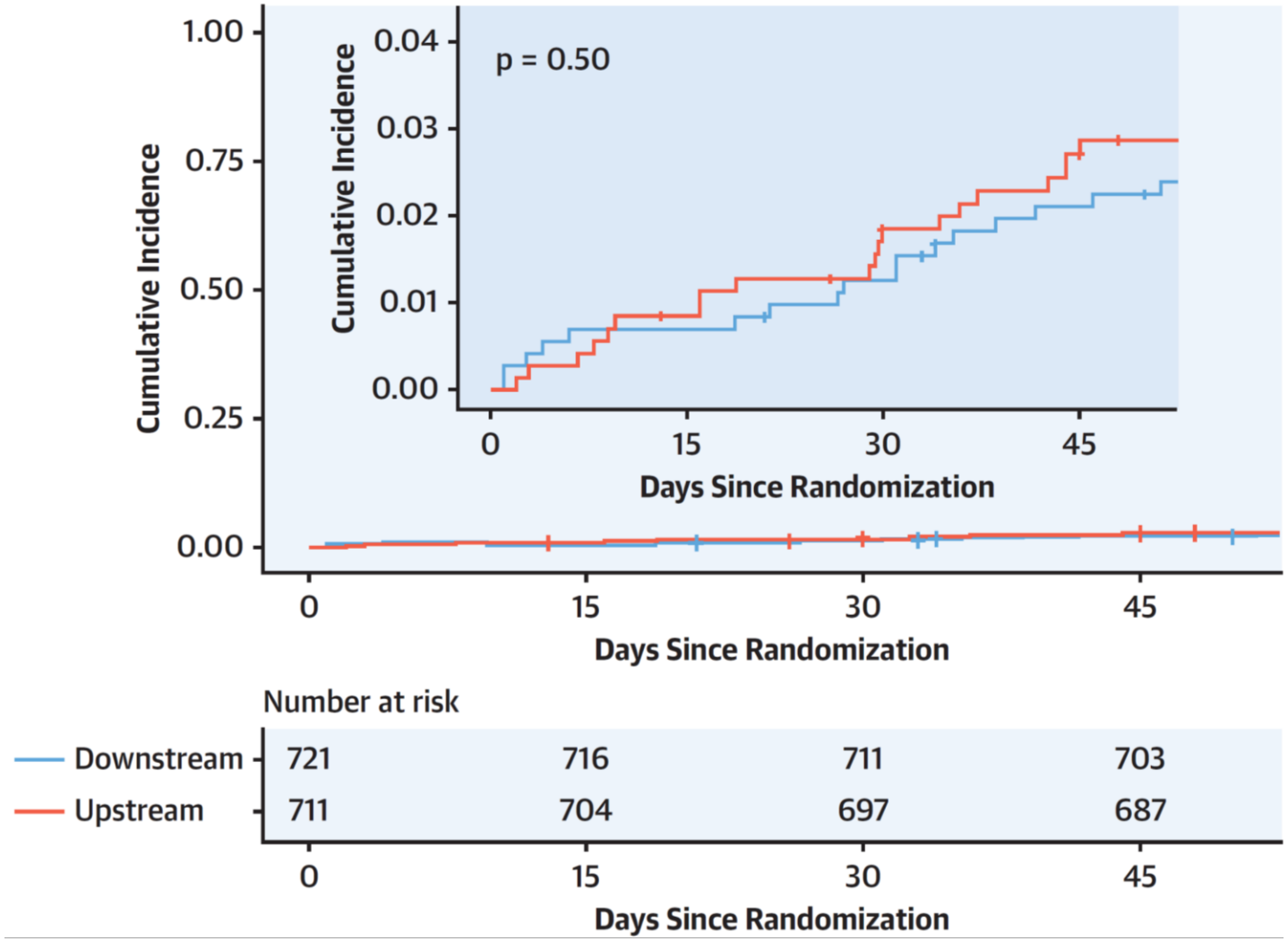
No. at Risk

Ticagrelor	2012	1877	1857	1835	1815	1801	1722
Prasugrel	2006	1892	1877	1862	1839	1829	1803



Schüpke et al, N Engl J Med 2019

DUBIUS



Tarantini et al, J Am Coll Cardiol 2020

64857 pazienti da "Swedish Coronary Angiography and Angioplasty Registry"

	No. (%)				
	Pretreated		Not pretreated		
Bivalirudin	9544 (15.9)	492 (1.3)	436 (8.8)	1 (0.1)	<.001
GP2b/3a receptor inhibitor	1555 (2.6)	1 (0.0)	97 (1.9)	1 (0.1)	.002
Unfractionated heparin	53 338 (89.1)	4 (0.1)	4485 (90.4)	1 (0.1)	.007

Clinical outcome	Patients, No. (%)				
	Pretreated (n = 59 894)	Not pretreated (n = 4963)	Missing	Adjusted OR (95% CI)	*P* value
Primary end point					
Death at 30 d[a,b]	846 (1.4)	125 (2.5)	0	1.44 (0.78-2.62)	.36
Secondary end point					
Death at 1 y[a,c]	2324 (4.3)	241 (7.1)	0	1.34 (0.77-2.34)	.30
Definite stent thrombosis at 30 d[a,d]	243 (0.2)	19 (0.2)	0	1.17 (0.64-2.16)	.60
In-hospital bleeding[a,e]	3562 (6.0)	380 (7.5)	11 (0.1)	1.49 (1.06-2.12)	.02

Dworeck et al, JAMA Network Open 2020

Ma è tutto così chiaro e semplice?

FABOLUS PRO

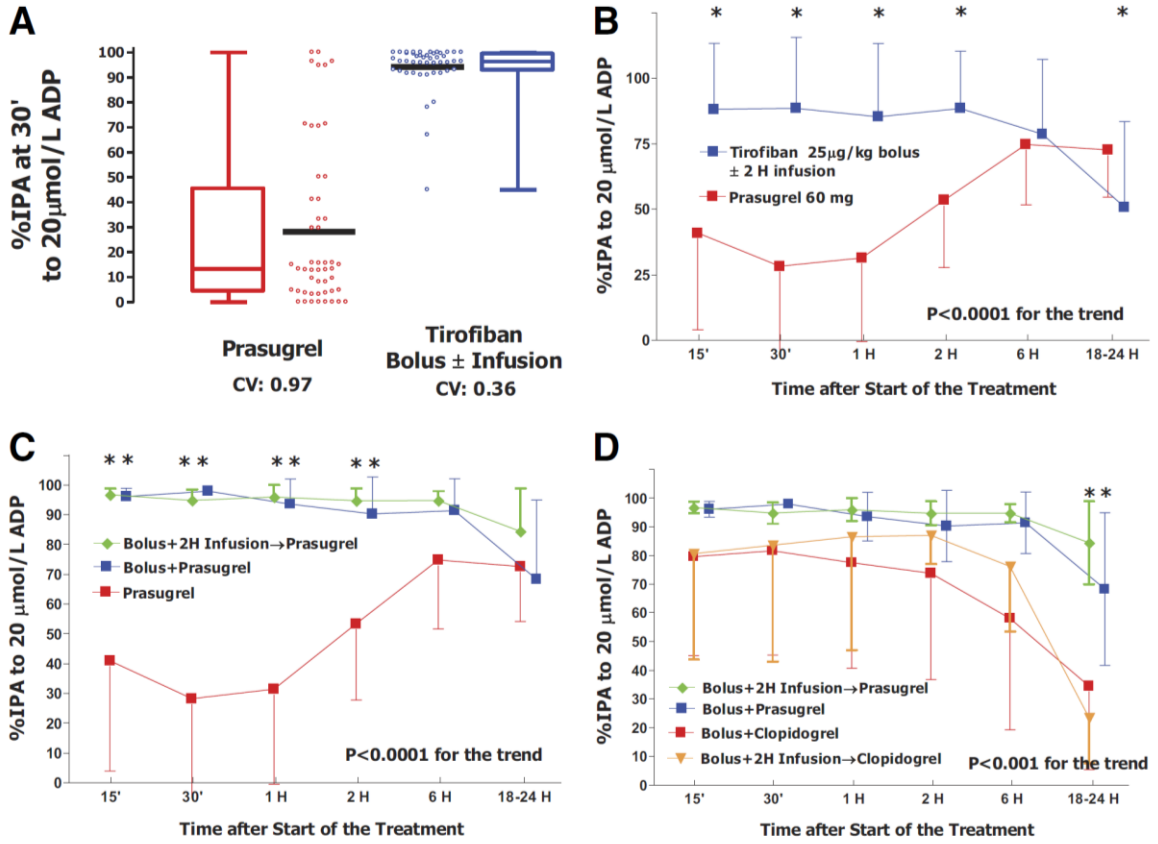


Figure 2. Kinetics of Platelet Inhibition Over Time After 20 µmol/l ADP

(A) Primary endpoint analysis; percentage of platelet inhibition (%IPA) after 20 µmol/l adenosine diphosphate (ADP) 30 min after start of the treatment. CV denotes the %IPA coefficient of variability, which has been calculated as the SD divided by the mean value. The **horizontal bars** in the scatter plot graph denote mean values; **(B)** %IPA in the tirofiban group versus prasugrel alone; **(C)** %IPA in patients treated with both tirofiban bolus with or without infusion versus the prasugrel-alone group; **(D)** %IPA in patients treated with tirofiban, with or without infusion and with or without prasugrel or clopidogrel.
*p = 0.05 versus %IPA measured in the prasugrel-alone group at post hoc analysis. **Vertical bars** represent SD of the mean value.

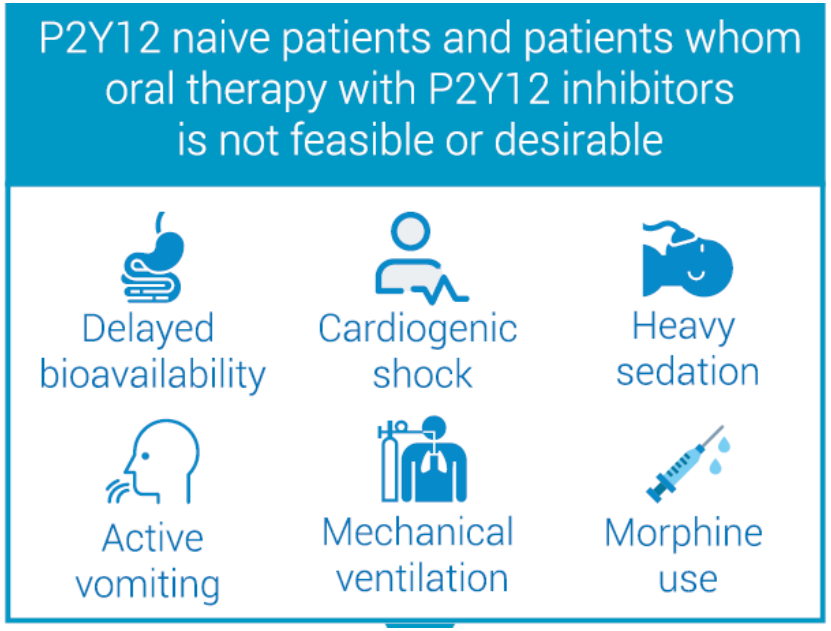
Valgimigli et al, J Am Coll Cardiol Intv 2012

Confronto tra inibitori P2Y12

	Clopidogrel	Prasugrel	Ticagrelor
Chemical class	Thienopyridine	Thienopyridine	Cyclopentyl-triazo-lopyrimidine
Route	Oral	Oral	Oral
Prodrug	Yes (pro-drug, CYP dependent, 2 steps)	yes (pro-drug, CYP dependent, 1 step)	No
Bioavailability	15%	79%	36%
Standard dosage	600 mg LD, then 75 mg once a day	60 mg LD, then 10 mg once a day	180 mg LD, then 90 mg twice a day
Reversibility of binding	Irreversible	Irreversible	Reversible
Onset of antiplate-let effect	2–6 h	0.5–4 h	0.5–2 h
Level of plate-let inhibition at steady state	40–60%	65–80%	65–80%
Offset of antiplate-let effect	3–10 days	5–10 days	3–4 days
Recommended stop of treatment before surgery	5 days	7 days	3–5 days
Excretion	50% renal, 46% biliary	68% renal, 27% feces	Biliary
Kidney failure	No dose adjustment	No dose adjustment	No dose adjustment
Dialysis or CrCl < 15 mL/min	Limited data	Limited data	Limited data

Kubica et al, Cardiology Journal 2024

Limiti degli inibitori orali del recettore P2Y12



Di conseguenza, molti pazienti potrebbero non raggiungere un'adeguata inibizione piastrinica al momento della PCI o subito dopo, con conseguente aumentato rischio di trombosi dello stent, infarto del miocardio e morte

Durata e antidoto: L'effetto di questi farmaci dura per diversi giorni, e non esiste un antidoto disponibile in commercio per ripristinare rapidamente la funzionalità piastrinica in caso di emorragia o necessità di un intervento chirurgico d'urgenza.

De Luca et al, J Am Heart Assoc 2021
Kubica et al, Cardiology Journal 2024

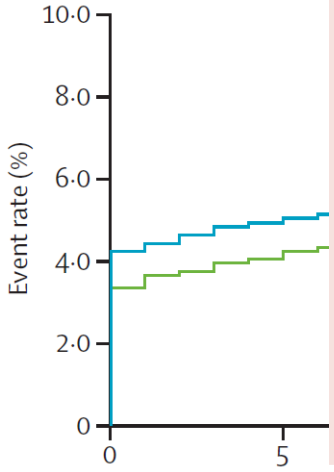
Confronto tra inibitori P2Y12

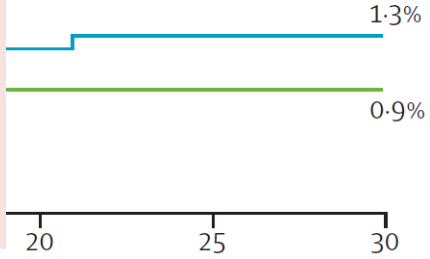
	Clopidogrel	Prasugrel	Ticagrelor	Cangrelor
Chemical class	Thienopyridine	Thienopyridine	Cyclopentyl-triazo-lopyrimidine	Adenosine triphos-phate analogue
Route	Oral	Oral	Oral	Intravenous
Prodrug	Yes (pro-drug, CYP dependent, 2 steps)	yes (pro-drug, CYP dependent, 1 step)	No	No
Bioavailability	15%	79%	36%	100%
Standard dosage	600 mg LD, then 75 mg once a day	60 mg LD, then 10 mg once a day	180 mg LD, then 90 mg twice a day	30 μg/kg bolus, then 4 μg/kg/min
Reversibility of binding	Irreversible	Irreversible	Reversible	Reversible
Onset of antiplate-let effect	2–6 h	0.5–4 h	0.5–2 h	2 min
Level of plate-let inhibition at steady state	40–60%	65–80%	65–80%	90–98%
Offset of antiplate-let effect	3–10 days	5–10 days	3–4 days	30–60 min
Recommended stop of treatment before surgery	5 days	7 days	3–5 days	1 h
Excretion	50% renal, 46% biliary	68% renal, 27% feces	Biliary	Not dependent on hepatic or renal clearance mecha-nisms
Kidney failure	No dose adjustment	No dose adjustment	No dose adjustment	No dose adjustment
Dialysis or CrCl < 15 mL/min	Limited data	Limited data	Limited data	Limited data

Kubica et al, Cardiology Journal 2024

CHAMPION-PCI, CHAMPION-PLATFORM, e CHAMPION-PHOENIX: Cangrelor Vs. Clopidogrel or placebo

	Cangrelor (n=12 565)	Clopidogrel (n=12 542)	OR (95% CI)	p*
GUSTO bleeding				
Severe/life threatening	28 (0·2%)	23 (0·2%)	1·22 (0·70–2·11)	0·4875
Moderate	76 (0·6%)	56 (0·4%)	1·36 (0·96–1·92)	0·0828
Severe/moderate	103 (0·8%)	79 (0·6%)	1·30 (0·97–1·75)	0·0762
Mild	2109 (16·8%)	1627 (13·0%)	1·35 (1·26–1·45)	<0·0001
Mild, excluding ecchymosis, oozing, and <5 cm haematoma	707 (5·6%)	515 (4·1%)	1·39 (1·24–1·56)	<0·0001
Any GUSTO bleed	2196 (17·5%)	1696 (13·5%)	1·35 (1·26–1·45)	<0·0001
TIMI bleeding				
Major	32 (0·3%)	28 (0·2%)	1·14 (0·69–1·90)	0·6101
Minor	77 (0·6%)	51 (0·4%)	1·51 (1·06–2·15)	0·0218
TIMI major/minor	109 (0·9%)	79 (0·6%)	1·38 (1·03–1·85)	0·0290



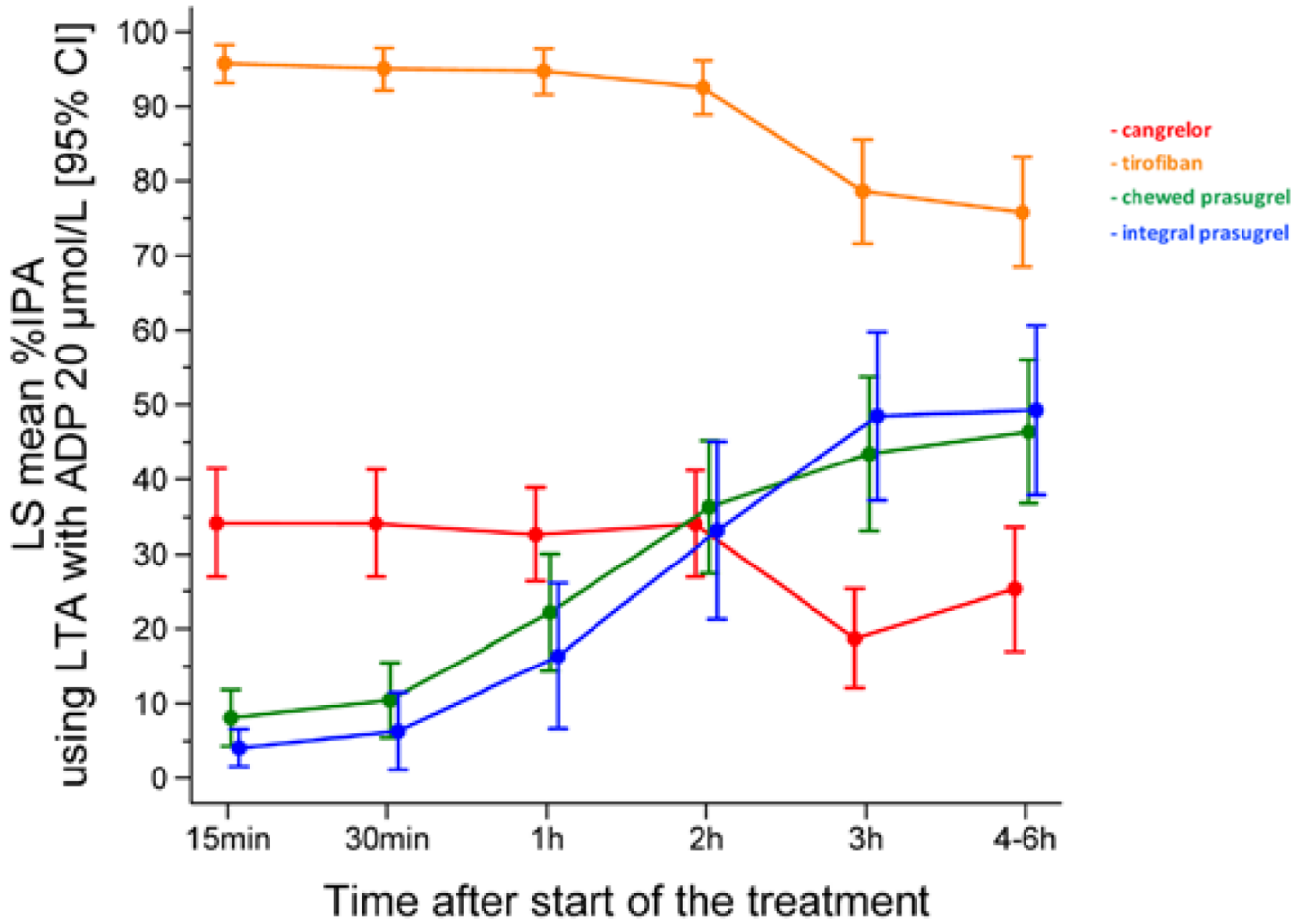


Favours cangrelor Favours comparator

Steg et al, Lancet 2013

Cangrelor con Ticagrelor e Prasugrel

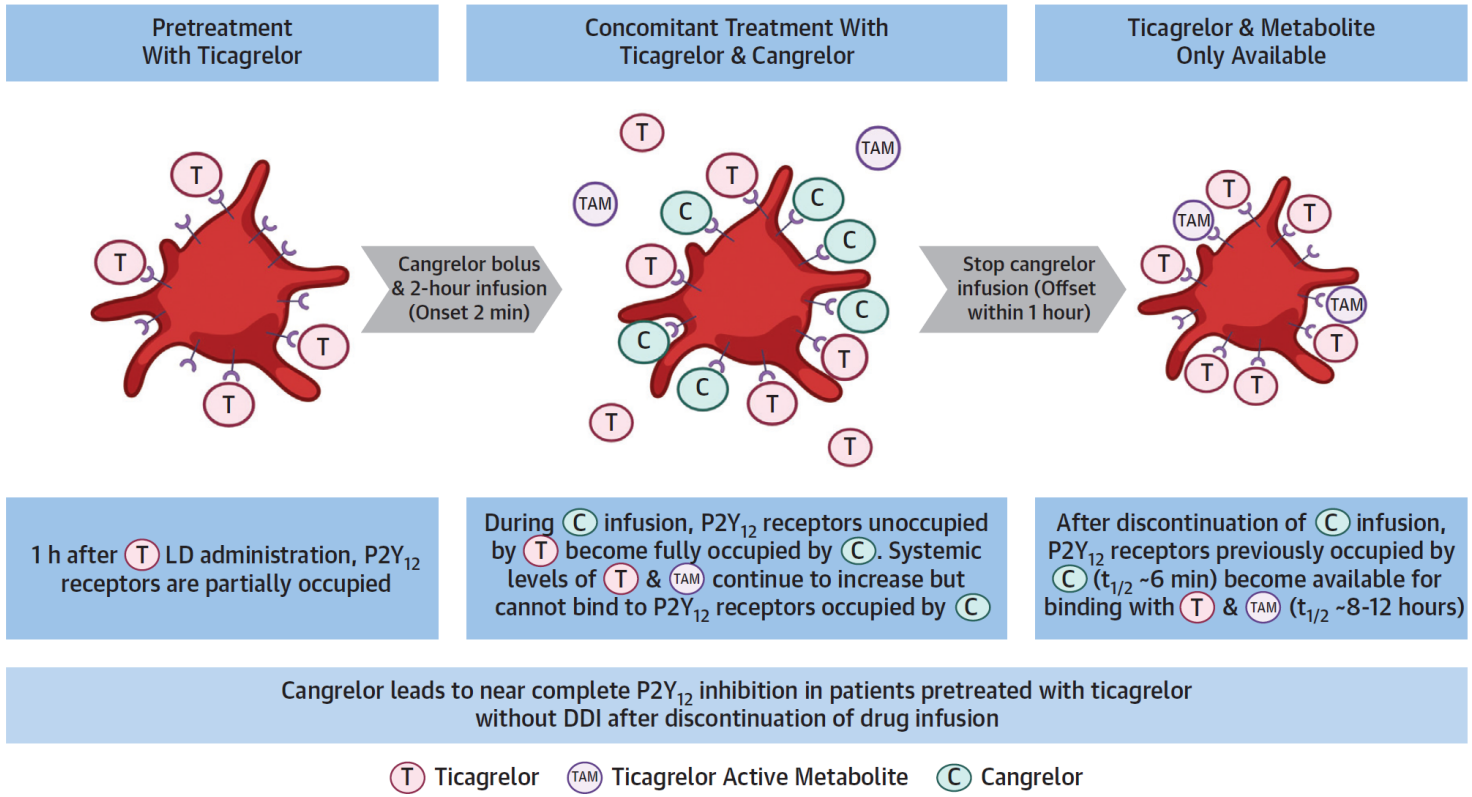
FABOLUS-FASTER



Gargiulo et al, Circulation 2020

SWAP-5 Study: Cangrelor in pazienti pretrattati con Ticagrelor

CENTRAL ILLUSTRATION **Pharmacokinetic and Pharmacodynamic Profiles Associated With the Use of Cangrelor in Patients With Coronary Artery Disease Pretreated With Ticagrelor**

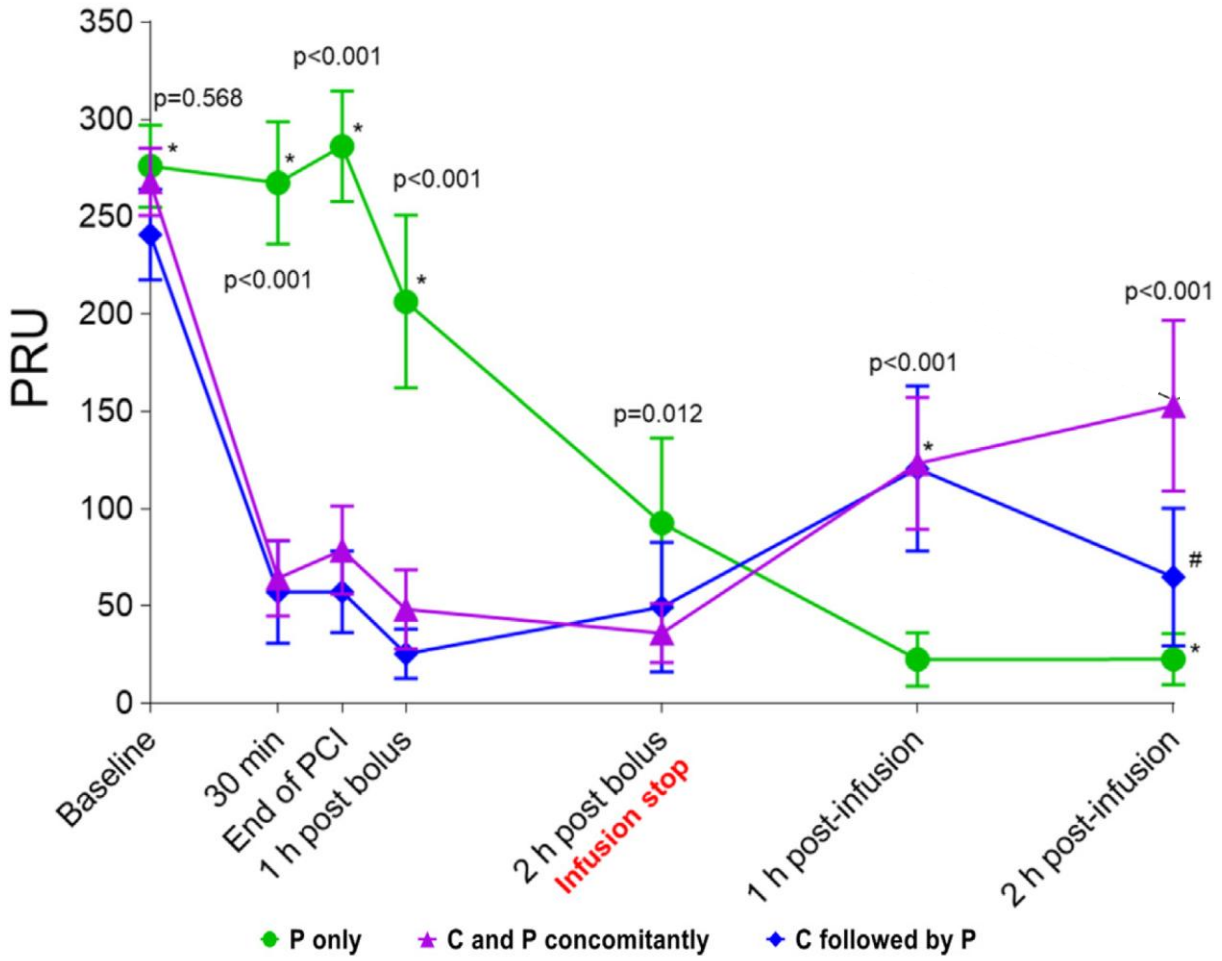


Franchi F, et al. J Am Coll Cardiol Intv. 2023;16(1):36-46.

The ticagrelor active metabolite is AR-C124910XX. DDI = drug-drug interaction; LD = loading dose; $t_{1/2}$ = half-life.

Franchi et al, J Am Coll Cardiol Intv 2023

SWAP-6 Study: Cangrelor in pazienti pretrattati con Prasugrel



Franchi et al, J Am Coll Cardiol Intv 2023

Ricordiamo che non esistono trial randomizzati di efficacia e safety di Cangrelor con Ticagrelor e Prasugrel

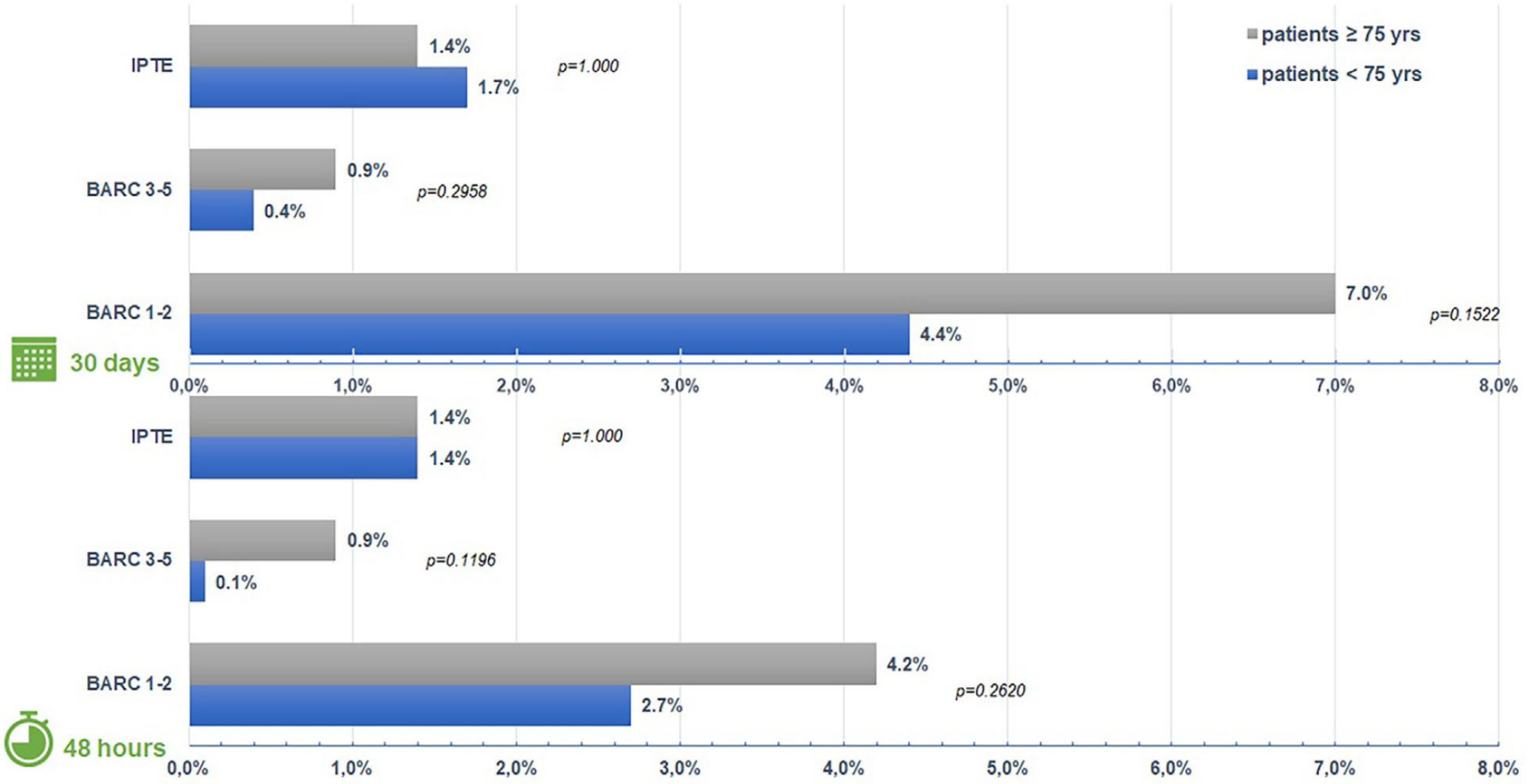
Cangrelor: dati real world

Esperienze Real-World con Cangrelor in uno studio registro monocentrico su 991 pazienti

Indication for cangrelor	
No pretreatment with oral P2Y12 inhibitor	950 (95.9%)
Pretreatment with oral P2Y12 inhibitor deemed insufficient	20 (2.0%)
Thrombus evolves during PCI without pretreatment with oral P2Y12 inhibitor	8 (0.8%)
Thrombus evolves during PCI despite pretreatment with oral P2Y12 inhibitor	7 (0.7%)
Uncertainty about bleeding and need for P2Y12 inhibition	6 (0.6%)
Aspirin prior to PCI	949 (95.8%)
Warfarin prior to PCI	17 (1.7%)
NOAC prior to PCI	27 (2.7%)
Oral P2Y12 inhibitor after PCI	
No	15 (1.5%)
Clopidogrel	95 (9.6%)
Ticagrelor	881 (88.9%)
Unfractionated heparin as adjunct to PCI	974 (98.3%)
Abciximab as adjunct to PCI	21 (2.1%)
Bivalirudin as adjunct to PCI	2 (0.2%)
Eptifibatide as adjunct to PCI	1 (0.1%)

Thim et al, Cardiology Research and Practice 2023

Lo Studio ARCANGELO nel paziente ≥ 75 anni



Capranzano et al, The American Journal of Cardiology 2025

ESC European Society of Cardiology
European Heart Journal (2023) **44**, 3720–3826
https://doi.org/10.1093/eurheartj/ehad191

ESC GUIDELINES

2023 ESC Guidelines for the management of acute coronary syndromes

Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC)

Il cangrelor può essere preso in considerazione nei pazienti naïve agli inibitori del recettore $P2Y_{12}$ che devono essere sottoposti a PCI[251-254].

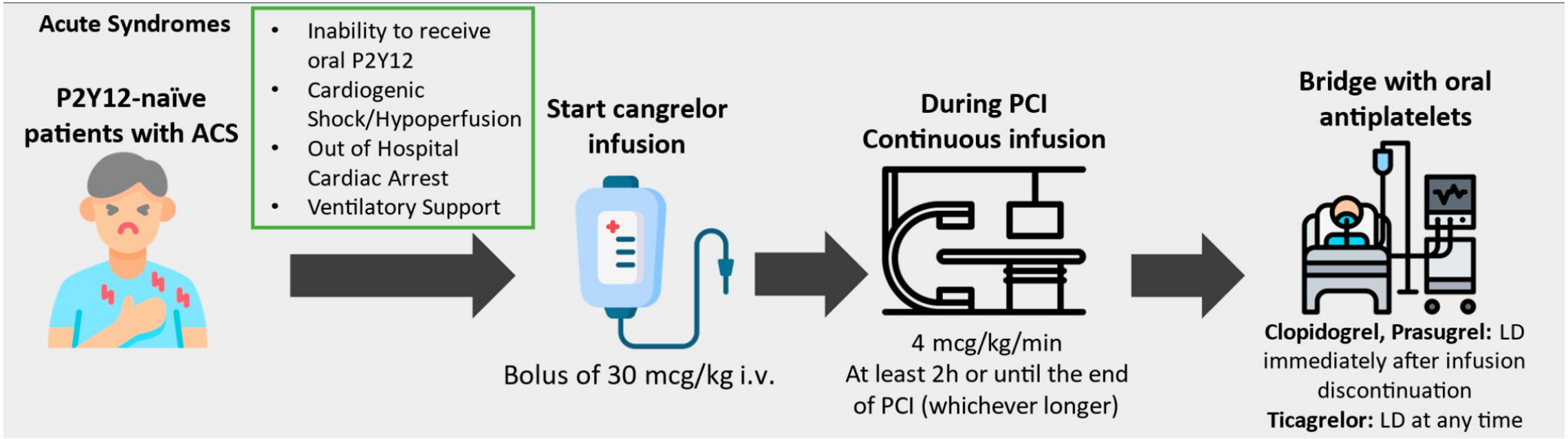
IIb	A

CLINICAL PRACTICE GUIDELINES

2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

COR	LOE	Recommendation
2b	B-R	1. Among patients with ACS undergoing PCI who have not received a P2Y12 inhibitor, intravenous cangrelor may be reasonable to reduce periprocedural ischemic events.*[1–4]

ESC guidelines on ACS, European Heart Journal 2023
ACC/AHA on ACS, Circulation 2025



Pyrpyris et al, Pharmaceuticals 2025

Take Home Message

- Numerose evidenze scientifiche hanno dimostrato che nelle SCA-NSTEMI il pretrattamento con gli inibitori del recettore P2Y12 non dà nessun vantaggio ed è spesso gravato da maggior rischio di sanguinamento
- Le linee guida hanno recepito pienamente questo messaggio e il pretrattamento con P2Y12i per os è in Classe III Liv. A
- Secondo le recenti Linee Guida Europee si può prendere in considerazione il pretrattamento solo nei pazienti NSTEMI *non HBR non candidati a coronarografia precoce* (> 24h) Classe IIb Liv. C
- La comparsa dell'effetto antiaggregante con Ticagrelor e Prasugrel può richiedere circa 2 ore dal carico orale
- Durante quella finestra temporale il paziente, magari sottoposto ad una PCI complessa, non risulta sufficientemente antiggregato
- Esistono, inoltre, molte situazioni in cui la somministrazione di farmaci per os risulta più complessa/meno efficace (shock cardiogeno, intubati, vomito, rallentamento di assorbimento intestinale in paziente acuti…)

Take Home Message

- Il Cangrelor è un inibitore P2Y12 somministrato per via endovenosa con un inizio di azione immediato e una quasi completa inibizione piastrinica
- Il Cangrelor supera i limiti di Prasugrel e Ticagrelor nei pazienti SCA
- Il Cangrelor ha un ottimo profilo di safety
- Sia le Linee Guida ESC che quelle ACC/AHA consigliano l'utilizzo di Cangrelor nei pazienti naïve agli inibitori del recettore P2Y12 Classe IIb Liv. A
- Le proprietà farmacologiche di Cangrelor possono essere particolarmente utili in scenari clinici in cui l'assorbimento degli inibitori P2Y12 somministrati per via orale è compromesso o non possibile e soprattutto nei pazienti sottoposti a PCI complessa
- La sicurezza e l'efficacia di Cangrelor in pazienti trattati con Ticagrelor o Prasugrel sono stati chiariti in maniera meno ampia rispetto a Clopidogrel

BIELLA CUORE
12-13 SETTEMBRE 2025

Take Home Message

- Numerose evidenze scientifiche hanno dimostrato che nelle SCA-NSTEMI il pretrattamento con gli inibitori del recettere P2Y12 non da nessun vantaggio ed è spesso gravato da maggior rischio di sanguinamento
- Le linee guida hanno recepito pienamente questo messaggio e il pretrattamento con P2Y12i è in Classe III liv. A
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- Il Cangrelor supera i limiti di Prasugrel e Ticagrelor nei pazienti SCA
- Il Cangrelor ha un ottimo profilo di safety
- Sia le Linee Guida ESC che quelle ACC/AHA consigliano l'utilizzo di Cangrelor nei pazienti naïve agli inibitori del recettore P2Y12 Classe Iib Liv. A
- Le proprietà farmacologiche di Cangrelor possono essere particolarmente utili in scenari clinici in cui l'assorbimento degli inibitori P2Y12 somministrati per via orale è compromesso o non possibile
- Soprattutto nei pazienti sottoposti a PCI complessa o in quelli in cui si ipotizza ridotta/tardiva efficacia dei farmaci per os, il Cangrelor potrebbe essere un'ottima alternativa
- La sicurezza e l'efficacia di Cangrelor rispetto a Ticagrelor o Prasugrel per quanto riguarda gli eventi ischemici sono stati chiariti in maniera meno ampia rispetto a Clopidogrel

- Cangrelor non ha metabolismo epatico e renale significativo
- Registri scaricati
- Shock cardiogeno
- Queste proprietà farmacologiche possono essere particolarmente utili in scenari clinici in cui l'assorbimento degli inibitori P2Y12 somministrati per via orale è compromesso o non possibile, nonché nei pazienti che necessitano di CABG o altri interventi chirurgici all'inizio dopo la PCI, quando l'interruzione prolungata di un inibitore P2Y12 potrebbe non essere sicura
- La sicurezza e l'efficacia di cangrelor rispetto a ticagrelor o prasugrel per quanto riguarda gli eventi ischemici non sono state stabilite

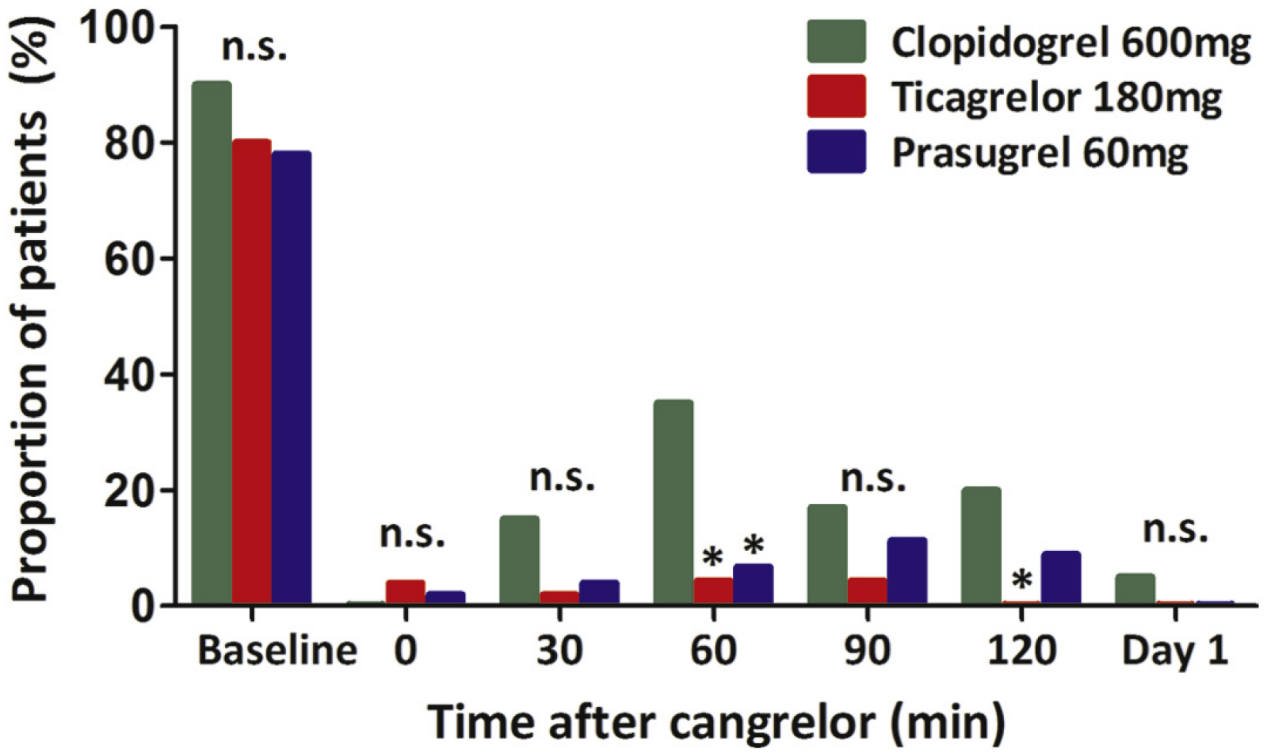
Pyrpyris et al, Pharmaceuticals 2025

ExcelsiorLOAD2 Trial

Cangrelor

Clopidogr
Loading
cangrelor
n =

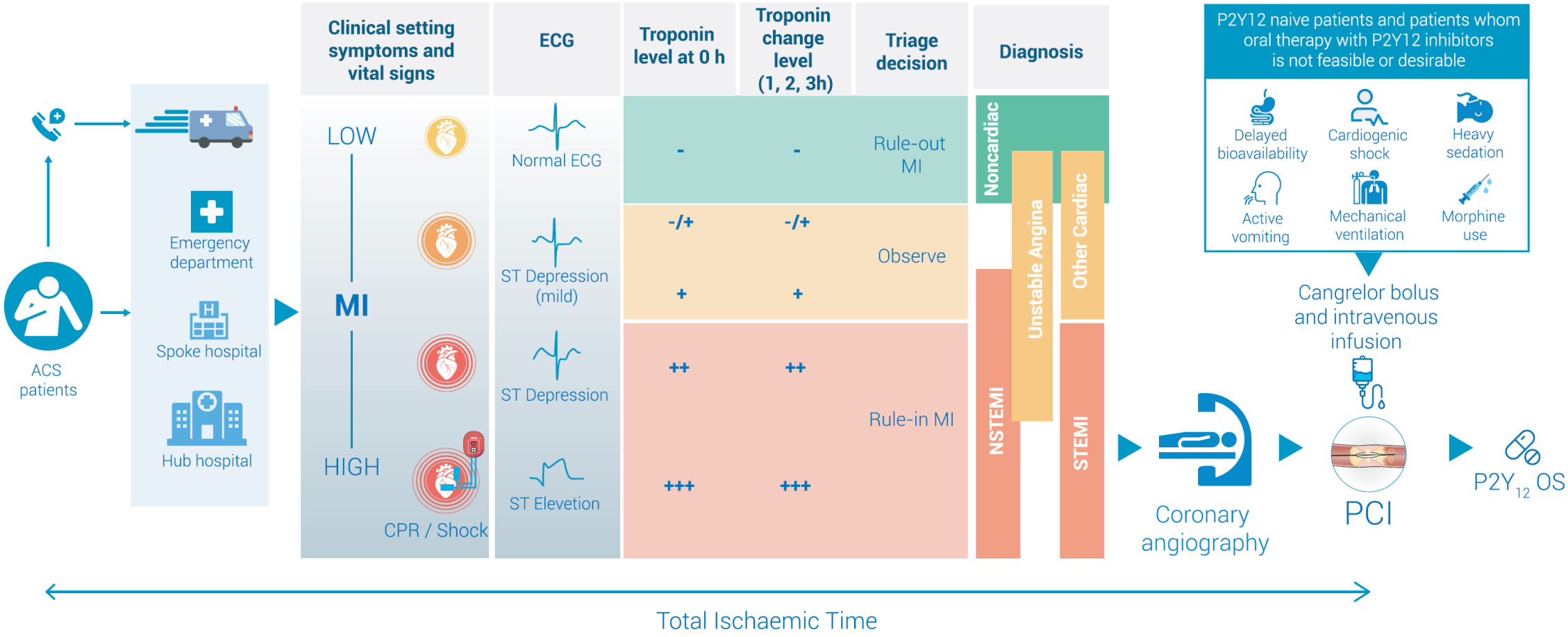
Proportion of Patients With High On-Treatment Platelet Reactivity



Prasugrel 60mg
Loading **at start** of
cangrelor infusion
n = 45

*p < 0.01 as compared with clopidogrel 600 mg. n.s. = not significant.

Hochholzer et al, Circulation 2020



De Luca et al, J Am Heart Assoc 2021

64857 pazienti da "Swedish Coronary Angiography and Angioplasty Registry"

Clinical outcome	Patients, No. (%)			Adjusted OR (95% CI)	*P* value
	Pretreated (n = 59 894)	Not pretreated (n = 4963)	Missing		
Primary end point					
Death at 30 d[a,b]	846 (1.4)	125 (2.5)	0	1.44 (0.78-2.62)	.36
Secondary end point					
Death at 1 y[a,c]	2324 (4.3)	241 (7.1)	0	1.34 (0.77-2.34)	.30
Definite stent thrombosis at 30 d[a,d]	243 (0.2)	19 (0.2)	0	1.17 (0.64-2.16)	.60
In-hospital bleeding[a,e]	3562 (6.0)	380 (7.5)	11 (0.1)	1.49 (1.06-2.12)	.02

Dworeck et al, JAMA Network Open 2020

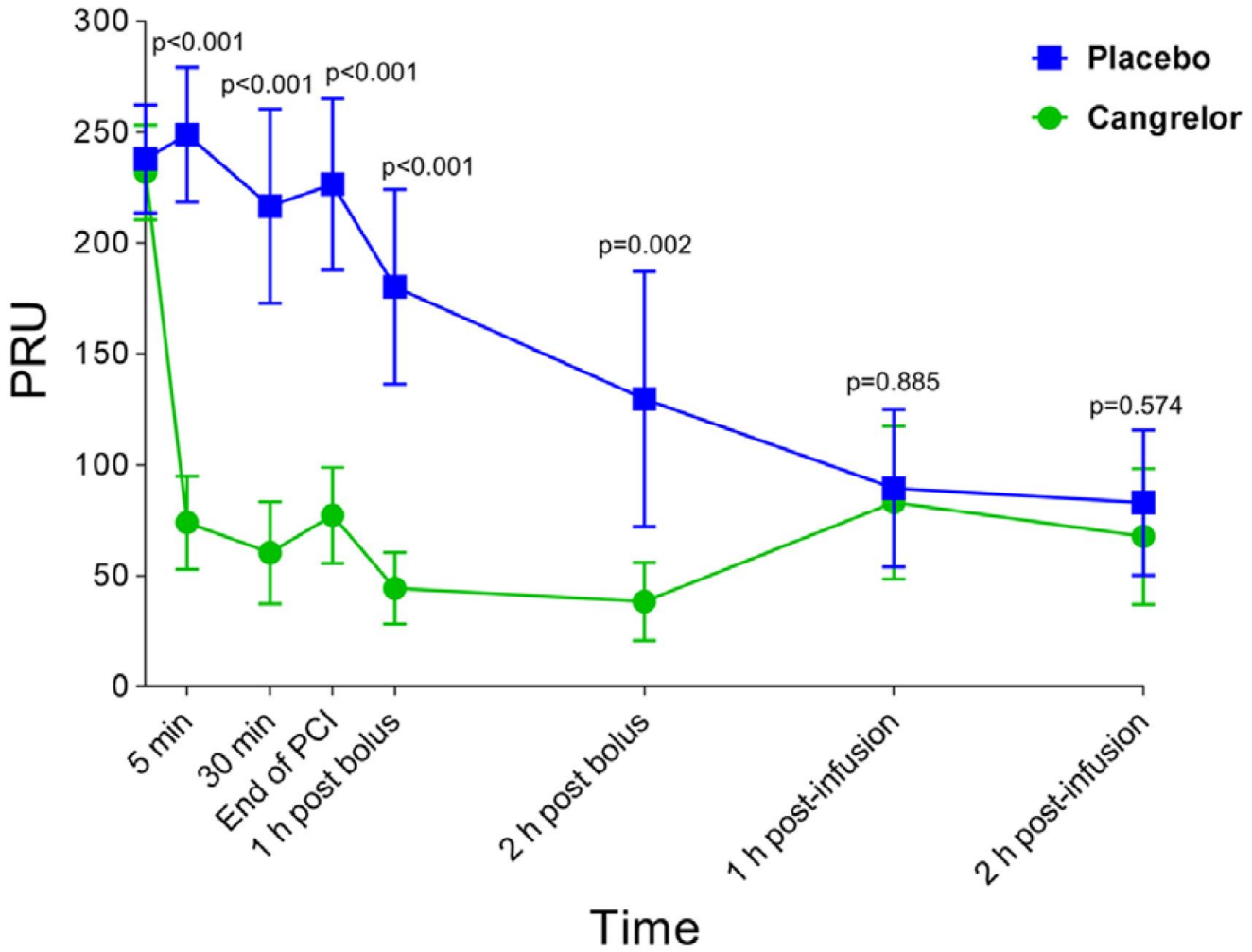
I. Antiplatelet drugs	
Aspirin	LD of 150–300 mg orally or 75–250 mg i.v. if oral ingestion is not possible, followed by oral MD of 75–100 mg o.d.; no specific dose adjustment in CKD patients.
$P2Y_{12}$ receptor inhibitors (oral or i.v.)	
Clopidogrel	LD of 300–600 mg orally, followed by an MD of 75 mg o.d.; no specific dose adjustment in CKD patients. Fibrinolysis: at the time of fibrinolysis an initial dose of 300 mg (75 mg for patients older than 75 years of age).
Prasugrel	LD of 60 mg orally, followed by an MD of 10 mg o.d. In patients with body weight <60 kg, an MD of 5 mg o.d. is recommended. In patients aged ≥75 years, prasugrel should be used with caution, but a MD of 5 mg o.d. should be used if treatment is deemed necessary. No specific dose adjustment in CKD patients. Prior stroke is a contraindication for prasugrel.
Ticagrelor	LD of 180 mg orally, followed by an MD of 90 mg b.i.d.; no specific dose adjustment in CKD patients.
Cangrelor	Bolus of 30 mcg/kg i.v. followed by 4 mcg/kg/min infusion for at least 2 h or the duration of the procedure (whichever is longer). In the transition from cangrelor to a thienopyridine, the thienopyridine should be administered immediately after discontinuation of cangrelor with an LD (clopidogrel 600 mg or prasugrel 60 mg); to avoid a potential DDI, prasugrel may also be administered 30 min before the cangrelor infusion is stopped. Ticagrelor (LD 180 mg) should be administered at the time of PCI to minimize the potential gap in platelet inhibition during the transition phase.
GP IIb/IIIa receptor inhibitors (i.v.)	
Eptifibatide	Double bolus of 180 mcg/kg i.v. (given at a 10-min interval) followed by an infusion of 2.0 mcg/kg/min for up to 18 h. For CrCl 30–50 mL/min: first LD, 180 mcg/kg i.v. bolus (max 22.6 mg); maintenance infusion, 1 mcg/kg/min (max 7.5 mg/h). Second LD (if PCI), 180 mcg/kg i.v. bolus (max 22.6 mg) should be administered 10 min after the first bolus. Contraindicated in patients with end-stage renal disease and with prior ICH, ischaemic stroke within 30 days, fibrinolysis, or platelet count <100 000/mm^3.
Tirofiban	Bolus of 25 mcg/kg i.v. over 3 min, followed by an infusion of 0.15 mcg/kg/min for up to 18 h. For CrCl ≤60 mL/min: LD, 25 mcg/kg i.v. over 5 min followed by a maintenance infusion of 0.075 mcg/kg/min continued for up to 18 h. Contraindicated in patients with prior ICH, ischaemic stroke within 30 days, fibrinolysis, or platelet count <100 000/mm^3.
II. Anticoagulant drugs	
UFH	Initial treatment: i.v. bolus 70–100 U/kg followed by i.v. infusion titrated to achieve an aPTT of 60–80 s. During PCI: 70–100 U/kg i.v. bolus or according to ACT in case of UFH pre-treatment.
Enoxaparin	Initial treatment: for treatment of ACS 1 mg/kg b.i.d. subcutaneously for a minimum of 2 days and continued until clinical stabilization. In patients whose CrCl is below 30 mL per minute (by Cockcroft–Gault equation), the enoxaparin dosage should be reduced to 1 mg per kg o.d. During PCI: for patients managed with PCI, if the last dose of enoxaparin was given less than 8 h before balloon inflation, no additional dosing is needed. If the last s.c. administration was given more than 8 h before balloon inflation, an i.v. bolus of 0.3 mg/kg enoxaparin sodium should be administered.
Bivalirudin	During PPCI: 0.75 mg/kg i.v. bolus followed by i.v. infusion of 1.75 mg/kg/h for 4 h after the procedure. In patients whose CrCl is below 30 mL/min (by Cockcroft–Gault equation), maintenance infusion should be reduced to 1 mg/kg/h.
Fondaparinux	Initial treatment: 2.5 mg/d subcutaneously. During PCI: A single bolus of UFH is recommended. Avoid if CrCl <20 mL/min.

ESC guidelines on ACS, European Heart Journal 2023

Oral P2Y12 inhibitor	Loading Dose	Timing of Loading Dose Administration
Clopidogrel	600 mg	Immediately after discontinuation of cangrelor
Prasugrel	60 mg	Immediately after discontinuation of cangrelor
Ticagrelor	180 mg	At any time during or immediately after discontinuation of cangrelor

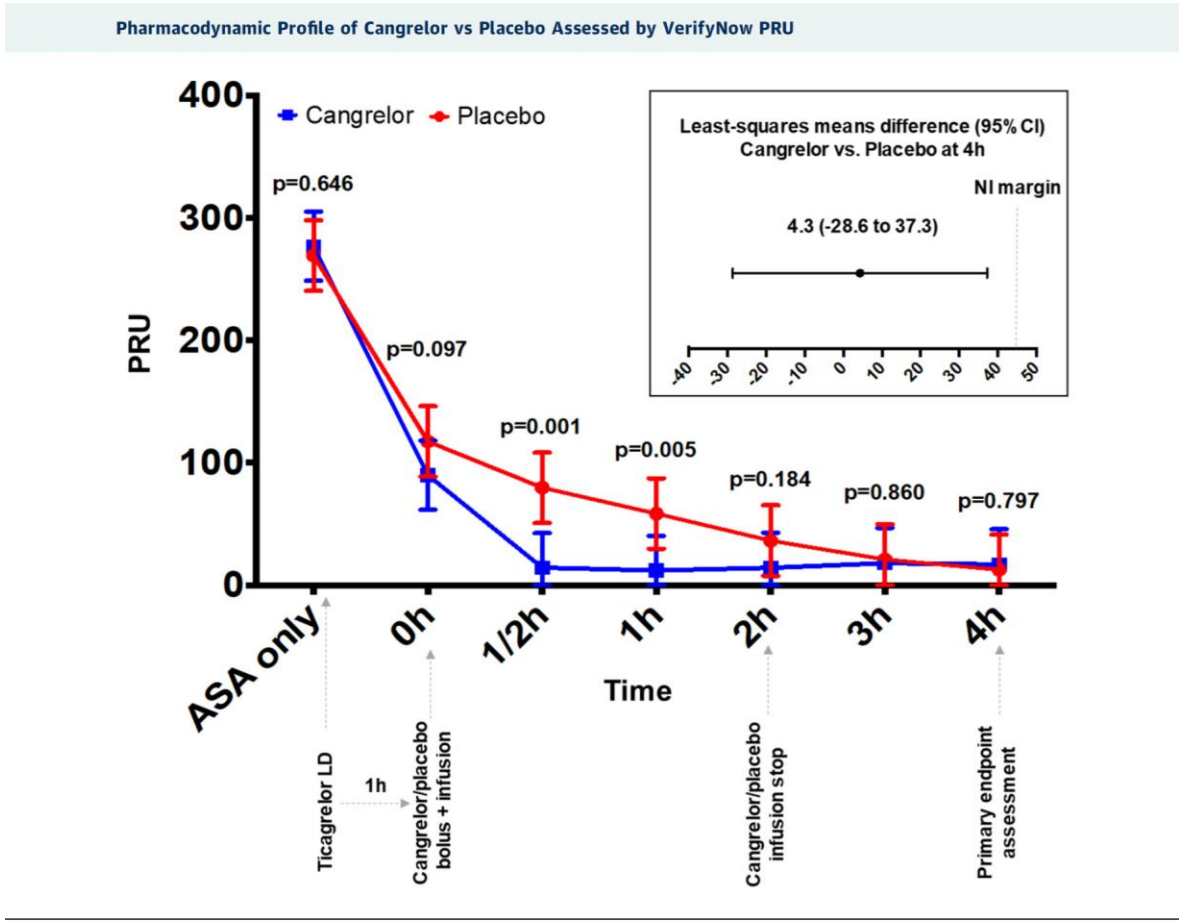
ACC/AHA on ACS, Circulation 2025

CANTIC Study: inibizione piastrinica con cangrelor e ticagrelor frantumato



Franchi et al, Circulation 2019

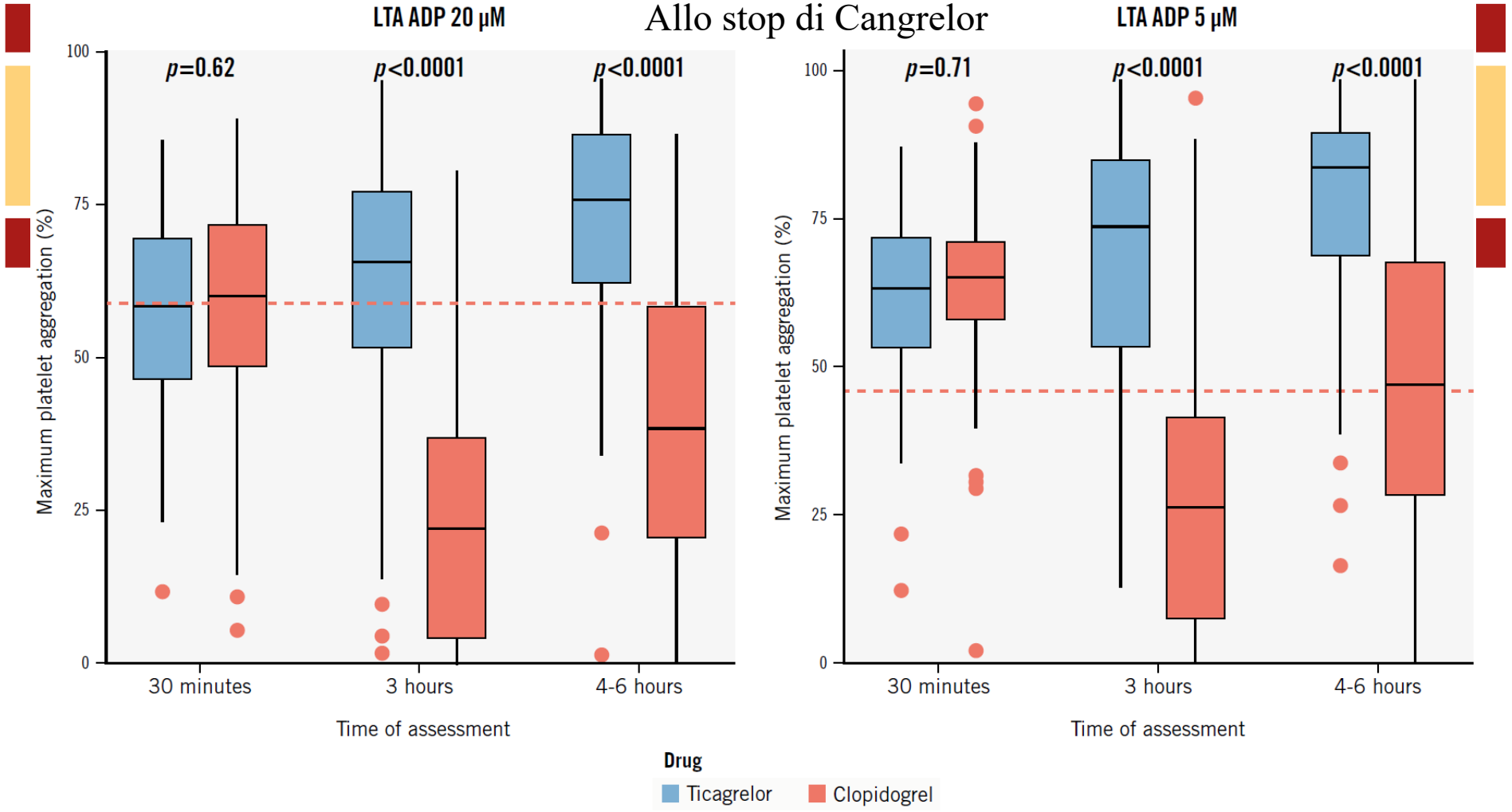
SWAP-5 Study: Cangrelor in pazienti pretrattati con Ticagrelor



$P2Y_{12}$ reaction units (PRU) measured by the VerifyNow $P2Y_{12}$ assay. Values are expressed as least-squares means. **Error bars** indicate 95% CIs. *P* values indicate comparisons between groups at each time point. ASA = acetylsalicylic acid; LD = loading dose; NI = noninferiority.

Franchi et al, J Am Coll Cardiol Intv 2023

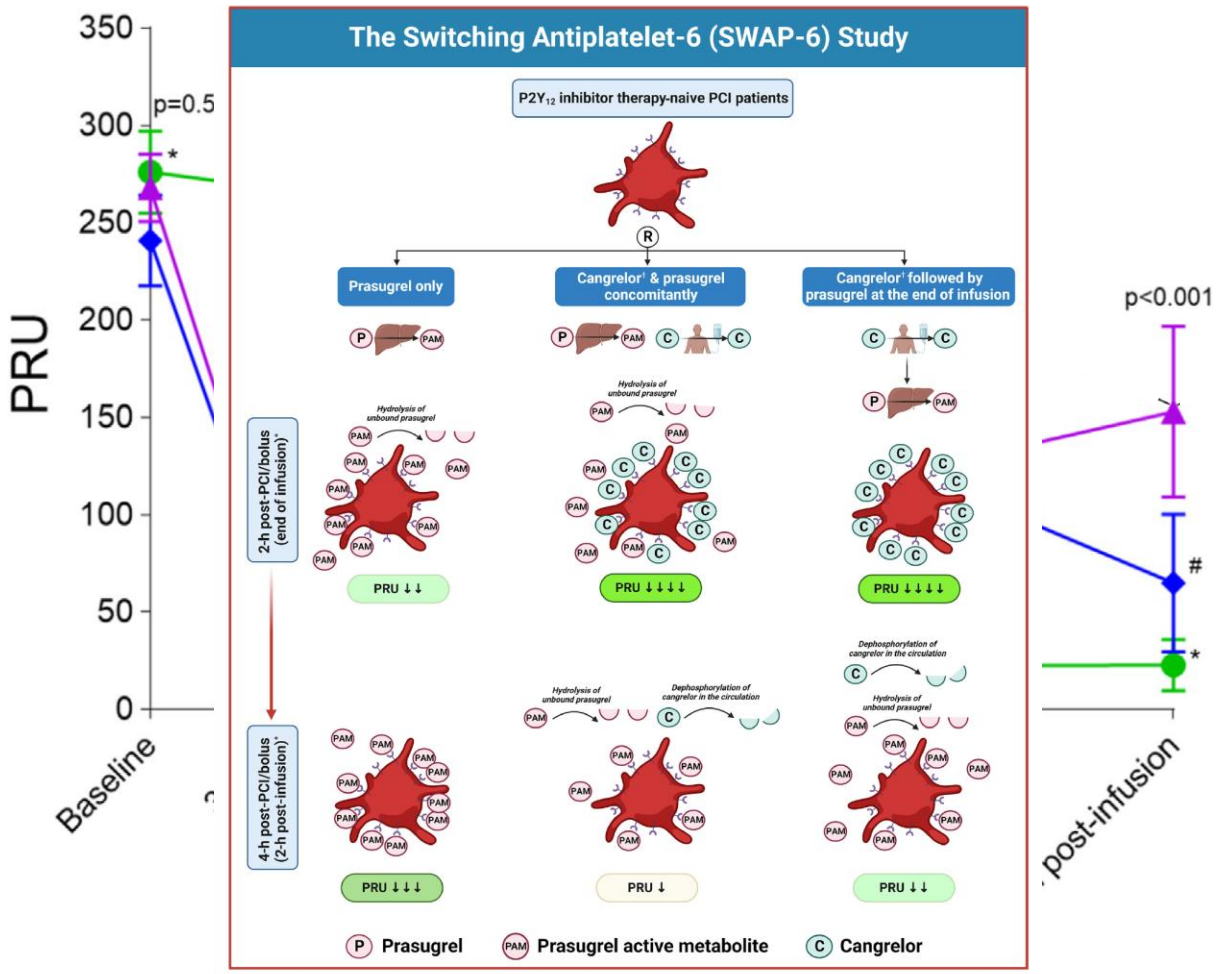
Registro POMPEII: effetti farmacodinamici di Cangrelor



Gargiulo et al, EuroIntervention 2025

SWAP-6 Study: Cangrelor in pazienti pretrattati con Prasugrel

CENTRAL ILLUSTRATION Pharmacokinetic and Pharmacodynamic Profiles Associated With Switching From Cangrelor to Prasugrel in Patients Undergoing Percutaneous Coronary Intervention



Franchi F, et al. J Am Coll Cardiol Intv. 2023;16(20):2528-2539.

Franchi et al, J Am Coll Cardiol Intv 2023

DAPT-SHOCK-AMI trial

DAPT SHOCK AMI

Randomised
multicentre
international
double-blind
placebo-controlled

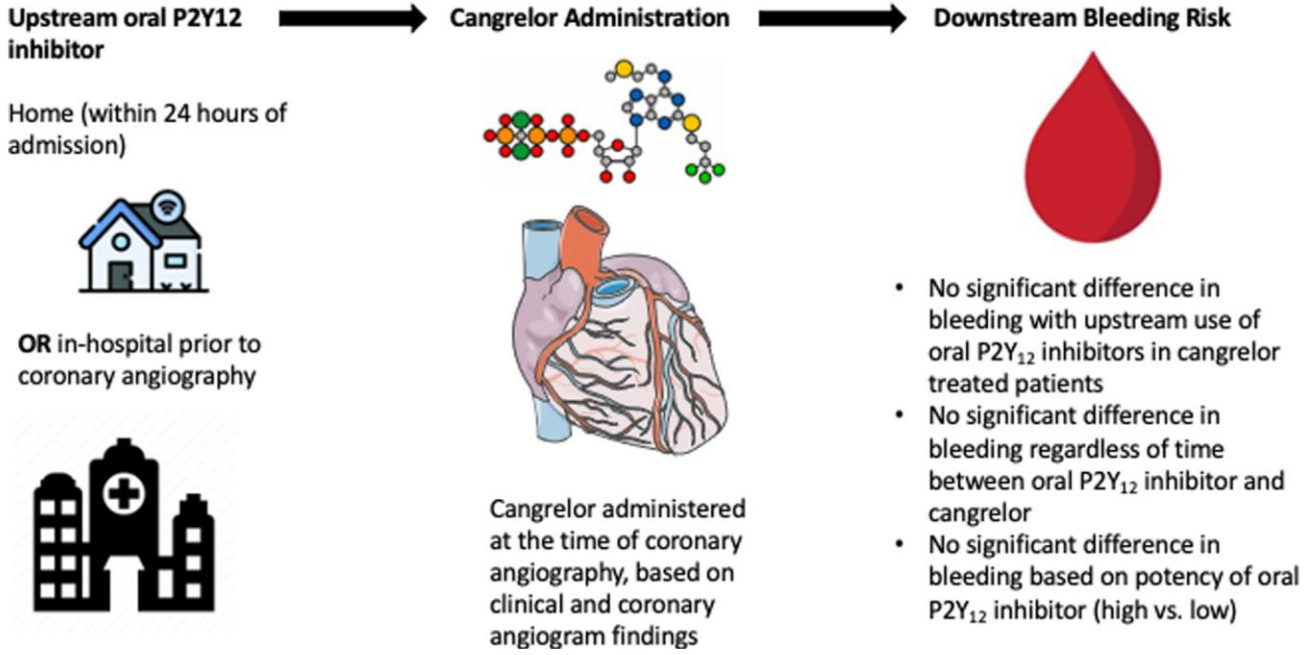
Comparison of initial $P2Y_{12}$ inhibitor treatment strategies based on

- → IV cangrelor or
- → crushed tablets of ticagrelor (180 mg)

1° EP: Death / MI / stroke within 30 days.
2° EPs: [1]Death / MI / UR / stroke / Major bleeding;
[2]CV death / MI / UR / HF;
[3]HF;
[4]CV death.
All [(1-4)] within 1 year.

Motovska et al, EuroIntervention 2024

Rischio di sanguinamento tra i pazienti trattati con Cangrelor a cui è stata somministrata la terapia UpStrem con P2Y12i: il registro CAMEO



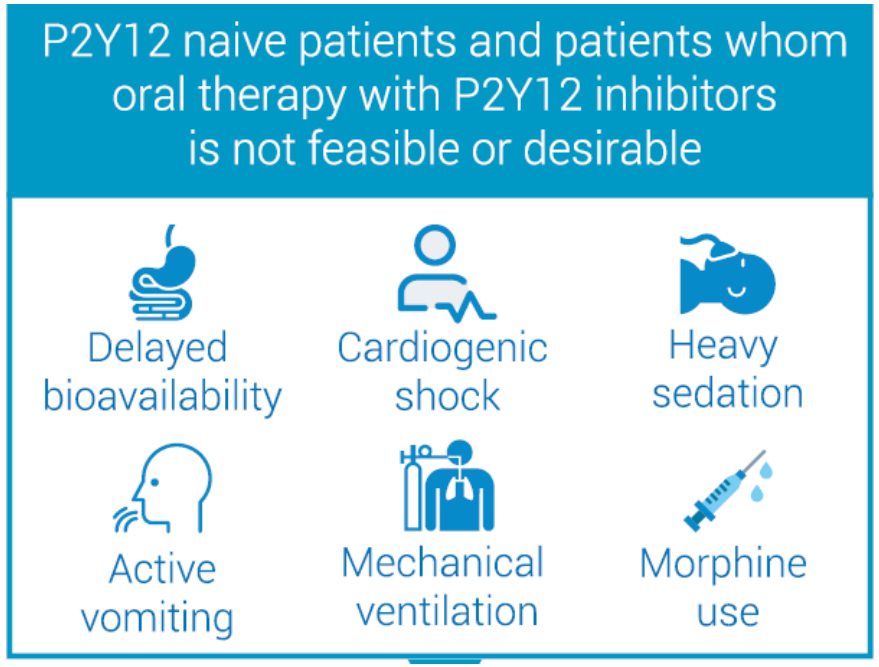
Outcome	n/N (%)	Unadjusted odds ratio (95% CI)	*P* value	Adjusted odds ratio (95% CI)	*P* value
Bleed event - pretreatment	25/384 (6.5%)	0.72 (0.46-1.13)	.154	0.62 (0.38-1.01)	.053
Bleed event - no pretreatment	122/1388 (8.8%)				

Time group, h	Bleed events[a], n/N (%)	Unadjusted odds ratio (95% CI)	*P*	Adjusted odds ratio (95% CI)	*P*
0-1	5/101 (5.0)	Ref.		Ref.	
1-3	11/103 (10.7)	2.30 (0.77-6.86)	.137	2.70 (0.87-8.32)	.084
>3	3/94 (3.2)	0.63 (0.15-2.73)	.539	0.65 (0.15-2.85)	.566

Rymer et al, JSCAI 2024

Confronto tra inibitori P2Y12

	Clopidogrel	Prasugrel	Ticagrelor
Chemical class	Thienopyridine	Thienopyridine	Cyclopentyl-triazo-lopyrimidine
Route	Oral	Oral	Oral
Prodrug	Yes (pro-drug, CYP dependent, 2 steps)	yes (pro-drug, CYP dependent, 1 step)	No
Bioavailability	15%	79%	36%
Standard dosage	600 mg LD, then 75 mg once a day	60 mg LD, then 10 mg once a day	180 mg LD, then 90 mg twice a day
Reversibility of binding	Irreversible	Irreversible	Reversible
Onset of antiplate-let effect	2–6 h	0.5–4 h	0.5–2 h
Level of plate-let inhibition at steady state	40–60%	65–80%	65–80%
Offset of antiplate-let effect	3–10 days	5–10 days	3–4 days
Recommended stop of treatment before surgery	5 days	7 days	3–5 days
Excretion	50% renal, 46% biliary	68% renal, 27% feces	Biliary
Kidney failure	No dose adjustment	No dose adjustment	No dose adjustment
Dialysis or CrCl < 15 mL/min	Limited data	Limited data	Limited data



Kubica et al, Cardiology Journal 2024
De Luca et al, J Am Heart Assoc 2021

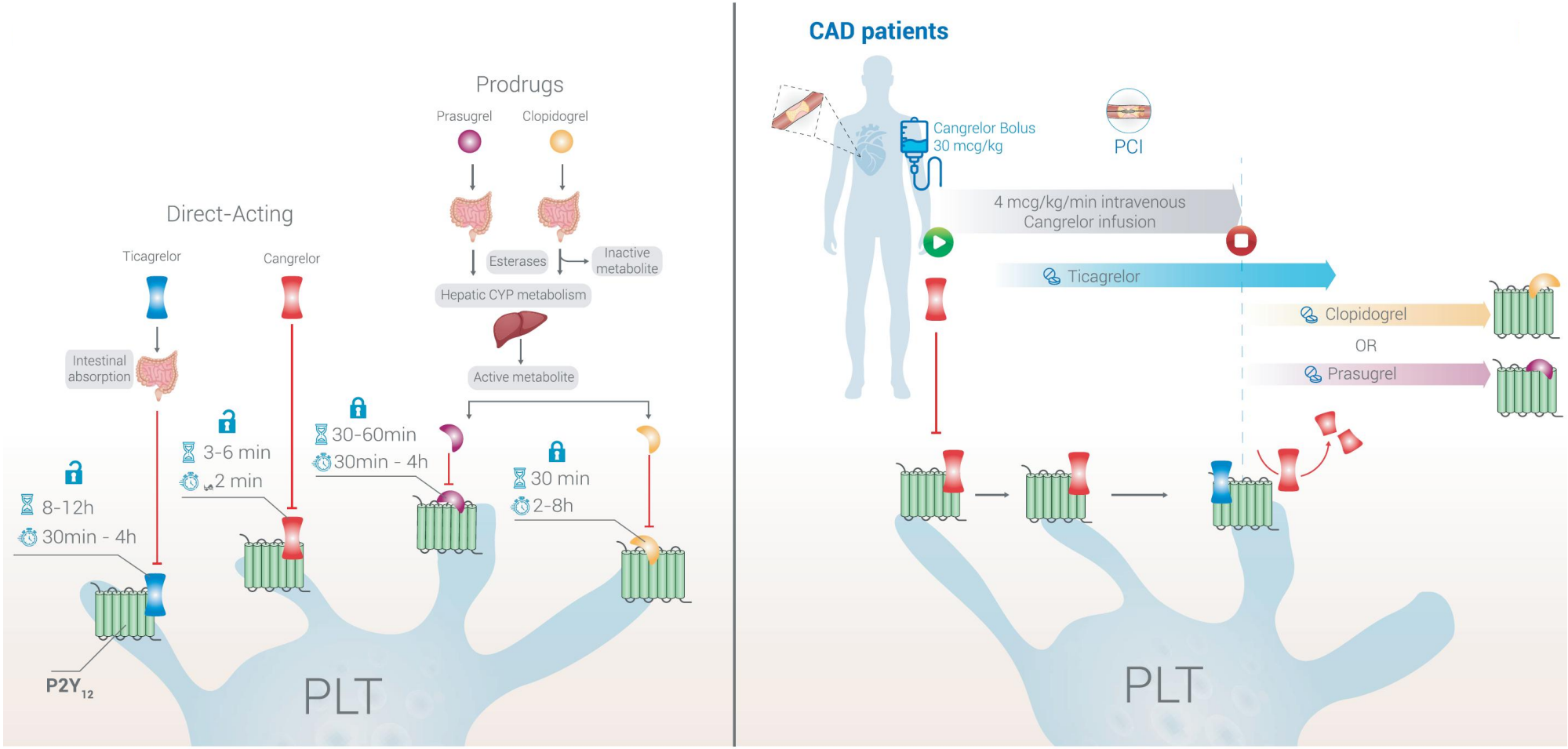
Limiti degli inibitori orali del recettore P2Y12

- **Ridotta biodisponibilità**: La biodisponibilità può essere alterata da un ridotto e/o rallentato assorbimento intestinale. Anche nausea, vomito, o l'incapacità di deglutire (ad esempio, in pazienti sedati, intubati o in shock) possono compromettere la biodisponibilità del farmaco.
- **Ridotta biodisponibilità in pazienti critici**: La biodisponibilità di questi farmaci è spesso ridotta nei pazienti con ACS, soprattutto nei pazienti STEMI o nei pazienti in condizioni critiche o in chi è stata somministrata morfina.
- **Variabilità individuale**: La farmacocinetica presenta una grande variabilità nella rapidità e potenza della risposta antiaggregante tra i pazienti, anche con farmaci più recenti come prasugrel o ticagrelor.

Di conseguenza, molti pazienti potrebbero non raggiungere un'adeguata inibizione piastrinica al momento della PCI o subito dopo, con conseguente aumentato rischio di trombosi dello stent, infarto del miocardio e morte

- **Durata e antidoto**: L'effetto di questi farmaci dura per diversi giorni, e non esiste un antidoto disponibile in commercio per ripristinare rapidamente la funzionalità piastrinica in caso di emorragia o necessità di un intervento chirurgico d'urgenza.

Kubica et al, Cardiology Journal 2024



De Luca et al, J Am Heart Assoc 2021


BIELLA CUORE
12-13 SETTEMBRE 2025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