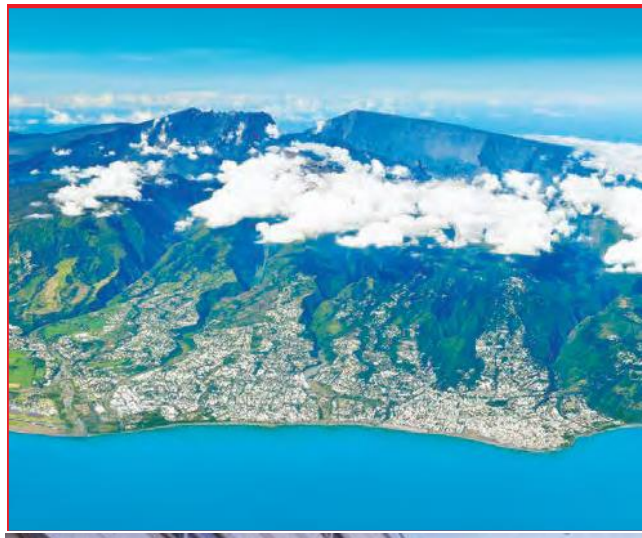
Quoi de neuf avec les antiagregants?

Hôpital Pitié-Salpêtrière AP-HP

G. Montalescot

ACTION Group



Dr. Montalescot reports research Grants to the Institution or Consulting/Lecture Fees from Abbott, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Boston Scientific,Bristol-Myers-Squibb, Cell-Prothera, CSL-Behring, Europa, Idorsia, Servier, Medtronic, MSD, Novartis, Pfizer, Quantum Genomics,Sanofi-Aventis.

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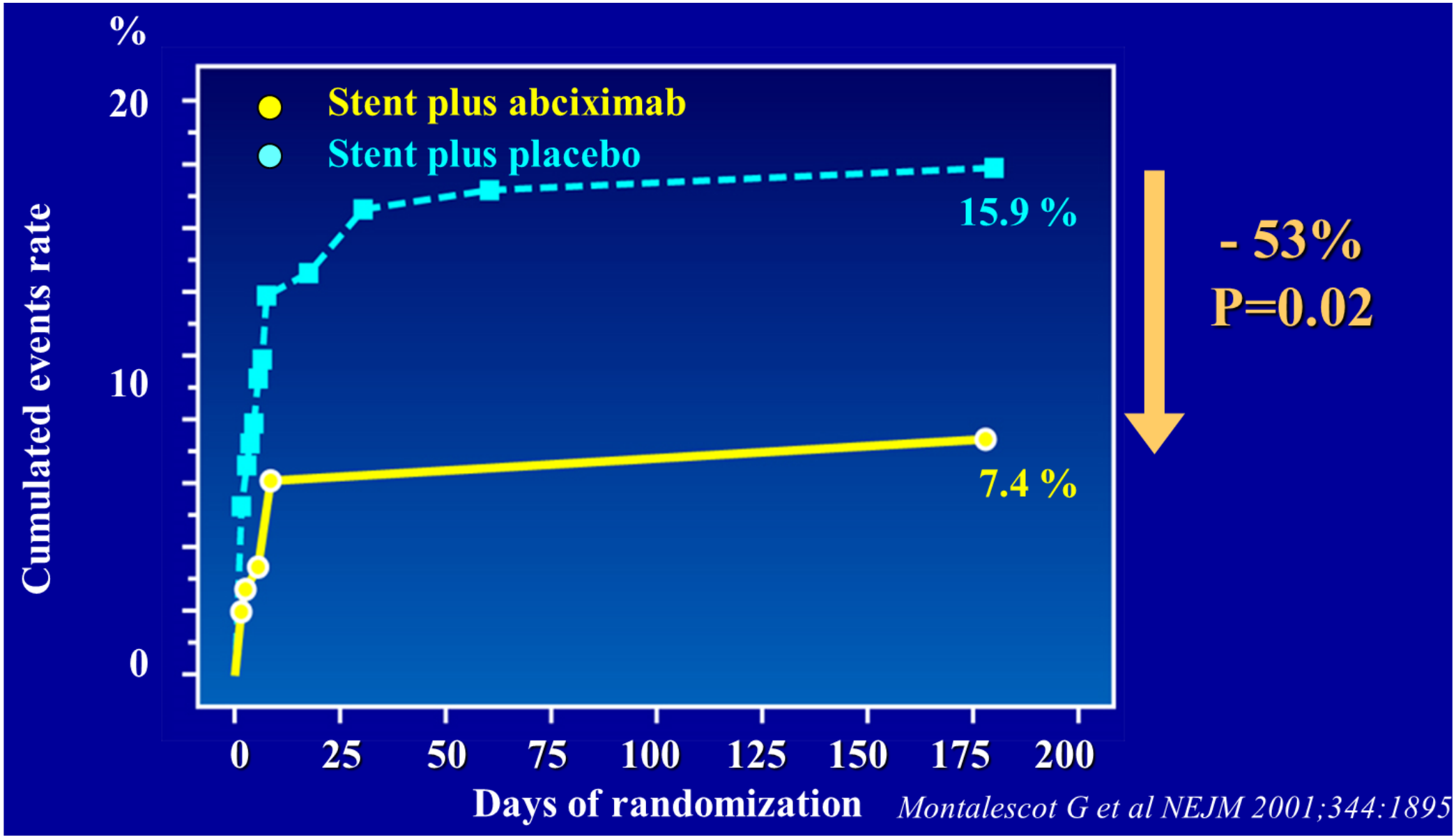
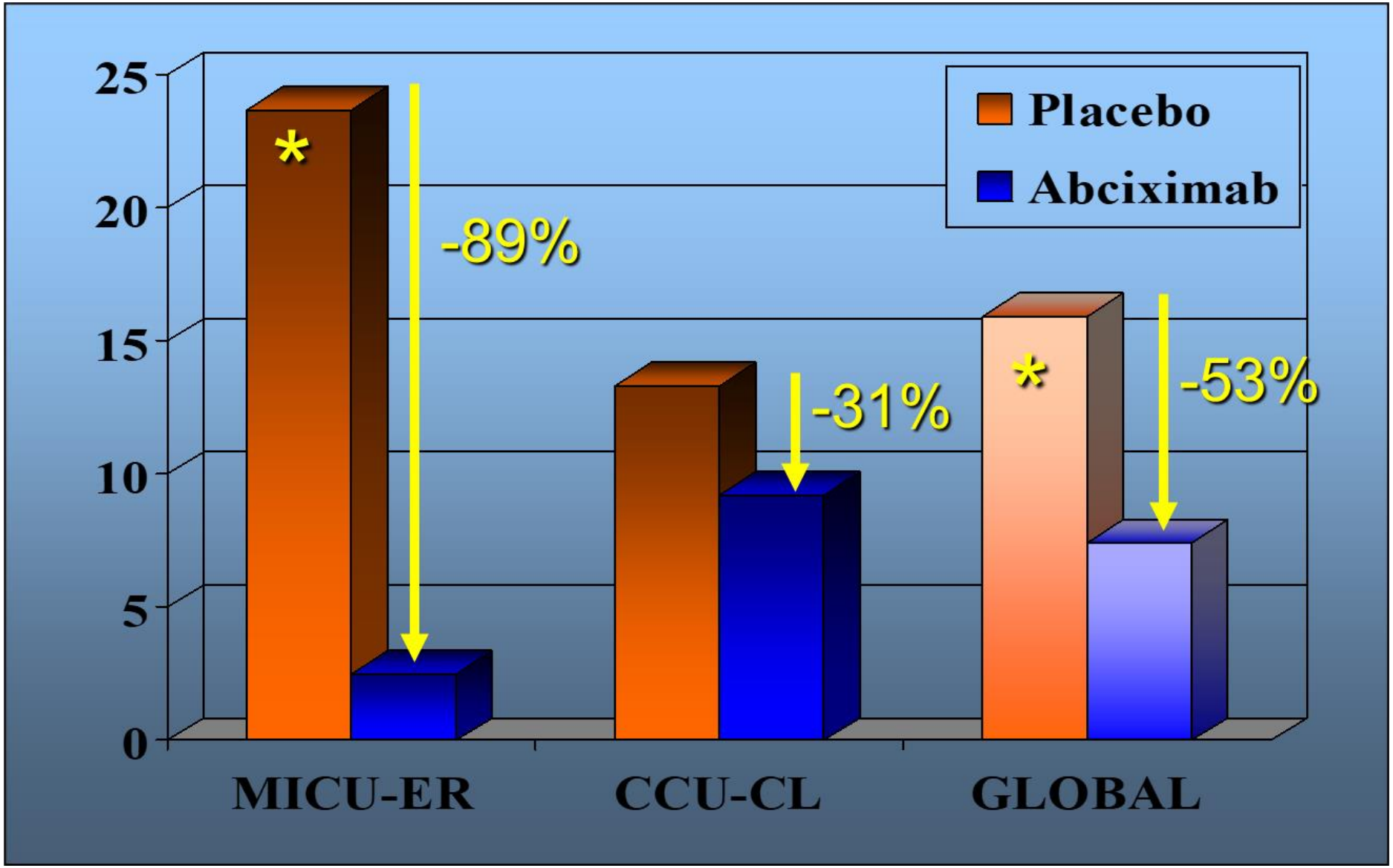
GPIIb/IIIa, le retour!

ADMIRAL, 1° EP : Death, MI, urg revasc



ADMIRAL 1° EP according to place of Rx

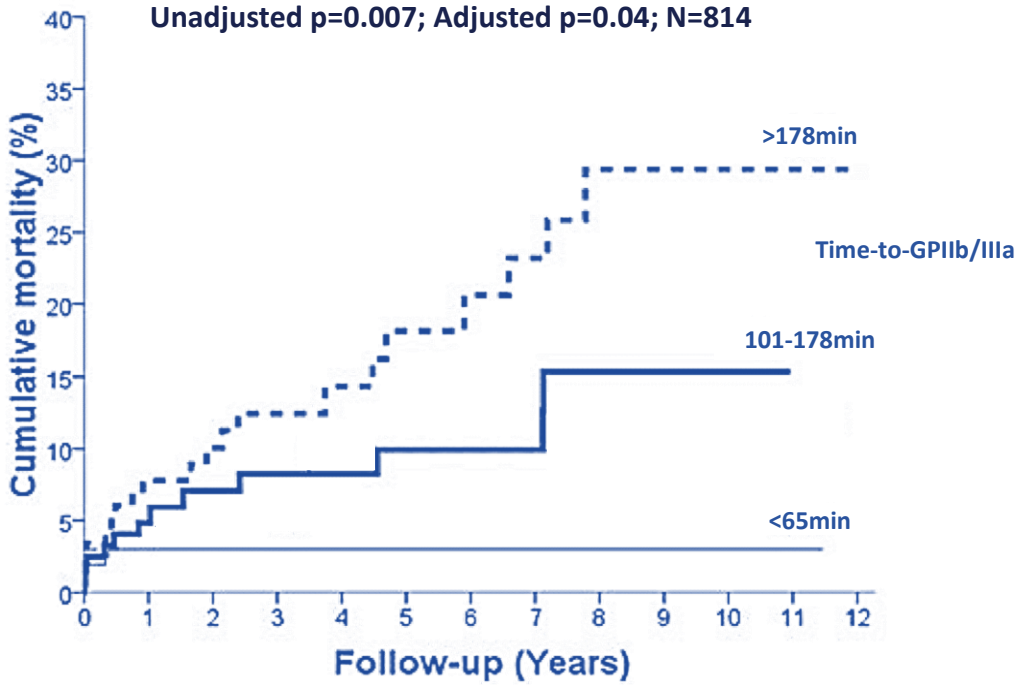


« optimal » use
Young patient
Anterior MI
Early presenter
Early administration
Intra-coronary

Earlier Administration Lowers Mortality

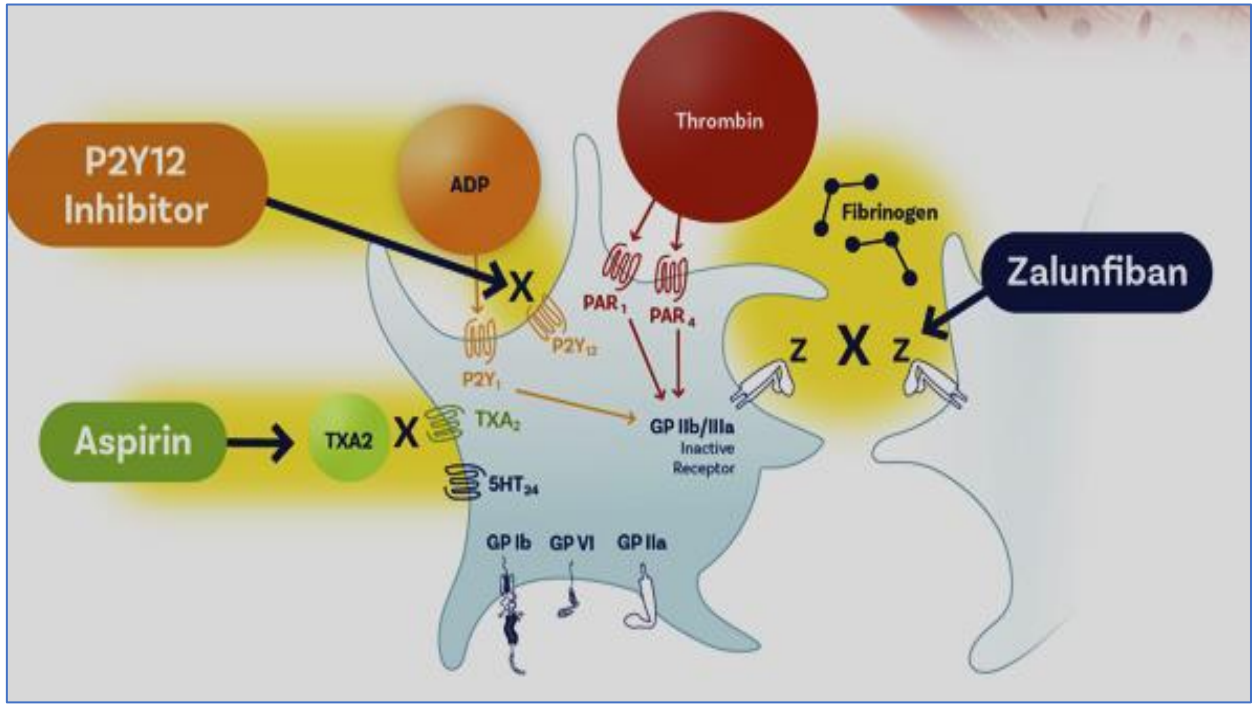
- The earlier the interventional platelet inhibitor can be introduced, the more heart muscle can be protected
- Consequently, the cumulative reduction in mortality grows over time
- In a study of patients who received GPIIb/IIIa inhibitors, the earlier they were administered, the lower the cumulative mortality was, up to a 12-year follow-up

GPIIb/IIIa Speed-to-Administration and Cumulative Patient Mortality (to 12 Years)

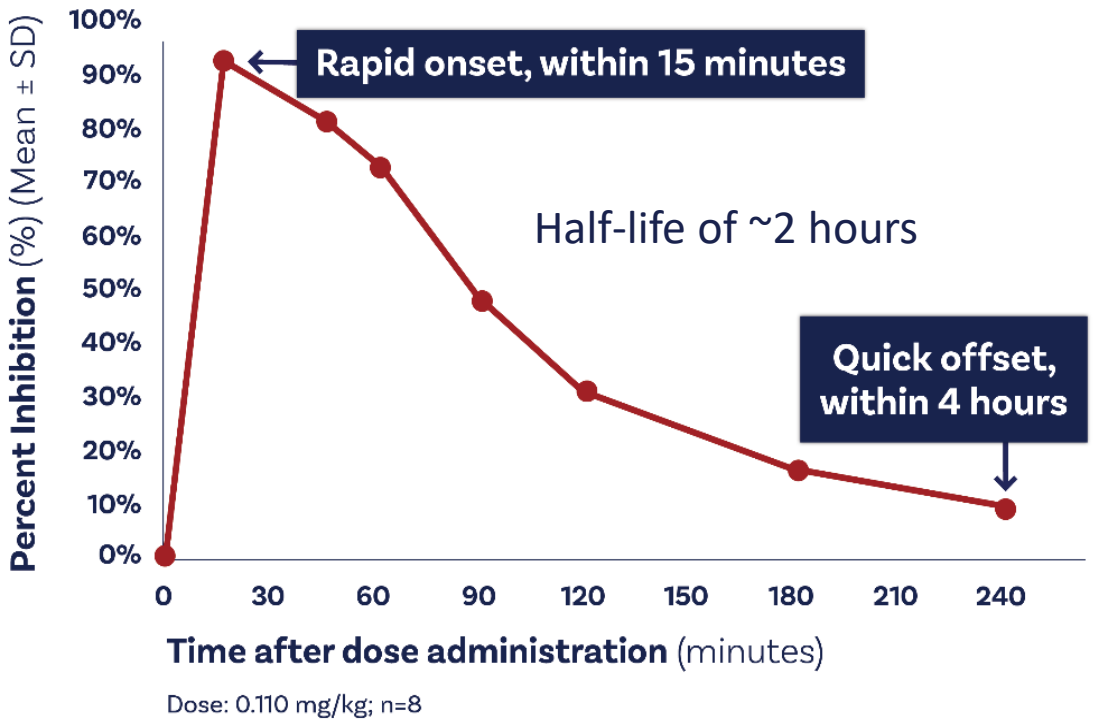


De Luca et al. / J Thromb Haemost 2011; 9: 2361–70.

Zalunfiban Has Fast Onset and Fast Offset



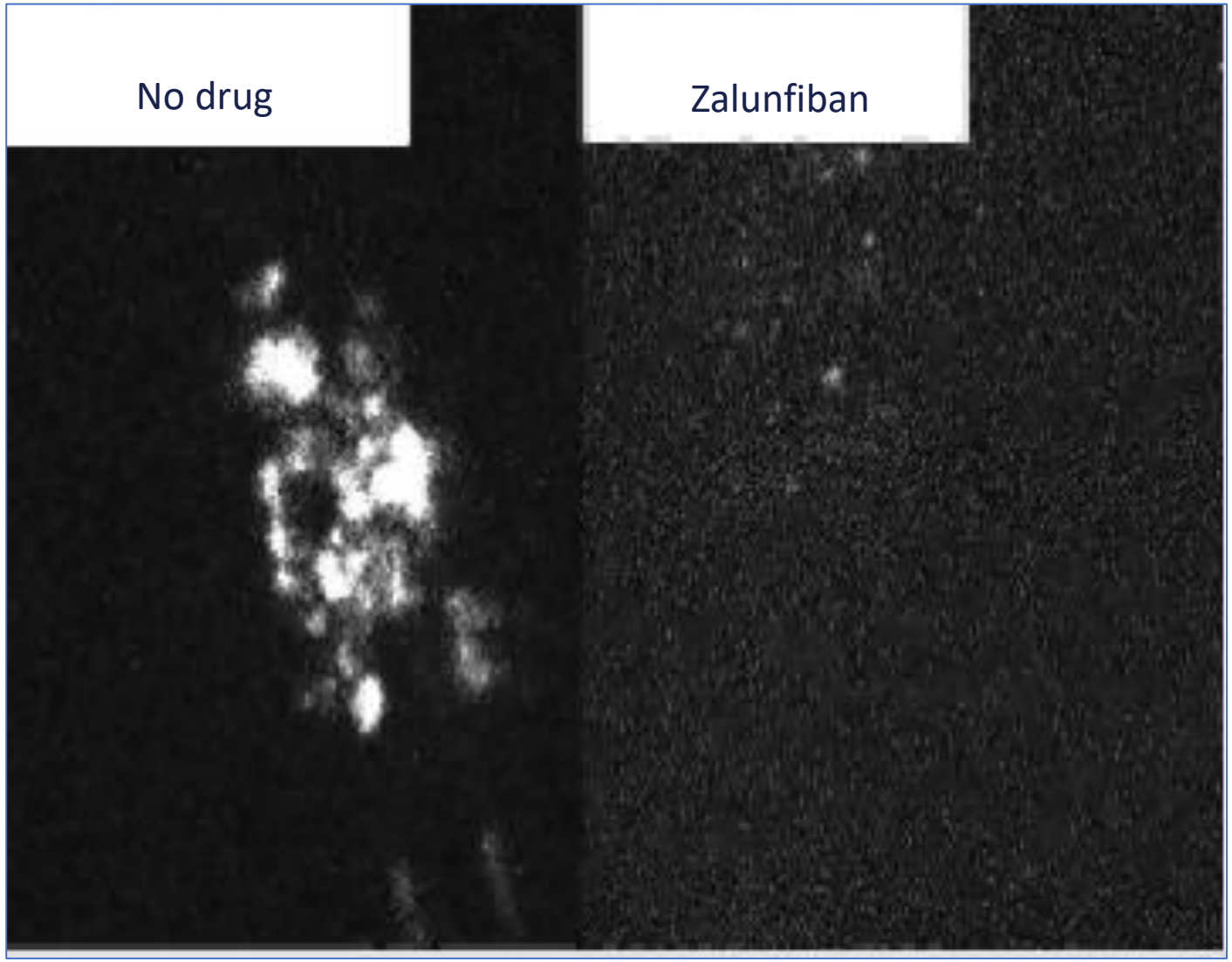
Inhibition of Platelet Aggregation Over Time



Dose: 0.110 mg/kg; n=8

1. Bor et al. / EuroIntervention. 2021 Aug 6;17(5):e401-e410.

Zalunfiban prevents trombosis in a Mouse Model



ClinicalTrials.gov Identifier: NCT04825743
Sponsor: Celecor Therapeutics.

CELEBRATE trial

Patient with STEMI (pre-hospital)

Eligibility criteria met?

No

Patient not eligible

Yes

Verbal or short written informed consent

No

Yes

Randomisation:
SC injection with
RUC-4 dose 1 (0.110 mg/kg),
RUC-4 dose 2 (0.130 mg/kg),
or placebo

Transfer to CCL\CCU PCI centre

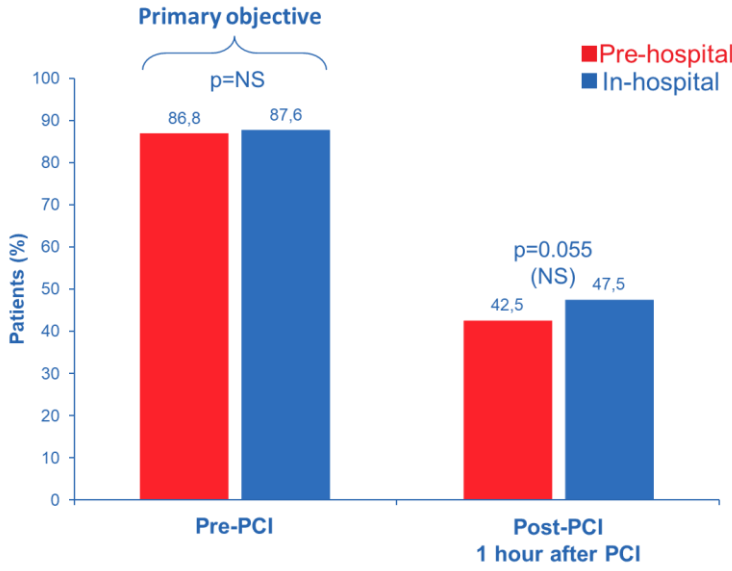
Hospitalisation

1) all-cause death through 30 days
2) hemorrhagic or ischemic stroke through 30 days
3) recurrent MI (type I to type IV) through 30 days
4) acute stent thrombosis at 24 hours post-PCI
5) new onset heart failure or rehospitalization for HF through 30 days
6) MI with hs-cTnT levels ≥10x ULN at 24 hours post-PCI
7) none of the above

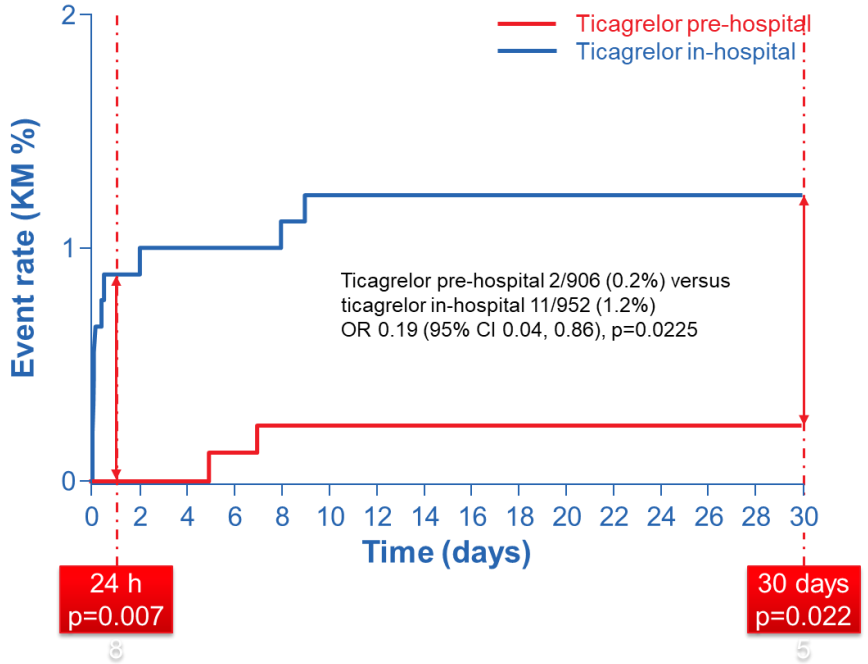
Primary endpoint:
Clinical outcome at 30 days as assessed on a ranked 7-point scale

P_2Y_{12} inhibitors, plus fort, plus tôt!

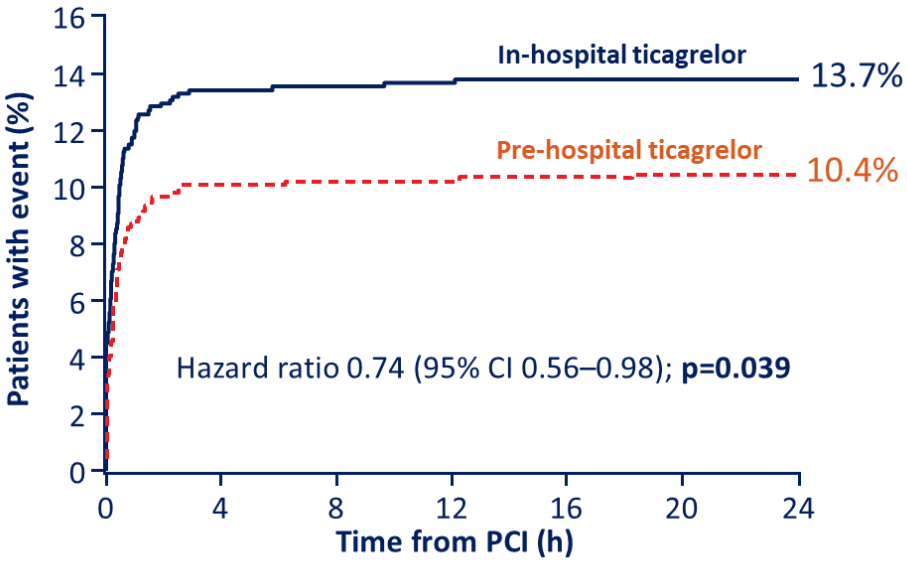
Time effect of $P2Y_{12}$ inhibition in STEMI



Absence of 70% ST elevation



Definite stent thrombosis



	Patients with event, no. (%)	Total no. of patients
Pre-hospital ticagrelor	83 (10.4)	799
In-hospital ticagrelor	114 (13.7)	830

Composite ischaemic endpoint: death, MI, urgent revasc, definite stent thrombosis or BO GP IIb/IIIa inhibitor

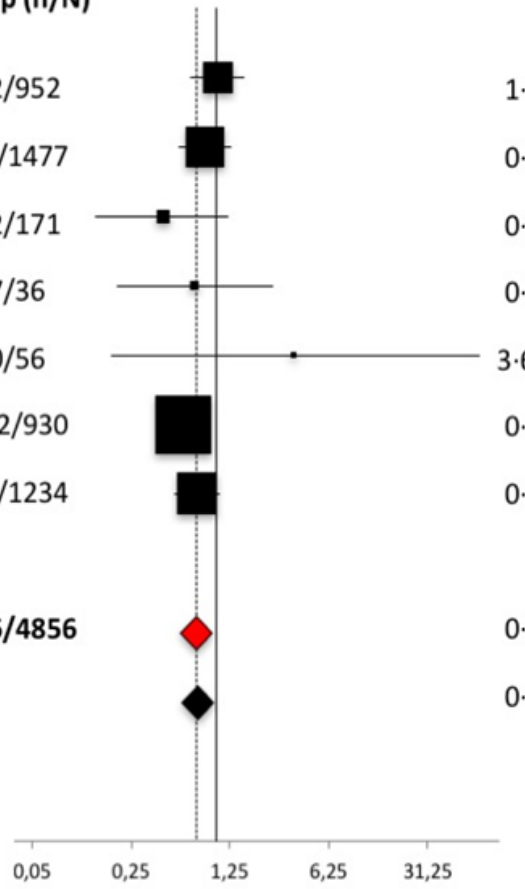
Montalescot et al. NEJM 2014

ATLANTIC

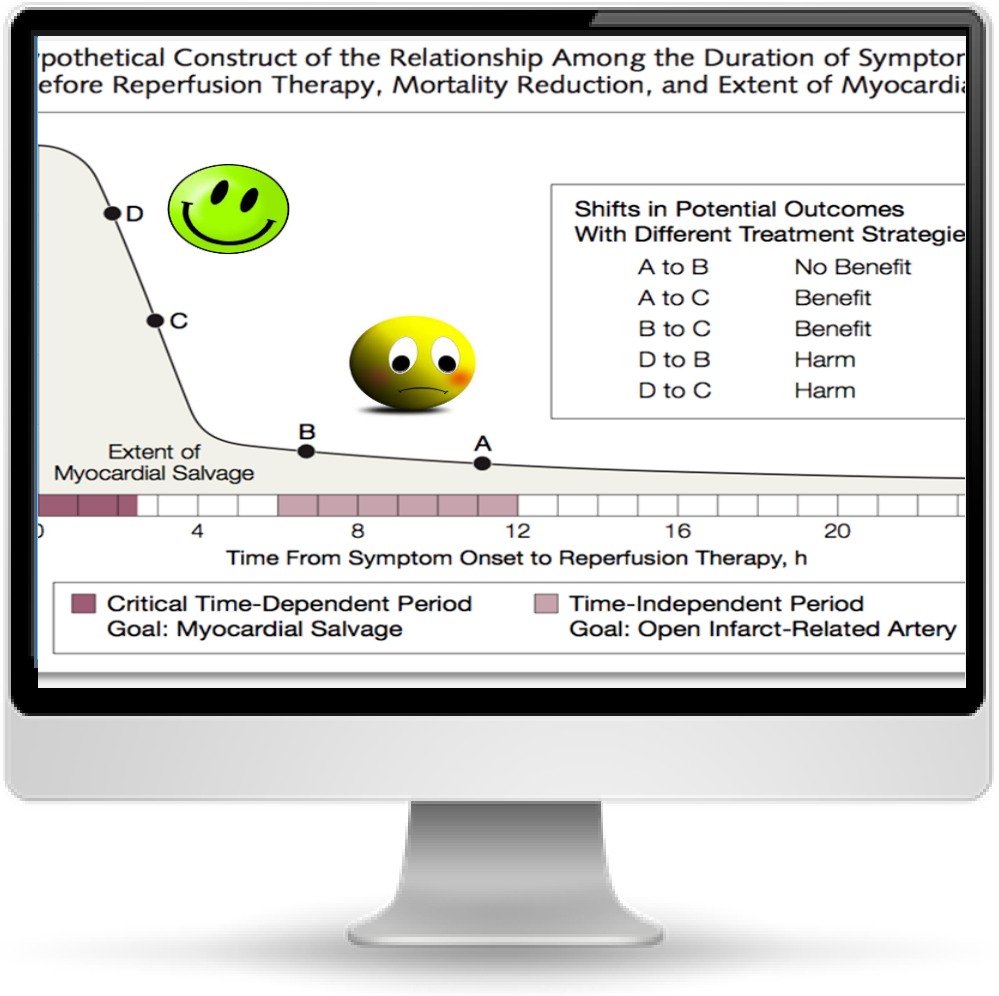
Montalescot et al. JACC Intv 2015

Early P2Y12 I. in STEMI

Study	« EARLY » group (n/N)	« DELAYED» group (n/N)	OR; 95%-CI*
ATLANTIC	41/906	42/952	1·03 (0·66-1·59)
CHAMPION STEMI	41/1407	51/1477	0·84 (0·55-1·27)
CIPAMI	5/164	12/171	0·42 (0·14-1·21)
ERASE MI	5/34	7/36	0·71 (0·20-2·51)
LOAD AND GO	3/112	0/56	3·61 (0·18-71·15
PCI CLARITY	70/933	112/930	0·59 (0·43-0·81)
TRITON STEMI	54/1236	72/1234	0·74 (0·51-1·06)
Fixed effect model	**219/4792**	**296/4856**	0·73 (0·61-0·88)
Random effects model			0·74 (0·61-0·90)



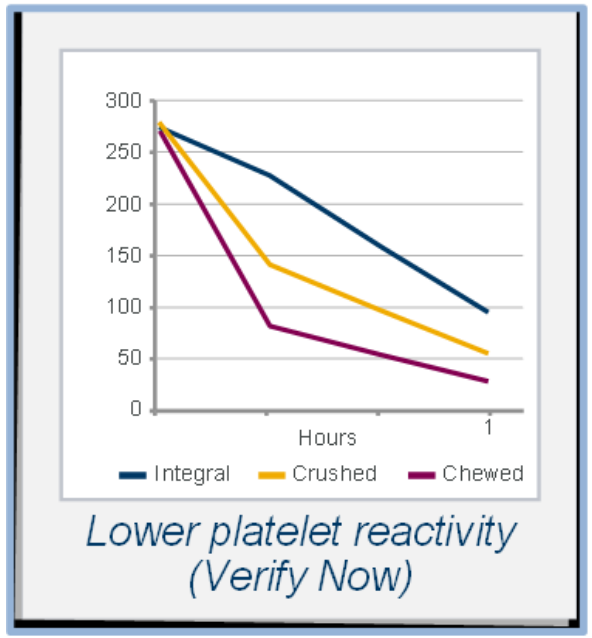
*Heterogeneity: : I-squared=9%, Q=6·61, df=6, P=0·36
Test for overall effect (fixed effect): p=0·0008
Test for overall effect (random effect): p=0·003



Bellemain-Appaix A. et al. EuroIntervention. 2018

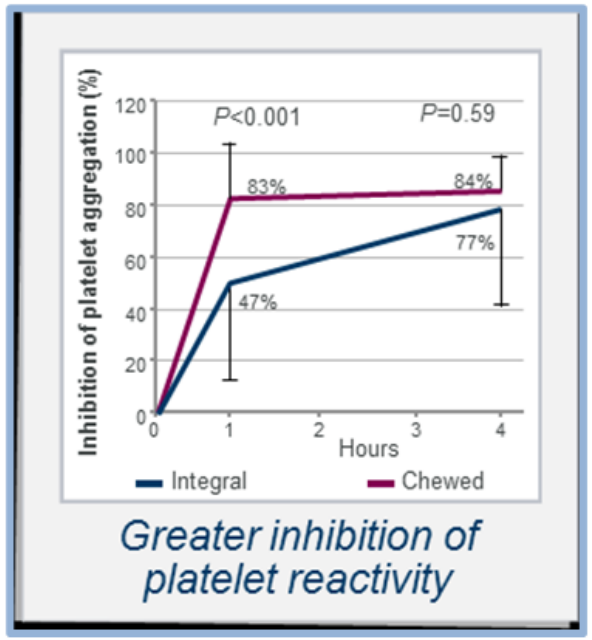
Crushing P2Y12 I. in STEMI

Ticagrelor



Lower platelet reactivity (Verify Now)

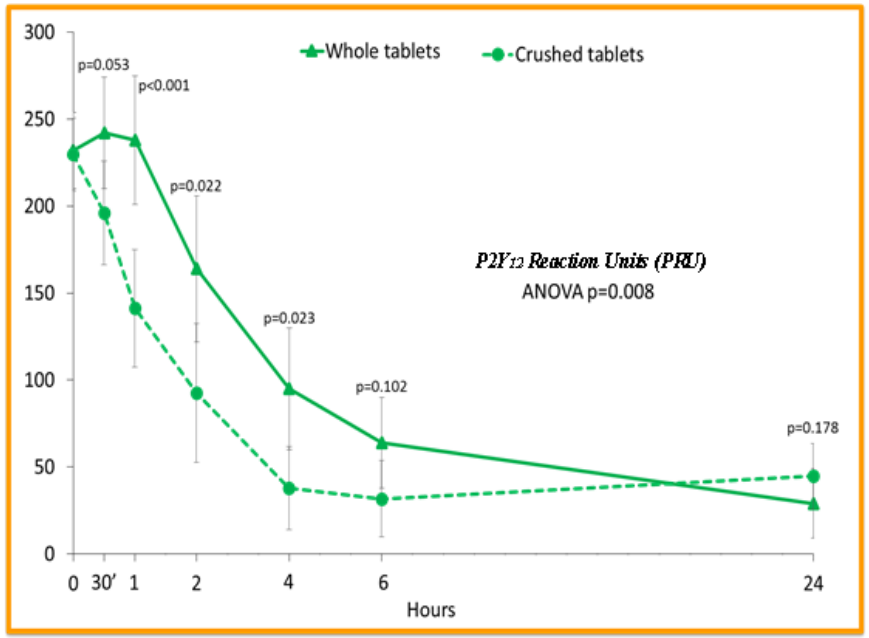
Venetsanos D *et al.*
Thromb Res 2017;149:88–94



Greater inhibition of platelet reactivity

Asher E *et al.*
Thromb Haemost 2017

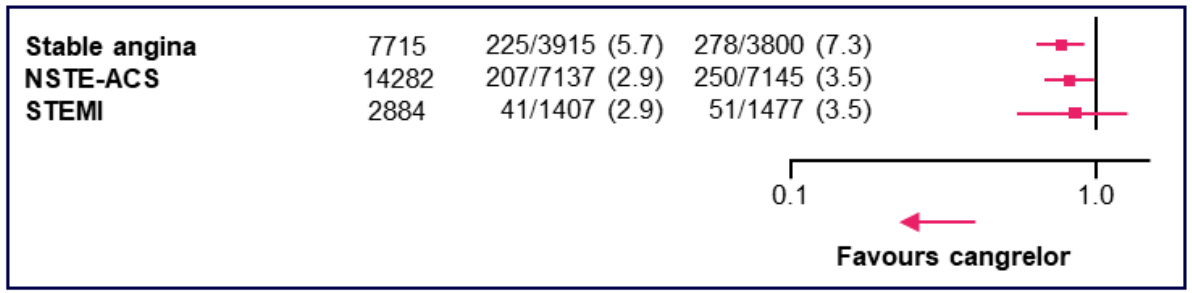
Prasugrel



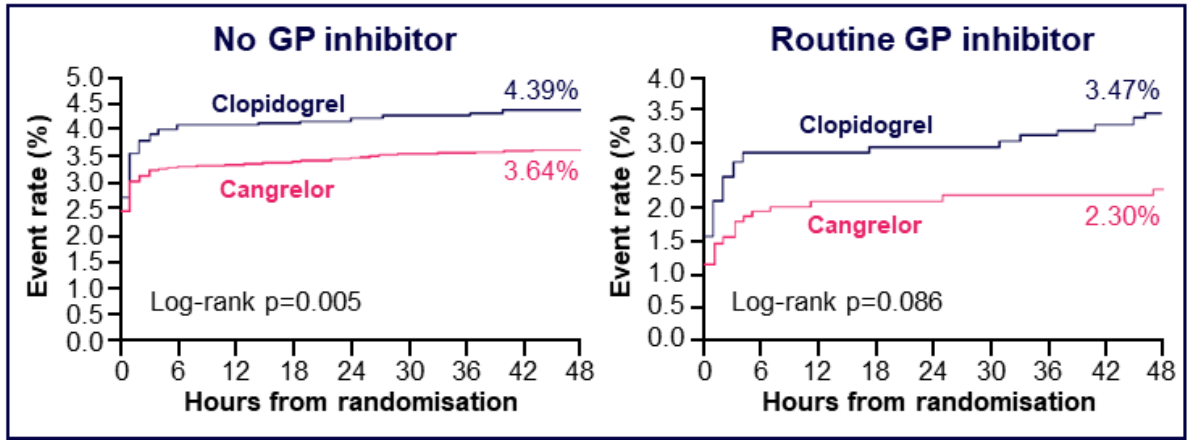
Rollini F et al.
JACC 2016

Cangrelor in STEMI

Pooled analysis of patient-level data[1]



Curves for primary efficacy endpoint[2,a]



- Rapid onset
- PD data
- Real-world data
- "Ideal" for pPCI

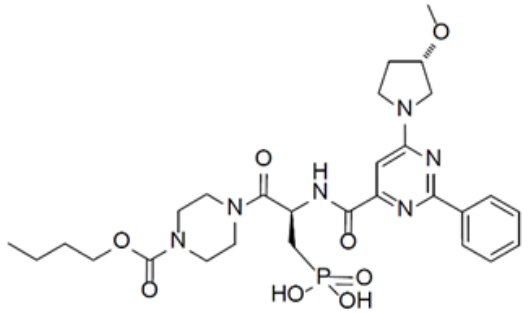
- Tested vs clopidogrel
- No RCT in STEMI
- No emergency room /ambulance use
- No RCT in cardiogenic shock (PRAGUE-23 ongoing)

[a] Composite of all-cause mortality, MI, ischaemia-driven revascularization, or stent thrombosis at 48 hours after randomization

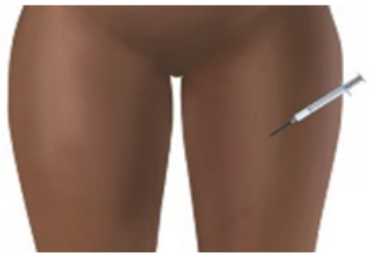
GP, glycoprotein; MI, myocardial infarction; NSTE-ACS, non ST-elevation acute coronary syndrome; PD, pharmacodynamics; pPCI, primary percutaneous coronary intervention; RCT, randomised controlled trial; STEMI, ST-elevation myocardial infarction

Adapted from: 1. Steg PG, et al. Lancet. 2013;382:1981-92; 2. Vaduganathan M, et al. J Am Coll Cardiol. 2017;69:176-85

Selatogrel: a new selective P2Y12 receptor agonist

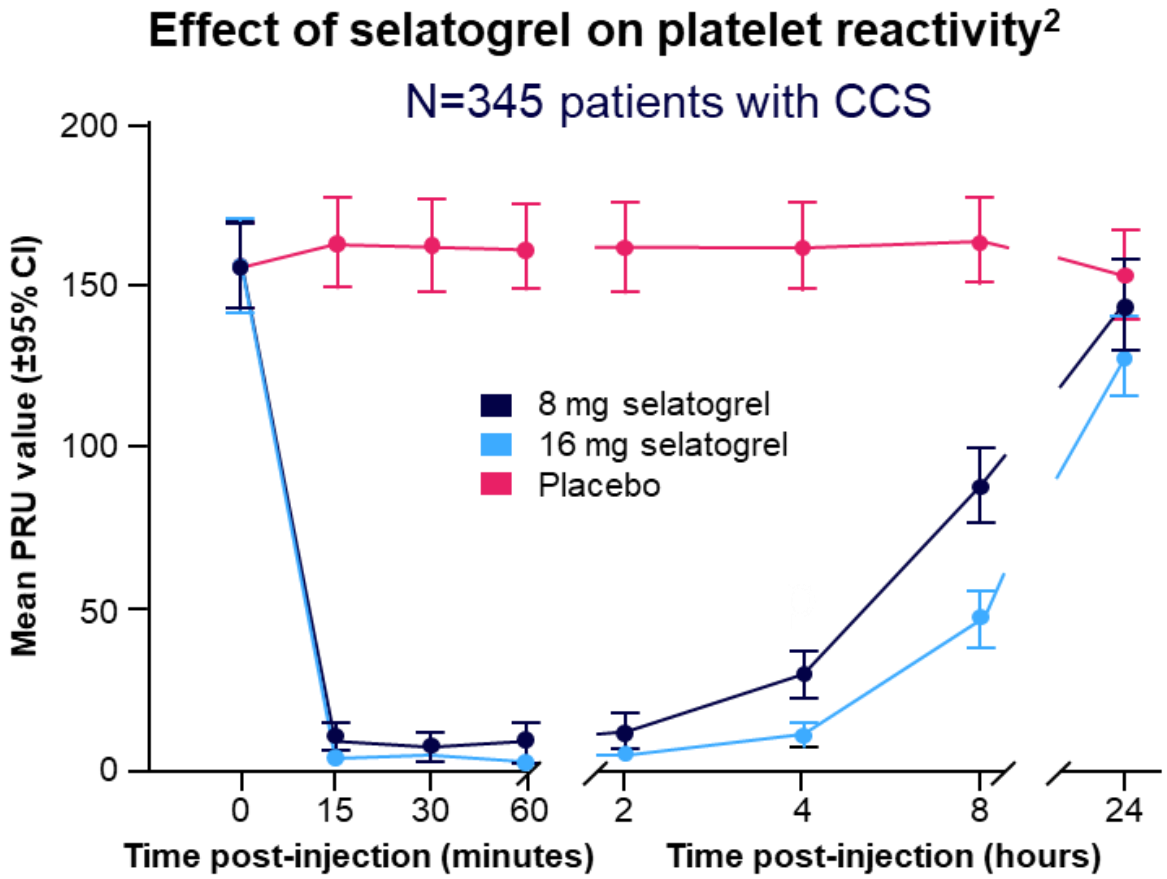


2-phenyl-pyrimidine derivative



PK and PD[1]

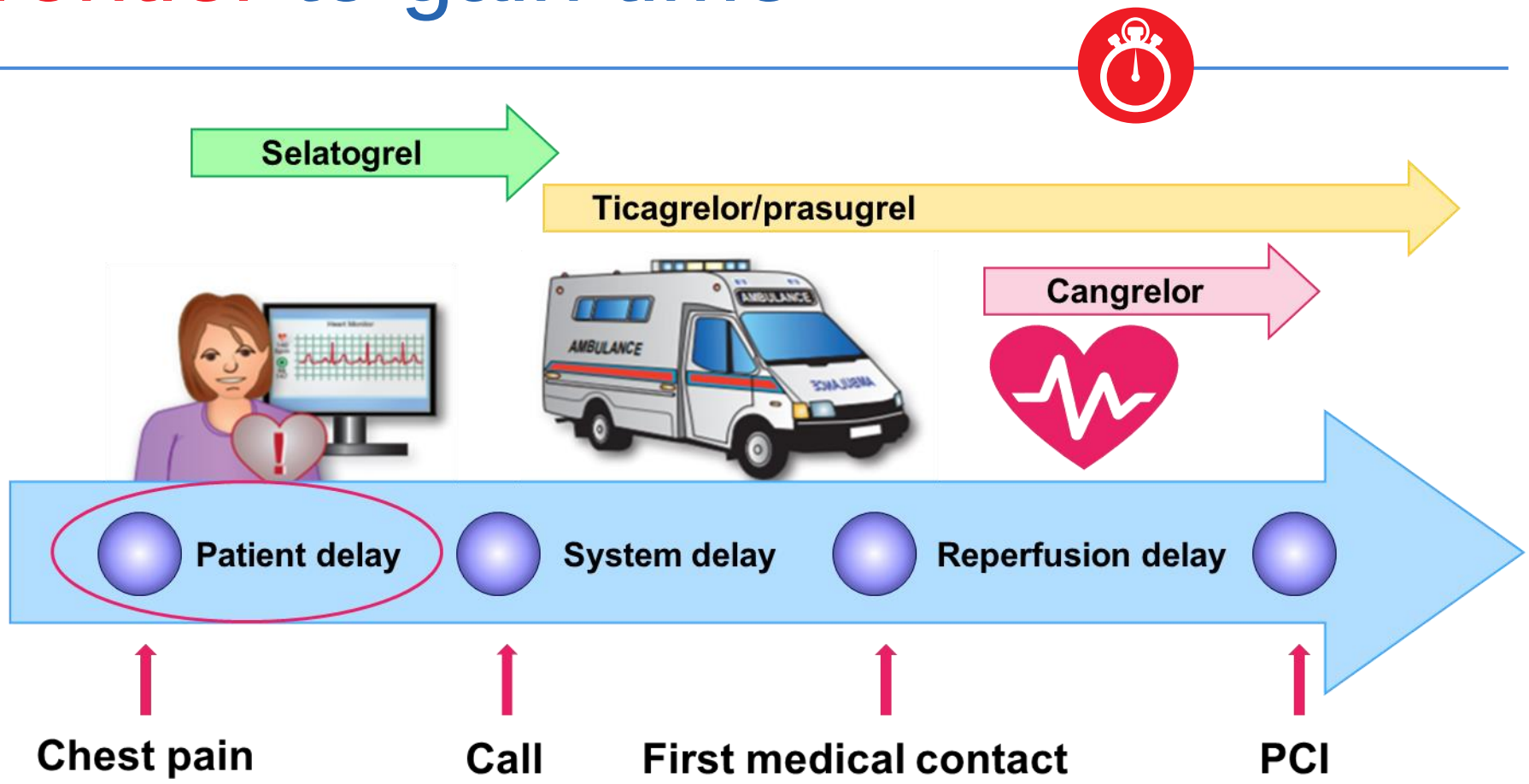
- **ADP** receptor antagonist
- **SC** administration
- **No metabolic** conversion
- **Onset** of action short
- **Potent** with >80% IPA for 6-8 hours
- **Reversible** → platelet function returns to baseline within ~24 hours
  - Terminal half-life: ~7 hours
- **Elimination** by biliary excretion



ADP, adenosine diphosphate; CCS, chronic coronary syndromes; IPA, inhibition of platelet aggregation; PD, pharmacodynamics; PK, pharmacokinetics; PRU, platelet reaction units; SC, subcutaneous

1. Schilling U, et al. Clin Pharmacokinet. 2020;59:545-66; 2. Adapted from: Storey RF, et al. Eur Heart J. 2020;41:3132-40

Next frontier to gain time



PCI, percutaneous coronary intervention

Adapted from: Hulot JS, Montalescot G. Eur Heart J. 2020;41:3141-43

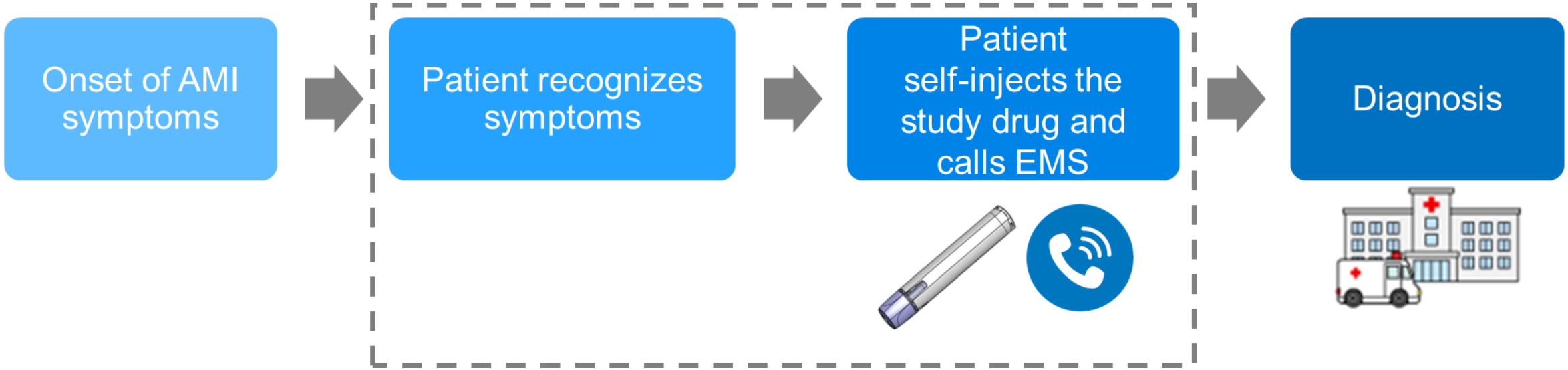
Selatogrel in acute MI (phase 3)

Selatogrel Outcome Study in suspected Acute Myocardial Infarction

Population:
Patients with an history of AMI at risk of recurrent AMI.

Training:
Participants will be trained on when and how to self-administer study treatment.

Study treatment:
Study drug (selatogrel or placebo) self-administered by patient using a ready-to use integrated drug delivery device.



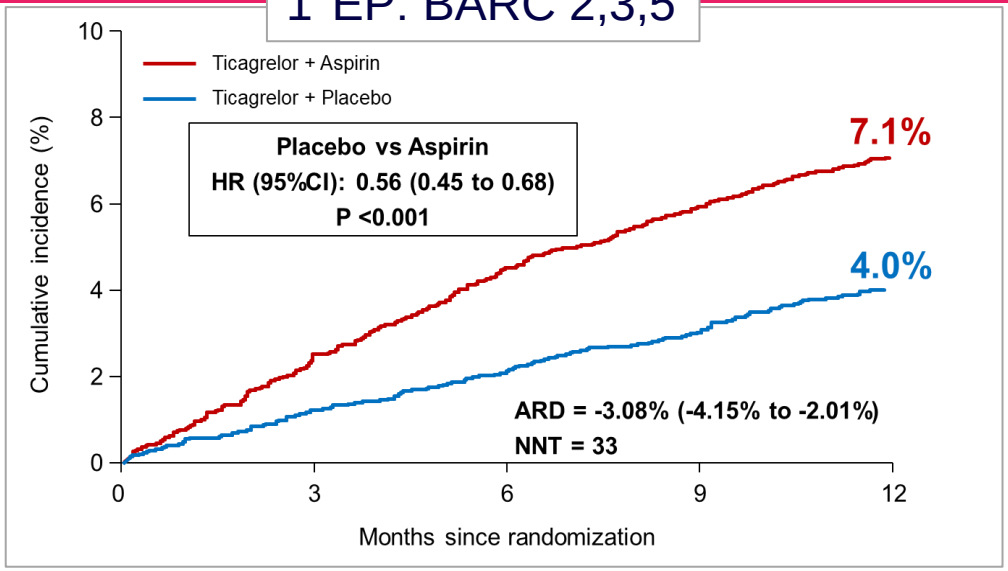
EMS, emergency medical services; MI, myocardial infarction
ClinicalTrials.gov Identifier: NCT04957719

Monotherapie pour tous, 30j après stenting?

TWILIGHT

(**3m^{ths}** post-PCI)

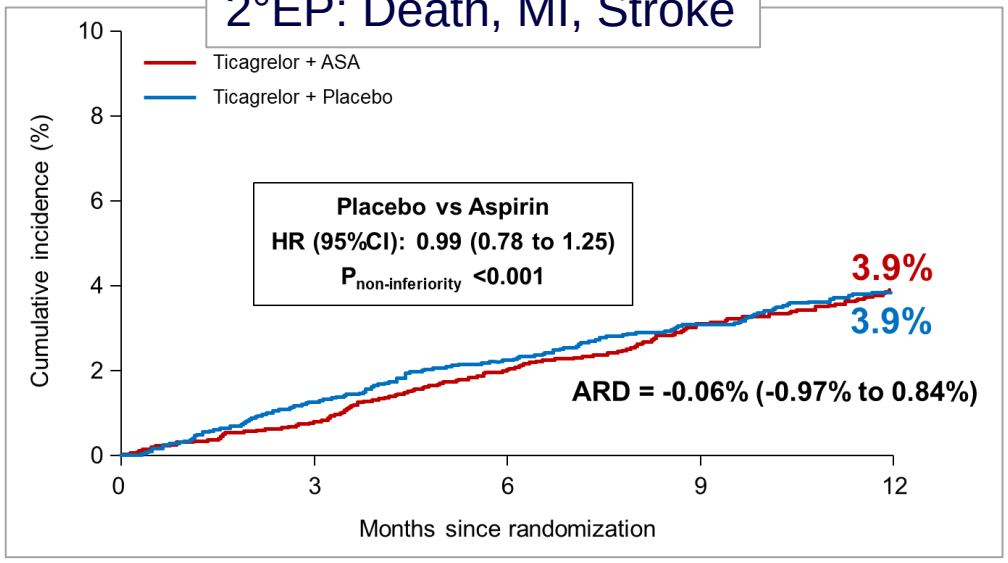
1°EP: BARC 2,3,5



N=7119
HBR/HBI
DB

Mehran R. NEJM 2019

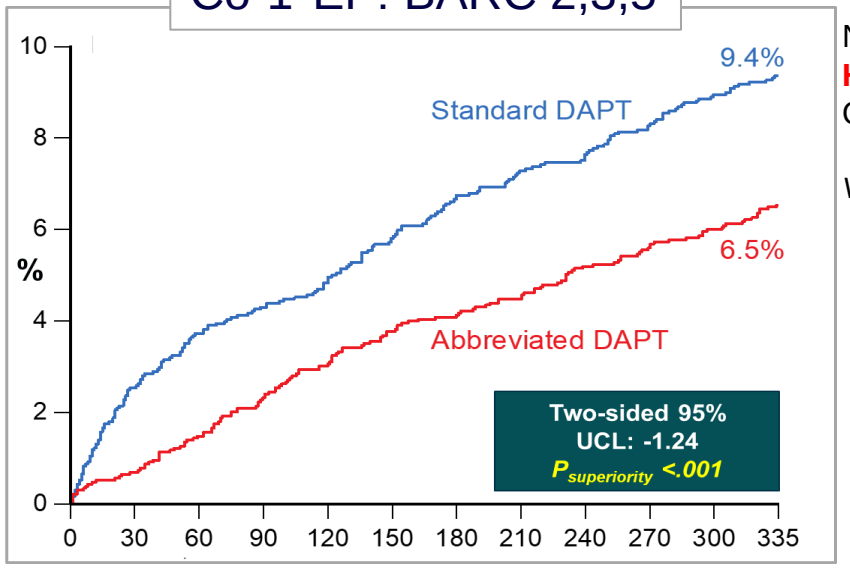
2°EP: Death, MI, Stroke



MASTER-DAPT

(**1mth** post-PCI)

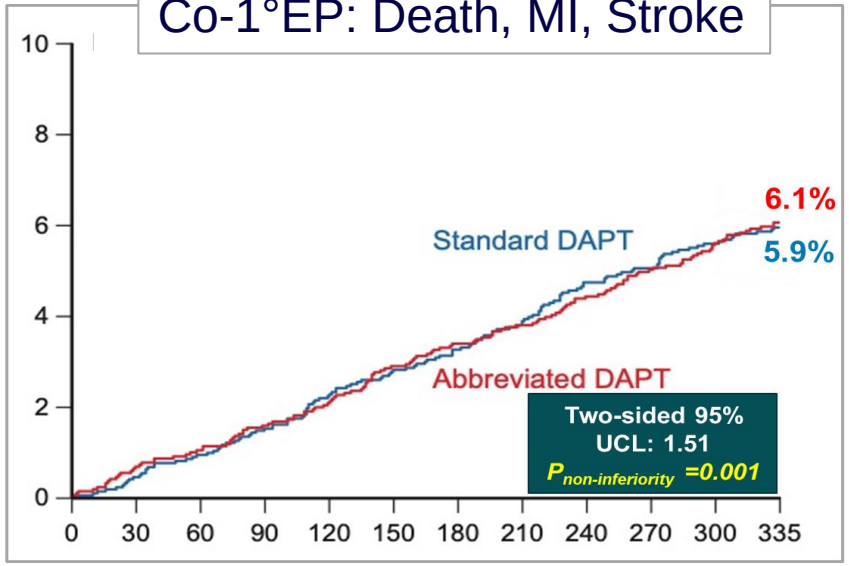
Co-1°EP: BARC 2,3,5



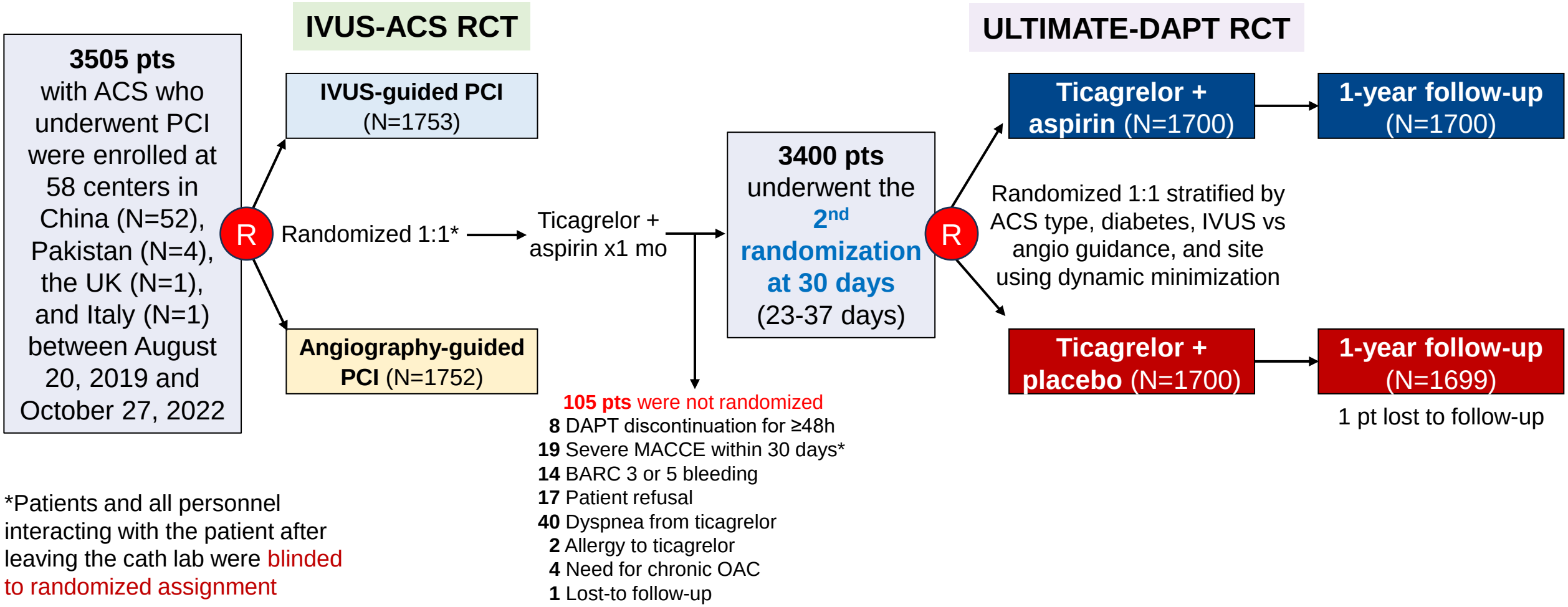
N=4579
HBR
OL

Valgimigli M. NEJM 2021

Co-1°EP: Death, MI, Stroke



PREVENT: 2x2 Randomization



*Patients and all personnel interacting with the patient after leaving the cath lab were blinded to randomized assignment

*Death, stroke, STEMI, definite ST, or clinically-driven TVR)

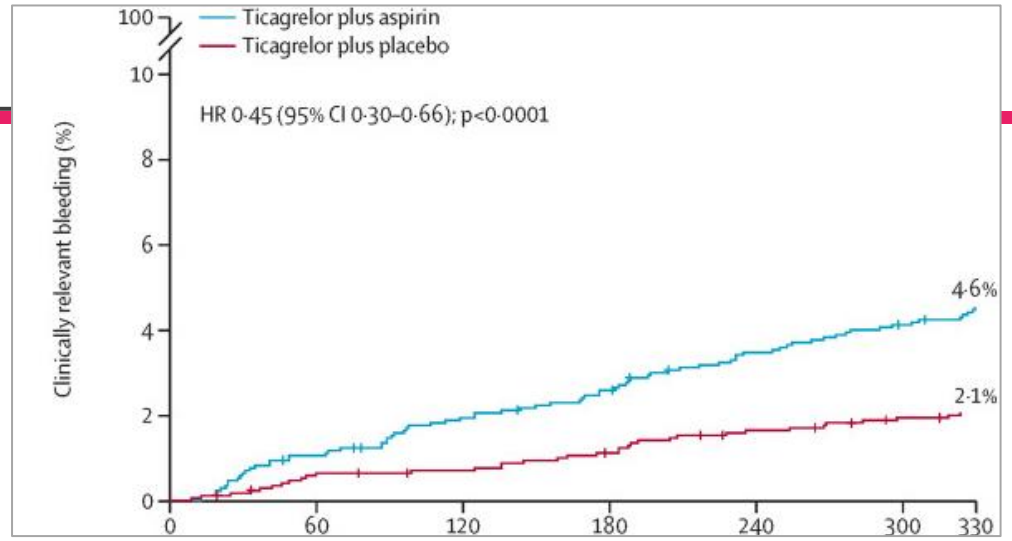
Lancet 2024

ULTIMATE-DAPT(1mth post-PCI)

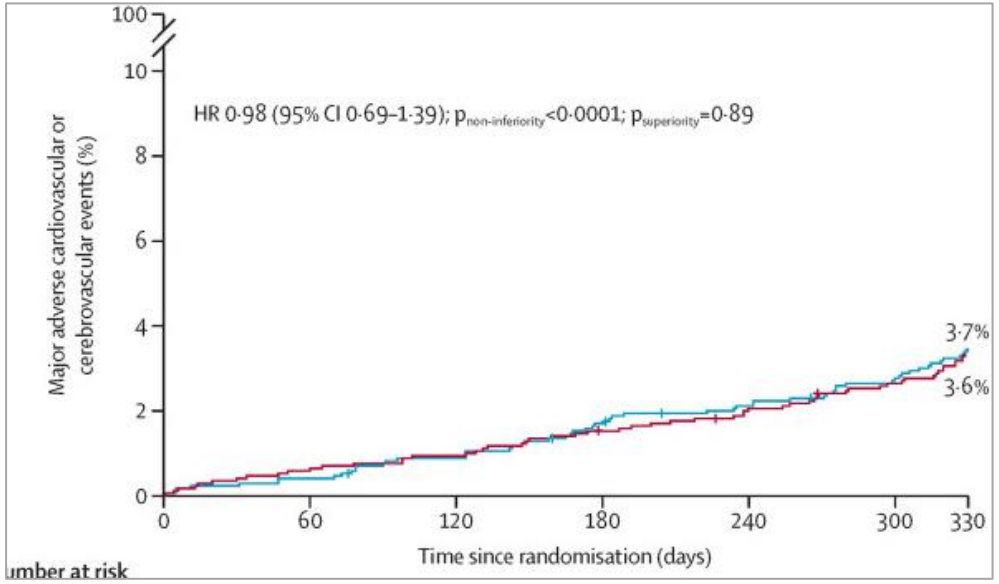
N=3400
100%ACS (IVUS-PCI)
DB

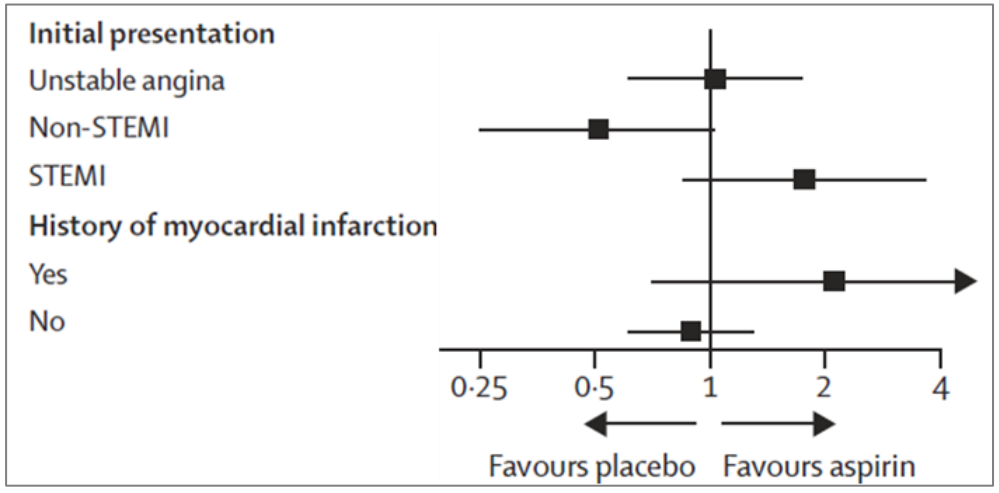
Ge Z. Lancet 2024

1° Efficacy EP: BARC 2-5



1°Safety EP: Death, MI, Stroke, ST, TVR





DAPT duration (months)

	Standard
Stable	1
MI	3-12

action-groupe.org

Pitié-Salpêtrière