UNIVERSITÀ DEGLI STUDI DI BRESCIA
DIPARTIMENTO DI SPECIALITA' MEDICO-CHIRURGICHE, SCIENZE RADIOLOGICHE E SANITA' PUBBLICA

Aggiornamenti in tema di

TERAPIA CARDIOVASCOLARE

03 Marzo 2018

Salò (BS) Hotel Conca d'Oro - via Zette 7

Nuove linee guida ESC sulla terapia antiaggregante

Riccardo Raddino

2015 ESC NSTE-ACS Guidelines

NSTE-ACS

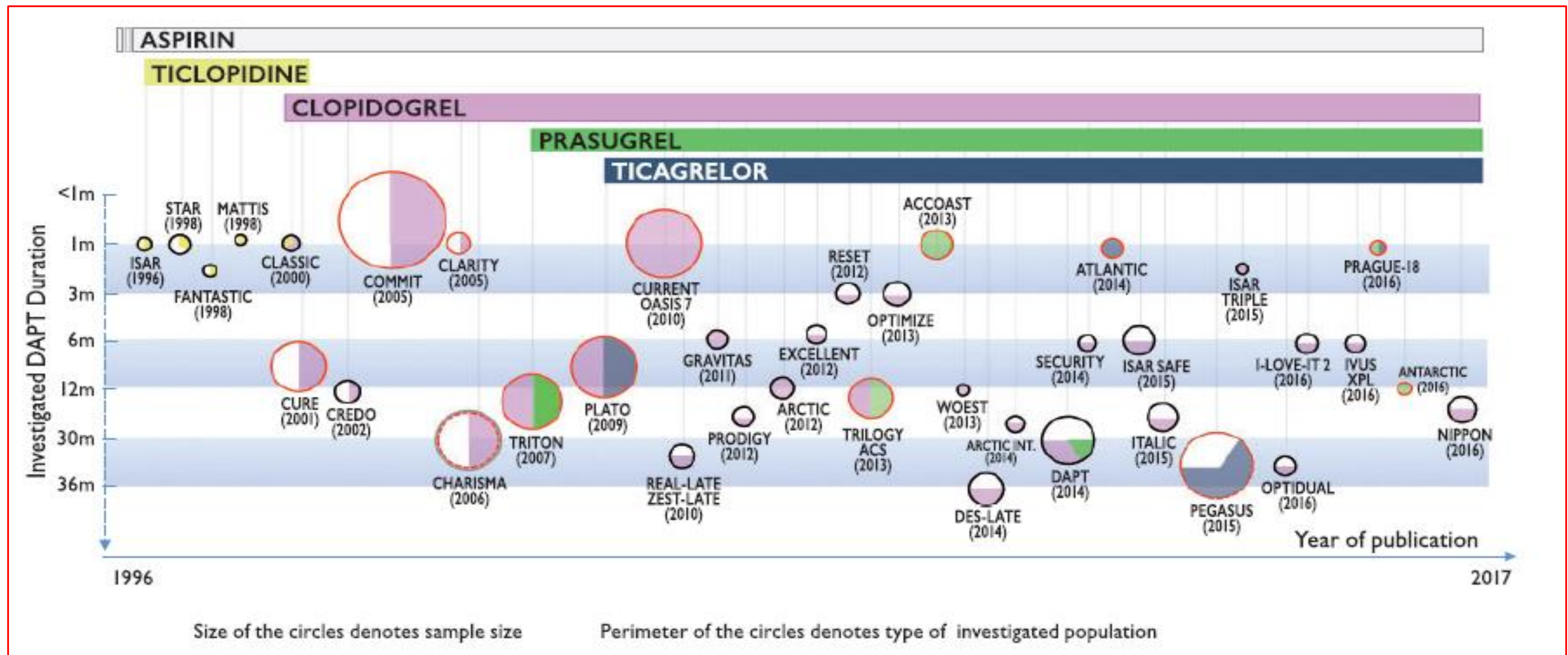
Recommendations	Class[a]	Level[b]	Ref.[c]
Oral antiplatelet therapy			
Aspirin is recommended for all patients without contraindications at an initial oral loading dose[d] of 150–300 mg (in aspirin-naive patients) and a maintenance dose of 75–100 mg/day long-term regardless of treatment strategy.	I	A	129–132
A $P2Y_{12}$ inhibitor is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds.	I	A	137, 148, 153
• Ticagrelor (180 mg loading dose, 90 mg twice daily) is recommended, in the absence of contraindications,[e] for all patients at moderate-to-high risk of ischaemic events (e.g. elevated cardiac troponins), regardless of initial treatment strategy and including those pretreated with clopidogrel (which should be discontinued when ticagrelor is started).	I	B	153
• Prasugrel (60 mg loading dose, 10 mg daily dose) is recommended in patients who are proceeding to PCI if no contraindication.[e]	I	B	148, 164
• Clopidogrel (300–600 mg loading dose, 75 mg daily dose) is recommended for patients who cannot receive ticagrelor or prasugrel or who require oral anticoagulation.	I	B	137
$P2Y_{12}$ inhibitor administration for a shorter duration of 3–6 months after DES implantation may be considered in patients deemed at high bleeding risk.	IIb	A	187–189, 192

European Heart Journal 2015; doi:10.1093/eurheartj/ehv320

2017 ESC Focused Update on Dual Antiplatelet Therapy in Coronary Artery Disease developed in collaboration with the EACTS*

*: European Association for Cardio-Thoracic Surgery

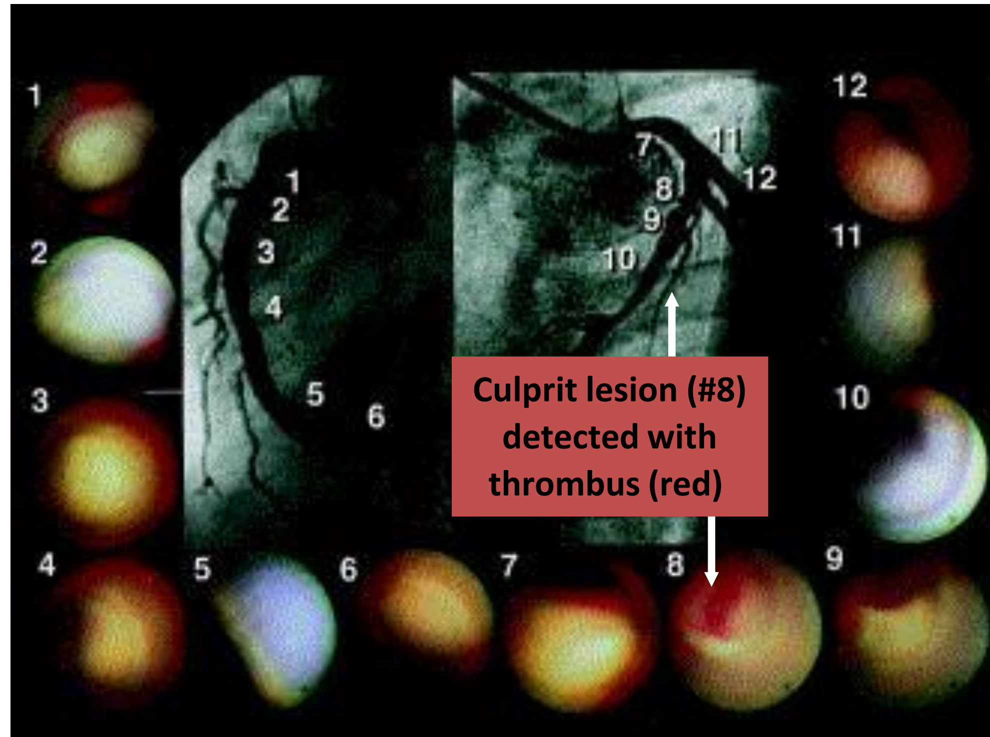
Efficacia e sicurezza della DAPT : 20 anni di studi



PERCHE' MANTENERE LA DAPT DOPO 1 EVENTO ACUTO?
Evidenza di vulnerabilità delle placche per almeno 12 mesi

Angiographic & angioscopic images in a 58-year-old man with anterior MI[Asakura 2001]

Multiple 'vulnerable' plaques detected in non-culprit segments 1–7



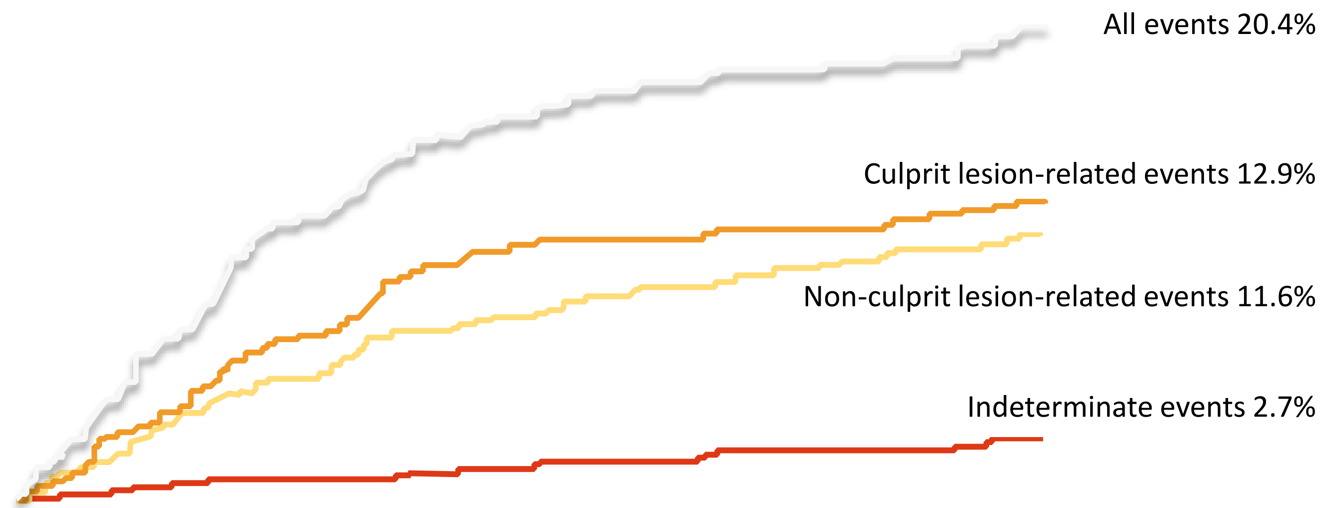
Multiple 'vulnerable' plaques detected in non-culprit segments 10–12

ACS, acute coronary syndrome; MI, myocardial infarction.
Asakura M *et al.* J Am Coll Cardiol 2001;37:1284–1288 (with permission).

AZ Medical Internal Use Only

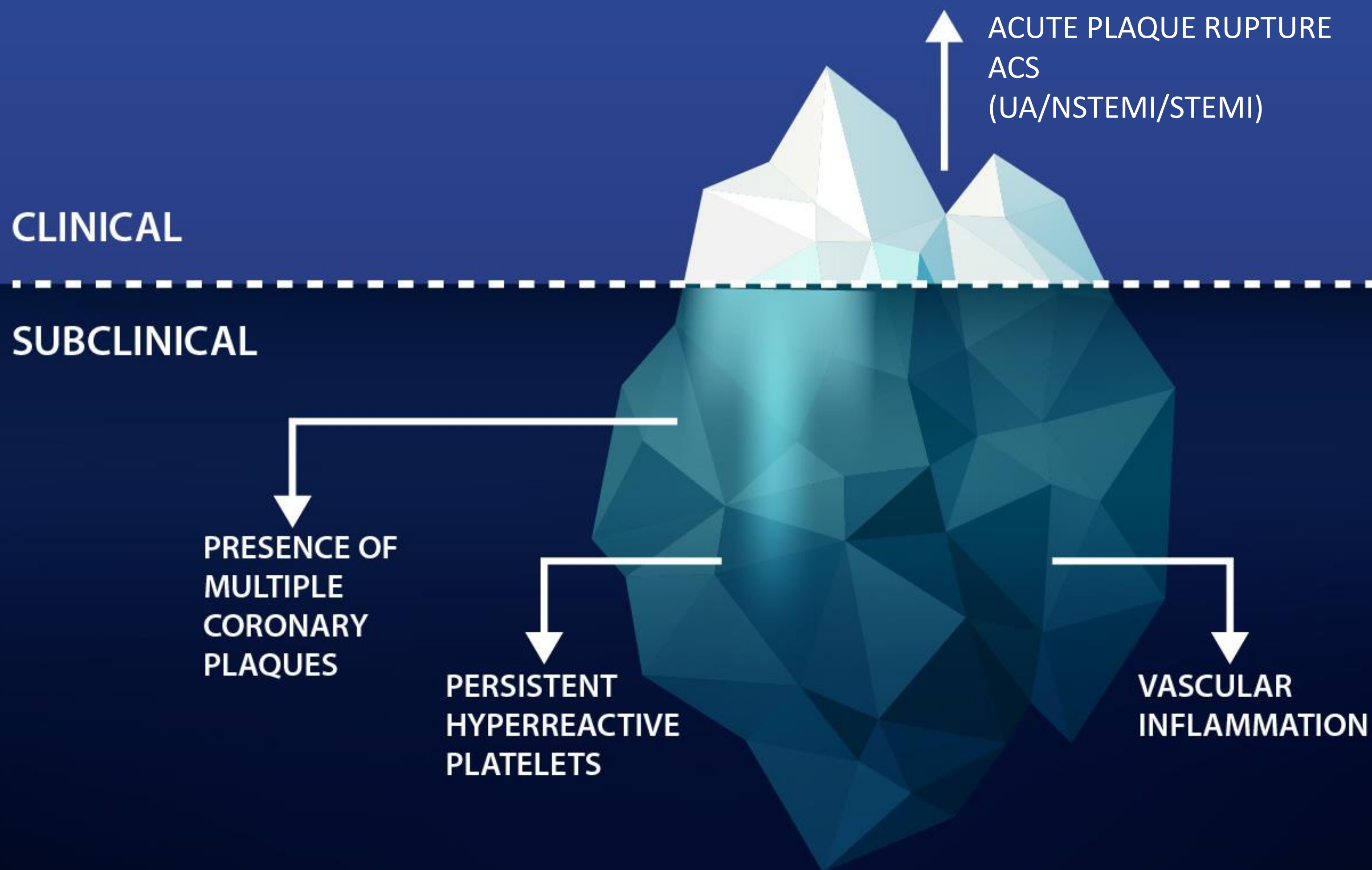
La recidiva di eventi coronarici dopo 1 evento indice può derivare sia dalla culprit che dalle alter placche non culprit nell'albero coronarico

PROSPECT study: Prospective study of the natural history of atherosclerosis over 3 years in patients with ACS who underwent PCI (n=697)[Stone 2011]



ACS, acute coronary syndrome; MACE, major adverse cardiac events; PCI, percutaneous coronary intervention; PROSPECT, Providing Regional Observations to Study Predictors of Events in the Coronary Tree.
Stone GW *et al.* N Engl J Med 2011;364:226–235.

La sindrome coronarica acuta non è che la punta dell'iceberg della malattia aterosclerotica



ACS, acute coronary syndrome; NSTEMI, non-ST segment elevation myocardial infarction; STEMI, ST segment elevation myocardial infarction; UA, unstable angina.

Goldstein JA. J Am Coll Cardiol 2002;39:1464–1467.

AZ Medical Internal Use Only

L'importanza della stratificazione del rischio ischemico ed emorragico

Recommendations	Class[a]	Level[b]
The use of risk scores designed to evaluate the benefits and risks of different DAPT durations[c] may be considered.[15,18]	IIb	A

L’importanza della stratificazione del rischio emorragico (PRECISE-DAPT) e ischemico (DAPT)

	PRECISE-DAPT score[18]	DAPT score[15]	
Time of use	At the time of coronary stenting	After 12 months of uneventful DAPT	
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)	Standard DAPT (12 months) vs. Long DAPT (30 months)	
Score calculation[a]	HB: ≥12, 11·5, 11, 10·5, ≤10 WBC: ≤5, 8, 10, 12, 14, 16, 18, ≥20 Age: ≤50, 60, 70, 80, ≥90 CrCl: ≥100, 80, 60, 40, 20, 0 Prior Bleeding: No, Yes Score Points: 0, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30	Age ≥75 65 to <75 <65 Cigarette smoking Diabetes mellitus MI at presentation Prior PCI or prior MI Paclitaxel-eluting stent Stent diameter <3 mm CHF or LVEF <30% Vein graft stent	 −2 pt −1 pt 0 pt +1 pt +1 pt +1 pt +1 pt +1 pt +1 pt +2 pt +2 pt
Score range	0 to 100 points	−2 to 10 points	
Decision making cut-off suggested	Score ≥25 → Short DAPT Score <25 → Standard/long DAPT	Score ≥2 → Long DAPT Score <2 → Standard DAPT	
Calculator	www.precisedaptscore.com	www.daptstudy.org	

PRECISE-DAPT = PREdicting bleeding Complications In patients undergoing Stent implantation and subsEquent Dual Anti Platelet Therapy;

QUALE ANTIAGGREGANTE ?

ESC European Society of Cardiology

ACS:

sia NSTE-ACS sia STE-ACS

SCAD

Recommendations	Class	Level
In patients with ACS, ticagrelor (180 mg loading dose, 90 mg twice daily) on top of aspirin is recommended, regardless of initial treatment strategy, including patients pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced) unless there are contra-indications.	I	B
In patients with ACS undergoing PCI, prasugrel (60 mg loading dose, 10 mg daily dose) on top of aspirin is recommended for $P2Y_{12}$ inhibitor-naïve patients with NSTE-ACS or initially conservatively managed STEMI if indication for PCI is established, or in STEMI patients undergoing immediate coronary catheterization unless there is a high-risk of life-threatening bleeding or other contra-indications.	I	B
Clopidogrel (600 mg loading dose, 75 mg daily dose) on top of aspirin is recommended in stable CAD patients undergoing coronary stent implantation and in ACS patients who cannot receive ticagrelor or prasugrel, including those with prior intracranial bleeding or indication for OAC.	I	A
Clopidogrel (300 mg loading dose in patients ≤75, 75 mg daily dose) is recommended on top of aspirin in STEMI patients receiving thrombolysis.	I	A

PROVVEDIMENTI PERIPROCEDURALI PER RIDURRE I RISCHI EMORRAGICI

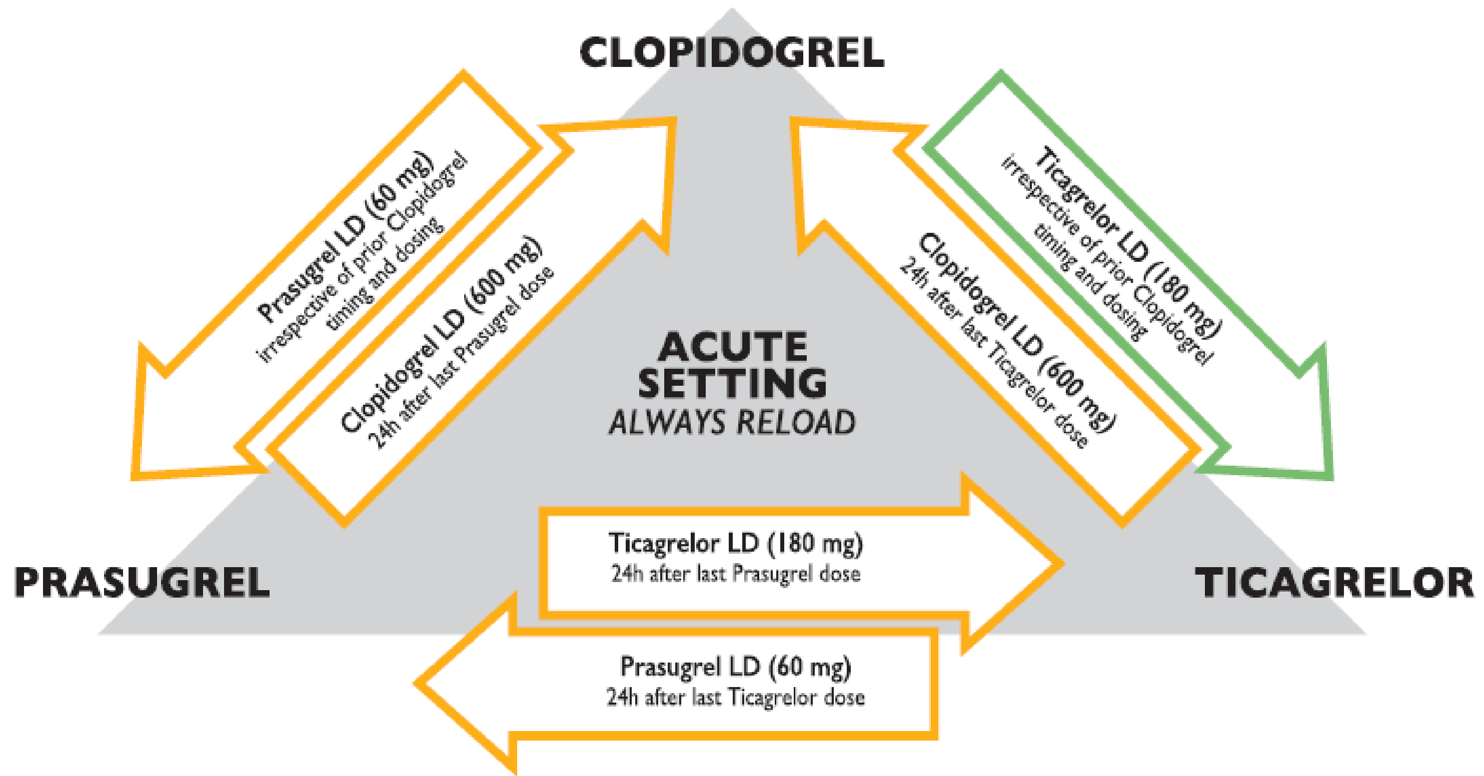
Measures to minimize bleeding while on dual antiplatelet therapy

Recommendations	Class[a]	Level[b]
Radial over femoral access is recommended for coronary angiography and PCI if performed by an expert radial operator.[43,44]	I	A
In patients treated with DAPT, a daily aspirin dose of 75 - 100 mg is recommended.[45–47,51,52]	I	A
A PPI in combination with DAPT[c] is recommended.[70,79,80,86,87]	I	B
Routine platelet function testing to adjust antiplatelet therapy before or after elective stenting is not recommended.[58–60]	III	A

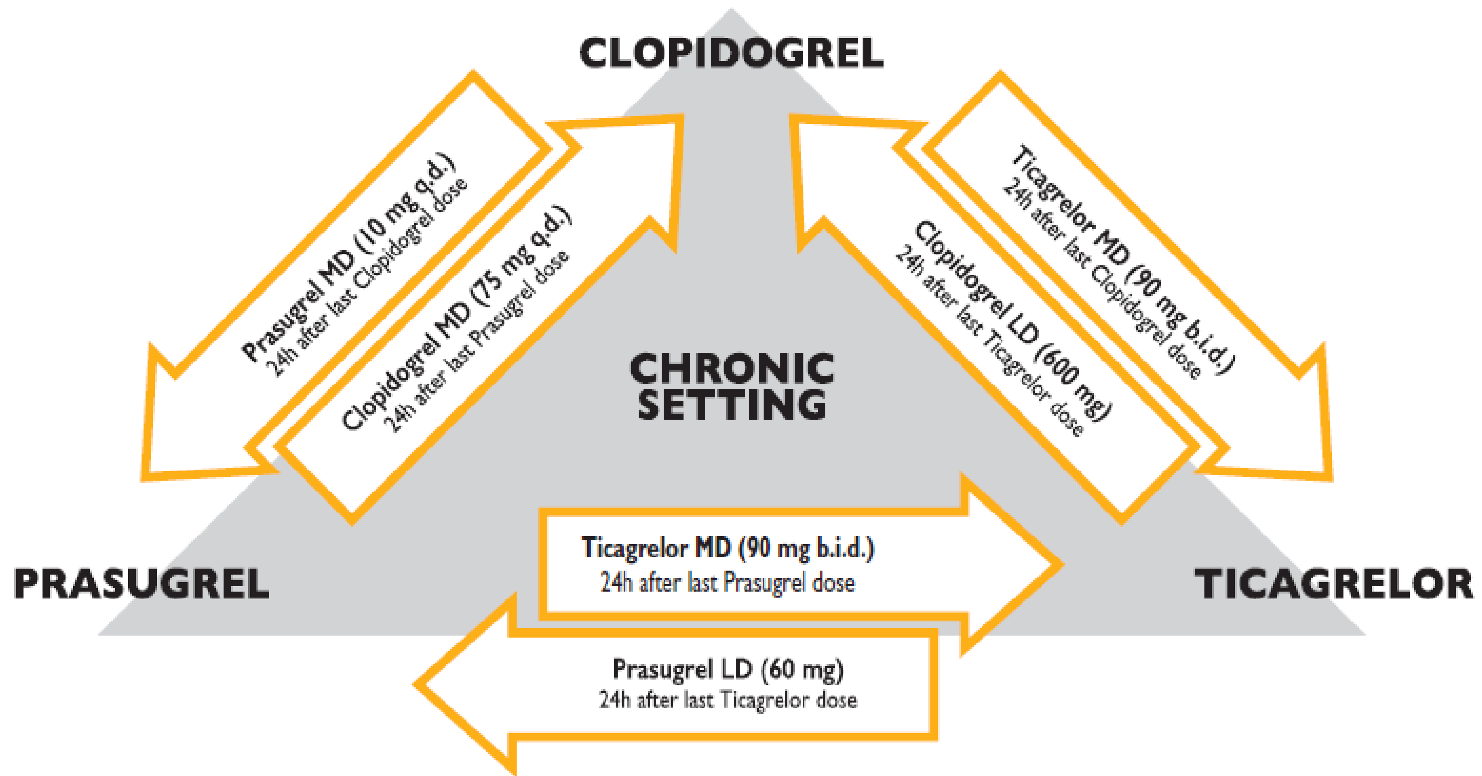
Switching tra i diversi inibitori orali di P2Y12

Recommendations	Class	Level
In patients with ACS who were previously exposed to clopidogrel, switching from clopidogrel to ticagrelor is recommended early after hospital admission at a loading dose of 180 mg irrespective of timing and loading dose of clopidogrel, unless contra-indications to ticagrelor exist.	I	B
Additional switching between oral $P2Y_{12}$ inhibitors may be considered in cases of side effects/drug intolerance according to the proposed algorithms.	IIb	C

SINDROME CORONARICA ACUTA

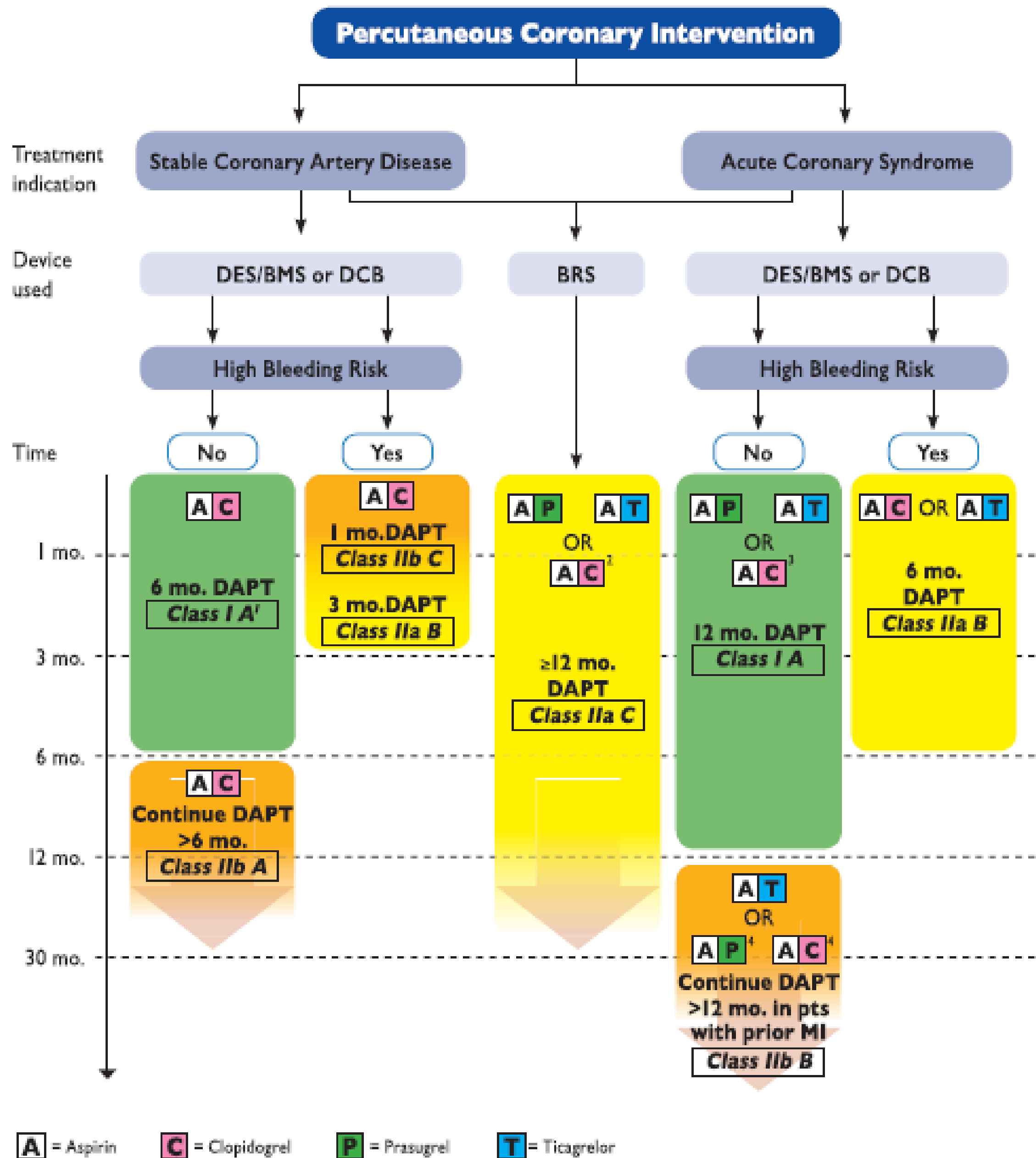


MALATTIA CORONARICA STABILE

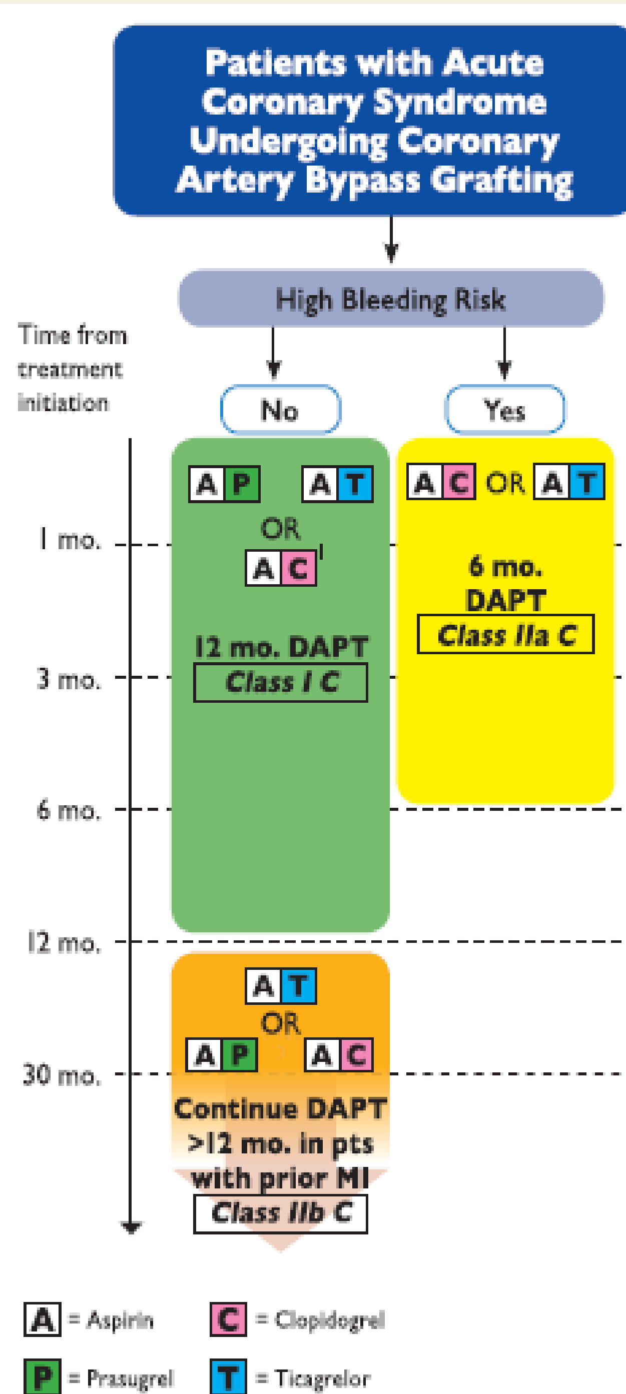


ALGORITMI PER LA GESTIONE DELLA DAPT NEI PAZIENTI CON MALATTIA CORONARICA

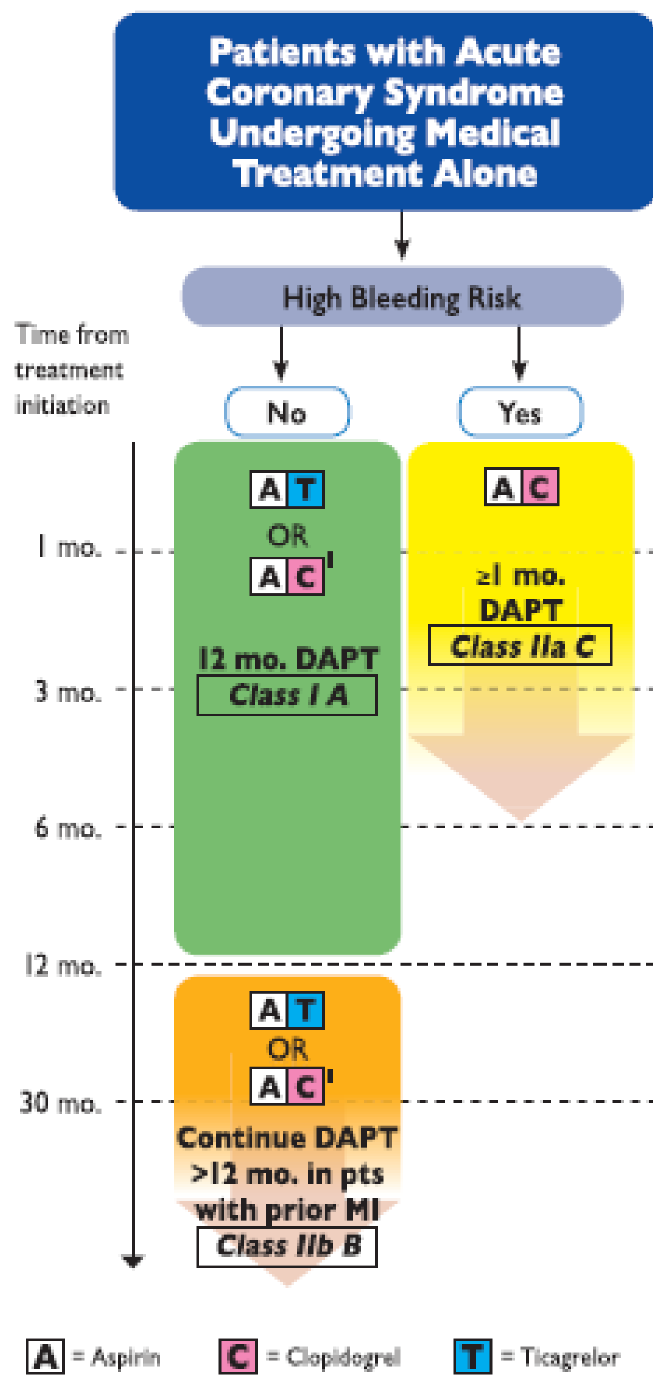
PTCA



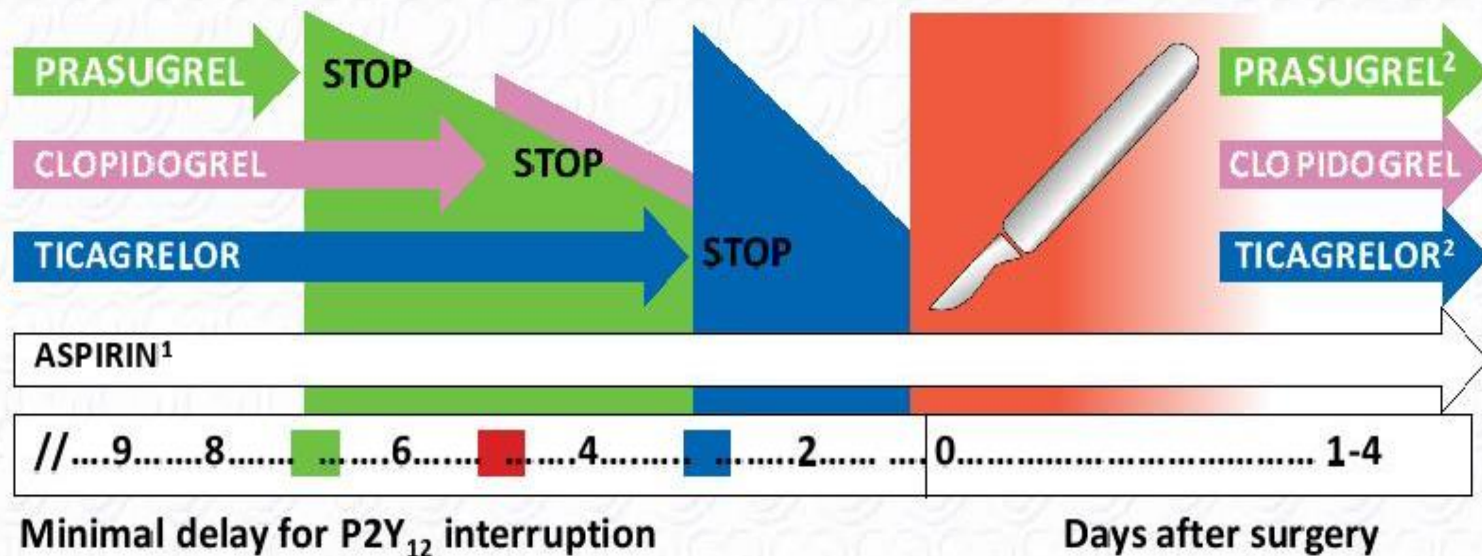
BPAC



Terapia medica



Timing della sospensione dei diversi inibitori orali di P2Y12 nella chirurgia maggiore non cardiaca



= Expected average platelet function recovery

[1] Decision to stop aspirin throughout surgery should be made on a single case basis taking into account the surgical bleeding risk.

[2] In patients not requiring OAC.

In alcuni pazienti andrebbe considerato (IIbA) il prolungamento della DAPT

European Heart Journal Advance Access published August 29, 2015

European Heart Journal
doi:10.1093/eurheartj/ehv320

ESC GUIDELINES

Recommendation	Class	Level	Ref.
A $P2Y_{12}$ inhibitor is recommended, in addition to aspirin, for 12 months unless there are contraindications such as excessive risk of bleeds.	I	A	137, 148, 153
Long-term $P2Y_{12}$ inhibition			
$P2Y_{12}$ inhibitor administration in addition to aspirin beyond 1 year may be considered after careful assessment of the ischaemic and bleeding risks of the patient.	IIb	A	184, 186

AHA/ACC expert consensus document on DAPT 2016

Accepted Manuscript

2016 ACC/AHA Guideline Focused Update on Duration of Dual Antiplatelet Therapy in Patients With Coronary Artery Disease

IIb	A SR	In patients with ACS treated with medical therapy alone (without revascularization or fibrinolytic therapy) who have tolerated DAPT without bleeding complication and who are not at high bleeding risk (e.g., prior bleeding on DAPT, coagulopathy, oral anticoagulant use), continuation of DAPT for longer than 12 months may be reasonable (28,30,40,41,43,53,71,141).

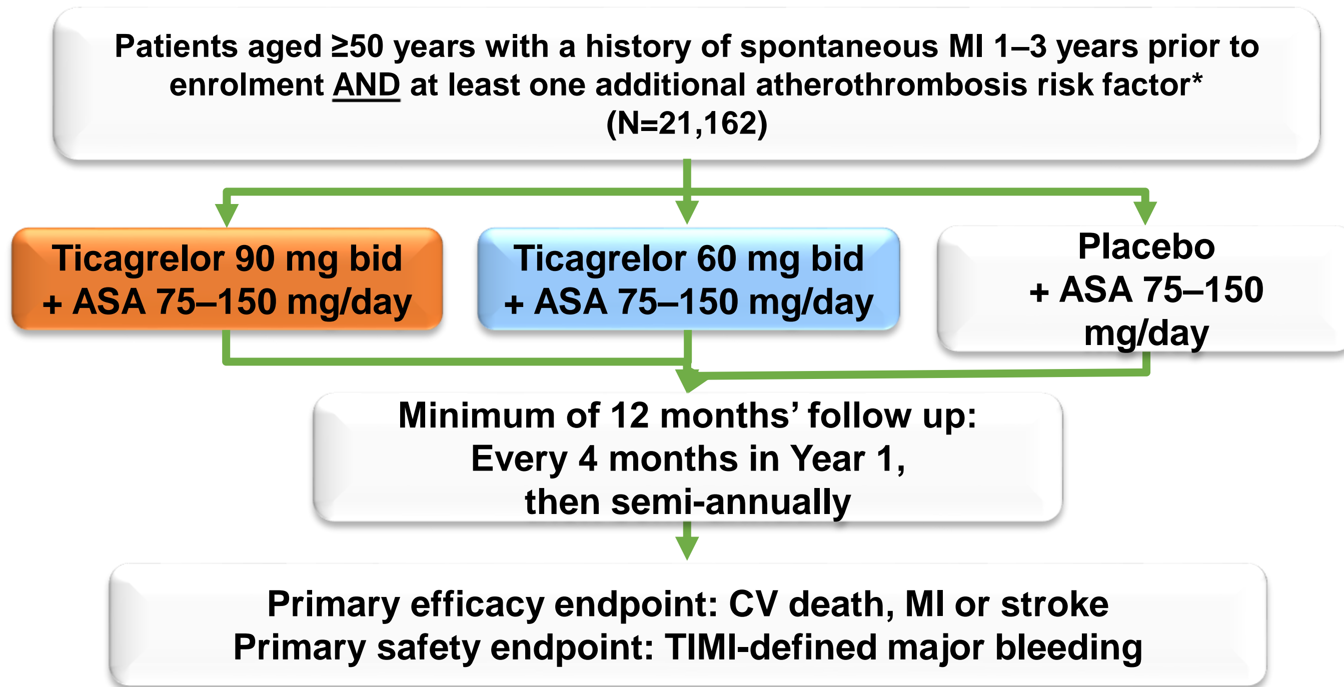
IIb	A SR	In patients with ACS (NSTE-ACS or STEMI) treated with coronary stent implantation who have tolerated DAPT without a bleeding complication and who are not at high bleeding risk (e.g., prior bleeding on DAPT, coagulopathy, oral anticoagulant use), continuation of DAPT (clopidogrel, prasugrel, or ticagrelor) for longer than 12 months may be reasonable (16,22-26,28,30,40,41,43,53,54,72).

Dual antiplatelet therapy duration in patients with acute coronary syndrome treated with percutaneous coronary intervention *(continued)*

ESC
European Society of Cardiology

Recommendations	Class	Level
In patients with ACS who have tolerated DAPT without a bleeding complication, continuation of DAPT for longer than 12 months may be considered.	IIb	A
In patients with MI and high ischaemic risk who have tolerated DAPT without a bleeding complication, ticagrelor 60 mg *b.i.d.* for longer than 12 months on top of aspirin may be preferred over clopidogrel or prasugrel.	IIb	B

PEGASUS-TIMI 54: Study Design



*Age ≥65 years, diabetes mellitus, second prior MI, multivessel CAD or chronic non-end stage renal disease
bid, twice daily; CAD, coronary artery disease; TIMI, Thrombolysis in Myocardial Infarction

Bonaca MP *et al. Am Heart J* 2014;167:437–444
Bonaca MP *et al. N Engl J Med* 2015 [Epub ahead of print]

Key inclusion and exclusion criteria

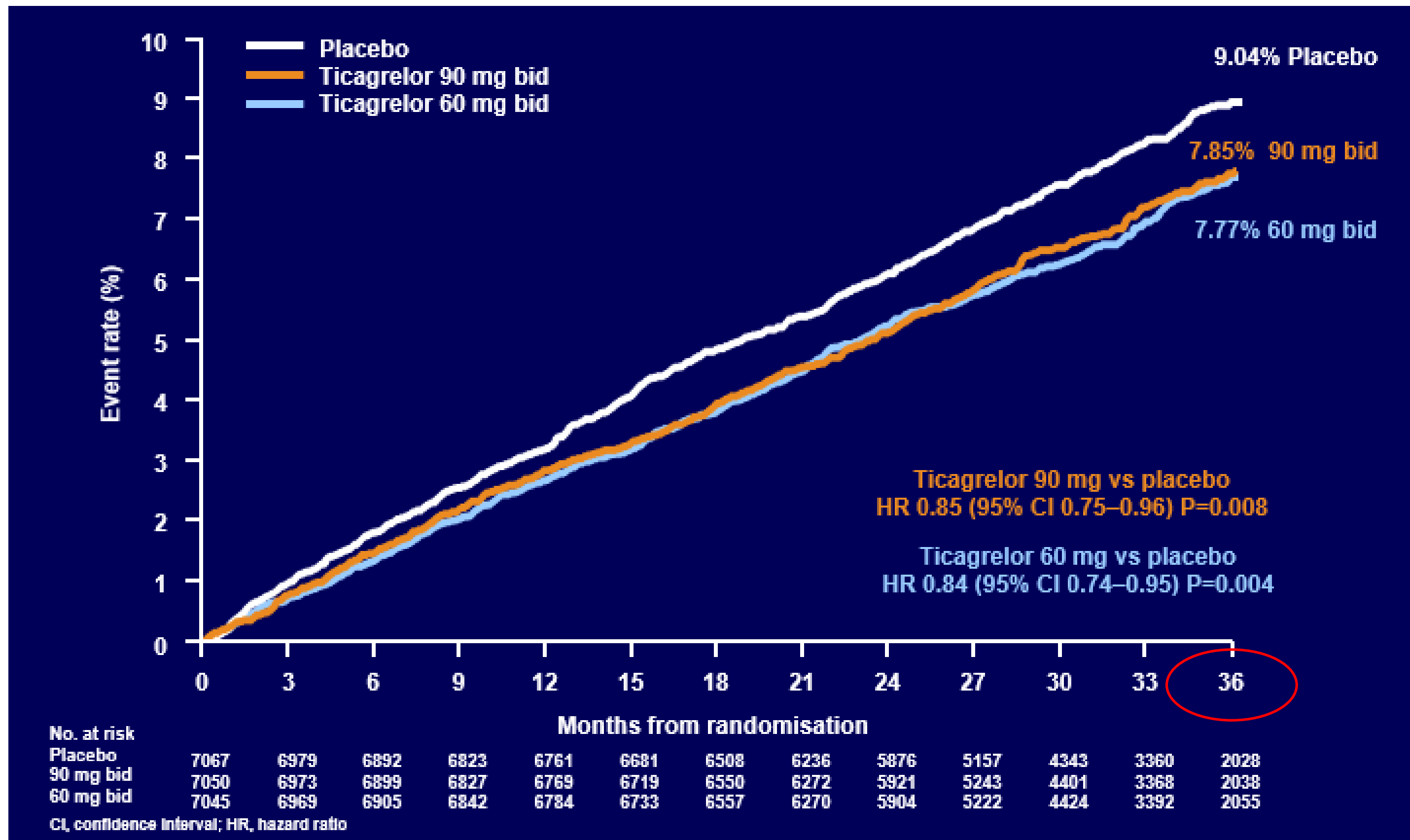
Key inclusion

- Age ≥50 years
- **At least 1 of the following**:
  - Age ≥65 years
  - Diabetes requiring medication
  - 2nd prior MI (>1 year ago)
  - Multivessel CAD
  - Chronic, non-end stage renal dysfunction (CrCl <60 mL/min, Cockcroft Gault equation)
- Tolerating ASA and able to be dosed at 75−150 mg/d

Key exclusion

- Planned use of $P2Y_{12}$ antagonist, dipyridamole, cilostazol, or anticoagulant
- Bleeding disorder
- History of ischaemic stroke, ICH, CNS tumour or vascular abnormality
- Recent GI bleed or major surgery
- At risk for bradycardia
- Dialysis or severe liver disease

PEGASUS-TIMI 54: Primary Endpoint

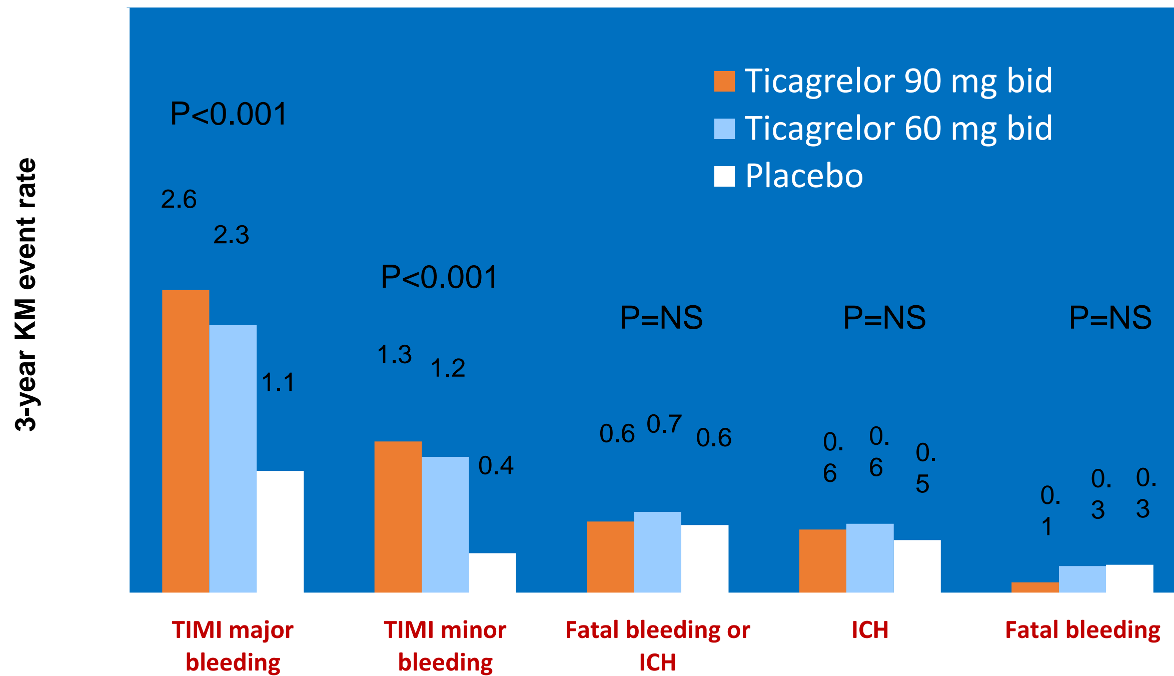


CI, confidence interval; HR, hazard ratio

Bonaca MP *et al. N Engl J Med* 2015 [Epub ahead of print]

In PEGASUS-TIMI 54, long-term treatment with ticagrelor significantly reduced the risk of the composite of CV death, MI or stroke by 15–16% in patients with a prior MI* within the previous 1–3 years

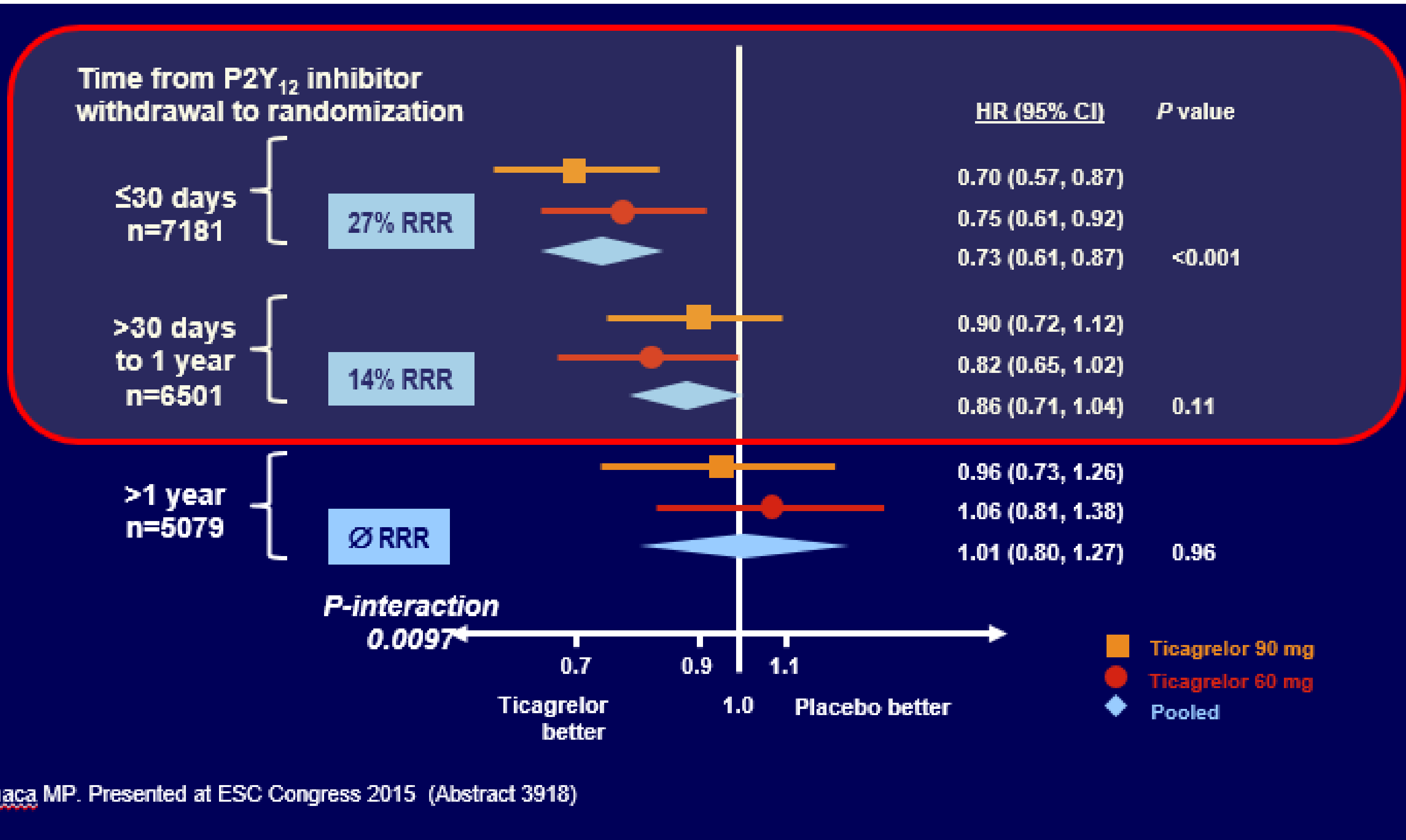
PEGASUS-TIMI 54: Bleeding



Rates are presented as 3-year Kaplan-Meier estimates
P<0.026 indicates statistical significance

Bonaca MP *et al. N Engl J Med* 2015 [Epub ahead of print]

ANALISI DEI SOTTOGRUPPI: La riduzione dell'end point primario (CV death, MI or stroke) è tanto maggiore quanto minore è il tempo trascorso dalla sospensione della DAPT



L'EMA ha approvato l'utilizzo di Ticagrelor 60 mg x 2/die in pazienti che hanno sospeso Ticagrelor 90 mg dopo almeno 1 anno di terapia; il trattamento con Ticagrelor 60 mg può essere iniziato SENZA sospendere Ticagrelor 90 mg .

A CHI?

QUANDO ?

PERCHE' ?

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Grazie

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