Planteamiento en SCASEST

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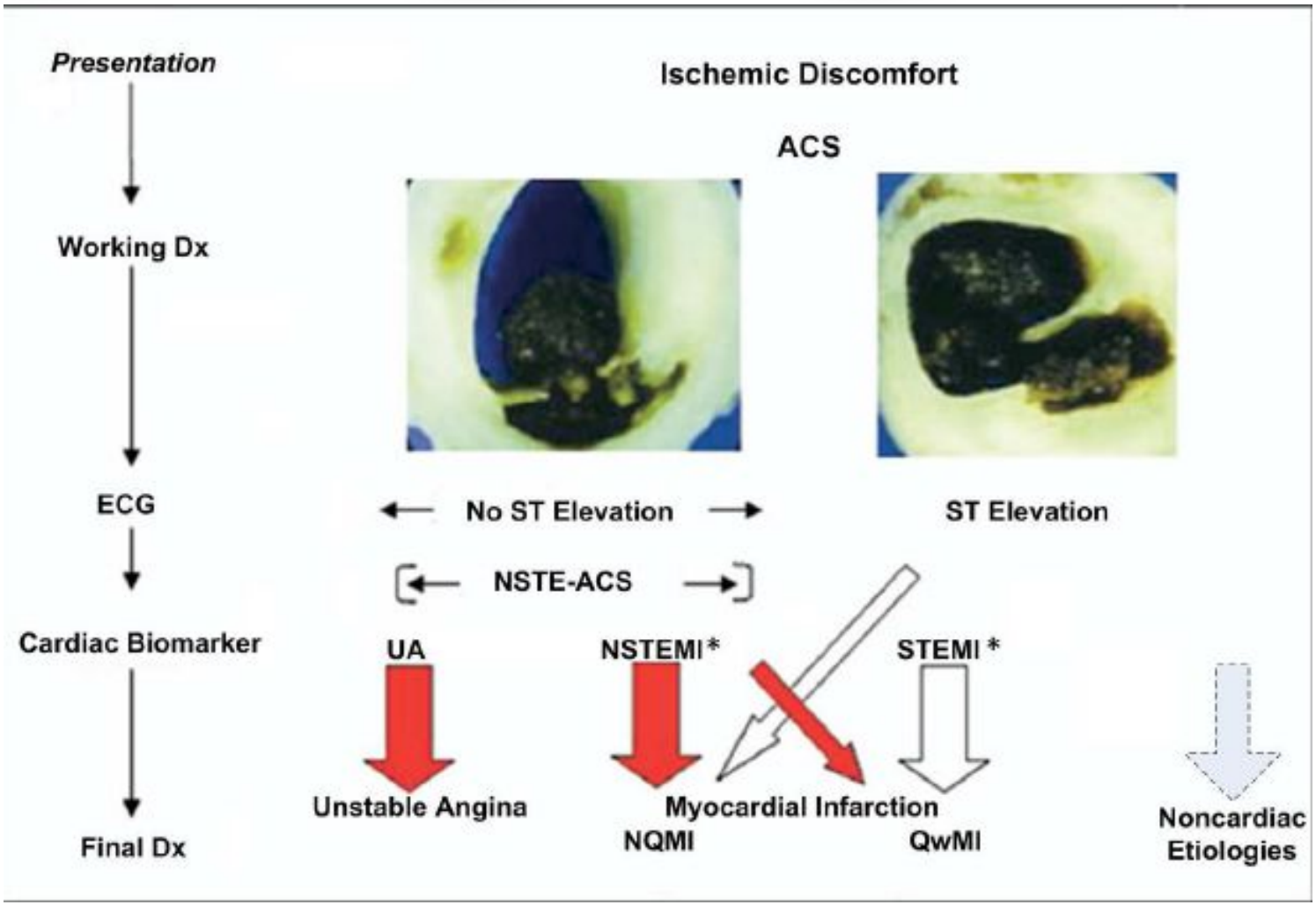
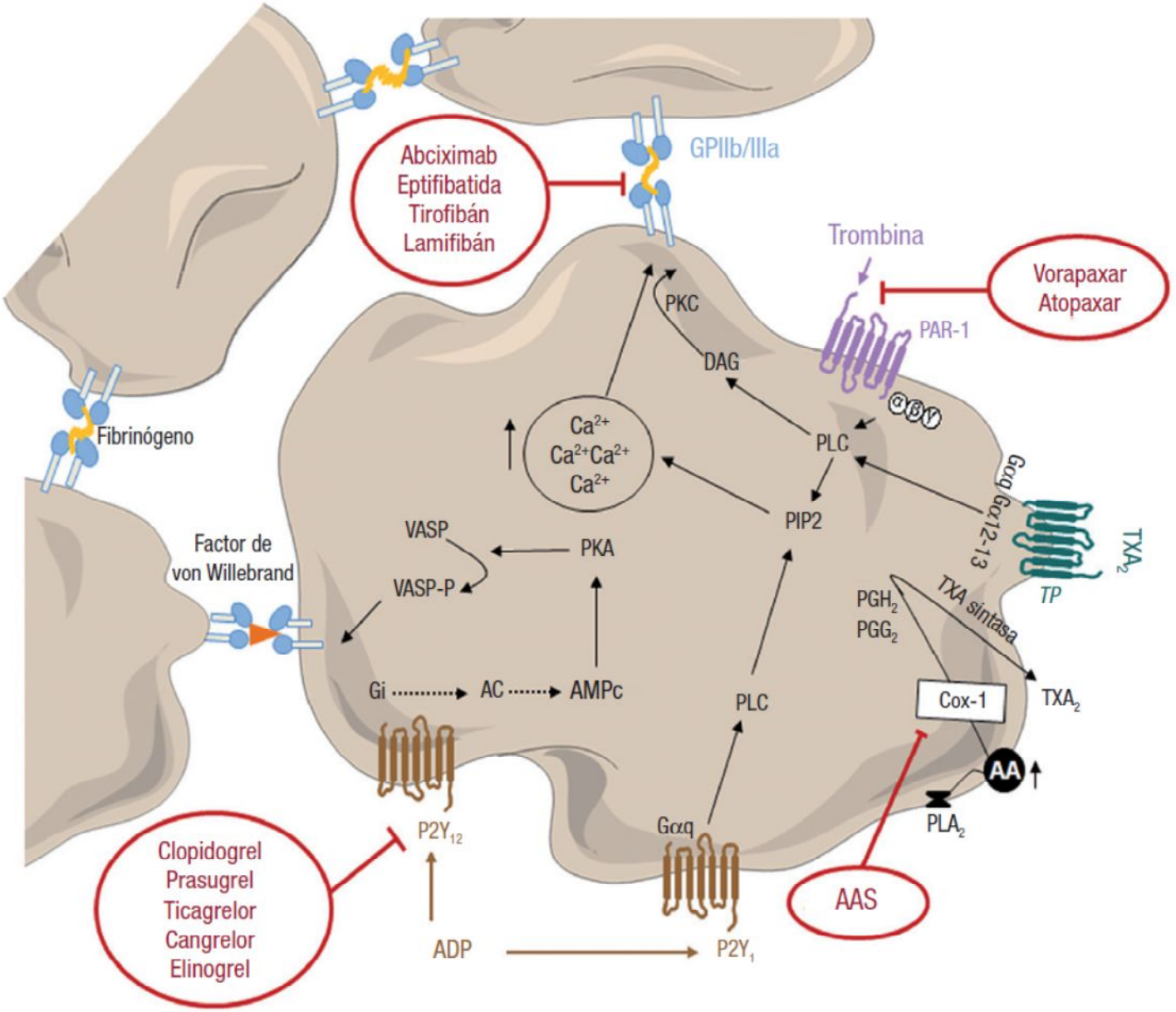
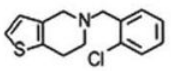

Presentation
Ischemic Discomfort
ACS
Working Dx
ECG
No ST Elevation
ST Elevation
NSTE-ACS
Cardiac Biomarker
UA
NSTEMI*
STEMI*
Unstable Angina
Myocardial Infarction
NQMI
QwMI
Noncardiac Etiologies
Final Dx


Abciximab
Eptifibatida
Tirofibán
Lamifibán
GPIIb/IIIa
Trombina
Vorapaxar
Atopaxar
PAR-1
PKC
DAG
Fibrinógeno
Ca2+
Ca2+Ca2+
Ca2+
PLC
αβγ
Gαq Gα12-13
TXA2
TP
PIP2
VASP
PKA
Factor de
von Willebrand
VASP-P
PGH2
PGG2
TXA sintasa
Gi
AC
AMPc
PLC
Cox-1
TXA2
AA
PLA2
Gαq
P2Y12
Clopidogrel
Prasugrel
Ticagrelor
Cangrelor
Elinogrel
AAS
ADP
P2Y1

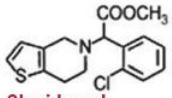
Tienopiridinas

Primera generación



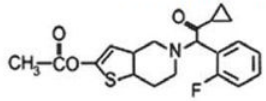
Ticlopidina
Administración: oral
Conversión metabólica: sí
Reversible: no
Vida media: 30-50 h
Duración acción: 5-10 días

Segunda generación



Clopidogrel
Administración: oral
Conversión metabólica: sí
Reversible: no
Vida media: 7 h
Duración acción: 5-10 días

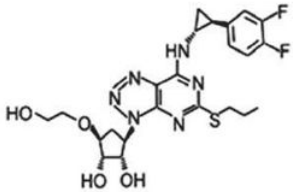
Tercera generación



Prasugrel
Administración: oral
Conversión metabólica: sí
Reversible: no
Vida media: 3,5 h
Duración acción: 5-10 días

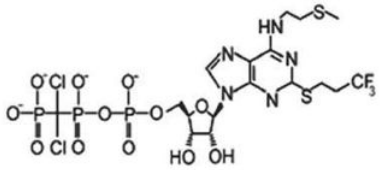
Análogos de nucleósido/nucleótido

Ciclo-pentil-triazol-pirimidina



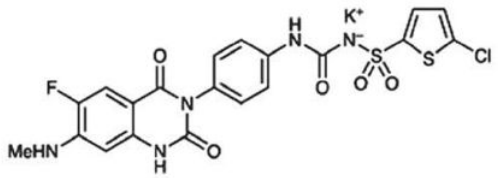
Ticagrelor
Administración: oral
Conversión metabólica: no
Reversible: sí
Vida media: 12 h
Duración acción: 1 día

Análogo del trifosfato de adenosina



Cangrelor
Administración: parenteral
Conversión metabólica: no
Reversible: sí
Vida media: 2-5 min
Duración acción: 1 h

Sulfonilurea



Elinogrel
Administración: oral y parenteral
Conversión metabólica: no
Reversible: sí
Vida media: oral, 12-14 h; parenteral, 50 min
Duración acción: oral, 1 día; parenteral, 2 h

PLATO study design

PLATO

NSTE-ACS (moderate-to-high risk) STEMI (if primary PCI)
Clopidogrel-treated or -naive;
randomised within 24 hours of index event
(N=18,624)

Clopidogrel
If pre-treated, no additional loading dose;
if naive, standard 300 mg loading dose,
then 75 mg qd maintenance;
(additional 300 mg allowed pre PCI)

Ticagrelor
180 mg loading dose, then
90 mg bid maintenance;
(additional 90 mg pre-PCI)

6–12-month exposure

Primary endpoint: CV death + MI + Stroke
Primary safety endpint: Total major bleeding

PCI = percutaneous coronary intervention; ASA = acetylsalicylic acid;
CV = cardiovascular; TIA = transient ischaemic attack

PLATO inclusion criteria

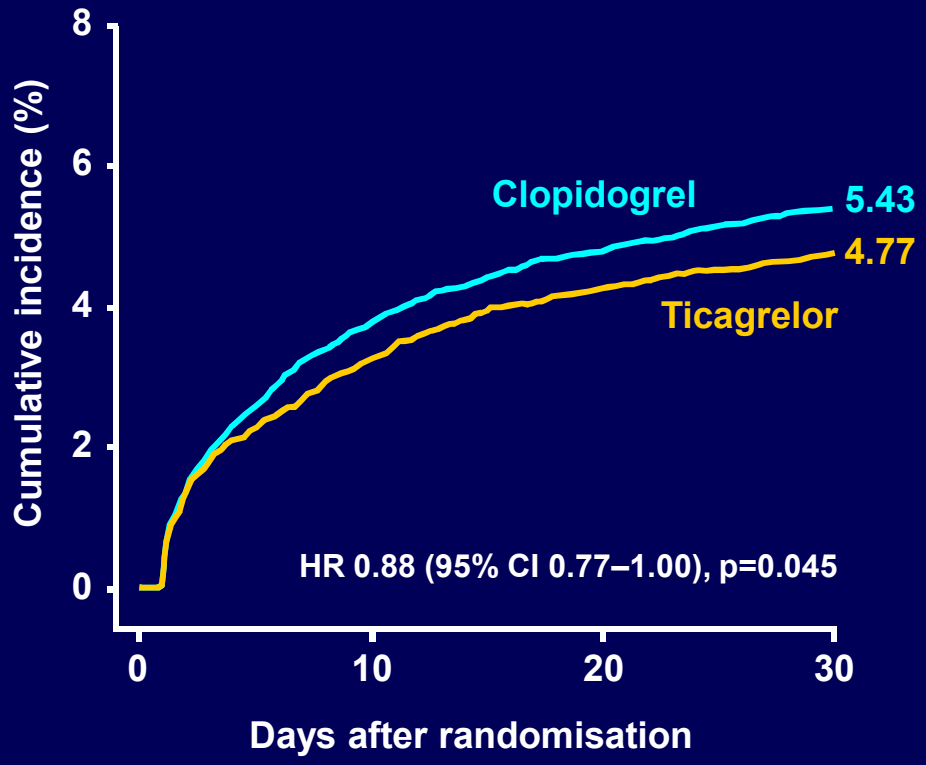
PLATO

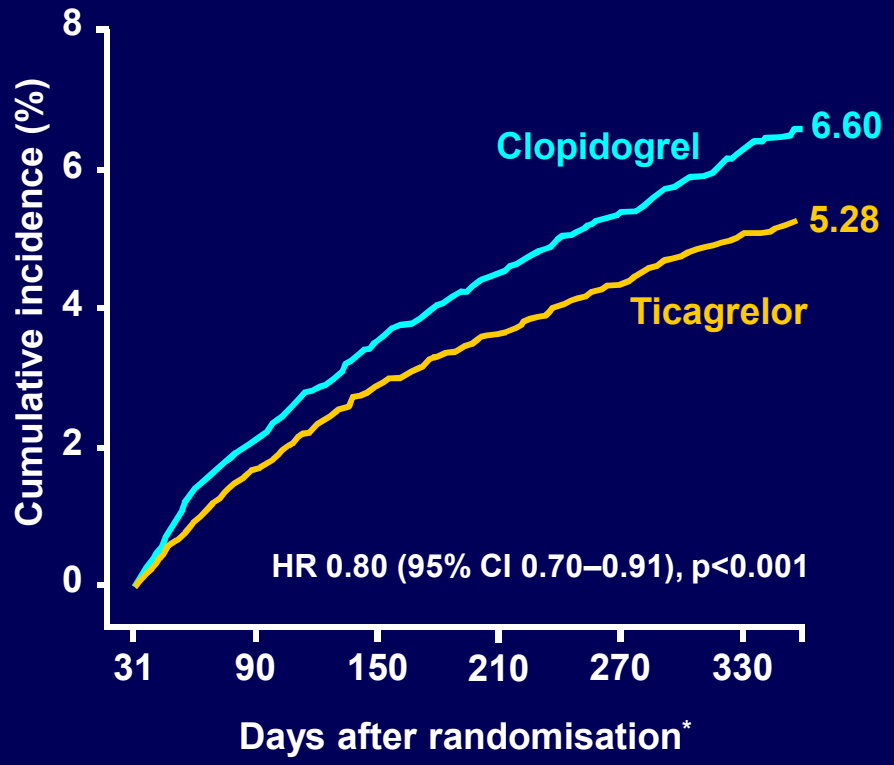
- Hospitalisation for STEMI or NSTEMI ACS, with onset during the previous 24 hours
- With STEMI, the following two inclusion criteria were required
  - Persistent STEMI or new LBBB
  - Primary PCI planned
- With NSTEMI ACS, at least two of the following three were required
  - ST-segment changes on ECG indicating ischaemia
  - Positive biomarker indicating myocardial necrosis
  - One of the following risk indicators
    - ≥60 years of age
    - Previous MI or CABG
    - CAD with ≥50% stenosis in ≥2 vessels
    - Previous ischaemic stroke, TIA, carotid stenosis (≥50%)
    - Diabetes mellitus
    - Peripheral artery disease
    - Chronic renal dysfunction (creatinine clearance <60 mL/min)

LBBB = left bundle branch block; ECG = elctrocardiogram; CABG = coronary artery bypass graft; CAD = coronary artery disease

Primary efficacy endpoint over time (composite of CV death, MI or stroke)

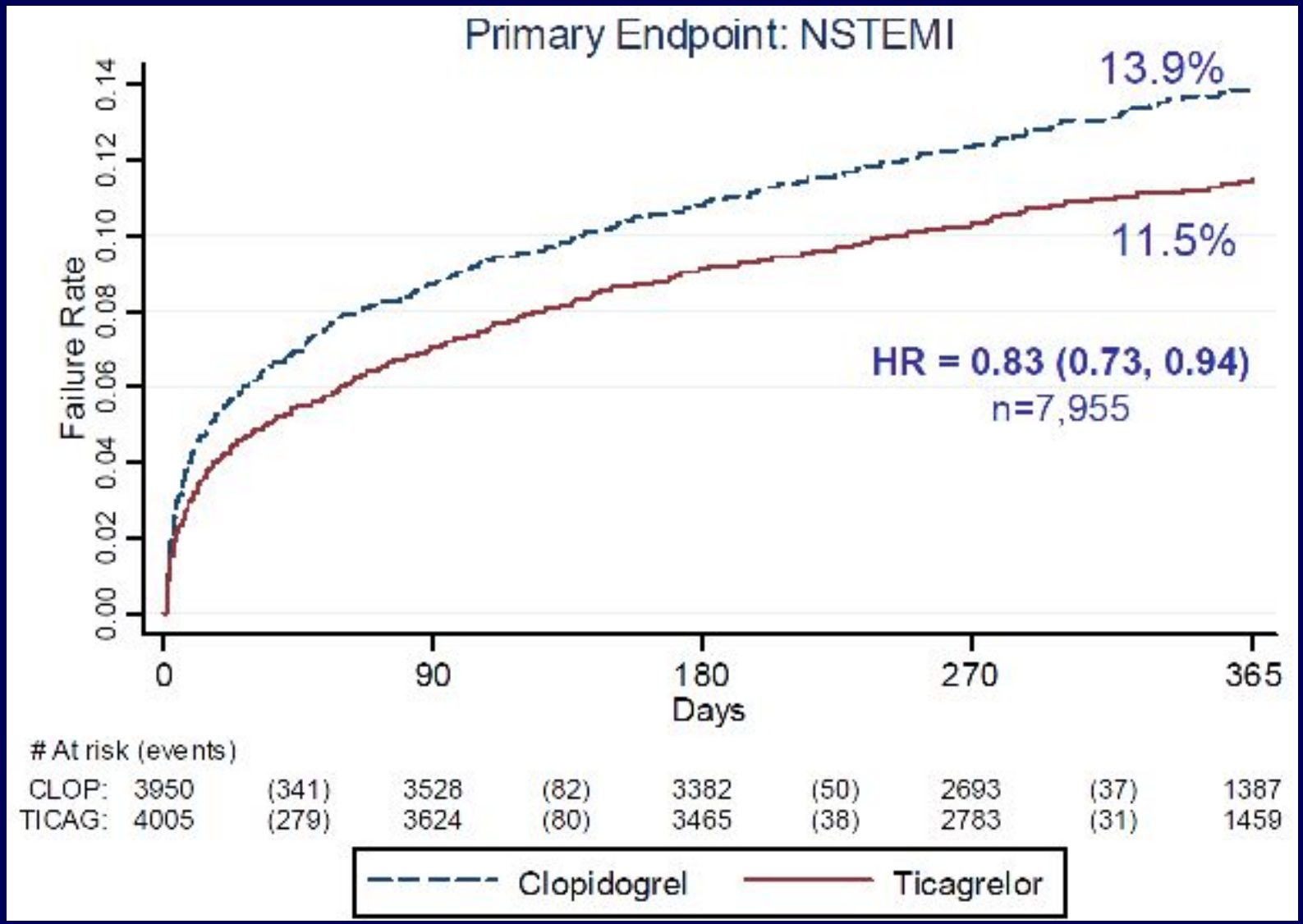
PLATO

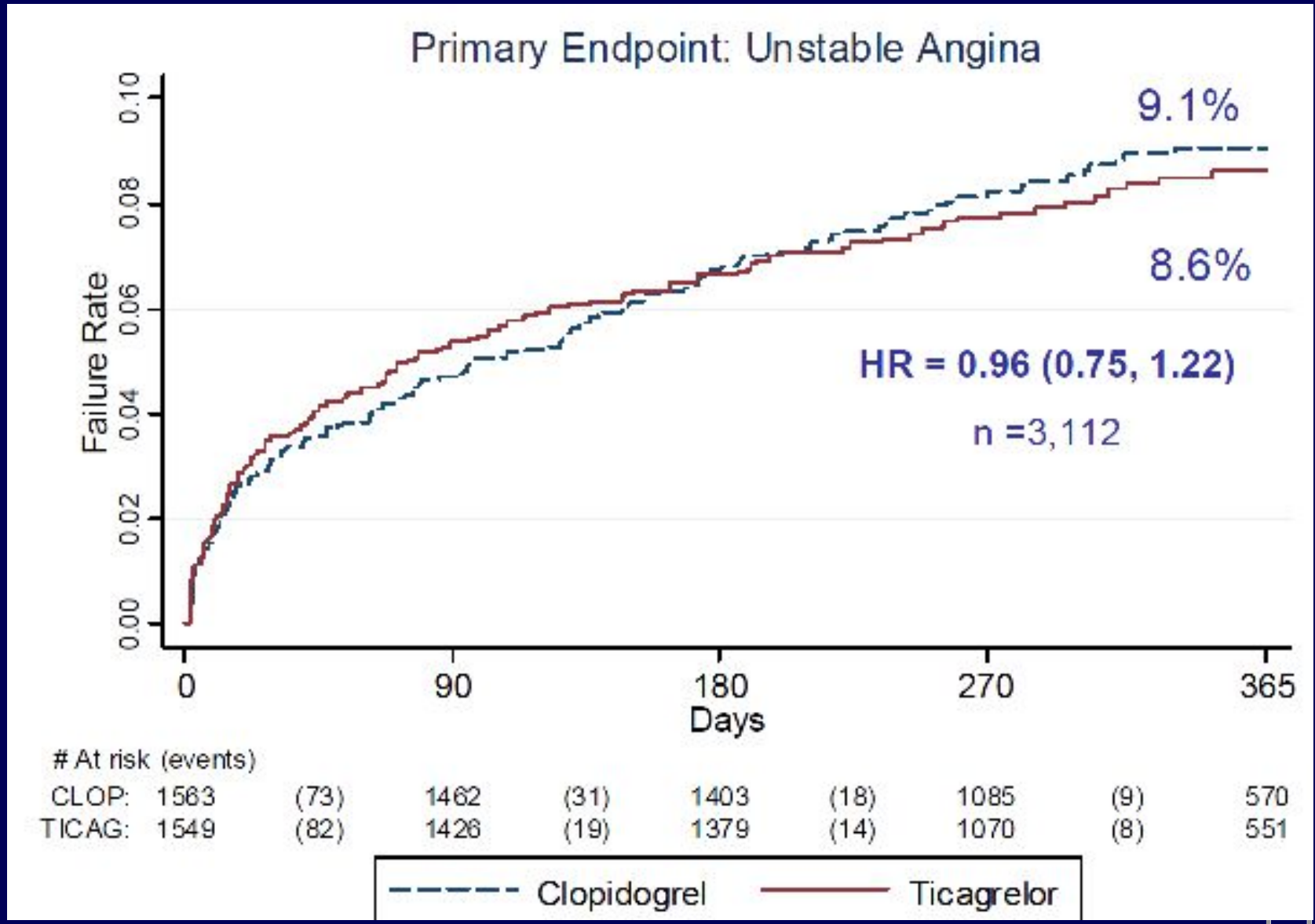




No. at risk										
Ticagrelor	9,333	8,942	8,827	8,763	8,673	8,543	8,397	7,028	6,480	4,822
Clopidogrel	9,291	8,875	8,763	8,688	8,688	8,437	8,286	6,945	6,379	4,751

*Excludes patients with any primary event during the first 30 days


Primary Endpoint: NSTEMI
13.9%
11.5%
HR = 0.83 (0.73, 0.94)
n=7,955
Failure Rate
0.00
0.02
0.04
0.06
0.08
0.10
0.12
0.14
0
90
180
270
365
Days
At risk (events)
CLOP: 3950 (341) 3528 (82) 3382 (50) 2693 (37) 1387
TICAG: 4005 (279) 3624 (80) 3465 (38) 2783 (31) 1459
Clopidogrel
Ticagrelor

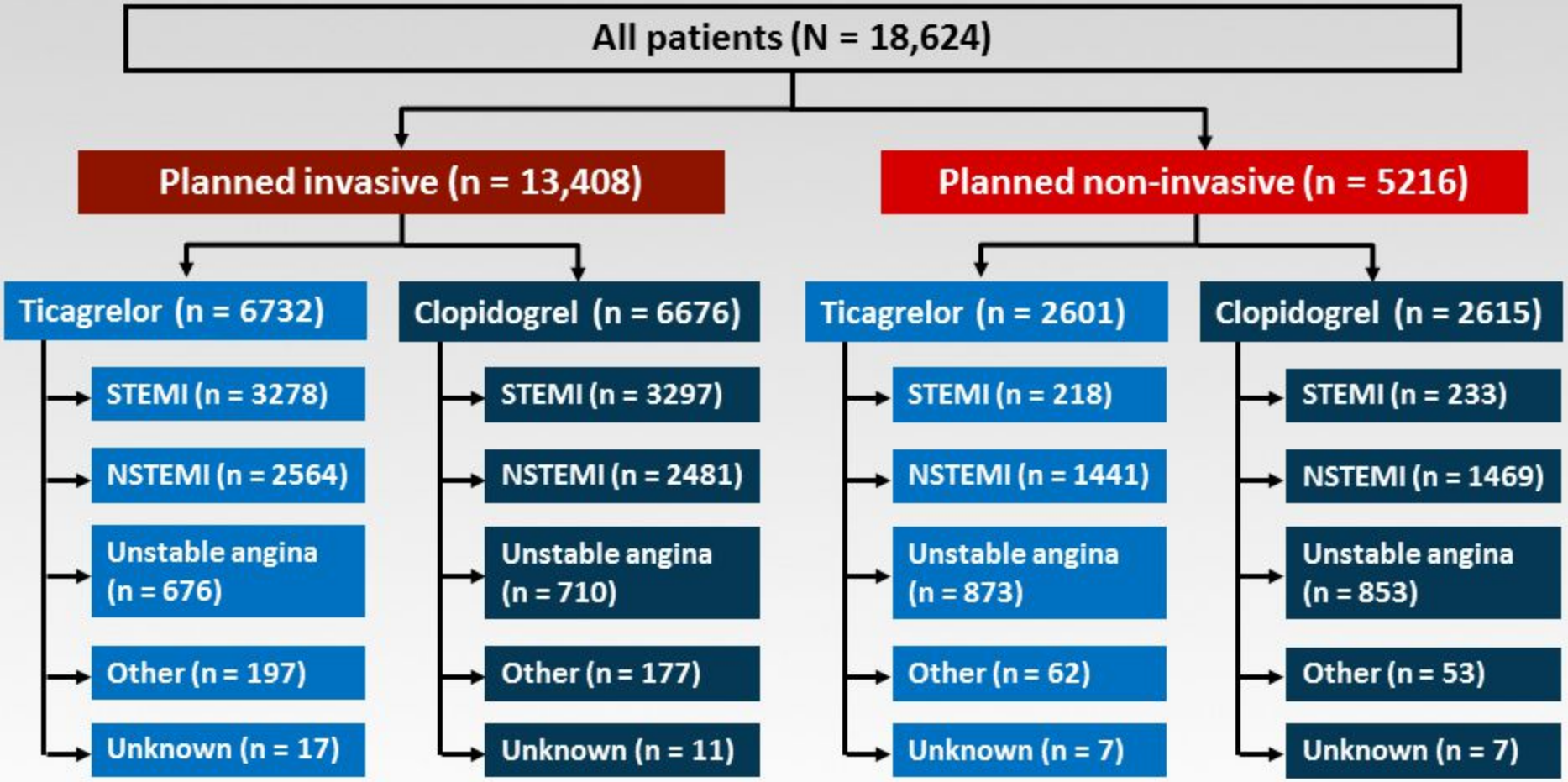

Primary Endpoint: Unstable Angina
9.1%
8.6%
HR = 0.96 (0.75, 1.22)
n =3,112
Failure Rate
0.00
0.02
0.04
0.06
0.08
0.10
0
90
180
270
365
Days
At risk (events)
CLOP: 1563 (73) 1462 (31) 1403 (18) 1085 (9) 570
TICAG: 1549 (82) 1426 (19) 1379 (14) 1070 (8) 551
Clopidogrel
Ticagrelor

Therapeutic considerations

PLATO

- Based on 1,000 patients admitted to hospital for ACS, using ticagrelor instead of clopidogrel for 12 months resulted in
  - 14 fewer deaths
  - 11 fewer myocardial infarctions
  - 6–8 fewer cases with stent thrombosis
  - No increase in bleedings requiring transfusion
  - 9 patients may switch to thienopyridine treatment because of reversible symptoms of dyspnoea
- Treating 54 patients with ticagrelor instead of with clopidogrel for one year will prevent one event of CV death, MI or stroke

PLATO:
Planned Invasive vs Medically Managed Patients



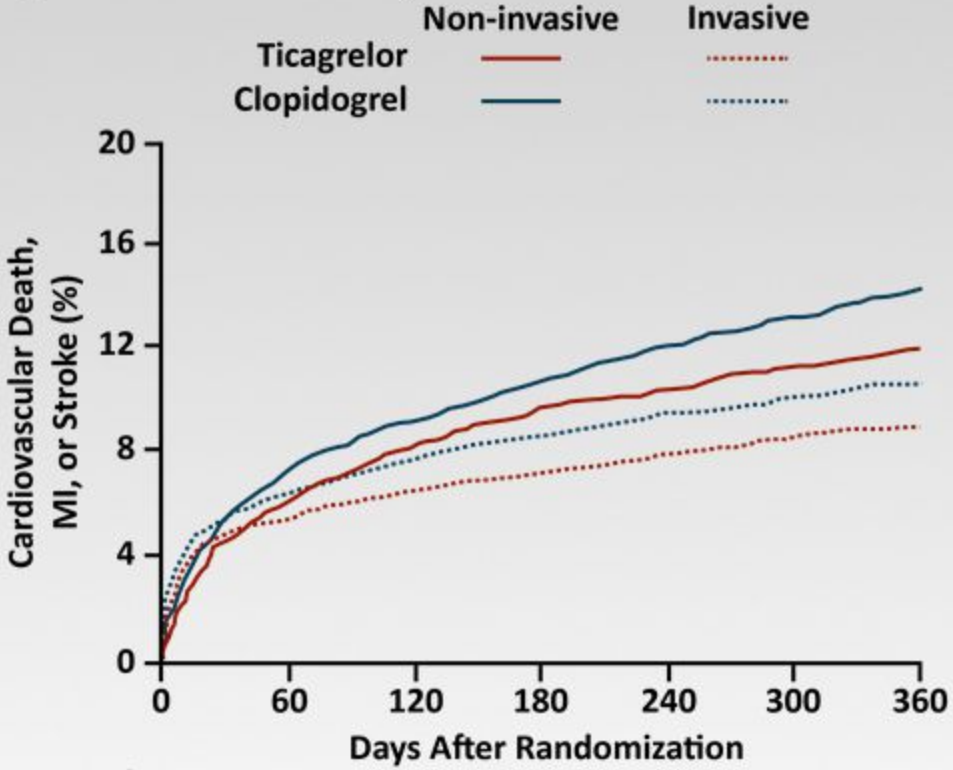
Acute Coronary SYNDROMES

James S, et al. *BMJ.* 2011;342:d3527 doi: 10.1136/bmj.d3527

the heart.org from WebMD

Medscape EDUCATION

PLATO Substudy:
Primary Composite Endpoint

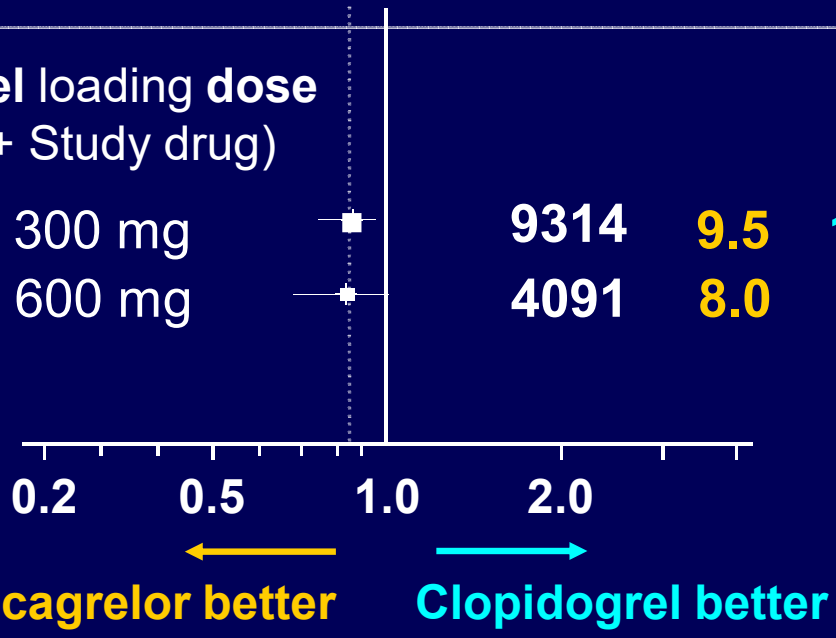


Number at Risk							
Invasive							
Ticagrelor	6732	6236	6134	5972	4889	3735	3048
Clopidogrel	6676	6129	6034	5881	4815	3680	2965
Non-invasive							
Ticagrelor	2601	2392	2326	2247	1854	1426	1099
Clopidogrel	2615	2392	2328	2243	1835	1416	1109

James S, et al. *BMJ.* 2011;342:d3527.

Primary efficacy endpoint by clopidogrel loading dose

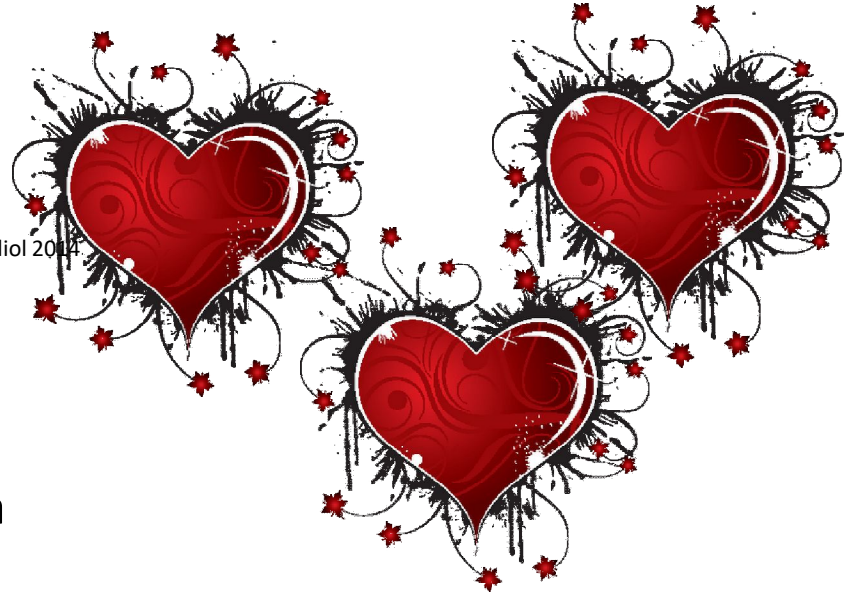
PLATO Invasive



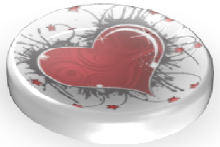
Characteristic	Hazard Ratio (95% CI)	Total Patients	KM % at Month 12 Ti.	KM % at Month 12 Cl.	HR (95% CI)	p value (Interaction)
Clopidogrel loading **dose** (Pre-rand. + Study drug)						0.917
300 mg		9314	9.5	11.2	0.85 (0.74, 0.96)	
600 mg		4091	8.0	9.5	0.83 (0.67, 1.03)	

DIOCLES

Pronóstico y manejo de síndrome coronario agudo en España 2012: estudio Diocles.Rev esp Cardiol 2014



- 10 de enero-15 junio 2012
- 70 centros aleatorizados
  - 35% Unidad críticos y hemodinámica
  - 45% solo unidad de críticos
  - 20% sin unidad de críticos ni hemodinámica
- 2557 pacientes
  - SCACEST 788 pac (30,8%)
  - SCASEST 1602 pac (62,7%)
  - Inclasificables 167 pac (6,5%)
- Mayor prescripción fármacos al alta. Clopidogrel incremento del 22,8% respecto a MASCARA
- Aumento tasa de revascularización hasta el 82% desde el 68% previo (MASCARA)

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement	Is recommended/is
	is not useful/effective, and in some cases may be harmful.	

Level of evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of evidence C	Consensus of opinion of the experts and/ or small studies, retrospective studies, registries.

2014 ESC/EACTS Guidelines on myocardial revascularization

The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

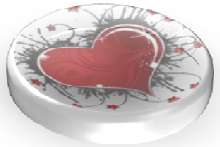
Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI)

Primary criteria
1. Relevant rise or fall in troponin
2. Dynamic ST- or T-wave changes (symptomatic or silent)
3. GRACE score >140
Secondary criteria
4. Diabetes mellitus
5. Renal insufficiency (eGFR <60 mL/min/1.73 m²)
6. Reduced LV function (ejection fraction <40%)
7. Early post-infarction angina
8. Recent PCI
9. Prior CABG
10. Intermediate to high GRACE risk score (http://www.gracescore.org)

,

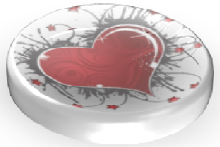
- RIESGO ELEVADO
  - Un factor primario de alto riesgo
  - 2-24 horas

- RIESGO INTERMEDIO
  - Al menos un factor secundario de alto riesgo
  - 24-72 horas
- RIESGO BAJO
  - Resto de pacientes
  - Test no invasivo
  - Antes del alta hospitalaria.

Recommendations for antithrombotic treatment in patients with NSTE-ACS undergoing PCI

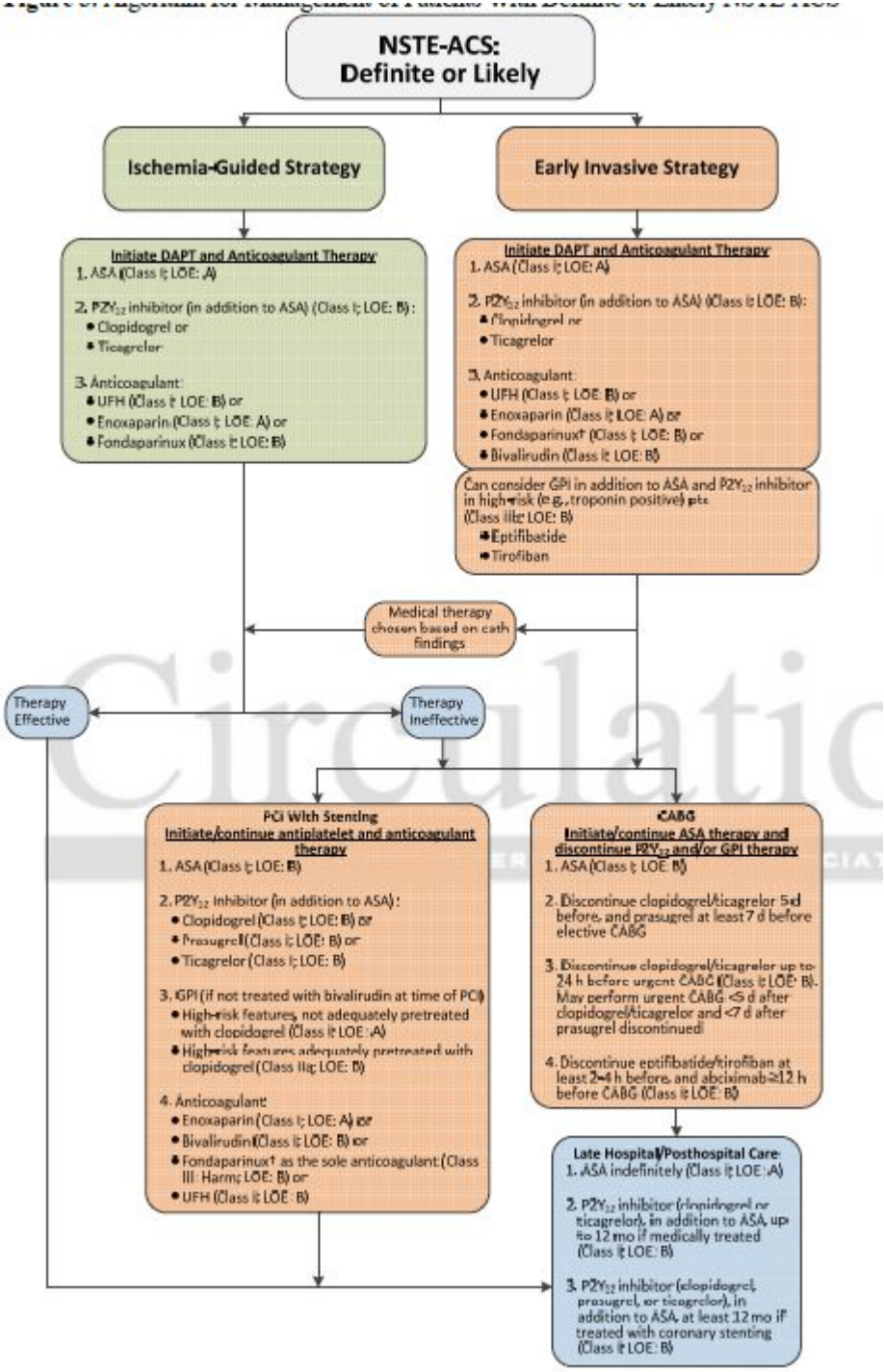
Recommendations	Class[a]	Level[b]
Antiplatelet therapy		
ASA is recommended for all patients without contraindications at an initial oral loading dose of 150–300 mg (or 80–150 mg I.v.), and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A
A $P2Y_{12}$ inhibitor is recommended in addition to ASA, and maintained over 12 months unless there are contraindications such as excessive risk of bleeding. Options are:	I	A
• Prasugrel (60 mg loading dose, 10 mg daily dose) in patients in whom coronary anatomy is known and who are proceeding to PCI if no contraindication.	I	B
• Ticagrelor (180 mg loading dose, 90 mg twice daily) for patients at moderate-to-high risk of ischaemic events, regardless of initial treatment strategy including those pre-treated with clopidogrel if no contraindication.	I	B
• Clopidogrel (600 mg loading dose, 75 mg daily dose), only when prasugrel or ticagrelor are not available or are contraindicated.	I	B
GP IIb/IIIa antagonists should be considered for bail-out situation or thrombotic complications.	IIa	C
Pre-treatment with prasugrel in patients in whom coronary anatomy not known, is not recommended.	III	B
Pre-treatment with GP IIb/IIIa antagonists in patients in not known, is not recommended.	III	A

Recommendations for antithrombotic treatment in patients undergoing PCI who require oral anticoagulation

Recommendations	Class[a]	Level[b]	Ref[c]
In patients with a firm indication for oral anticoagulation (e.g. atrial fibrillation with CHA_2DS_2-VASc score ≥2, venous thromboembolism, LV thrombus, or mechanical valve prosthesis), oral anticoagulation is recommended in addition to antiplatelet therapy.	I	C	
New-generation DES are preferred over BMS among patients requiring oral anticoagulation if bleeding risk is low (HAS-BLED ≤2).	IIa	C	
In patients with SCAD and atrial fibrillation with CHA_2DS_2-VASc score ≥2 at low bleeding risk (HAS-BLED ≤2), initial triple therapy of (N)OAC and ASA (75–100 mg/day) and clopidogrel 75 mg/day should be considered for a duration of at least one month after BMS or new-generation DES followed by dual therapy with (N)OAC and aspirin 75–100 mg/day or clopidogrel (75 mg/day) continued up to 12 months.	IIa	C	
DAPT should be considered as alternative to initial triple therapy for patients with SCAD and atrial fibrillation with a CHA_2DS_2-VASc score ≤1.	IIa	C	
In patients with ACS and atrial fibrillation at low bleeding risk (HAS-BLED≤2), initial triple therapy of (N)OAC and ASA (75–100 mg/day) and clopidogrel 75 mg/day should be considered for a duration of 6 months irrespective of stent type followed by (N)OAC and aspirin 75–100 mg/day or clopidogrel (75 mg/day) continued up to 12 months.	IIa	C	
In patients requiring oral anticoagulation at high bleeding risk (HAS BLED ≥3), triple therapy of (N)OAC and ASA (75–100 mg/day) and clopidogrel 75 mg/day should be considered for a duration of one month followed by (N)OAC and aspirin 75–100 mg/day or clopidogrel (75 mg/day) irrespective of clinical setting (SCAD or ACS) and stent type (BMS or new-generation DES).	IIa	C	
Dual therapy of (N)OAC and clopidogrel 75 mg/day may be considered as an alternative to initial triple therapy in selected patients.	IIb	B	865,870
The use of ticagrelor and prasugrel as part of initial triple therapy is not recommended	III	C	
Anticoagulation therapy after PCI in ACS patients			
In selected patients who receive ASA and clopidogrel, low-dose rivaroxaban (2.5 mg twice daily) may be considered in the setting of PCI for ACS if the patient is at low bleeding risk.	IIb	B	855
Anticoagulation during PCI in patients on oral anticoagulation			
It is recommended to use additional parenteral anticoagulation, regardless of the timing of the last dose of (N)OAC.	I	C	
Periprocedural parenteral anticoagulants (bivalirudin, enoxaparin or UFH) should be discontinued immediately after primary PCI.	IIa	C	

Aspirin				
• Non–enteric-coated aspirin to *all* patients promptly after presentation	162 mg–325 mg	I	A	(288-290)
• Aspirin maintenance dose continued indefinitely	81 mg/d–162 mg/d	I	A	(288-290)
P2Y$_{12}$ inhibitors				
• Clopidogrel loading dose followed by daily maintenance dose in patients unable to take aspirin	75 mg	I	B	(291)
• P2Y$_{12}$ inhibitor, in addition to aspirin, for up to 12 mo for patients treated initially with either an early invasive or initial ischemia-guided strategy:		I	B	
– Clopidogrel	300-mg or 600-mg loading dose, then 75 mg/d			(289, 292)
– Ticagrelor*	180-mg loading dose, then 90 mg BID			(293, 294)
• P2Y$_{12}$ inhibitor therapy (clopidogrel, prasugrel, or ticagrelor) continued for at least 12 mo in post–PCI patients treated with coronary stents	N/A	I	B	(293, 296, 302, 330, 331)
• Ticagrelor in preference to clopidogrel for patients treated with an early invasive or ischemia-guided strategy	N/A	IIa	B	(293, 294)
GP IIb/IIIa inhibitors				
• GP IIb/IIIa inhibitor in patients treated with an early invasive strategy and DAPT with intermediate/high-risk features (e.g., positive troponin)	• Preferred options are eptifibatide or tirofiban	IIb	B	(43, 94, 295)


NSTE-ACS:
Definite or Likely
Ischemia-Guided Strategy
Early Invasive Strategy
Initiate DAPT and Anticoagulant Therapy
1. ASA (Class I; LOE: A)
2. P2Y12 inhibitor (in addition to ASA) (Class I; LOE: B):
Clopidogrel or
Ticagrelor
3. Anticoagulant:
UFH (Class I; LOE: B) or
Enoxaparin (Class I; LOE: A) or
Fondaparinux (Class I; LOE: B)
Initiate DAPT and Anticoagulant Therapy
1. ASA (Class I; LOE: A)
2. P2Y12 inhibitor (in addition to ASA) (Class I; LOE: B):
Clopidogrel or
Ticagrelor
3. Anticoagulant:
UFH (Class I; LOE: B) or
Enoxaparin (Class I; LOE: A) or
Fondaparinux† (Class I; LOE: B) or
Bivalirudin (Class I; LOE: B)
Can consider GPI in addition to ASA and P2Y12 inhibitor in high-risk (e.g., troponin positive) pts (Class IIb; LOE: B)
Eptifibatide
Tirofiban
Medical therapy chosen based on cath findings
Therapy Effective
Therapy Ineffective
PCI With Stenting
Initiate/continue antiplatelet and anticoagulant therapy
1. ASA (Class I; LOE: B)
2. P2Y12 Inhibitor (in addition to ASA):
Clopidogrel (Class I; LOE: B) or
Prasugrel (Class I; LOE: B) or
Ticagrelor (Class I; LOE: B)
3. GPI (if not treated with bivalirudin at time of PCI)
High-risk features, not adequately pretreated with clopidogrel (Class I; LOE: A)
High-risk features adequately pretreated with clopidogrel (Class IIa; LOE: B)
4. Anticoagulant:
Enoxaparin (Class I; LOE: A) or
Bivalirudin (Class I; LOE: B) or
Fondaparinux† as the sole anticoagulant (Class III: Harm; LOE: B) or
UFH (Class I; LOE: B)
CABG
Initiate/continue ASA therapy and discontinue P2Y12 and/or GPI therapy
1. ASA (Class I; LOE: B)
2. Discontinue clopidogrel/ticagrelor 5 d before, and prasugrel at least 7 d before elective CABG
3. Discontinue clopidogrel/ticagrelor up to 24 h before urgent CABG (Class I; LOE: B). May perform urgent CABG <5 d after clopidogrel/ticagrelor and <7 d after prasugrel discontinued
4. Discontinue eptifibatide/tirofiban at least 2–4 h before, and abciximab ≥12 h before CABG (Class I; LOE: B)
Late Hospital/Posthospital Care
1. ASA indefinitely (Class I; LOE: A)
2. P2Y12 inhibitor (clopidogrel or ticagrelor), in addition to ASA, up to 12 mo if medically treated (Class I; LOE: B)
3. P2Y12 inhibitor (clopidogrel, prasugrel, or ticagrelor), in addition to ASA, at least 12 mo if treated with coronary stenting (Class I; LOE: B)