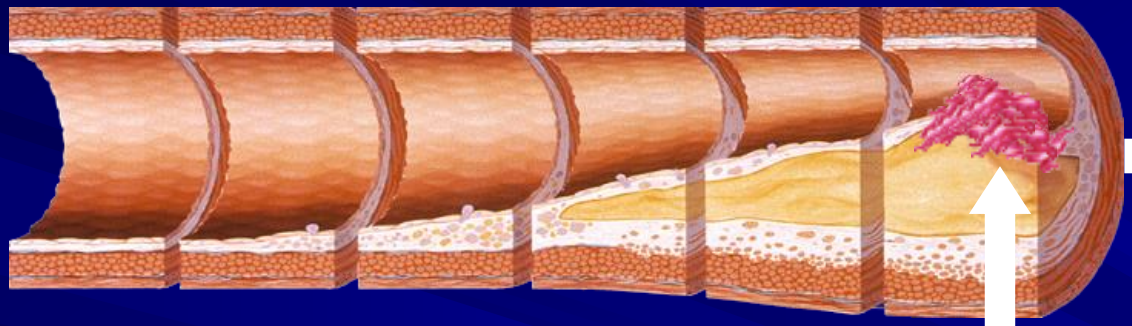
Acute Coronary Syndrome and Antiplatelet Treatment

דר מוחמד ג'בארין

מנהל היחידה לאי ספיקת לב ורצף טיפולי

מערך הלב , מרכז רפואי העמק

Atherothrombosis: A Generalized and Progressive Process



- Unstable angina
- MI

ACS

- Ischemic stroke/TIA
- Critical leg ischemia
- Cardiovascular death

Atherosclerosis → Atherothrombosis

Stable angina
Intermittent claudication

Adapted from Stary HC et al. *Circulation*. 1995; 92: 1355–74, and Fuster V *et al*. *Vasc Med*.
1998; 3: 231–9.

ג.ר. בן 52. פקיד.

מעשן כבד. אחרי TIA בגיל 45.

התקבל בזמן STEMI תחתון.

במסגרת צינטור דחוף טופל RCA חסום באמצעו.

מחלה חד כלית.

LVEF בעקבות הארוע – 55%. MR קל.

השתחרר מביה"ח תחת אספירין וברילינטה.

א.ב. בן 75. פנסיונר.

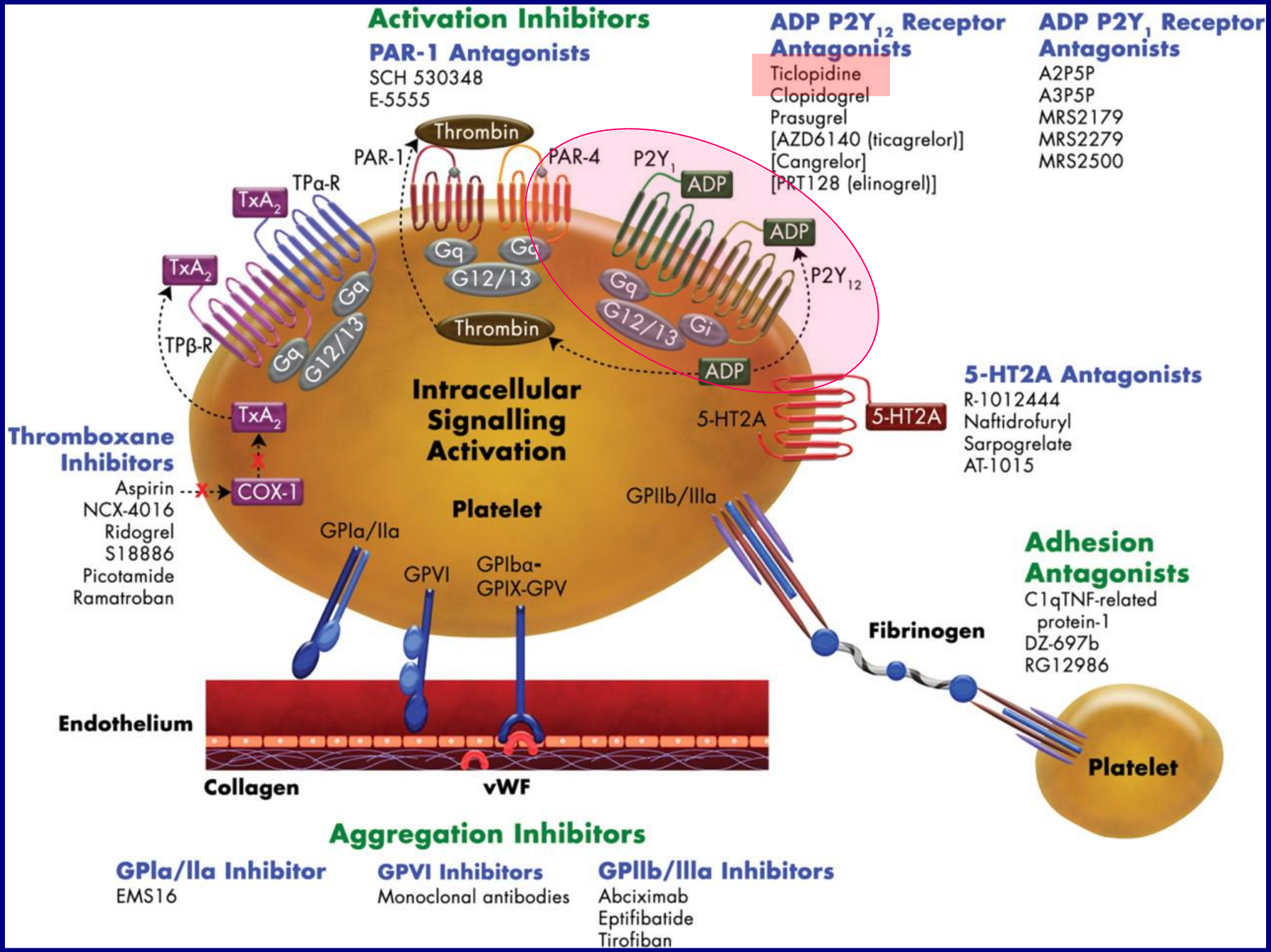
היפרטנסיבי. מטופל באליקוויס לפרפור עליות.

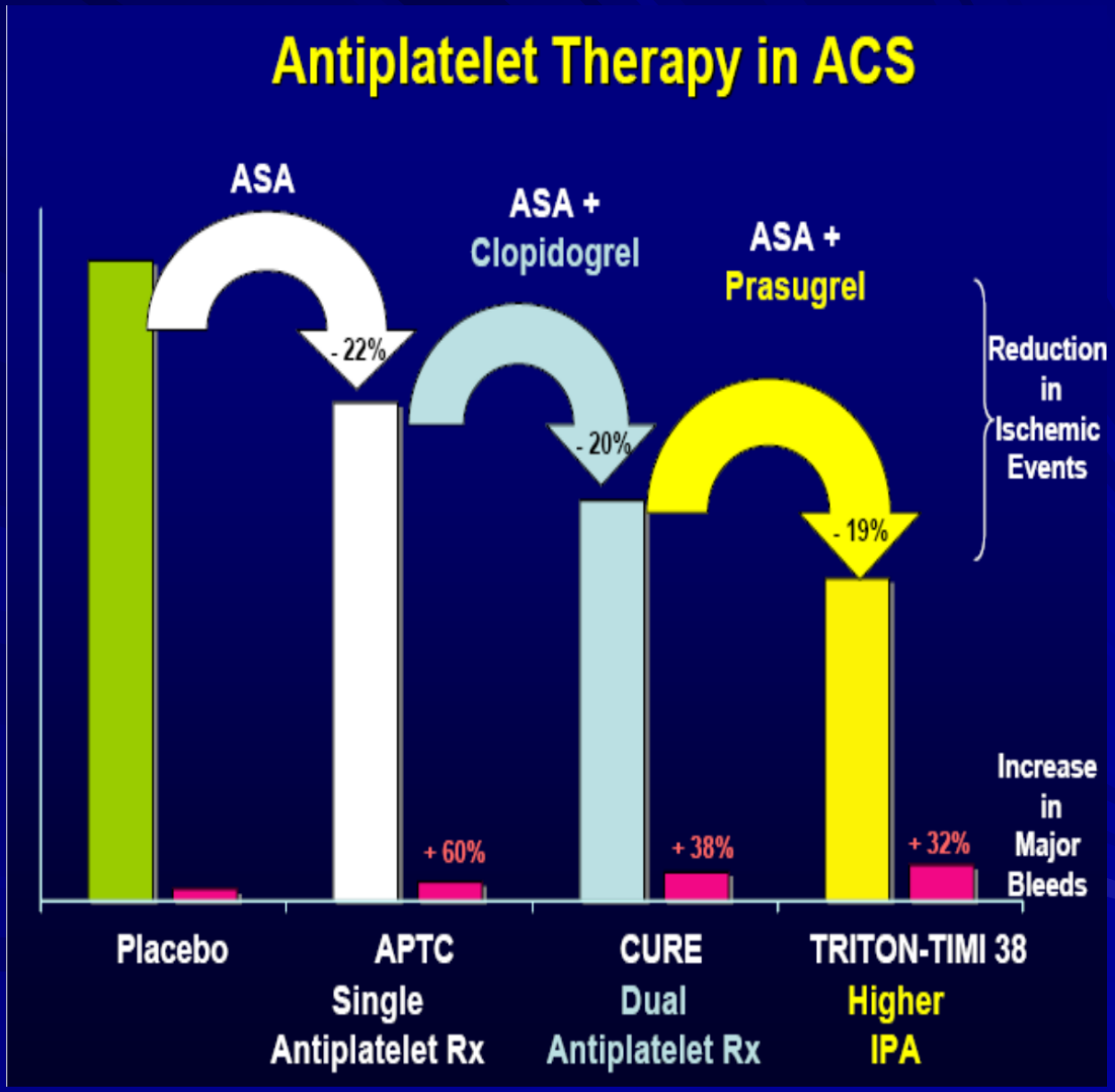
התקבל בזמן NSTEMI.

במסגרת צינטור טופל בסטנט ל- CX .

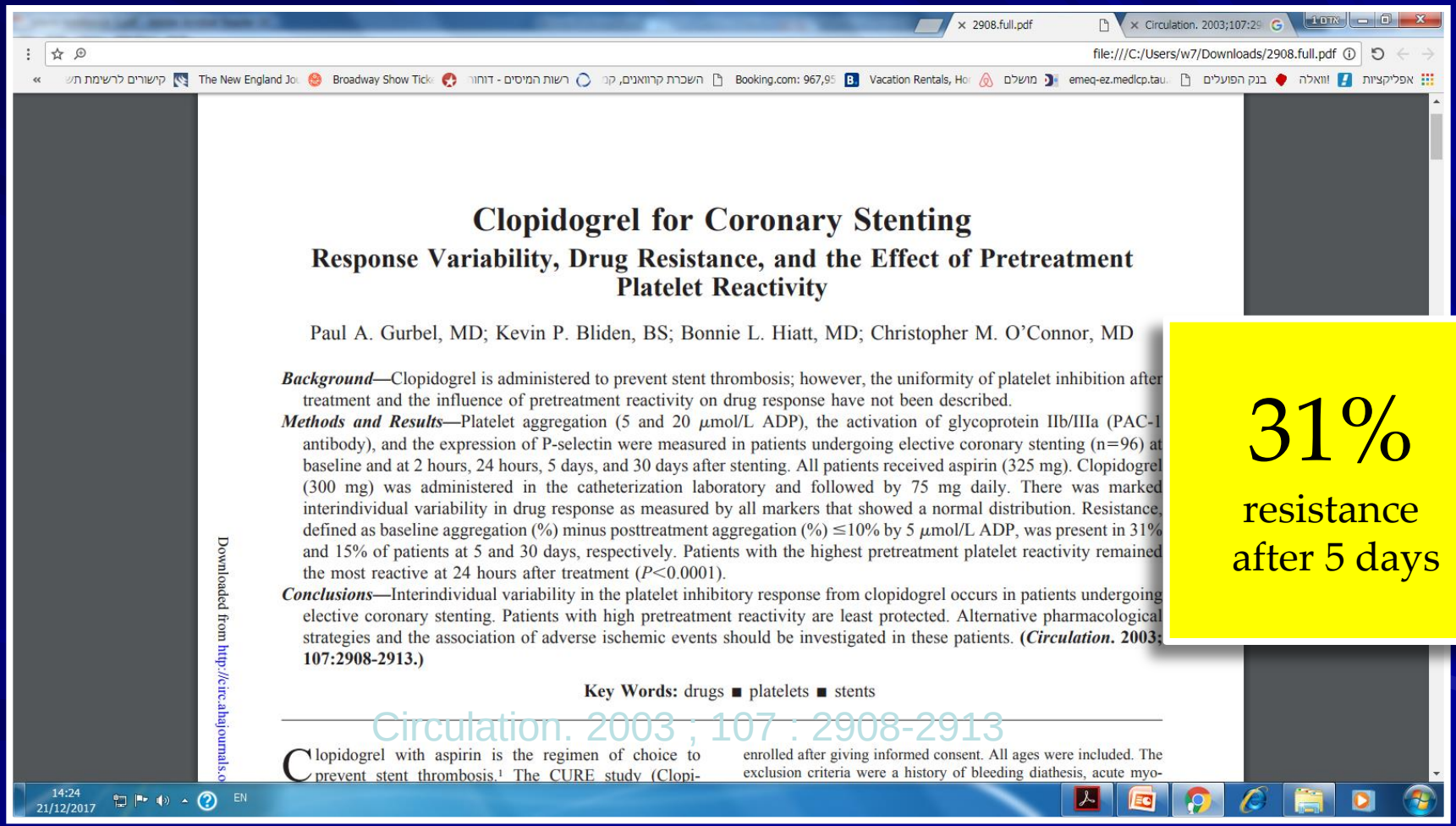
LVEF בעקבות הארוע – 50%. MR קל.

השתחרר מביה"ח תחת אספירין ופלביקס.


Activation Inhibitors
PAR-1 Antagonists
SCH 530348
E-5555
ADP P2Y12 Receptor Antagonists
Ticlopidine
Clopidogrel
Prasugrel
[AZD6140 (ticagrelor)]
[Cangrelor]
[PRT128 (elinogrel)]
ADP P2Y1 Receptor Antagonists
A2P5P
A3P5P
MRS2179
MRS2279
MRS2500
Thrombin
PAR-1
PAR-4
P2Y1
ADP
TPα-R
TxA2
Gq
G12/13
P2Y12
Gi
TPβ-R
Intracellular Signalling Activation
5-HT2A
5-HT2A Antagonists
R-1012444
Naftidrofuryl
Sarpogrelate
AT-1015
Thromboxane Inhibitors
Aspirin
NCX-4016
Ridogrel
S18886
Picotamide
Ramatroban
COX-1
Platelet
GPIIb/IIIa
GPIa/IIa
GPVI
GPIba-GPIX-GPV
Adhesion Antagonists
C1qTNF-related protein-1
DZ-697b
RG12986
Fibrinogen
Endothelium
Collagen
vWF
Platelet
Aggregation Inhibitors
GPIa/IIa Inhibitor
EMS16
GPVI Inhibitors
Monoclonal antibodies
GPIIb/IIIa Inhibitors
Abciximab
Eptifibatide
Tirofiban


Antiplatelet Therapy in ACS
ASA
ASA + Clopidogrel
ASA + Prasugrel
- 22%
- 20%
- 19%
Reduction in Ischemic Events
+ 60%
+ 38%
+ 32%
Increase in Major Bleeds
Placebo
APTC
Single Antiplatelet Rx
CURE
Dual Antiplatelet Rx
TRITON-TIMI 38
Higher IPA

From Clinical Evidence to Standard Therapy



Clopidogrel for Coronary Stenting

Response Variability, Drug Resistance, and the Effect of Pretreatment Platelet Reactivity

Paul A. Gurbel, MD; Kevin P. Bliden, BS; Bonnie L. Hiatt, MD; Christopher M. O'Connor, MD

***Background*—**Clopidogrel is administered to prevent stent thrombosis; however, the uniformity of platelet inhibition after treatment and the influence of pretreatment reactivity on drug response have not been described.

***Methods and Results*—**Platelet aggregation (5 and 20 μmol/L ADP), the activation of glycoprotein IIb/IIIa (PAC-1 antibody), and the expression of P-selectin were measured in patients undergoing elective coronary stenting (n=96) at baseline and at 2 hours, 24 hours, 5 days, and 30 days after stenting. All patients received aspirin (325 mg). Clopidogrel (300 mg) was administered in the catheterization laboratory and followed by 75 mg daily. There was marked interindividual variability in drug response as measured by all markers that showed a normal distribution. Resistance, defined as baseline aggregation (%) minus posttreatment aggregation (%) ≤10% by 5 μmol/L ADP, was present in 31% and 15% of patients at 5 and 30 days, respectively. Patients with the highest pretreatment platelet reactivity remained the most reactive at 24 hours after treatment ($P<0.0001$).

***Conclusions*—**Interindividual variability in the platelet inhibitory response from clopidogrel occurs in patients undergoing elective coronary stenting. Patients with high pretreatment reactivity are least protected. Alternative pharmacological strategies and the association of adverse ischemic events should be investigated in these patients. **(*Circulation*. 2003; 107:2908-2913.)**

Key Words: drugs ■ platelets ■ stents

Clopidogrel with aspirin is the regimen of choice to prevent stent thrombosis.[1] The CURE study (Clopi- enrolled after giving informed consent. All ages were included. The exclusion criteria were a history of bleeding diathesis, acute myo-

31%

resistance after 5 days

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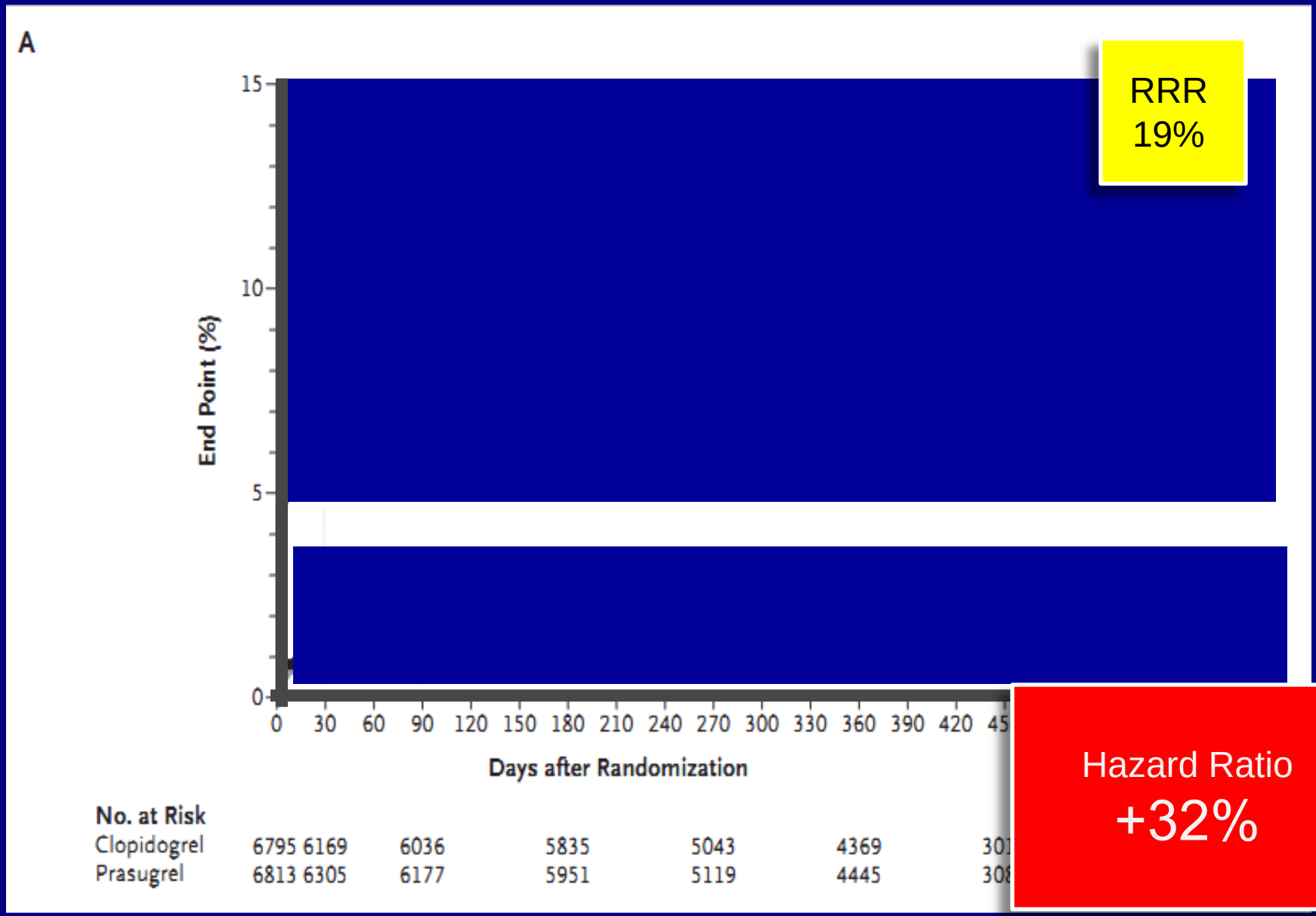
Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes

Stephen D. Wiviott, M.D., Eugene Braunwald, M.D., Carolyn H. McCabe, B.S., Gilles Montalescot, M.D., Ph.D., Witold Ruzyllo, M.D., Shmuel Gottlieb, M.D., Franz-Joseph Neumann, M.D., Diego Ardissino, M.D., Stefano De Servi, M.D., Sabina A. Murphy, M.P.H., Jeffrey Riesmeyer, M.D., Govinda Weerakkody, Ph.D., C. Michael Gibson, M.D., and Elliott M. Antman, M.D., for the TRITON–TIMI 38 Investigators*

STEMI

SCHEDUELED PCI


A
RRR
19%
End Point (%)
15
10
5
0
0 30 60 90 120 150 180 210 240 270 300 330 360 390 420 45
Days after Randomization
No. at Risk
Clopidogrel 6795 6169 6036 5835 5043 4369
Prasugrel 6813 6305 6177 5951 5119 4445
Hazard Ratio
+32%

The NEW ENGLAND JOURNAL of MEDICINE

Ticagrelor versus Clopidogrel in Patients with Acute Coronary Syndromes

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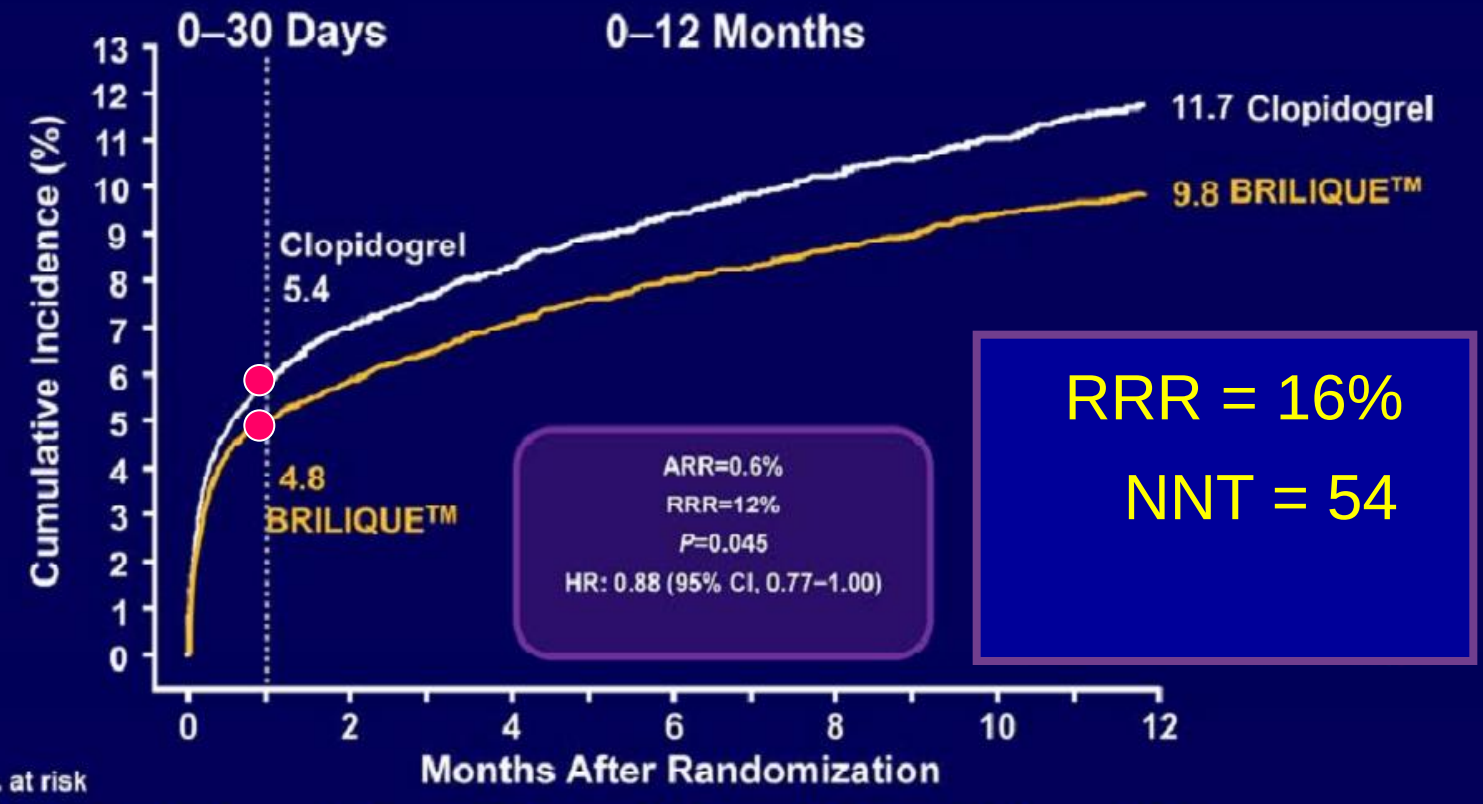
N Engl J Med 2009;361.

PLATO: Primary Efficacy Endpoint (Composite of CV Death, MI, or Stroke)



RRR = 16%

NNT = 54

No. at risk

BRILIQUE™	9,333	8,628	8,460	8,219	6,743	5,161	4,147
Clopidogrel	9,291	8,521	8,362	8,124	6,650	5,096	4,047

Both groups included aspirin.
*NNT at one year.

Ticagrelor Vs. Prasugrel

STEMI :
primary combined endpoint

Prasugrel	Clopidogrel
6.5 % (significant)	**9.5 %**

TRÎTON TIMI-38

Lancet 2009; 373: 723-31

Ticagrelor	Clopidogrel
9.4 % (p = 0.07)	**10.8 %**

PLATO

Circulation. 2010;122:2131-2141

Risk Reduction by the new drug as compared to Clopidogrel

Risk Increase by the new drug as compared to Clopidogrel

DIABETES:
primary combined endpoint

Prasugrel	Clopidogrel
12.2 % (significant)	**17.0 %**

Ticagrelor	Clopidogrel
14.1 % (not signif.)	**16.2 %**

TRÎTON TIMI-38

PLATO

Risk Reduction by the new drug as compared to Clopidogrel

Risk Increase by the new drug as compared to Clopidogrel

J Am Coll Cardiol 2013;61:1601–6

Vol. 61, No. 15, 2013
ISSN 0735-1097/$36.00
http://dx.doi.org/10.1016/j.jacc.2013.01.024

Comparison of Prasugrel and Ticagrelor Loading Doses in ST-Segment Elevation Myocardial Infarction Patients

RAPID (Rapid Activity of Platelet Inhibitor Drugs) Primary PCI Study

Guido Parodi, MD, PhD, Renato Valenti, MD, Benedetta Bellandi, MD, Angela Migliorini, MD, Rossella Marcucci, MD, Vincenzo Comito, MD, Nazario Carrabba, MD, Alberto Santini, MD, Gian Franco Gensini, MD, Rosanna Abbate, MD, David Antoniucci, MD

Florence, Italy

50 pts
Primary EP : Plts reactivity
Secondary EP : In hospital outcome

Objectives ...ation myocardial infarc-

Background ...elet inhibition 2 h after a loading dose (LD). However, the pharmacodynamic measurements after prasugrel and ticagrelor LD have been provided by assessing only healthy volunteers or subjects with stable coronary artery disease.

Methods Fifty patients with STEMI undergoing PPCI with bivalirudin monotherapy were randomized to receive 60 mg prasugrel LD (n = 25) or 180 mg ticagrelor LD (n = 25). Residual platelet reactivity was assessed by VerifyNow at baseline and 2, 4, 8, and 12 h after LD.

Results Platelet reactivity units (PRU) 2 h after the LD (study primary endpoint) were 217 (12 to 279) and 275 (88 to 305) in the prasugrel and ticagrelor groups, respectively (p = NS), satisfying pre-specified noninferiority criteria. High residual platelet reactivity (HRPR) (PRU ≥240) was found in 44% and 60% of patients (p = 0.258) at 2 h. The mean time to achieve a PRU <240 was 3 ± 2 h and 5 ± 4 h in the prasugrel and ticagrelor groups, respectively. The independent predictors of HRPR at 2 h were morphine use (odds ratio: 5.29; 95% confidence interval: 1.44 to 19.49; p = 0.012) and baseline PRU value (odds ratio: 1.014; 95% confidence interval: 1.00 to 1.03; p = 0.046).

Conclusions In patients with STEMI, prasugrel showed to be noninferior as compared with ticagrelor in terms of residual platelet reactivity 2 h after the LD. The 2 drugs provide an effective platelet inhibition 2 h after the LD in only a half of patients, and at least 4 h are required to achieve an effective platelet inhibition in the majority of patients. Morphine use is associated with a delayed activity of these agents. (Rapid Activity of Platelet Inhibitor Drugs Study, NCT01510171) (J Am Coll Cardiol 2013;61:1601–6) © 2013 by the American College of Cardiology Foundation

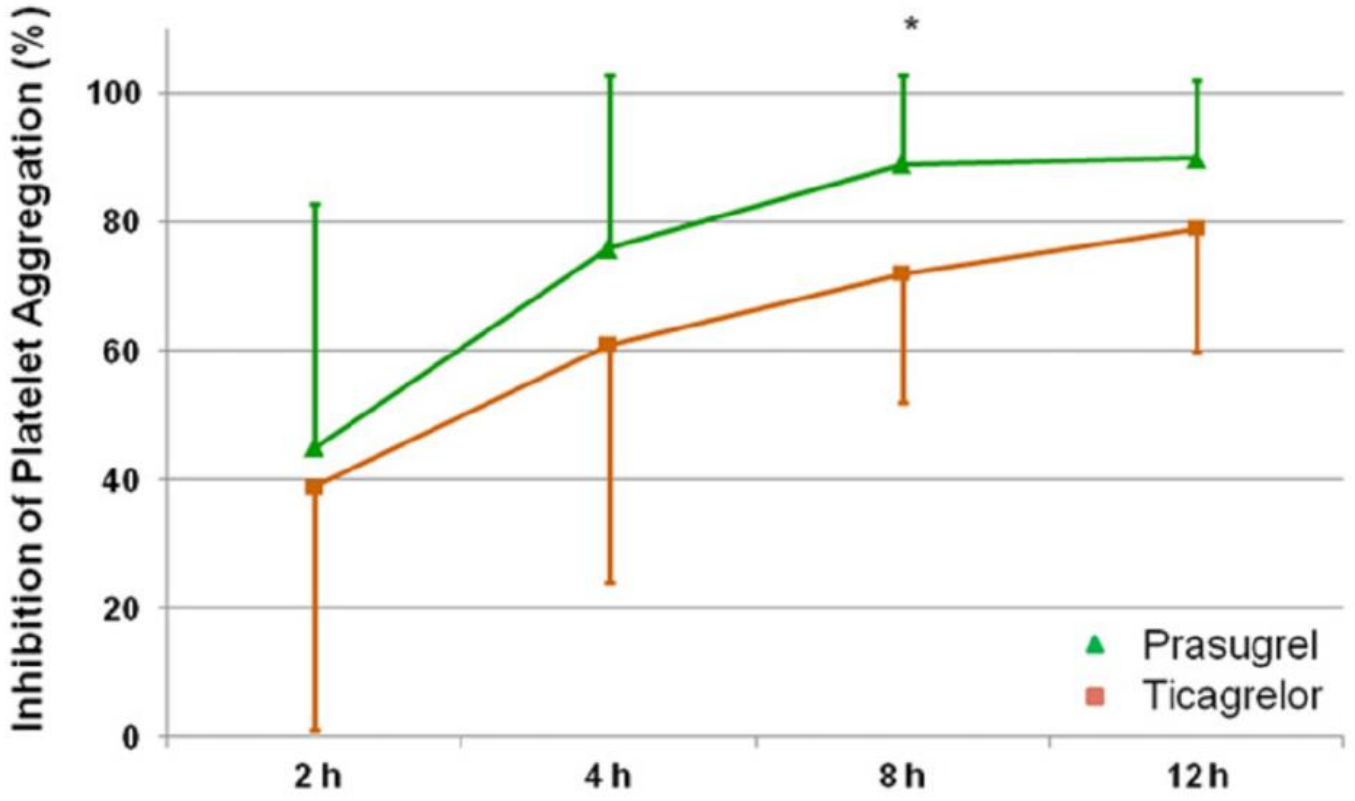


Figure 4 **Inhibition of Platelet Aggregation Over Time**

Inhibition of platelet aggregation by VerifyNow at 2, 4, 8, and 12 h after drug loading dose in patients with prasugrel **(triangles)** and ticagrelor **(squares)**. *$p < 0.01$ versus ticagrelor.

Contraindications for New DAPTS

Prasugrel

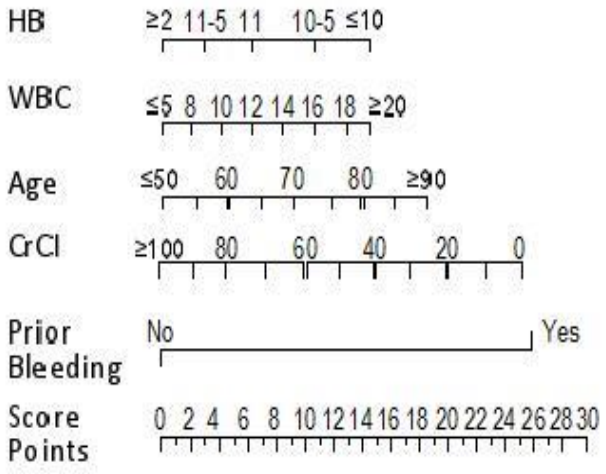
Age > 75y.
Or
Weight < 60Kg.
Or
Past stroke / TIA
GFR<30 ESRD.

Ticagrelor

Past hemorrhagic stroke.
Or
Active Asthma/COPD.
Or
conduction defect / Bradycardia.
GFR<30; ESRD

Risk scores validated for dual antiplatelet therapy duration decision-making

ESC European Society of Cardiology

	PRECISE-DAPT score	DAPT score	
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		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	

2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS
(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Recommendations for oral antiplatelet agents

Recommendations	Class [a]	Level [b]	Ref [c]
Aspirin should be given to all patients without contraindications at an initial loading dose of 150–300 mg, and at a maintenance dose of 75–100 mg daily long-term regardless of treatment strategy.	I	A	107, 108
A $P2Y_{12}$ inhibitor should be added to aspirin as soon as possible and maintained over 12 months, unless there are contraindications such as excessive risk of bleeding.	I	A	110, 130, 132
A proton pump inhibitor (preferably not omeprazole) in combination with DAPT is recommended in patients with a history of gastrointestinal haemorrhage or peptic ulcer, and appropriate for patients with multiple other risk factors (*H. elicobacter pylori* infection, age ≥65 years, concurrent use of anticoagulants or steroids).	I	A	125–127
anent withdrawal of $P2Y_{12}$ inhibitors within 12 months after the index event is discouraged unless	I	C	-
ischaemic events (e	I	B	132
oading dose, 10-mg daily dose) is recommended for $P2Y_{12}$-inhibitor-naive patients (especially			
prasugrel.	I	A	147
A 600-mg loading dose of clopidogrel (or a supplementary 300-mg dose at PCI following an initial 300-mg loading dose) is recommended for patients scheduled for an invasive strategy when ticagrelor or prasugrel is not an option.	I	B	108, 114, 115
A higher maintenance dose of clopidogrel 150 mg daily should be considered for the first 7 days in patients managed with PCI and without increased risk of bleeding.	IIa	B	108
Increasing the maintenance dose of clopidogrel based on platelet function testing is not advised as routine, but may be considered in selected cases.	IIb	B	124
Genotyping and/or platelet function testing may be considered in selected cases when clopidogrel is used.	IIb	B	119, 121
In patients pre-treated with $P2Y_{12}$ inhibitors who need to undergo non-emergent major surgery (including CABG), postponing surgery at least for 5 days after cessation of ticagrelor or clopidogrel, and 7 days for prasugrel, if clinically feasible and unless the patient is at high risk of ischaemic events should be considered.	IIa	C	-
Ticagrelor or clopidogrel should be considered to be (re-) started after CABG surgery as soon as considered safe.	IIa	B	134
The combination of aspirin with an NSAID (selective COX-2 inhibitors and non-selective NSAID) is not recommended.	III	C	-

Ticagrelor

regardless of initial treatment strategy

Prasugrel

in whom coronary anatomy is known and who are proceeding to PCI

[a]Class of recommendation.
[b]Level of evidence.
[c]References.
[d]Prasugrel is in the 'Guidelines on Revascularization'[148] given a IIa recommendation as the overall indication including clopidogrel-pre-treated patients a
anatomy. The class I recommendation here refers to the specifically defined subgroup.
CABG = coronary artery bypass graft; COX = cyclo-oxygenase; DAPT = dual (oral) antiplatelet therapy; NSAID = non-steroidal anti-inflammatory
coronary intervention.

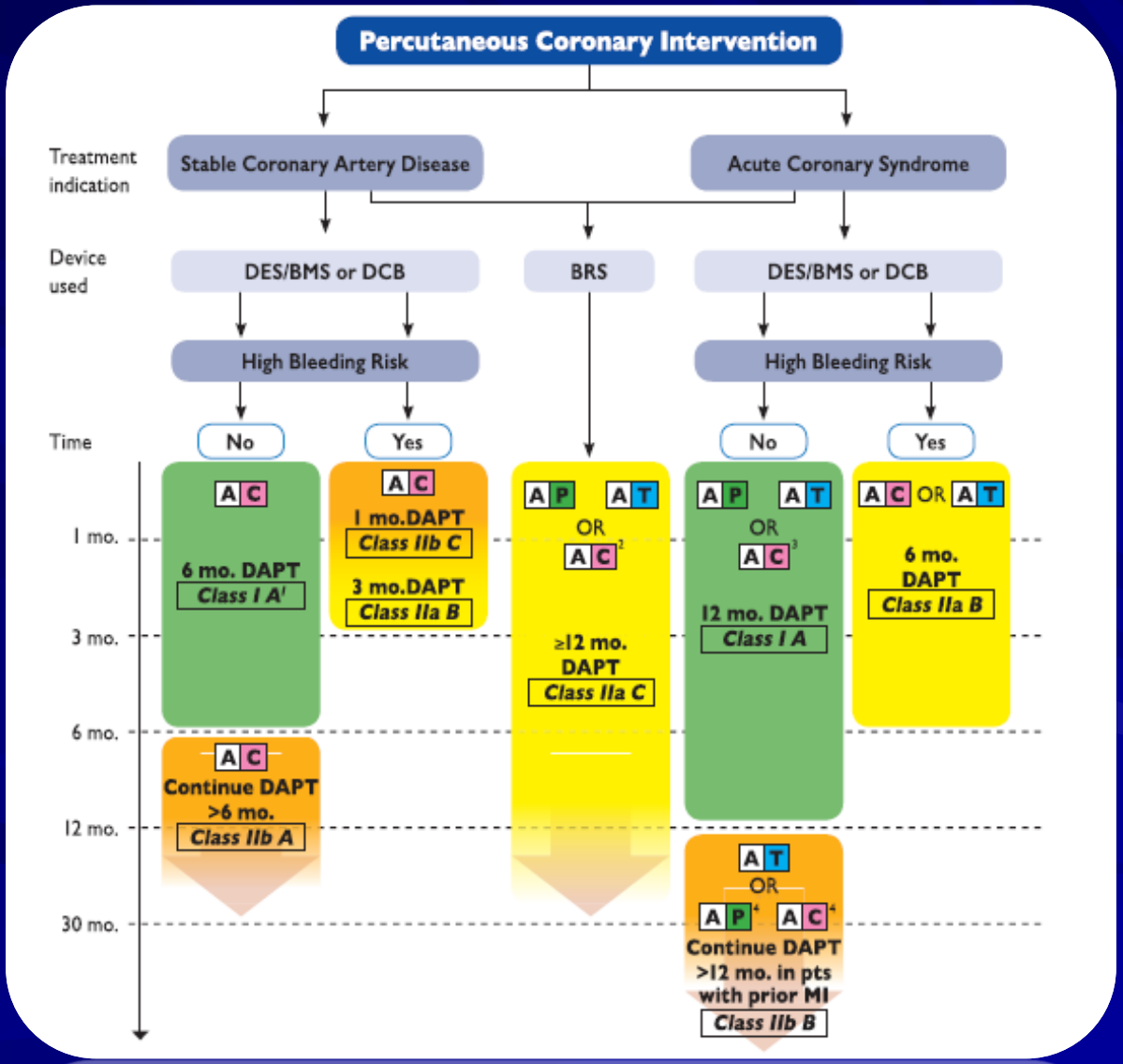
NSTEMI

Table 22 Routine therapies in the acute, subacute and long term phase of ST-segment elevation myocardial infarction

Recommendations	Class [a]	Level [b]	Ref [c]
Active smokers with STEMI must receive counselling and be referred to a smoking cessation programme.	I	B	225
Each hospital participating in the care of STEMI patients must have a smoking cessation protocol.	I	C	-
Exercise-based rehabilitation is recommended.	I	B	232, 233
Antiplatelet therapy with low dose aspirin (75–100 mg) is indicated indefinitely after STEMI.	I	A	237
In patients who are intolerant to aspirin, clopidogrel is indicated as an alternative to aspirin.	I	B	243
DAPT with a combination of aspirin and prasugrel or aspirin and ticagrelor is recommended (over aspirin and clopidogrel) in patients treated with PCI.	I	A	109, 110
DAPT with aspirin and an oral ADP receptor antagonist must be continued for up to 12 months after STEMI, with a strict minimum of:	I	C	245–247, 283
• 1 month for patients receiving BMS	I	C	
• 6 months for patients receiving DES	IIb	B	
In patients with left ventricular thrombus, anticoagulation should be instituted for a minimum of 3 months.	IIa	B	344–346
In patients with a clear indication for oral anticoagulation (e.g. atrial fibrillation with CHA_2DS_2-VASc Score ≥2 or mechanical valve prosthesis), oral anticoagulation must be implemented in addition to antiplatelet therapy.	I	C	-
If patients require triple antithrombotic therapy, combining DAPT and OAC, e.g. because of stent placement and an obligatory indication for OAC, the duration of dual antiplatelet therapy should be minimized to reduce bleeding risk.	I	C	-
In selected patients who receive aspirin and clopidogrel, low-dose rivaroxaban (2.5 mg twice daily) may be considered if the patient is at low bleeding risk.	IIb	B	262
DAPT should be used up to 1 year in patients with STEMI who did not receive a stent.	IIa	C	-
Gastric protection with a proton pump inhibitor should be considered for the duration of DAPT therapy in patients at high risk of bleeding.	IIa		
Oral treatment with beta-blockers should be considered during hospital stay and continued thereafter in all STEMI patients without contraindications.	IIa		

STEMI

ACS Scenario



ACS Scenario

In patients with ACS, ticagrelor (180 mg loading dose, 90 mg twice daily) on top of aspirin[c] is recommended, regardless of initial treatment strategy, including patients pre-treated with clopidogrel (which should be discontinued when ticagrelor is commenced) unless there are contraindications.[20]	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[c] unless there is a high risk of life-threatening bleeding or other contraindications.[23]	I	B
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[c] of clopidogrel, unless contraindications to ticagrelor exist.[20]	I	B

DAPT & OAC

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Prevention of Bleeding in Patients with Atrial Fibrillation Undergoing PCI

C. Michael Gibson, M.D., Roxana Mehran, M.D., Christoph Bode, M.D., Jonathan Halperin, M.D., Freek W. Verheugt, M.D., Peter Wildgoose, Ph.D., Mary Birmingham, Pharm.D., Juliana Ianus, Ph.D., Paul Burton, M.D., Ph.D., Martin van Eickels, M.D., Serge Korjian, M.D., Yazan Daaboul, M.D., Gregory Y.H. Lip, M.D., Marc Cohen, M.D., Steen Husted, M.D., Eric D. Peterson, M.D., M.P.H., and Keith A. Fox, M.B., Ch.B.

ABSTRACT

BACKGROUND

In patients with atrial fibrillation undergoing percutaneous coronary intervention (PCI) with placement of stents, standard anticoagulation with a vitamin K antagonist plus dual antiplatelet therapy (DAPT) with a $P2Y_{12}$ inhibitor and aspirin reduces the risk of thrombosis and stroke but increases the risk of bleeding. The effectiveness and safety of anticoagulation with rivaroxaban plus either one or two antiplatelet agents are uncertain.

METHODS

We randomly assigned 2124 participants with nonvalvular atrial fibrillation who had undergone PCI with stenting to receive, in a 1:1:1 ratio, low-dose rivaroxaban (15 mg once daily) plus a $P2Y_{12}$ inhibitor for 12 months (group 1), very-low-dose rivaroxaban (2.5 mg twice daily) plus DAPT for 1, 6, or 12 months (group 2), or standard therapy with a dose-adjusted vitamin K antagonist (once daily) plus DAPT for 1, 6, or 12 months (group 3). The primary safety outcome was clinically significant bleeding (a composite of major bleeding or minor bleeding according to Thrombolysis in Myocardial Infarction [TIMI] criteria or bleeding requiring medical attention).

RESULTS

The rates of clinically significant bleeding were lower in the two groups receiving rivaroxaban than in the group receiving standard therapy (16.8% in group 1, 18.0% in group 2, and 26.7% in group 3; hazard ratio for group 1 vs. group 3, 0.59; 95% confidence interval [CI], 0.47 to 0.76; P<0.001; hazard ratio for group 2 vs. group 3, 0.63; 95% CI, 0.50 to 0.80; P<0.001). The rates of death from cardiovascular causes, myocardial infarction, or stroke were similar in the three groups (Kaplan–Meier estimates, 6.5% in group 1, 5.6% in group 2, and 6.0% in group 3; P values for all comparisons were nonsignificant).

CONCLUSIONS

In participants with atrial fibrillation undergoing PCI with placement of stents, the administration of either low-dose rivaroxaban plus a $P2Y_{12}$ inhibitor for 12 months or very-low-dose rivaroxaban plus DAPT for 1, 6, or 12 months was associated with a lower rate of clinically significant bleeding than was standard therapy with a vitamin K antagonist plus DAPT for 1, 6, or 12 months. The three groups had similar efficacy rates, although the observed broad confidence intervals diminish the surety of any conclusions regarding efficacy. (Funded by Janssen Scientific Affairs and Bayer Pharmaceuticals; PIONEER AF-PCI ClinicalTrials.gov number, NCT01830543.)

From the Cardiovascular Division, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston (C.M.G., S.K., Y.D.); the Cardiovascular Institute, Mount Sinai Medical Center, Icahn School of Medicine at Mount Sinai, New York (R.M., J.H.); Heart Center, Department for Cardiology and Angiology I, University of Freiburg, Freiburg (C.B.), and Bayer Pharmaceuticals, Leverkusen (M.E.) — both in Germany; Onze Lieve Vrouwe Gasthuis (OLVG), Amsterdam (F.W.V.); Janssen Pharmaceuticals, Titusville (P.W., M.B., J.I., P.B.), and the Division of Cardiology, Newark Beth Israel Medical Center, Newark (M.C.) — both in New Jersey; University of Birmingham Institute of Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom (G.Y.H.L.); Aarhus University Hospital, Medical Department, Hospital Unit West, Herning, Denmark (S.H.); Duke Clinical Research Institute, Durham, NC (E.D.P.); and the Centre for Cardiovascular Science, University of Edinburgh and Royal Infirmary of Edinburgh, Edinburgh (K.A.F.). Address reprint requests to Dr. Gibson at Harvard Medical School, Beth Israel Deaconess Medical Center, 330 Brookline Ave., Overland 540, Boston, MA 02215, or at mgibson@bidmc.harvard.edu.

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DOI: 10.1056/NEJMoa1611594

PIONEER AF-PCI

XARELTO
&
DAPT

N Engl J Med 2016;375:2423-34.

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Dual Antithrombotic Therapy with Dabigatran after PCI in Atrial Fibrillation

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ABSTRACT

BACKGROUND

Triple antithrombotic therapy with warfarin plus two antiplatelet agents is the standard of care after percutaneous coronary intervention (PCI) for patients with atrial fibrillation, but this therapy is associated with a high risk of bleeding.

METHODS

In this multicenter trial, we randomly assigned 2725 patients with atrial fibrillation who had undergone PCI to triple therapy with warfarin plus a $P2Y_{12}$ inhibitor (clopidogrel or ticagrelor) and aspirin (for 1 to 3 months) (triple-therapy group) or dual therapy with dabigatran (110 mg or 150 mg twice daily) plus a $P2Y_{12}$ inhibitor (clopidogrel or ticagrelor) and no aspirin (110-mg and 150-mg dual-therapy groups). Outside the United States, elderly patients (≥80 years of age; ≥70 years of age in Japan) were randomly assigned to the 110-mg dual-therapy group or the triple-therapy group. The primary end point was a major or clinically relevant nonmajor bleeding event during follow-up (mean follow-up, 14 months). The trial also tested for the noninferiority of dual therapy with dabigatran (both doses combined) to triple therapy with warfarin with respect to the incidence of a composite efficacy end point of thromboembolic events (myocardial infarction, stroke, or systemic embolism), death, or unplanned revascularization.

RESULTS

The incidence of the primary end point was 15.4% in the 110-mg dual-therapy group as compared with 26.9% in the triple-therapy group (hazard ratio, 0.52; 95% confidence interval [CI], 0.42 to 0.63; P<0.001 for noninferiority; P<0.001 for superiority) and 20.2% in the 150-mg dual-therapy group as compared with 25.7% in the corresponding triple-therapy group, which did not include elderly patients outside the United States (hazard ratio, 0.72; 95% CI, 0.58 to 0.88; P<0.001 for noninferiority). The incidence of the composite efficacy end point was 13.7% in the two dual-therapy groups combined as compared with 13.4% in the triple-therapy group (hazard ratio, 1.04; 95% CI, 0.84 to 1.29; P=0.005 for noninferiority). The rate of serious adverse events did not differ significantly among the groups.

CONCLUSIONS

Among patients with atrial fibrillation who had undergone PCI, the risk of bleeding was lower among those who received dual therapy with dabigatran and a $P2Y_{12}$ inhibitor than among those who received triple therapy with warfarin, a $P2Y_{12}$ inhibitor, and aspirin. Dual therapy was noninferior to triple therapy with respect to the risk of thromboembolic events. (Funded by Boehringer Ingelheim; RE-DUAL PCI ClinicalTrials.gov number, NCT02164864.)

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*A complete list of investigators in the Randomized Evaluation of Dual Antithrombotic Therapy with Dabigatran versus Triple Therapy with Warfarin in Patients with Nonvalvular Atrial Fibrillation Undergoing Percutaneous Coronary Intervention (RE-DUAL PCI) trial is provided in the Supplementary Appendix, available with the full text of this article at NEJM.org.

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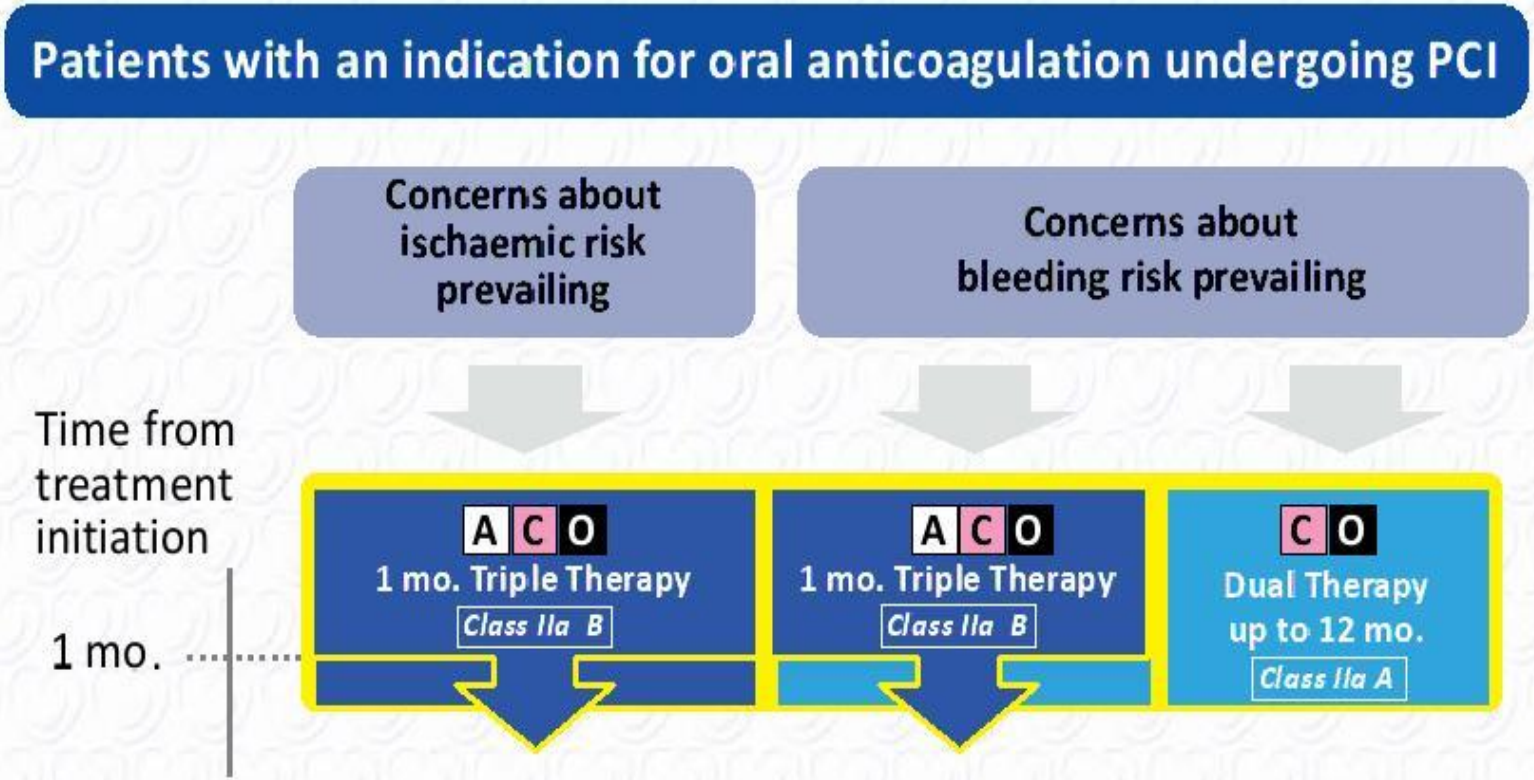
REDUAL-PCI

PRADAXA
&
DAPT

N Engl J Med 2017;377:1513-24.

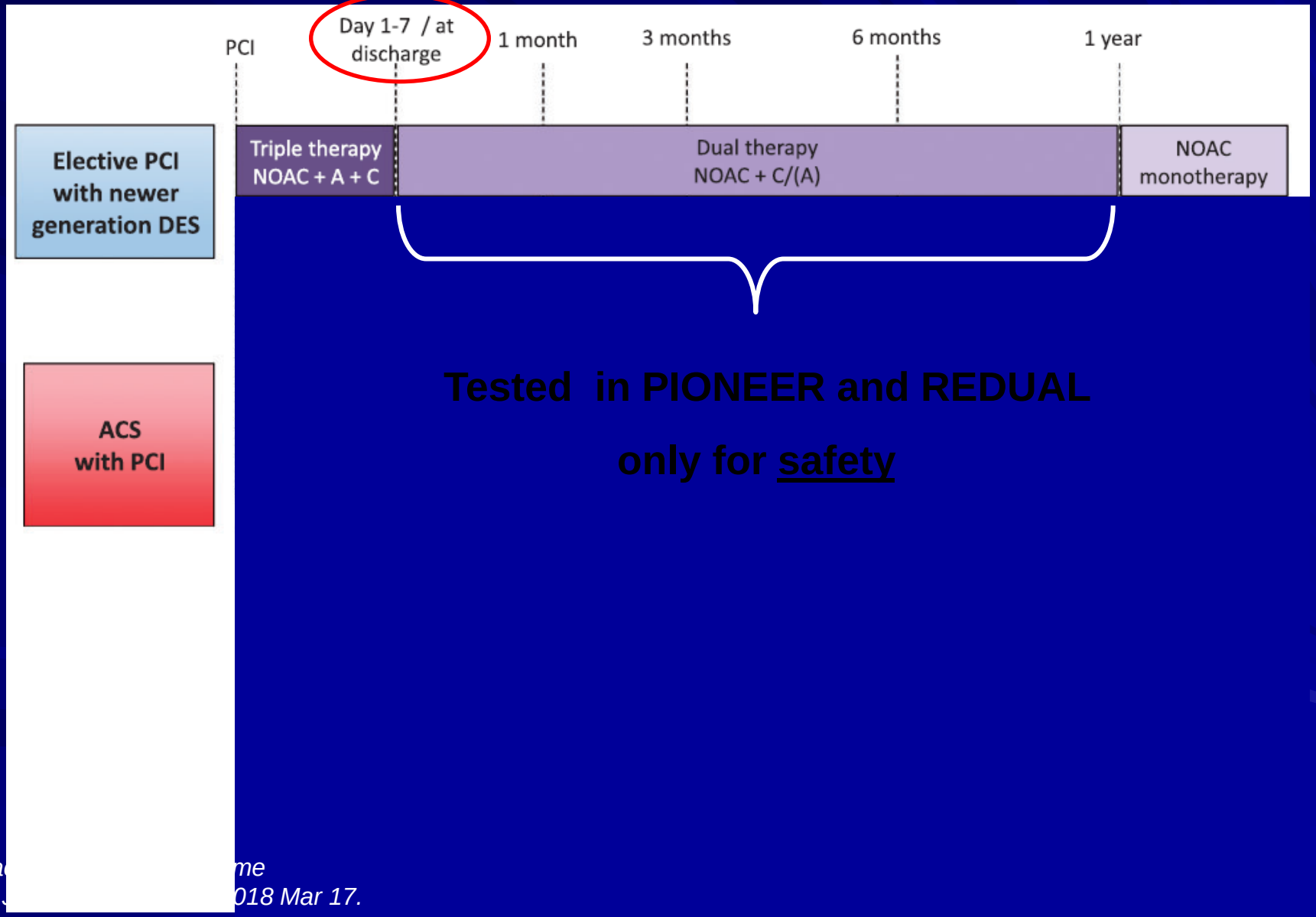
Algorithm for dual antiplatelet therapy (DAPT) in patients with an indication for oral anticoagulation Undergoing percutaneous coronary intervention (PCI)

ESC European Society of Cardiology

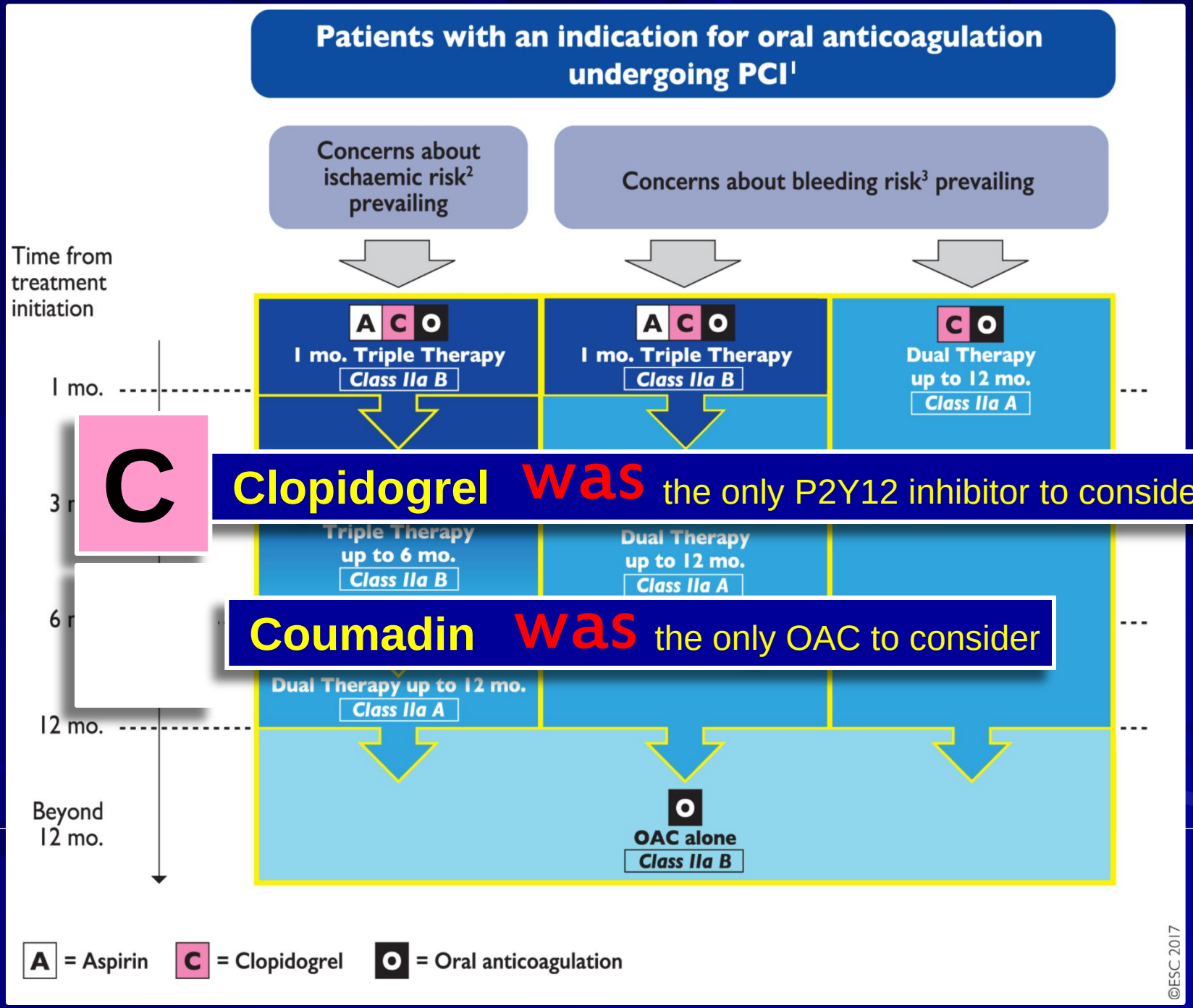


2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Long term treatment of patients on NOAC therapy after elective PCI or ACS



ACS, a me
Steffel J 018 Mar 17.


Patients with an indication for oral anticoagulation undergoing PCI[1]
Concerns about ischaemic risk[2] prevailing
Concerns about bleeding risk[3] prevailing
Time from treatment initiation
1 mo.
3 mo.
6 mo.
12 mo.
Beyond 12 mo.
A C O
1 mo. Triple Therapy
Class IIa B
A C O
1 mo. Triple Therapy
Class IIa B
C O
Dual Therapy up to 12 mo.
Class IIa A
Triple Therapy up to 6 mo.
Class IIa B
Dual Therapy up to 12 mo.
Class IIa A
Dual Therapy up to 12 mo.
Class IIa A
O
OAC alone
Class IIa B
C
Clopidogrel was the only P2Y12 inhibitor to consider
Coumadin was the only OAC to consider
A = Aspirin
C = Clopidogrel
O = Oral anticoagulation
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אחרי TIA

ג.ר. בן 52. פקיד.

מעשן כבד. אחרי TIA בגיל 45.

התקבל בזמן STEMI תחתון.

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מטופל באליקוויס לפרפור עליות

א.ב. בן 75. פנסיונר.

היפרטנסיבי. מטופל באליקוויס לפרפור עליות.

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Pre-Op Discontinuation

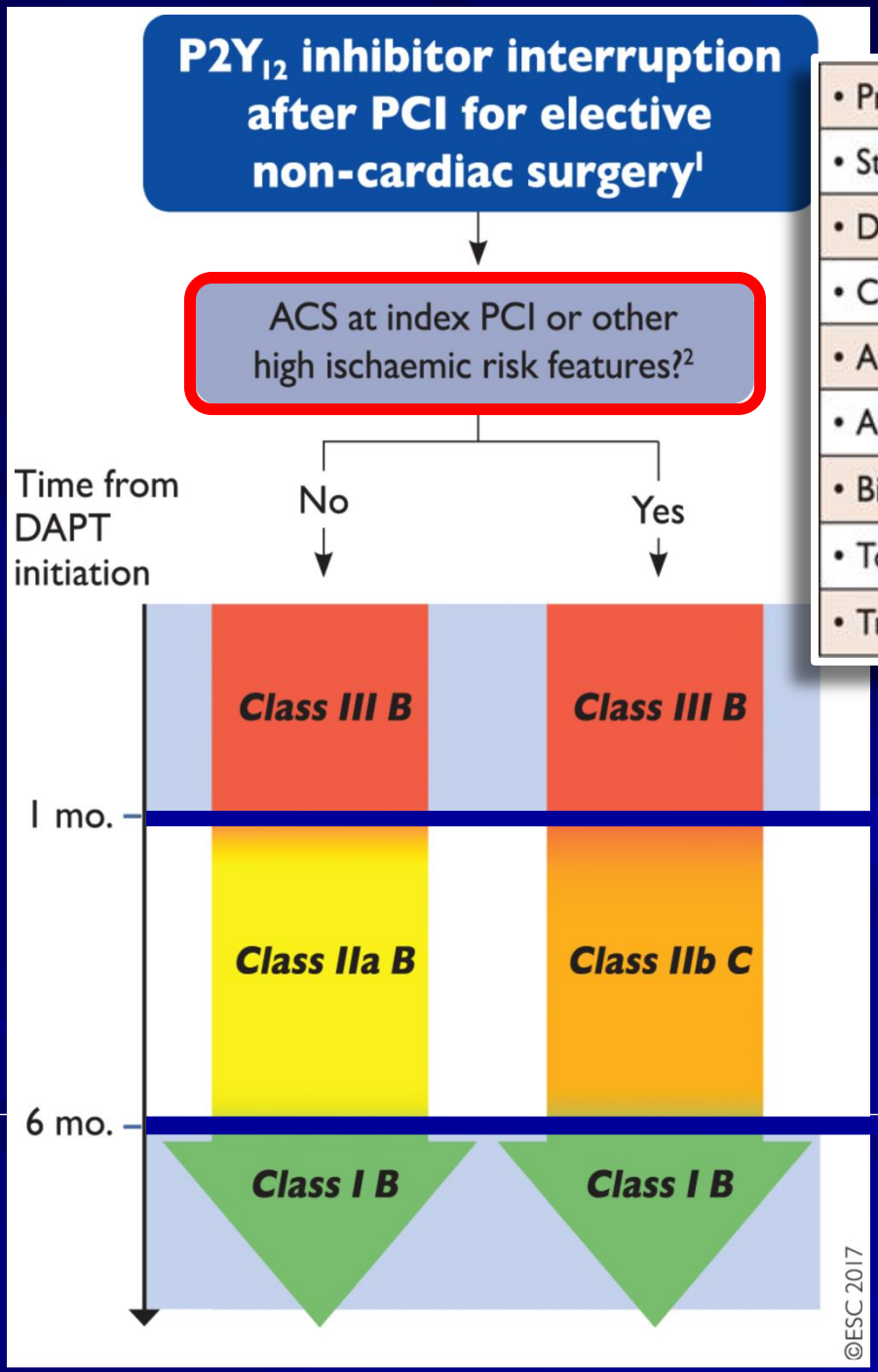
8. Elective non-cardiac surgery in patients on dual antiplatelet therapy

It is estimated that 5–25% of patients with coronary stents may require non-cardiac surgery within the year after stent implantation.[205] Management of patients on DAPT who are referred for surgical procedures involves consideration of: (1) the risk of stent thrombosis (particularly if DAPT needs to be interrupted); (2) the consequences of delaying the surgical procedure; and (3) the increased intra- and periprocedural bleeding risk and possible consequences of [illegible]. Given the complexity of these considerations, a multidisciplinary approach—involving interventional cardiologists, cardiologists, anaesthetists, haematologists, and surgeons—is required to determine the patient's risk for bleeding and thrombosis and to choose the best management strategy. Surgical [illegible] groups, with estimated 30-day cardiac event rates for cardiac death or MI of < 1%, 1–5%, and ≥5%, respectively.[205,209] A practical classification of the bleeding risk associated with each type of non-cardiac surgery has been recently proposed by the Stent After Surgery group.[210]

Risk of thrombosis

Risk of bleeding

Consequence of delaying surgery

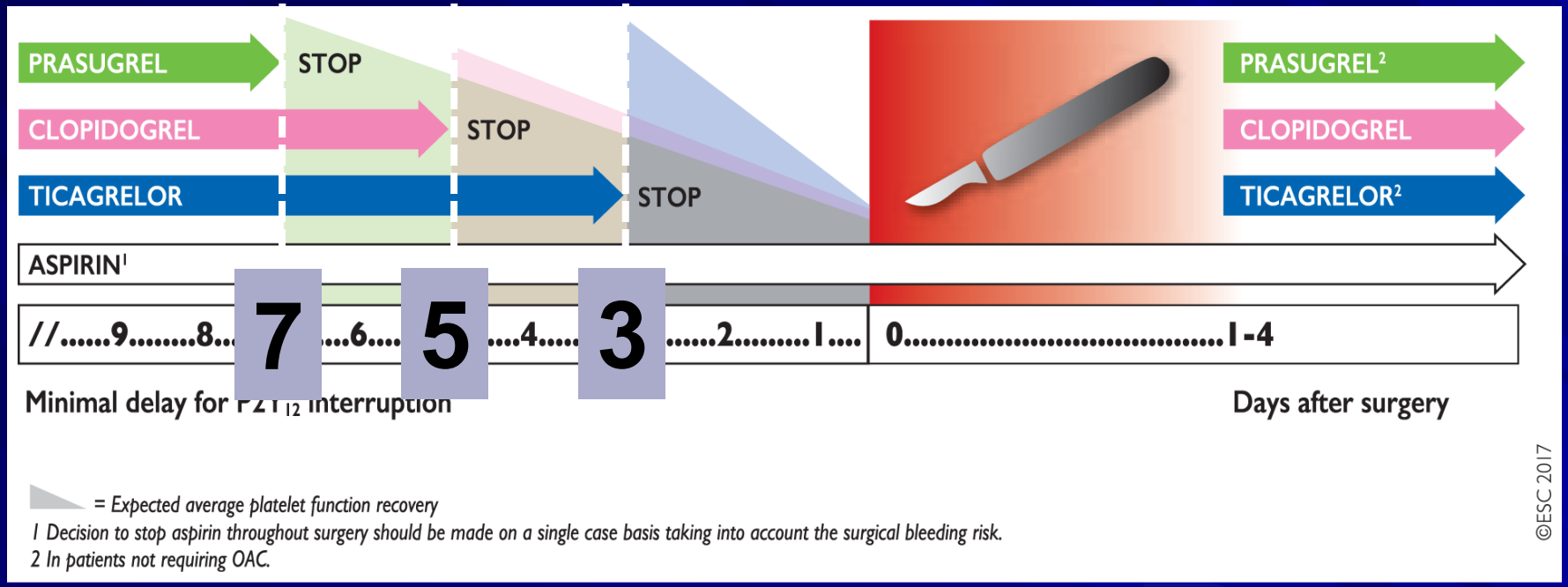


• Prior stent thrombosis on adequate antiplatelet therapy
• Stenting of the last remaining patent coronary artery
• Diffuse multivessel disease especially in diabetic patients
• Chronic kidney disease (i.e. creatinine clearance <60 mL/min)
• At least three stents implanted
• At least three lesions treated
• Bifurcation with two stents implanted
• Total stent length >60 mm
• Treatment of a chronic total occlusion

Danger zone

Zone in doubt

Safe zone


PRASUGREL
STOP
CLOPIDOGREL
STOP
TICAGRELOR
STOP
ASPIRIN[1]
PRASUGREL[2]
CLOPIDOGREL
TICAGRELOR[2]
//.....9.....8...
7
...6....
5
....4.....
3
.....2.....1....
0.....1-4
Minimal delay for P2Y12 interruption
Days after surgery
= 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.
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Thank you for your attention