Traitement antithrombotique du coronarien

Quel traitement Anti-thrombotique chez le coronarien

Un AAP ?
Deux AAP ?
1 AAP + 1 AC ?
1 AC seul ?

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

*: European Association for Cardio-Thoracic Surgery

ESC
European Society of Cardiology

Déjà non à jour avant ESC 2017

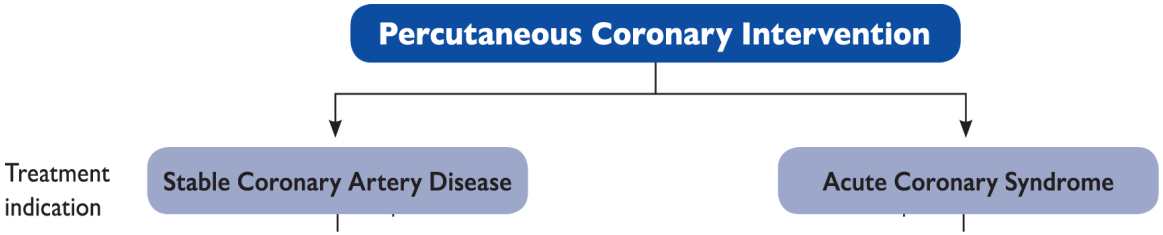
Classes of recommendations

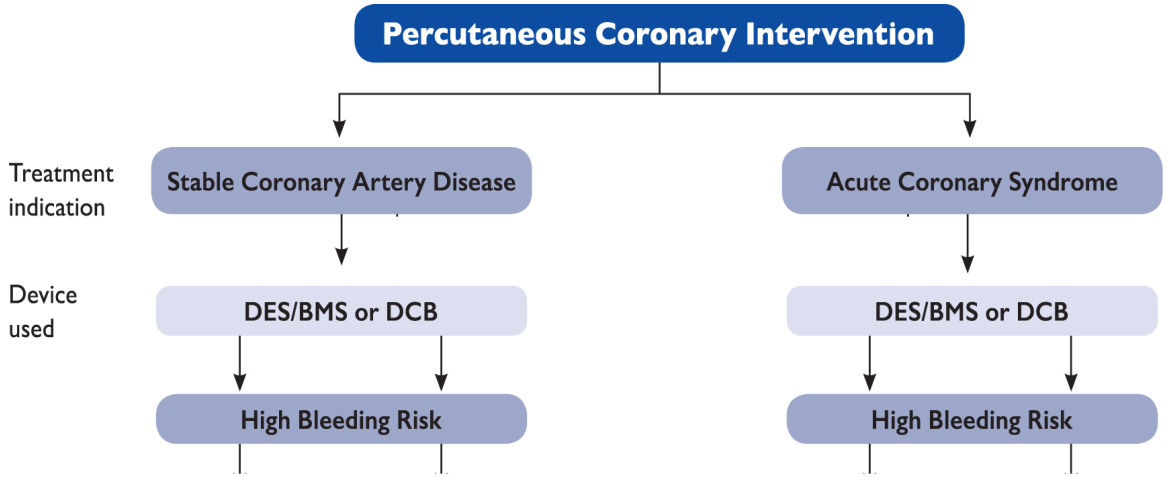
ESC
European Society of Cardiology

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/ is indicated.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered.
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered.
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended.

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

Code couleurs


Percutaneous Coronary Intervention
Treatment indication
Stable Coronary Artery Disease
Acute Coronary Syndrome


Percutaneous Coronary Intervention
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Device used
DES/BMS or DCB
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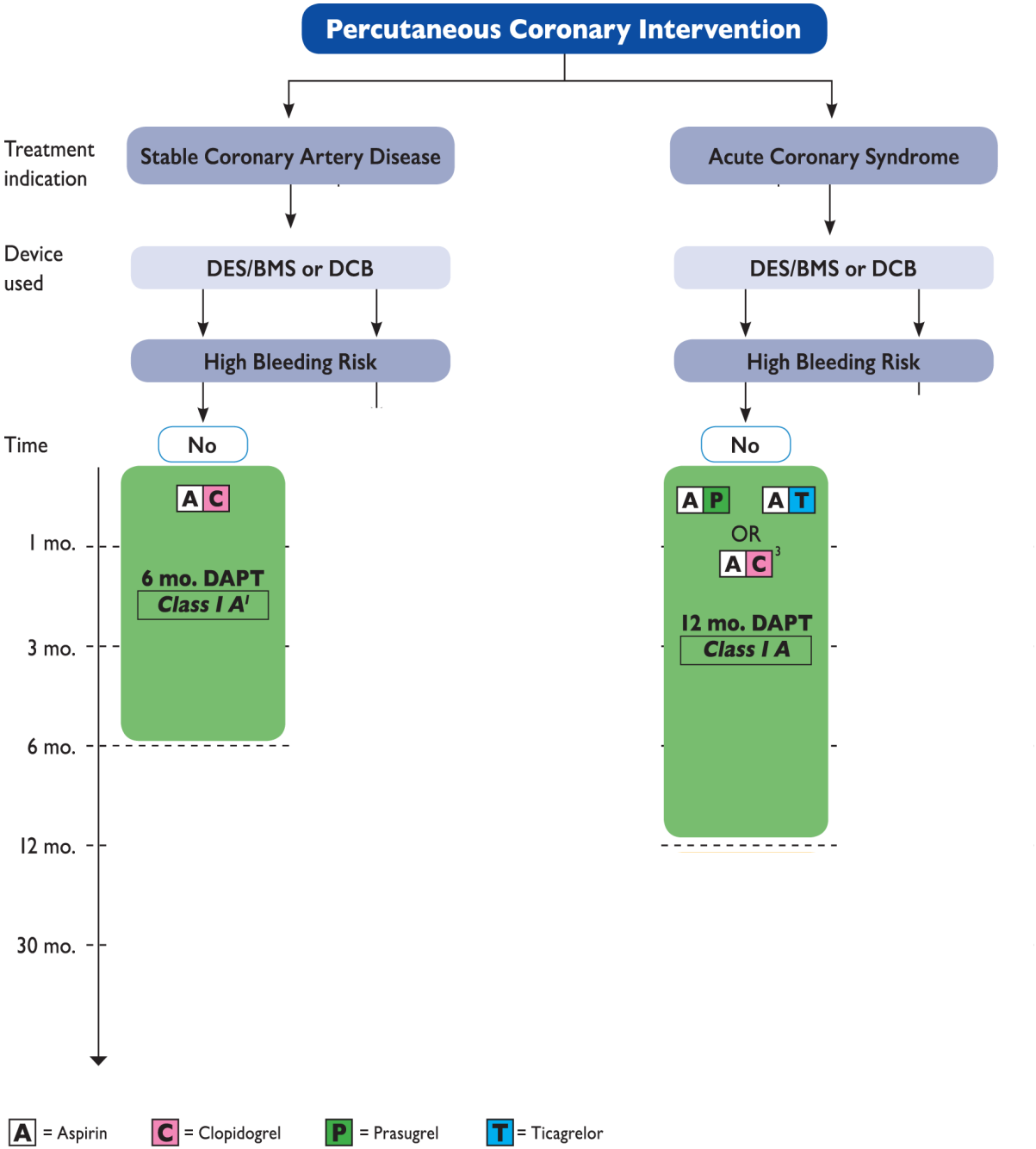
High Bleeding Risk
High Bleeding Risk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DES/BMS or DCB
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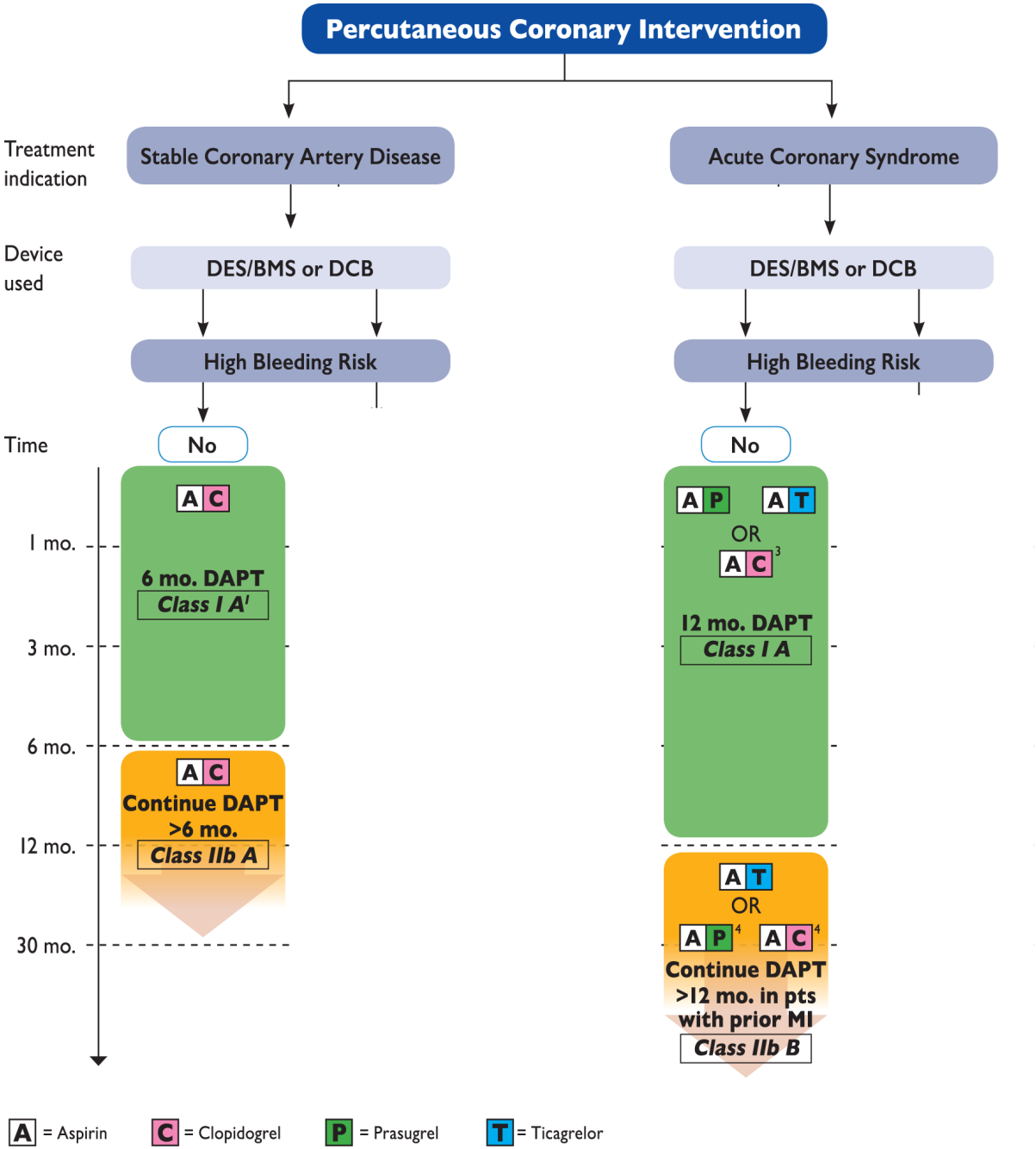
Time
No
No
A C
6 mo. DAPT
Class I A[1]
A P
A T
OR
A C[3]
12 mo. DAPT
Class I A
1 mo.
3 mo.
6 mo.
12 mo.
30 mo.
A = Aspirin
C = Clopidogrel
P = Prasugrel
T = Ticagrelor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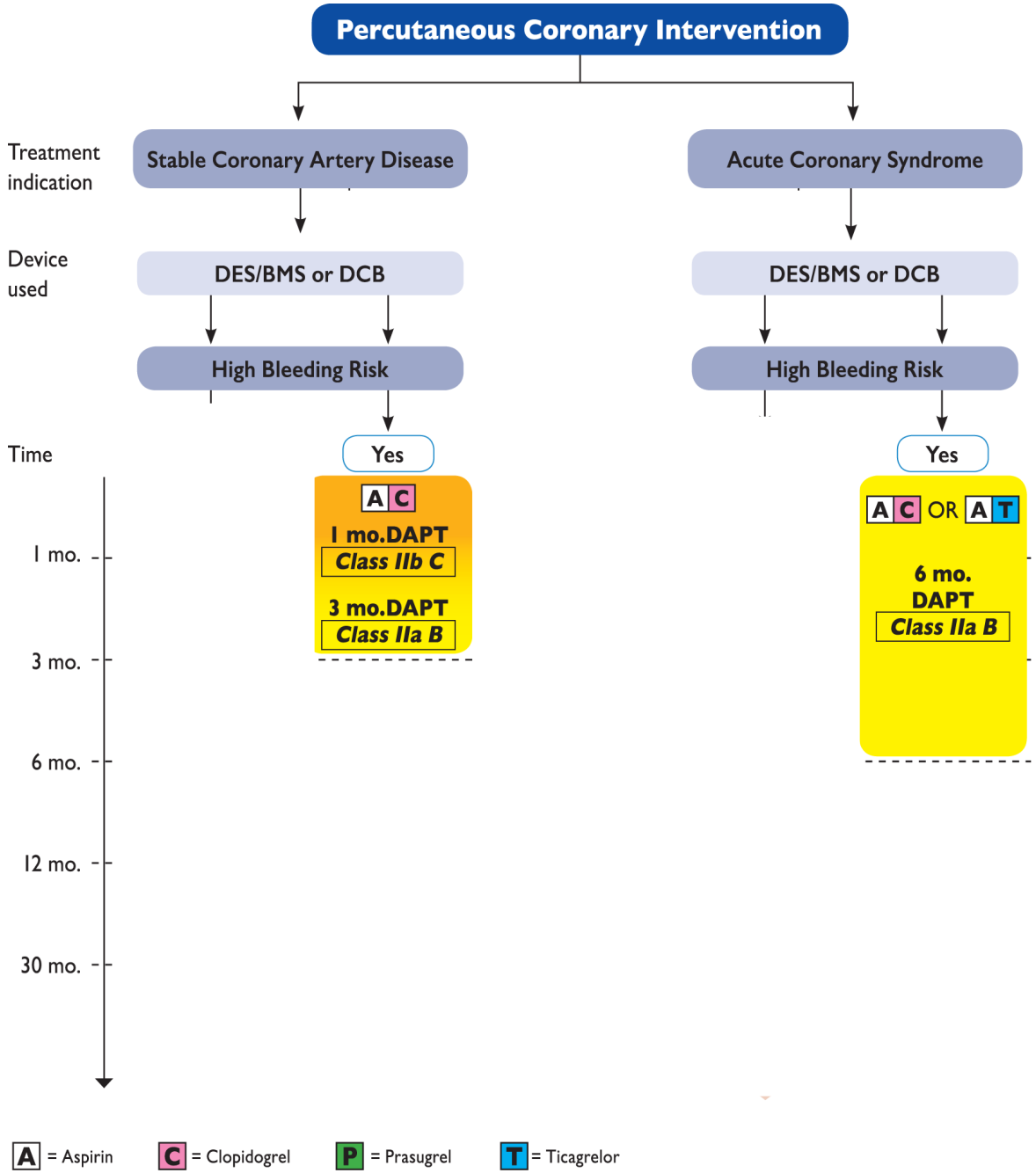
Device used
DES/BMS or DCB
DES/BMS or DCB
High Bleeding Risk
High Bleeding Risk
Time
No
No
A C
1 mo.
6 mo. DAPT
Class I A[1]
3 mo.
6 mo.
A C
Continue DAPT >6 mo.
Class IIb A
12 mo.
30 mo.
A P
A T
OR
A C[3]
12 mo. DAPT
Class I A
A T
OR
A P[4]
A C[4]
Continue DAPT >12 mo. in pts with prior MI
Class IIb B
A = Aspirin
C = Clopidogrel
P = Prasugrel
T = Ticagrelor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Device used
DES/BMS or DCB
DES/BMS or DCB
High Bleeding Risk
High Bleeding Risk
Time
Yes
Yes
A C
1 mo.DAPT
Class IIb C
3 mo.DAPT
Class IIa B
A C OR A T
6 mo.
DAPT
Class IIa B
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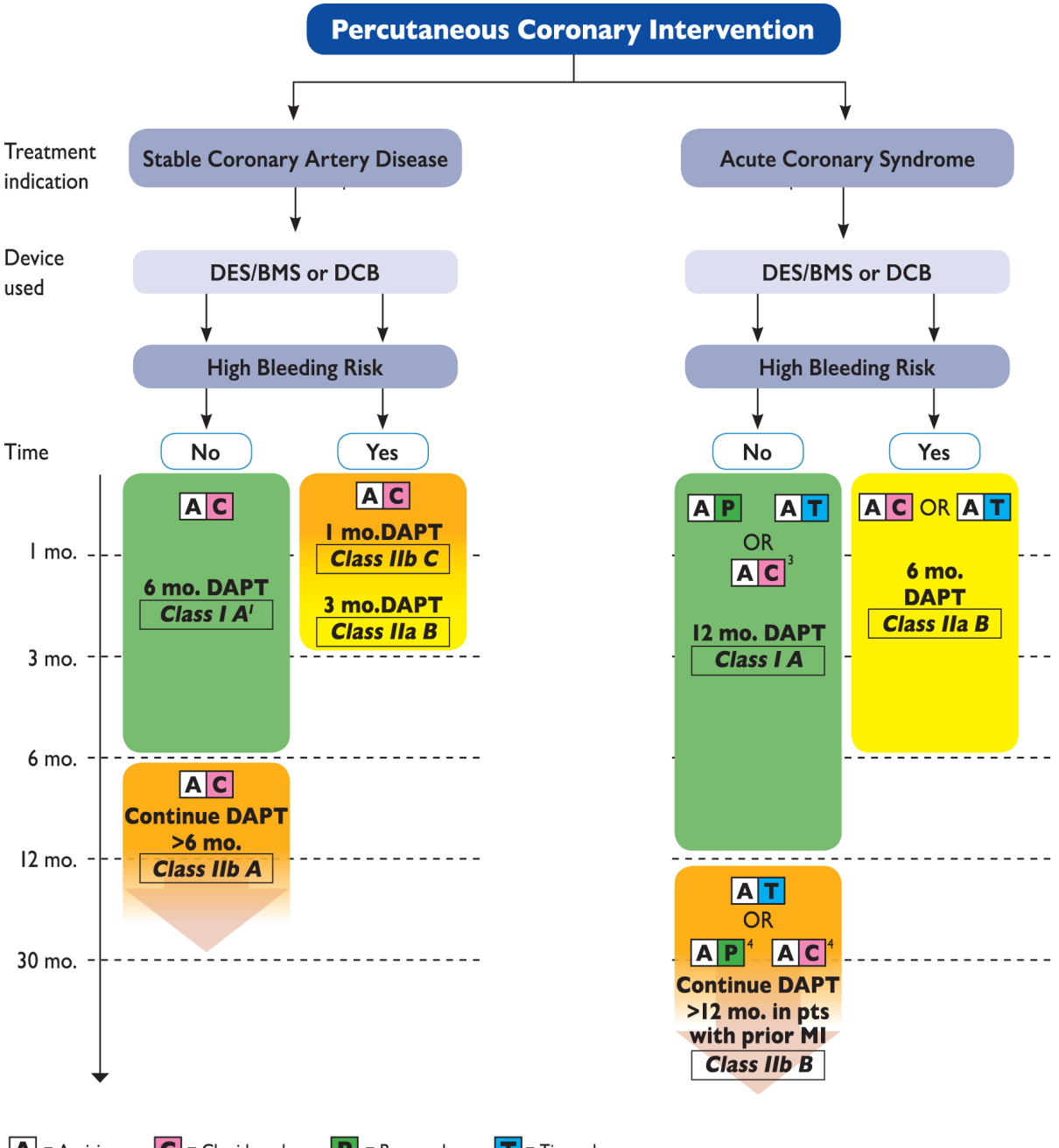
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Yes
No
Yes
1 mo.
3 mo.
6 mo.
12 mo.
30 mo.
A C
6 mo. DAPT
Class I A1
A C
1 mo.DAPT
Class IIb C
3 mo.DAPT
Class IIa B
A C
Continue DAPT >6 mo.
Class IIb A
A P A T
OR
A C3
12 mo. DAPT
Class I A
A C OR A T
6 mo. DAPT
Class IIa B
A T
OR
A P4 A C4
Continue DAPT >12 mo. in pts with prior MI
Class IIb B
A = Aspirin
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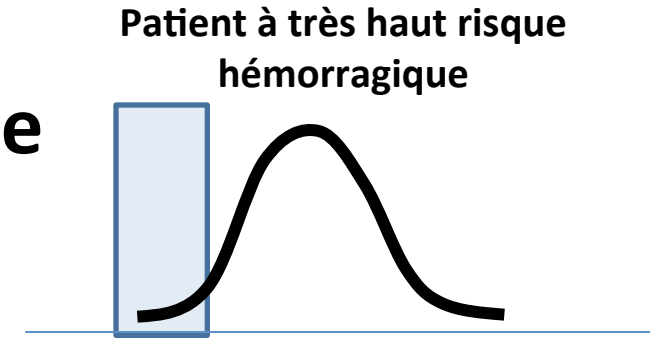
Comment peut-on décider que l'on réduira la durée de la bithérapie ?

Le très haut risque hémorragique



- 15% des patients ?
- Mieux vaut l'anticiper
- Comment le calculer ?
- Quel risque fait-on courir ?
- Attention aux publicités de certains industriels

PRECISEDAPT

Haemoglobin

unit

14

- (•) g/dl
- ( ) mmol/L

Age (years)

61

White blood cells

unit

9.5

- ( ) u/mcL
- (•) 10^9/L

Creatinine Clearance (ml/min)

67

Prior Bleeding [ ]

CALCULATE

RESET

PRECISEDAPT

Haemoglobin unit

14

g/dl

mmol/L

Age (years)

61

White blood cells unit

9.5

u/mcL

10^9/L

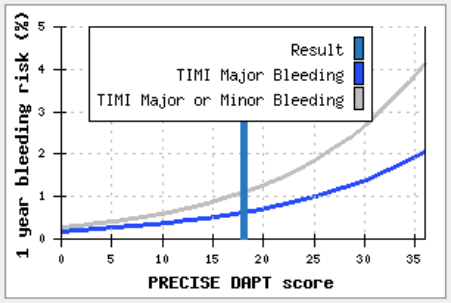
Creatinine Clearance (ml/min)

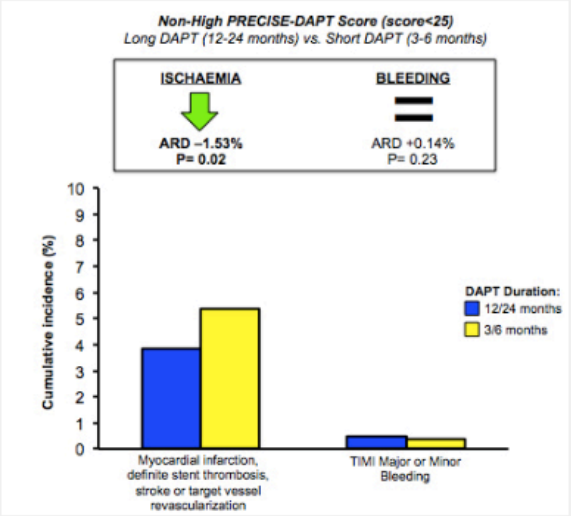
67

Prior Bleeding

CALCULATE

RESET





In patients without high PRECISE-DAPT score (Score<25) a long DAPT (12-24 months) as compared with a short DAPT (3-6 months) was associated with a lower

RESULT:

Cluster of risk:

Moderate

Score Calculated

18

12 months risk of TIMI major or minor Bleeding

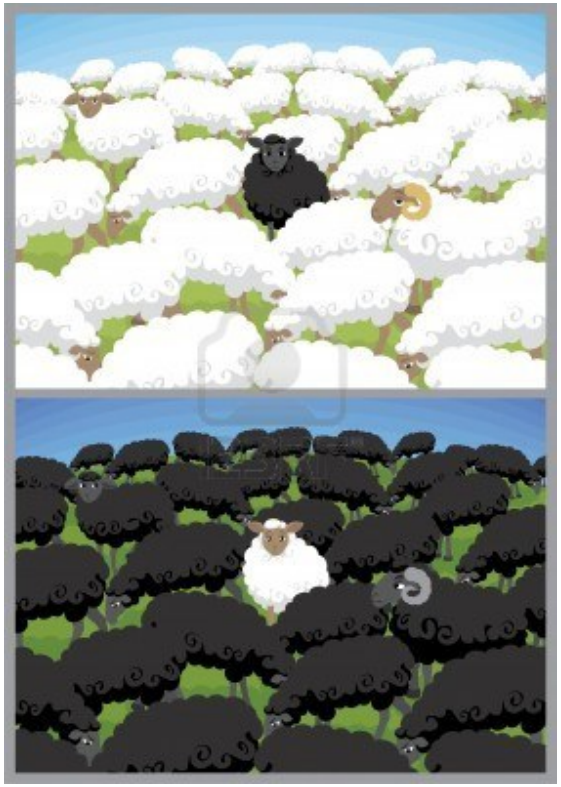
1.1%

12 months risk of TIMI Major Bleeding

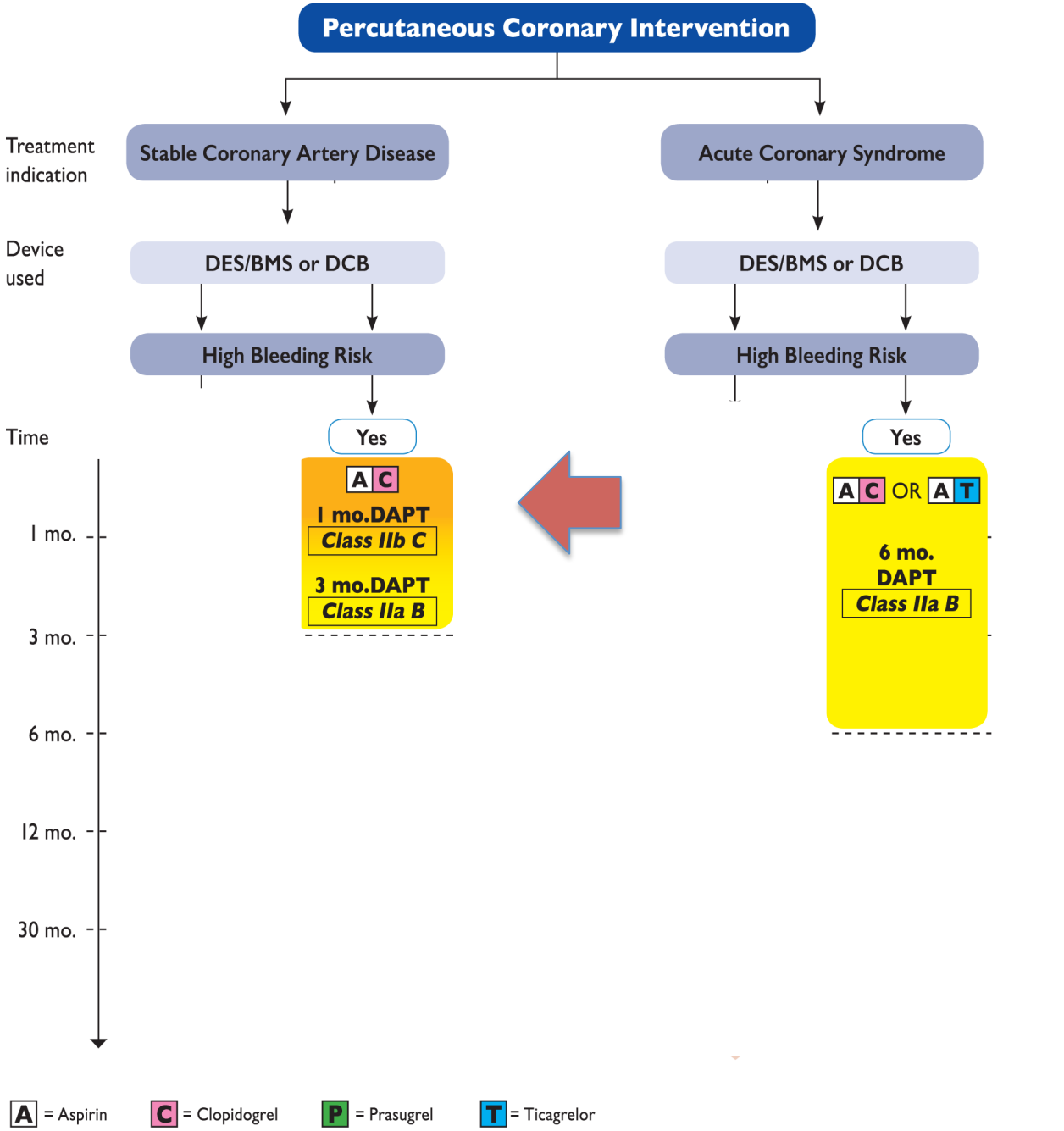
0.6%

Copy to clipboard

Les scores sont meilleurs à l'échelle d'une population qu'à l'échelle du patient



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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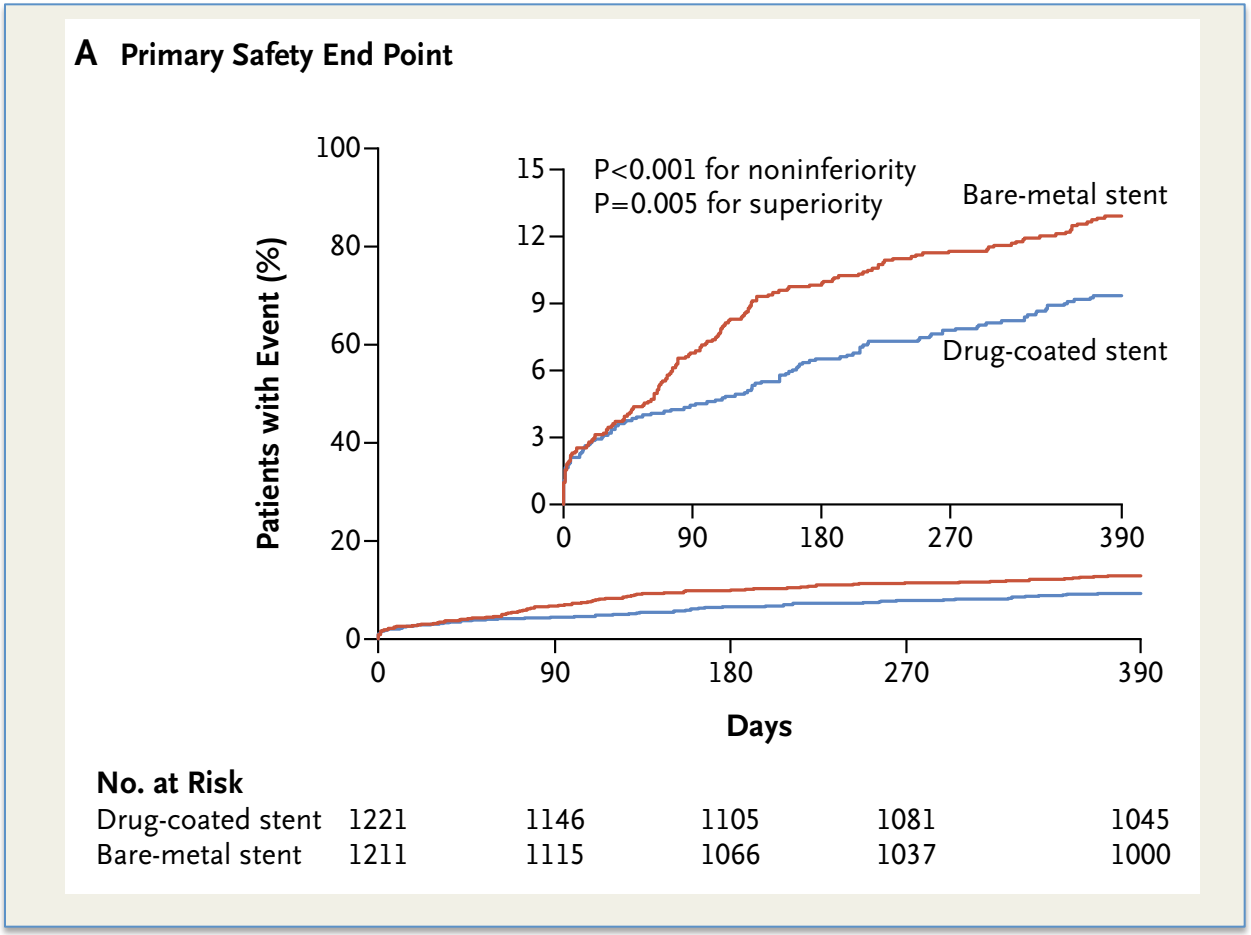
DAPT 1 mois: Stent nu vs Stent biolimus

- *Parmi des patients à haut risque hémorragique qui bénéficient d'une angioplastie coronaire. Un stent au biolimus est supérieur à un Stent nu lorsqu'une bithérapie est utilisée* ***pendant 1 mois****.*



Urban P et al. LEADERS FREE. N Engl J Med 2015
Polymer-free drug-coated coronary stents in patients at high bleeding risk.

Le traitement court se solde par .....un taux d'évènements très très élevé

Table 2. Primary and Secondary End Points.*

End Point	Drug-Coated Stent (N = 1221)	Bare-Metal Stent (N = 1211)	Hazard Ratio (95% CI)	P Value
	no. of events (% of patients)			
Primary safety end point: cardiac death, myocardial infarction, or stent thrombosis	112 (9.4)	154 (12.9)	0.71 (0.56–0.91)	0.005†

9,4% /an

2% de Thrombose de stent

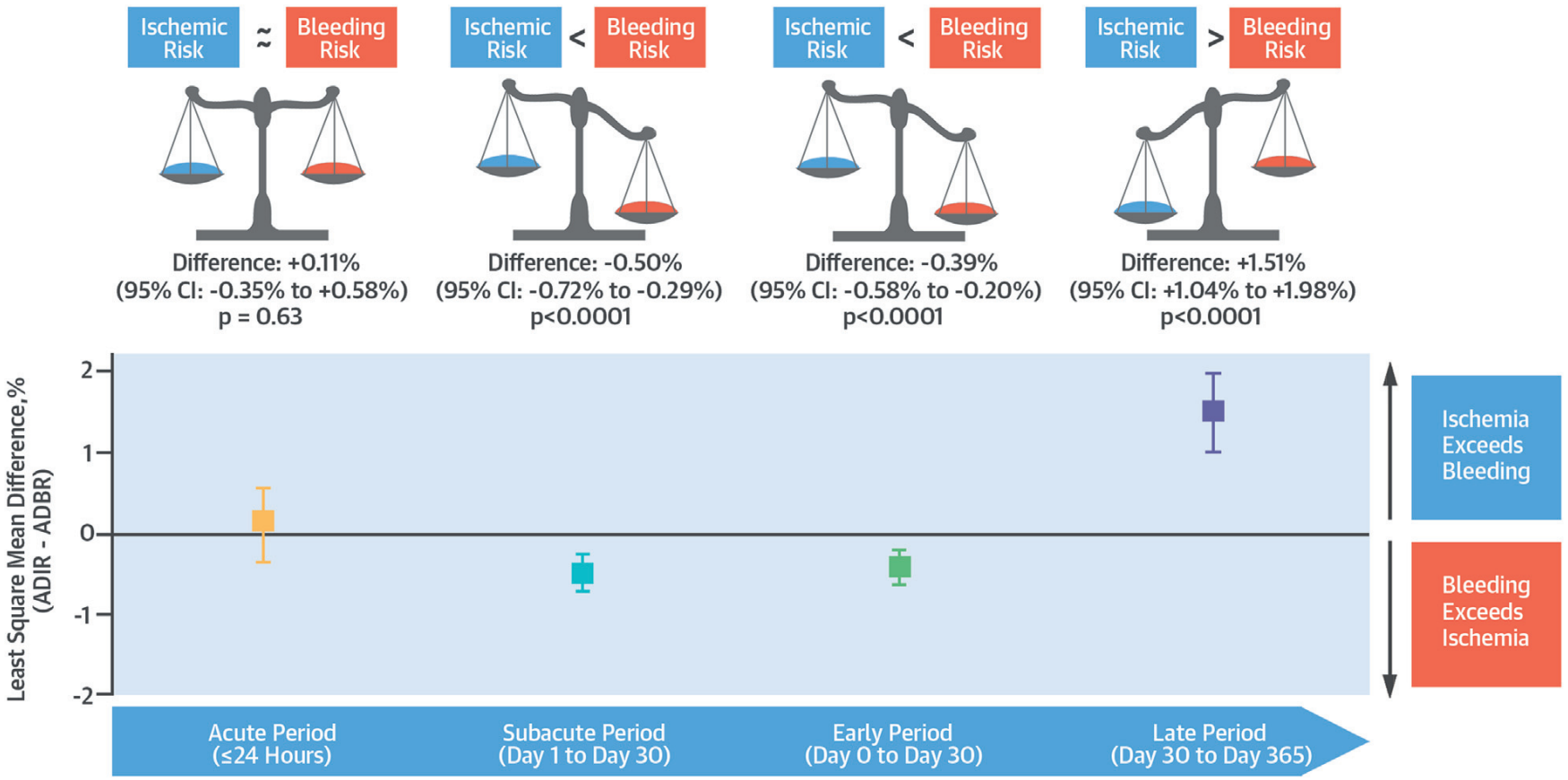
7.2% de saignements graves (BARC 3-5)

Attention aux trt AAP trop court

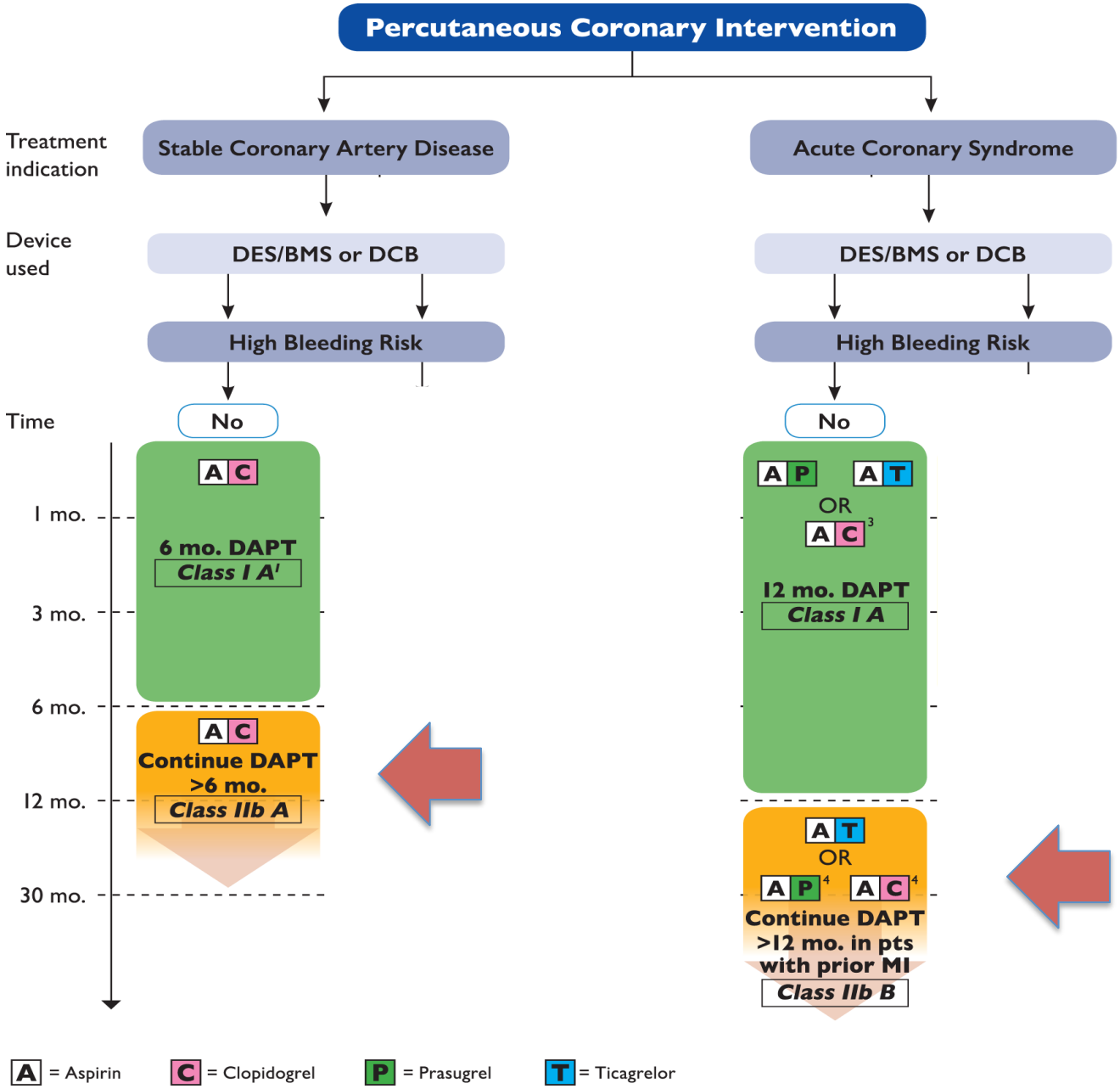
- **Malgré la totale conscience de la gravité d'un saignement chez le coronarien…..**
- **Ne pas galvauder la solution d'un raccourcissement exagéré d'une bithérapie**
- **Les saignements surviennent surtout en début de trt. Un arrêt à 1 mois épargnera moins de saignements qu'il ne générera de complications thrombotiques.**

J1 J30 > J30

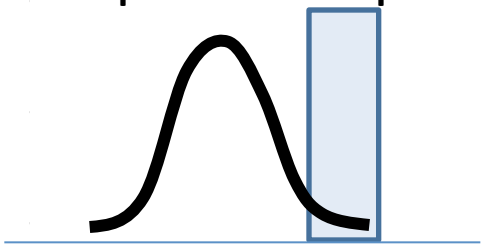
CENTRAL ILLUSTRATION **Temporal Differences in Ischemic and Bleeding Rates After Primary PCI for STEMI**



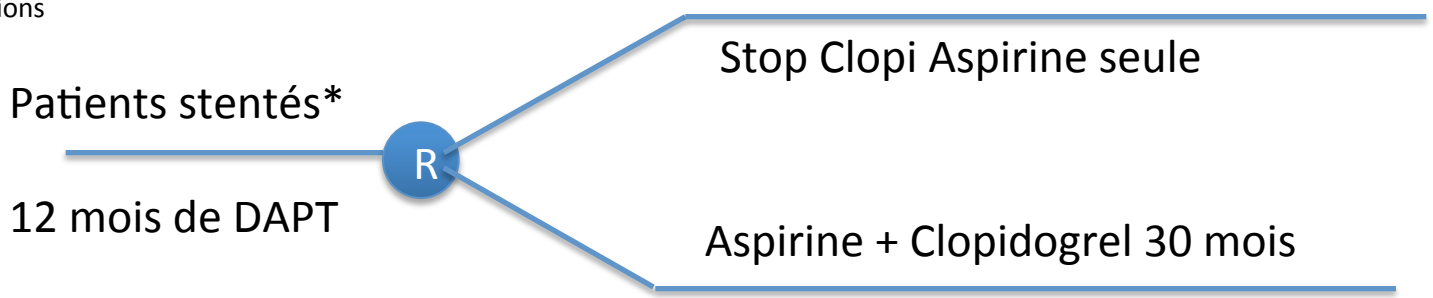
Giustino, G. et al. J Am Coll Cardiol. 2017;70(15):1846-57.



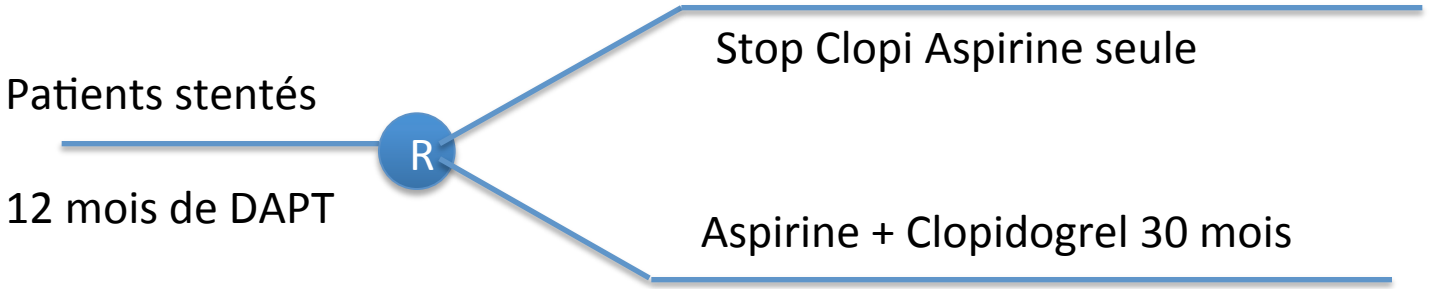
Patient à très haut risque thrombotique



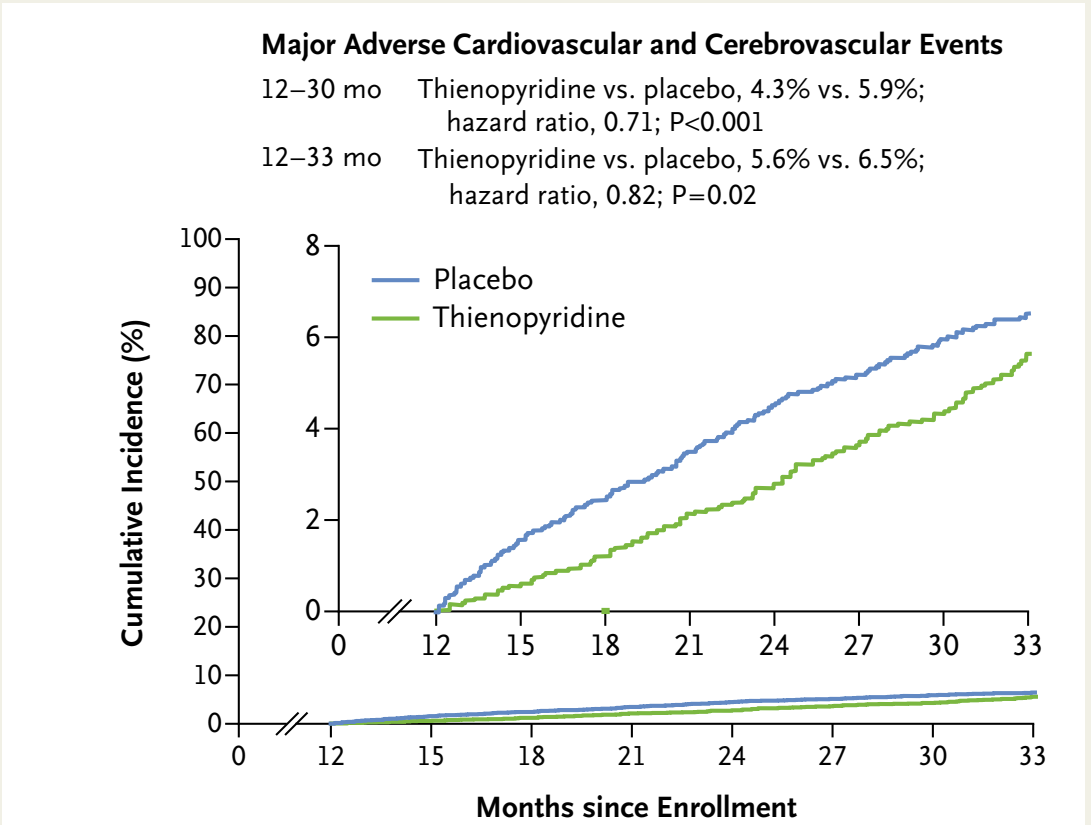
*Toutes situations



Mauri L et al. DAPT Study. N Engl J Med 2014 Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents.



29% de Réduction des MACES



Mauri L et al. DAPT Study. N Engl J Med 2014 Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents.

Le bénéfice dans DAPT : pas seulement sur la thrombose de stent

Table 2. Stent Thrombosis and Major Adverse Cardiovascular and Cerebrovascular Events.*

Outcome	Continued Thienopyridine (N = 5020)	Placebo (N = 4941)	Hazard Ratio, Thienopyridine vs. Placebo (95% CI)†	P Value†
	no. of patients (%)			
Stent thrombosis‡	19 (0.4)	65 (1.4)	0.29 (0.17–0.48)	<0.001
Definite	15 (0.3)	58 (1.2)	0.26 (0.14–0.45)	<0.001
Probable	5 (0.1)	7 (0.1)	0.71 (0.22–2.23)	0.55
Major adverse cardiovascular and cerebrovascular events§	211 (4.3)	285 (5.9)	0.71 (0.59–0.85)	<0.001
Death	98 (2.0)	74 (1.5)	1.36 (1.00–1.85)	0.05
Cardiac	45 (0.9)	47 (1.0)	1.00 (0.66–1.52)	0.98
Vascular	5 (0.1)	5 (0.1)	0.98 (0.28–3.39)	0.98
Noncardiovascular	48 (1.0)	22 (0.5)	2.23 (1.32–3.78)	0.002
Myocardial infarction	99 (2.1)	198 (4.1)	0.47 (0.37–0.61)	<0.001
Stroke	37 (0.8)	43 (0.9)	0.80 (0.51–1.25)	0.32
Ischemic	24 (0.5)	34 (0.7)	0.68 (0.40–1.17)	0.16
Hemorrhagic	13 (0.3)	9 (0.2)	1.20 (0.50–2.91)	0.68
Type uncertain	0	1 (<0.1)	—	0.32

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LA PROLONGATION DU CLOPIDOGREL AU DELA DE 12 MOIS EVITE DES THROMBOSES TARDIVES DE STENT MAIS AUSSI DE NOUVEAUX EVENEMENTS SUR D'AUTRES SITES

Mauri L et al. DAPT Study. N Engl J Med 2014 Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents.

DAPT : les mauvais résultats

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LA PROLONGATION DU CLOPIDOGREL AU DELA DE 12 MOIS MULTIPLIE PAR 2 LES SAIGNEMENTS, N'EVITE PAS LES AVC ET S'ACCOMPAGNE D'UN MAUVAIS SIGNAL SUR LA MORTALITE

Mauri L et al. DAPT Study. N Engl J Med 2014 Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents.

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

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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

Pourquoi une reco de grade IIb ?

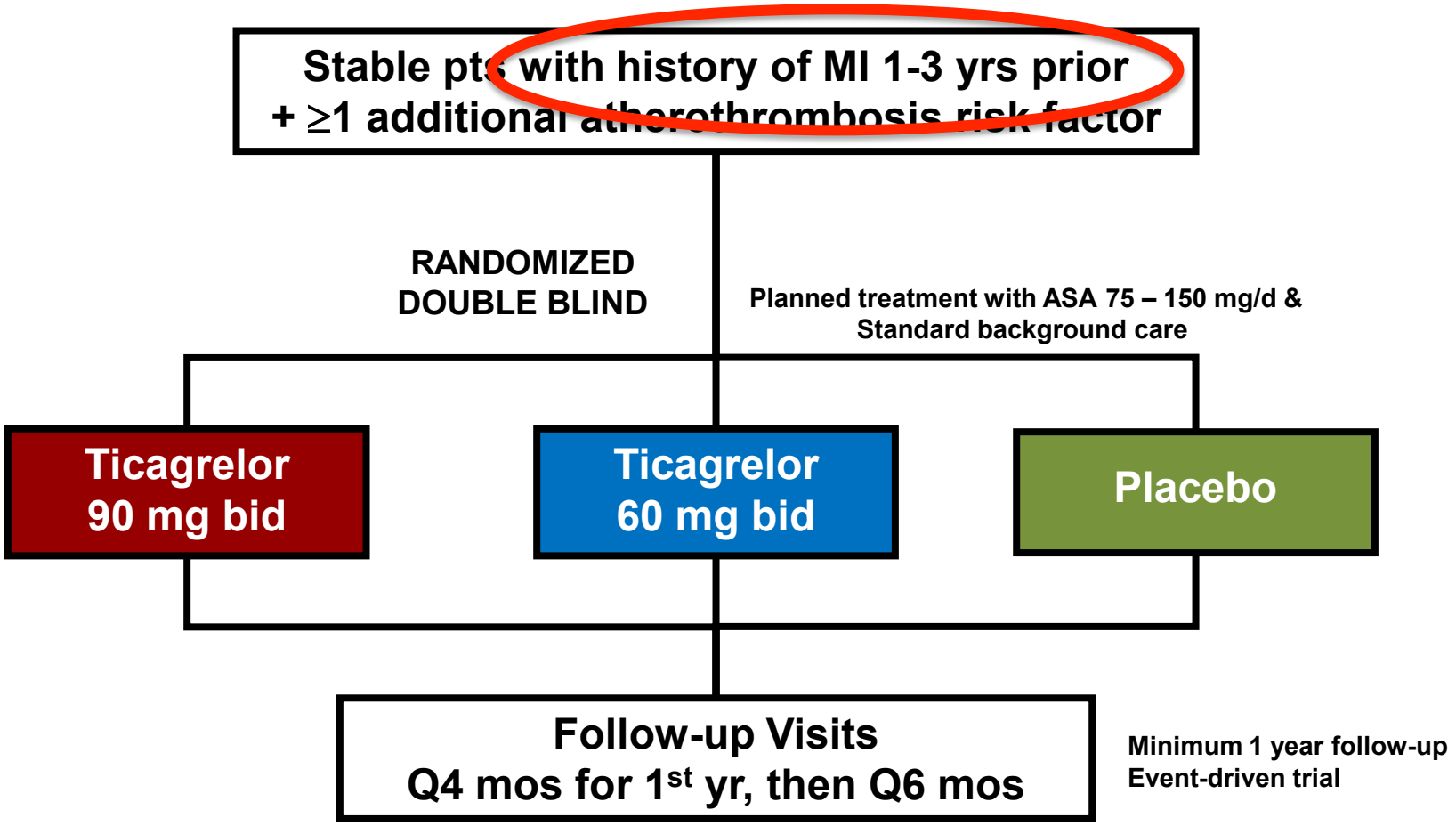
- D'autres essais n'ont pas retrouvé la même chose

- DAPT n'a pas inclus le nb de patients attendus

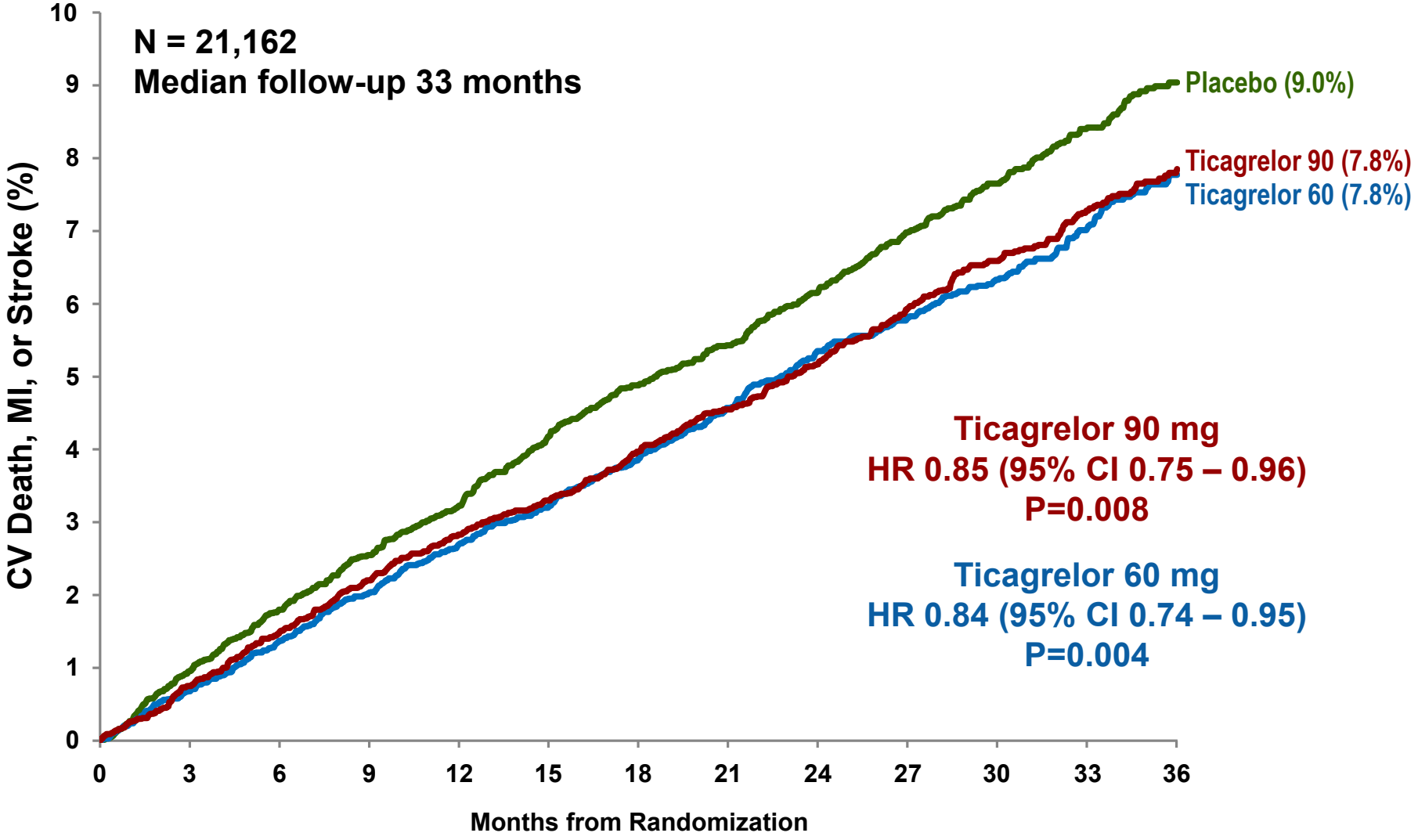
- …..Taux de mortalité plus élevé dans le bras qui continue la bithérapie au dela d'un an

….Il y a peut être mieux à faire…..

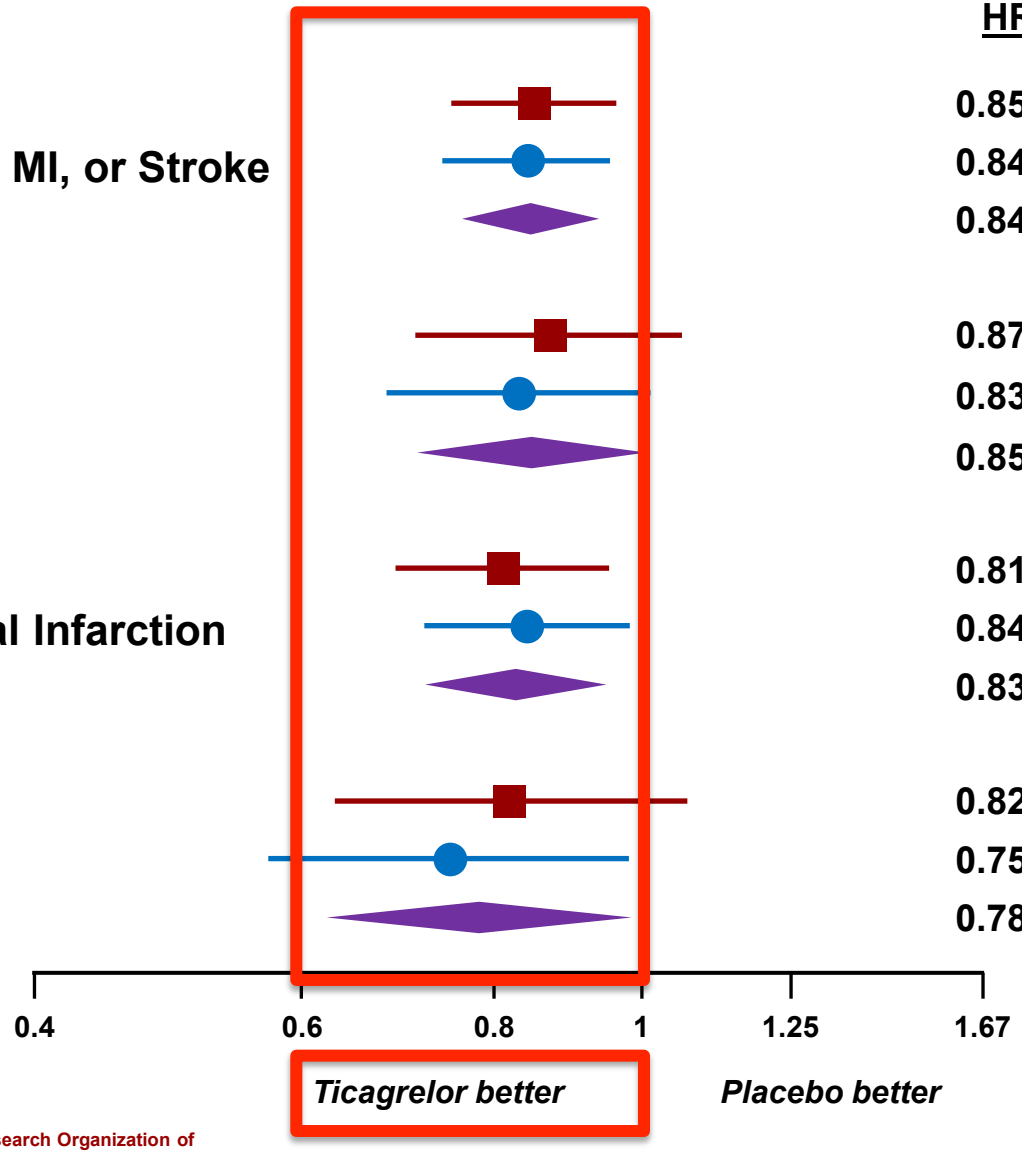
Trial Design



Primary Endpoint



Components of Primary Endpoint



Endpoint	HR (95% CI)	P value
CV Death, MI, or Stroke (1558 events)	0.85 (0.75-0.96)	0.008
	0.84 (0.74-0.95)	0.004
	0.84 (0.76-0.94)	0.001
CV Death (566 events)	0.87 (0.71-1.06)	0.15
	0.83 (0.68-1.01)	0.07
	0.85 (0.71-1.00)	0.06
Myocardial Infarction (898 events)	0.81 (0.69-0.95)	0.01
	0.84 (0.72-0.98)	0.03
	0.83 (0.72-0.95)	0.005
Stroke (313 events)	0.82 (0.63-1.07)	0.14
	0.75 (0.57-0.98)	0.03
	0.78 (0.62-0.98)	0.03

Ticagrelor 90 mg
Ticagrelor 60 mg
Pooled

Other Adverse Events

Adverse Event	Ticagrelor 90 mg bid (N=6988)	Ticagrelor 60 mg bid (N=6958)	Placebo (N=6996)	Ticagrelor 90 vs Placebo p-value	Ticagrelor 60 vs Placebo p-value
	3-yr KM rate (%)				
Dyspnea AE	18.9	15.8	6.4	P<0.001	P<0.001
Leading to study drug d/c	6.5	4.6	0.8	P<0.001	P<0.001
Severe	1.2	0.6	0.2	P<0.001	P<0.001
Bradyarrhythmia	2.0	2.3	2.0	P=0.31	P=0.10
Gout	2.3	2.0	1.5	P<0.001	P=0.01

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

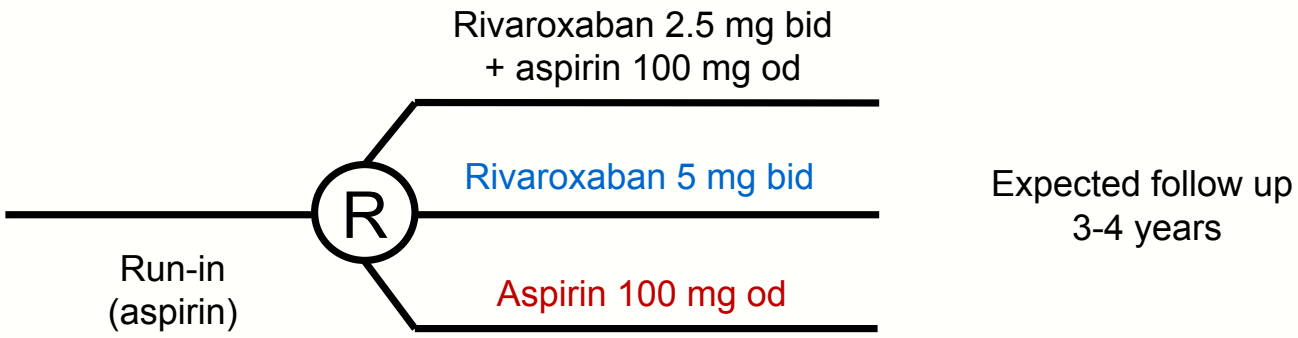
ESC European Society of Cardiology

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

Les reco de 2017 sont déjà dépassées ….

COMPASS design

Stable CAD or PAD
2,200 with a primary outcome event



Primary: CV death, stroke , MI

	Riva +Asp (n=9152)	Asp (n=9126)		
	%	%	HR (95% CI)	p
CV death, stroke, MI	**4.1%**	**5.4%**	**0.76 (0.66-0.86)**	**<0.0001**

Compass: NEJM 2017

Primary components

	Riva +Asp (n=9152)	Asp (n=9126)		
	%	%	HR (95% CI)	p
CV death	**1.7%**	**2.2%**	**0.78 (0.64-0.96)**	**<0.02**
Stroke	**0.9%**	**1.6%**	**0.58 (0.44-0.76)**	**<0.0001**
MI	**1.9%**	**2.2%**	**0.86 (0.70-1.05)**	**0.14**
Death	**3.4%**	**4.1%**	**0.82 (0.71-0.96)**	**0.01**

Primary components

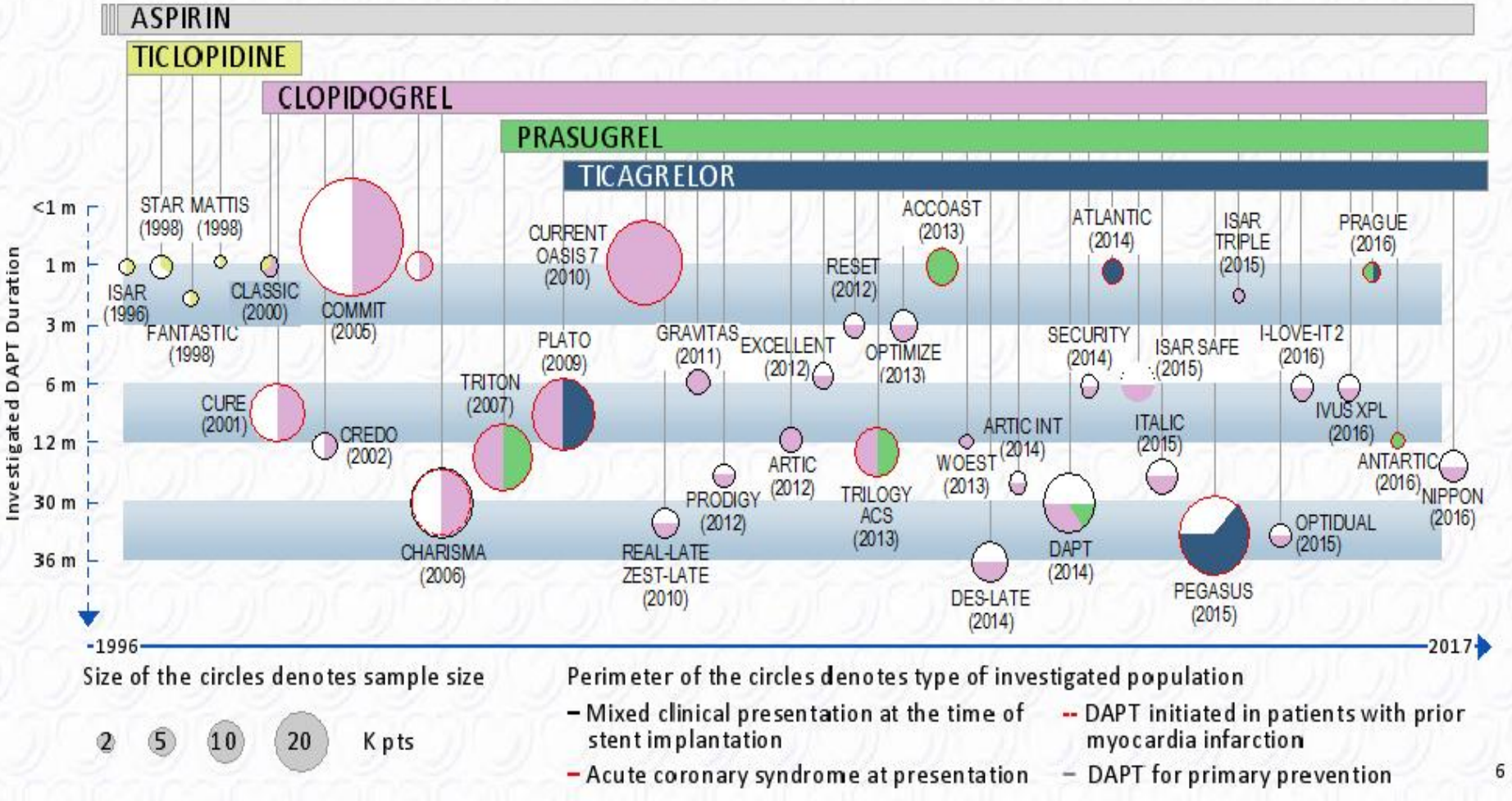
	Riva +Asp (n=9152)	A[illegible]		
			0.58 (0.44-0.76)	<0.0001
	1.9%	**2.2%**	**0.86 (0.70-1.05)**	**0.14**
Death	**3.4%**	**4.1%**	**0.82 (0.71-0.96)**	**0.01**

UNE PETITE DOSE DE RIVAROXABAN EN SUS DE L'ASPIRINE CHEZ UN CORONARIEN STABLE OU UN ARTERITIQUE

- **REDUIT LES MACE**
- **REDUIT LES AVC**
- **REDUIT LA MORTALITE**
- **AU PRIX D'UN SUR-RISQUE HEMORRAGIQUE**

History of dual antiplatelet therapy (DAPT) in patients with coronary artery disease

ESC European Society of Cardiology



Size of the circles denotes sample size

2 5 10 20 K pts

Perimeter of the circles denotes type of investigated population

- Mixed clinical presentation at the time of stent implantation
- Acute coronary syndrome at presentation
- DAPT initiated in patients with prior myocardia infarction
- DAPT for primary prevention

1 700 000 Patients inclus dans ces études

Recommendations on $P2Y_{12}$ inhibitor selection and timing	Class[a]	Level[b]
In patients with ACS, ticagrelor (180 mg loading dose, 90 mg *b.i.d.*) 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 contraindications.[c]	I	B
In patients with ACS undergoing PCI, prasugrel (60 mg loading dose, 10 mg *o.d.*) 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 contraindications.[c]	I	B
Pre-treatment with a $P2Y_{12}$ inhibitor is generally recommended in patients in whom coronary anatomy is known and the decision to proceed to PCI is made, as well as in patients with STEMI.	I	A
Clopidogrel (600 mg loading dose, 75 mg *o.d.*) 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 aged ≤75, 75 mg *o.d.*) is recommended on top of aspirin in STEMI patients receiving thrombolysis.	I	A
In NSTE-ACS patients in whom coronary anatomy is not known, it is not recommended to administer prasugrel.	III	B
Measures to minimize bleeding while on dual antiplatelet therapy		
Radial over femoral access is recommended for coronary angiography and PCI if performed by an expert radial operator.	I	A
In patients treated with DAPT, a daily aspirin dose of 75 - 100 mg is recommended.	I	A
A PPI in combination with DAPT is recommended.[d]	I	B
Routine platelet function testing to adjust antiplatelet therapy before or after elective stenting is not recommended.	III	A
Switching between oral $P2Y_{12}$ inhibitors		
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 contraindications to ticagrelor exist.[c]	I	B
Dual antiplatelet therapy duration in patients with acute coronary syndrome treated with percutaneous coronary intervention		
In patients with ACS treated with coronary stent implantation, DAPT with a $P2Y_{12}$ inhibitor on top of aspirin is recommended for 12 months unless there are contraindications such as excessive risk of bleeding (e.g. PRECISE-DAPT ≥25).	I	A
Dual antiplatelet therapy duration in patients with acute coronary syndrome undergoing medical therapy management		
In patients with ACS who are managed with medical therapy alone and treated with DAPT, it is recommended to continue $P2Y_{12}$ inhibitor therapy (either ticagrelor or clopidogrel) for 12 months.	I	A
Ticagrelor is recommended over clopidogrel, unless the bleeding risk outweighs the potential ischaemic benefit.	I	B
Prasugrel is not recommended in medically managed ACS patients.	III	B
Dual antiplatelet therapy in patients undergoing elective cardiac and non-cardiac surgery		
It is recommended to continue aspirin perioperatively if the bleeding risk allows, and to resume the recommended antiplatelet therapy as soon as possible post-operatively.	I	B
It is not recommended to discontinue DAPT within the first month of treatment in patients undergoing elective non-cardiac surgery.	III	B
Gender considerations		
Similar type and duration of DAPT are recommended in male and female patients.	I	A

Faut-il pré-traiter les Angioplasties programmées des Angors stables ?

$P2Y_{12}$ inhibitor selection and timing *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
Pre-treatment with a $P2Y_{12}$ inhibitor is generally recommended in patients in whom coronary anatomy is known and the decision to proceed to PCI is made as well as in patients with STEMI.	I	A
In patients with NSTE-ACS undergoing invasive management, ticagrelor administration (180 mg loading dose, 90 mg twice daily), or clopidogrel (600 mg loading dose, 75 mg daily dose) if ticagrelor is not an option, should be considered as soon as the diagnosis is established.	IIa	C
In patients with stable CAD pre-treatment with clopidogrel may be considered if the probability of PCI is high.	IIb	C

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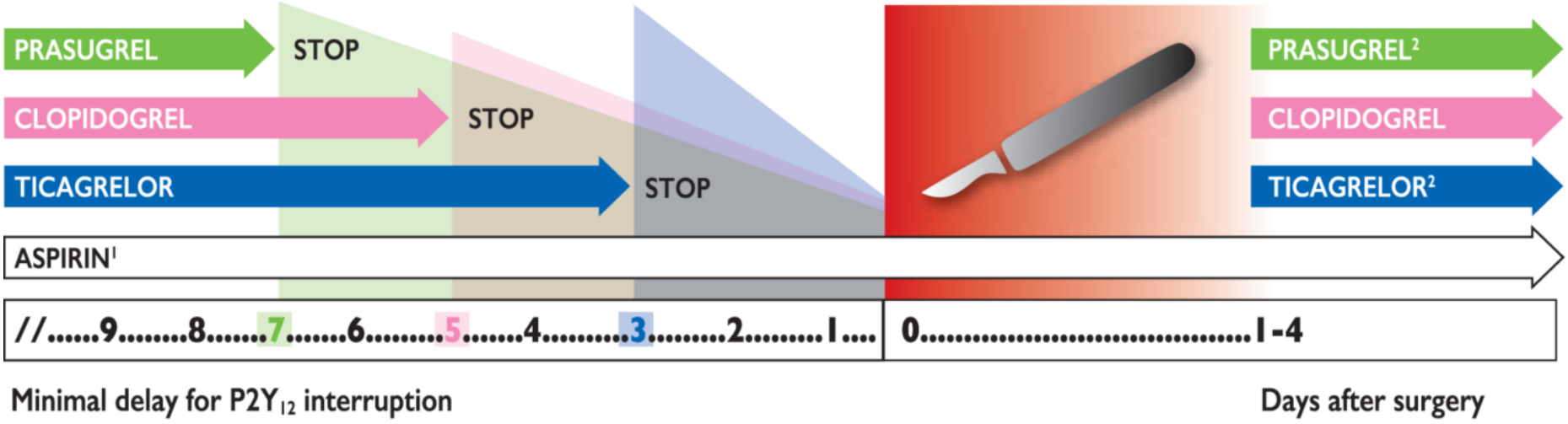
(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Quid des Arrêts des AAP pour un geste hémorragique ?



= *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.

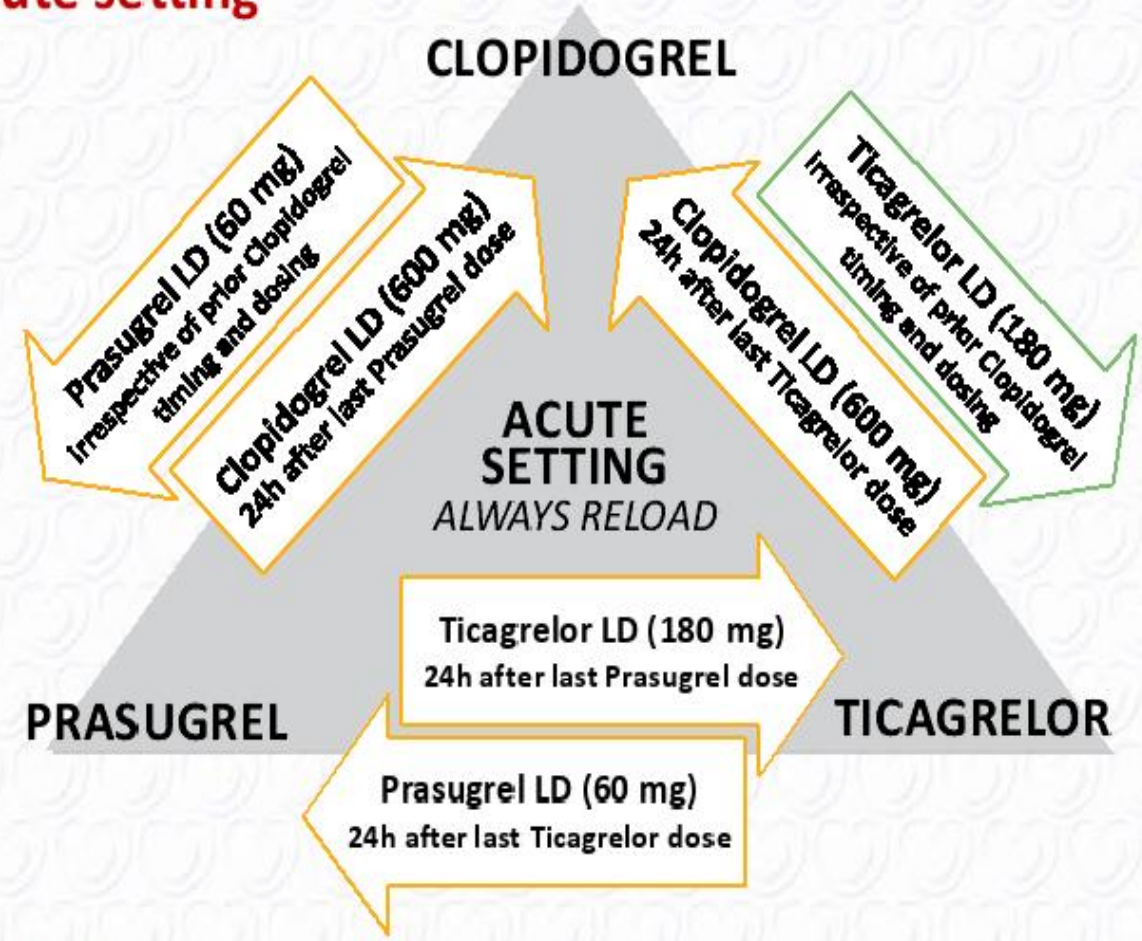
2 In patients not requiring OAC.

Il est recommandé de ne pas arrêter la bithérapie durant le 1er mois chez les sujets qui vont à une chirurgie

III

Les switch ?

Algorithm for switching between oral $P2Y_{12}$ inhibitors in the acute setting



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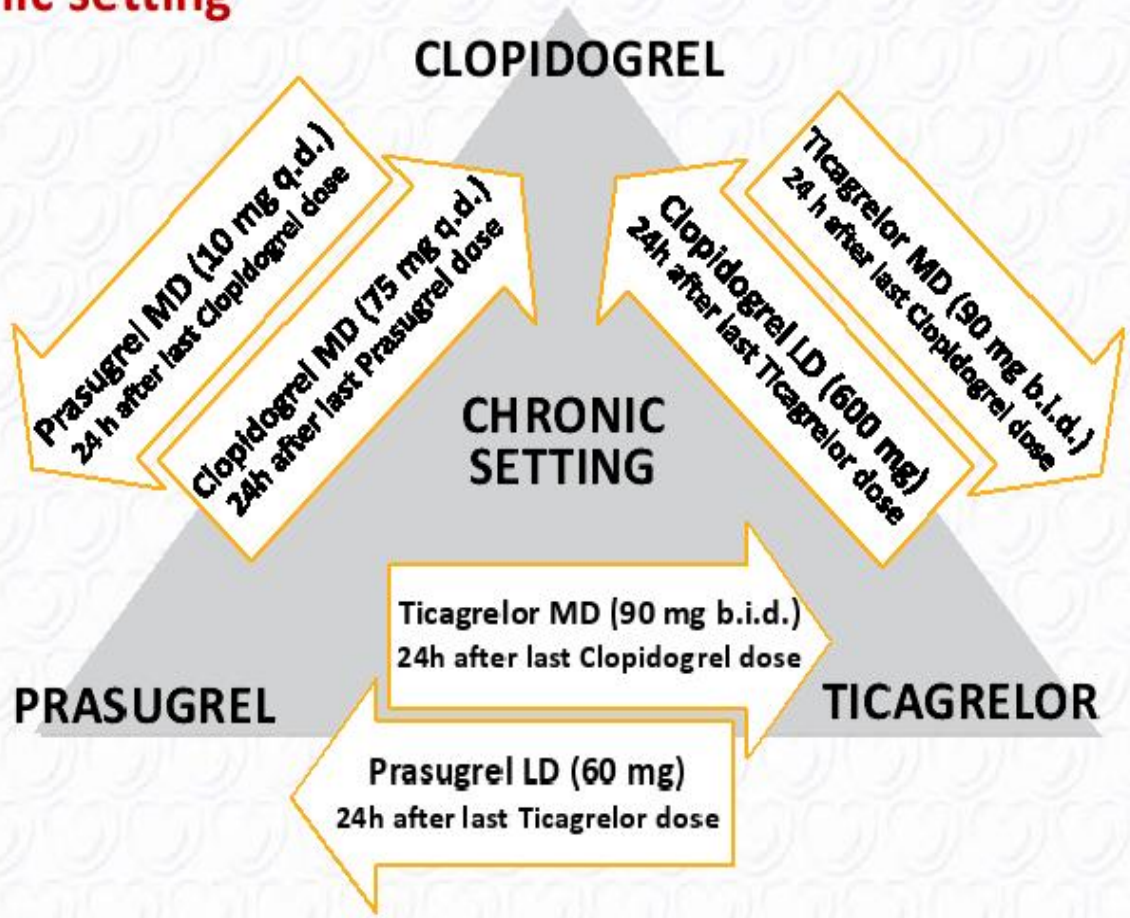
Algorithm for switching between oral $P2Y_{12}$ inhibitors in the chronic setting



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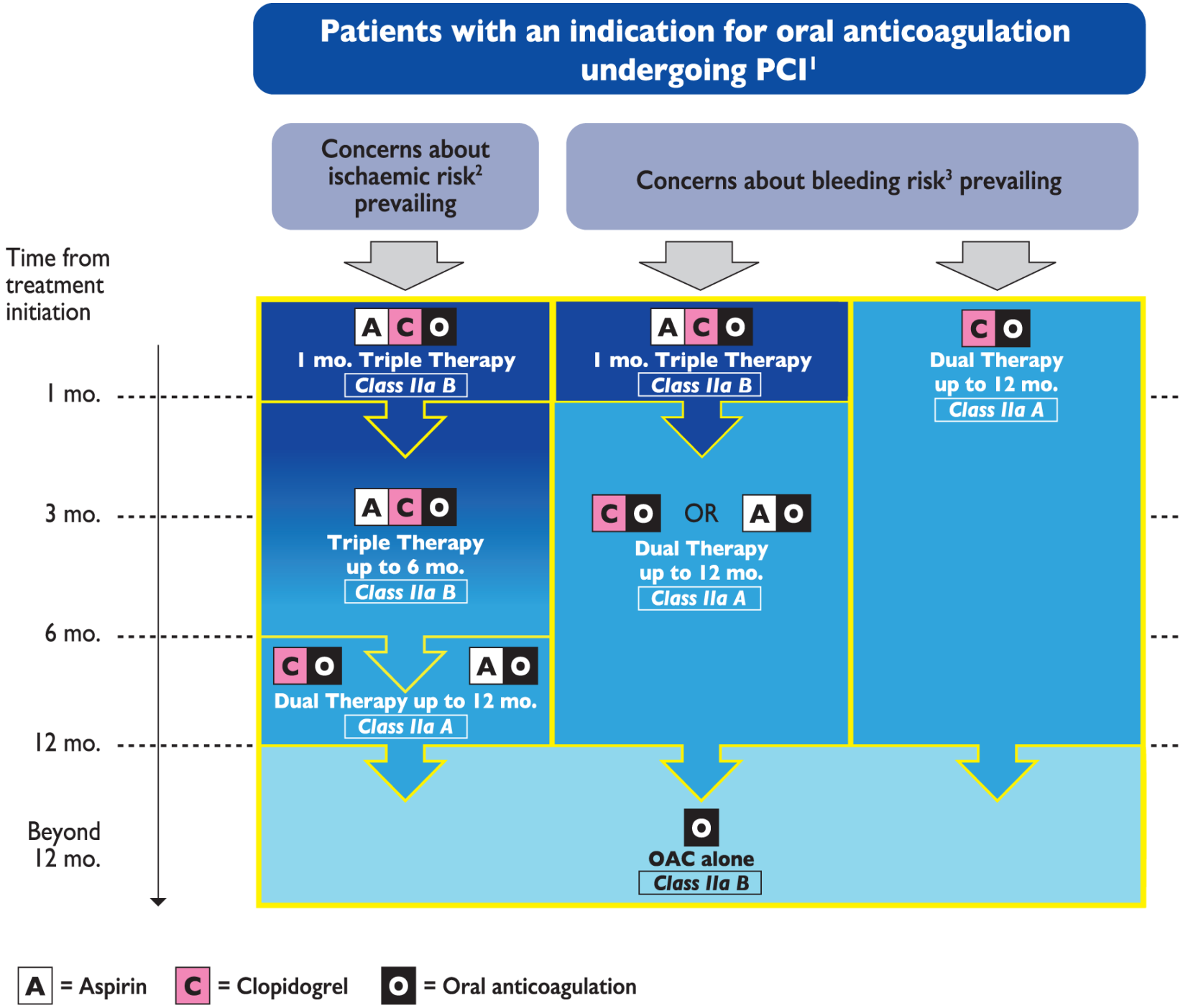
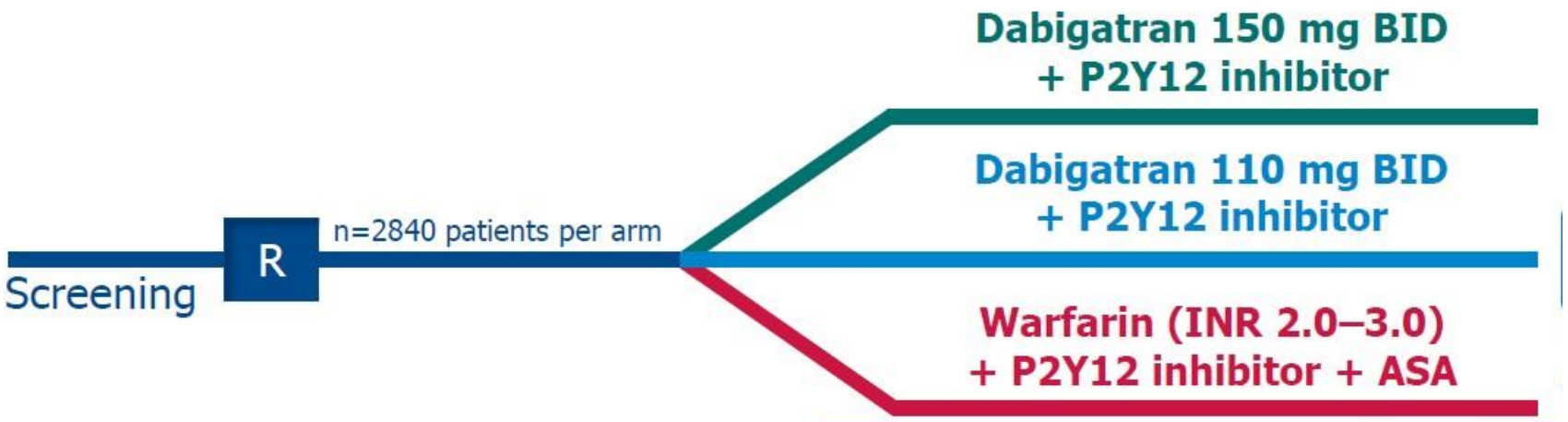
(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

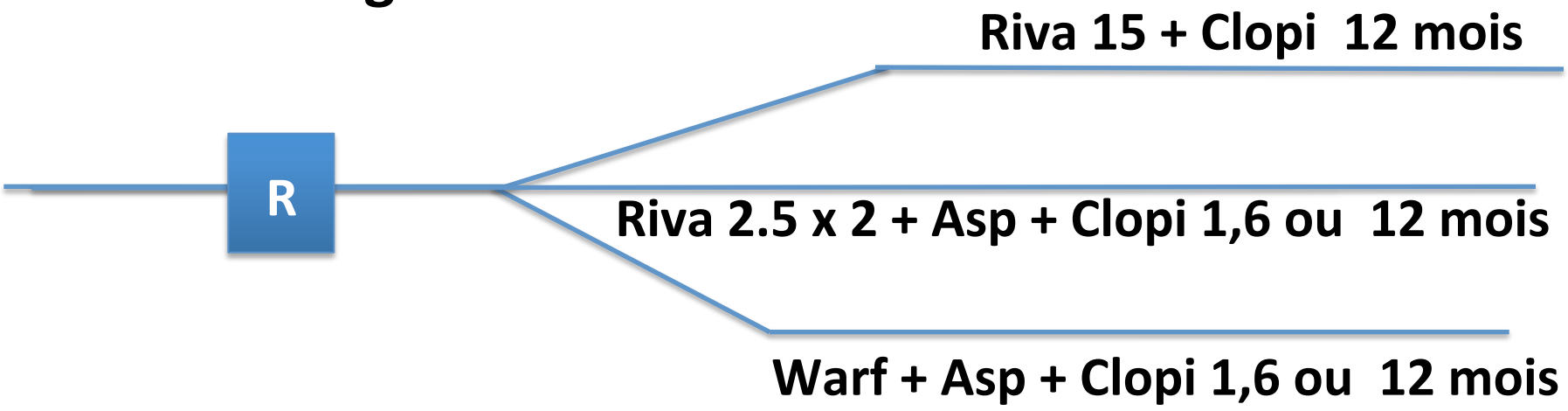
Quid chez les coronariens en FA ?


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
A C O
Triple Therapy up to 6 mo.
Class IIa B
C O OR A O
Dual Therapy up to 12 mo.
Class IIa A
C O
A O
Dual Therapy up to 12 mo.
Class IIa A
O
OAC alone
Class IIa B
A = Aspirin
C = Clopidogrel
O = Oral anticoagulation

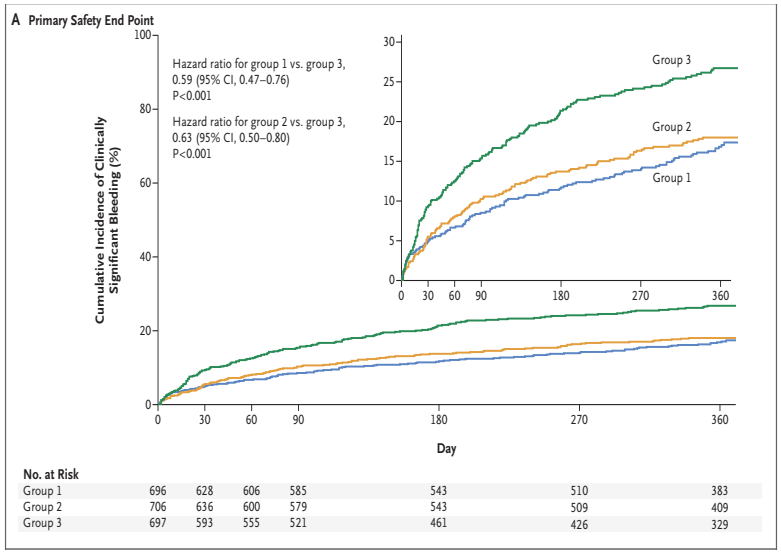
RE-DUAL PCI design



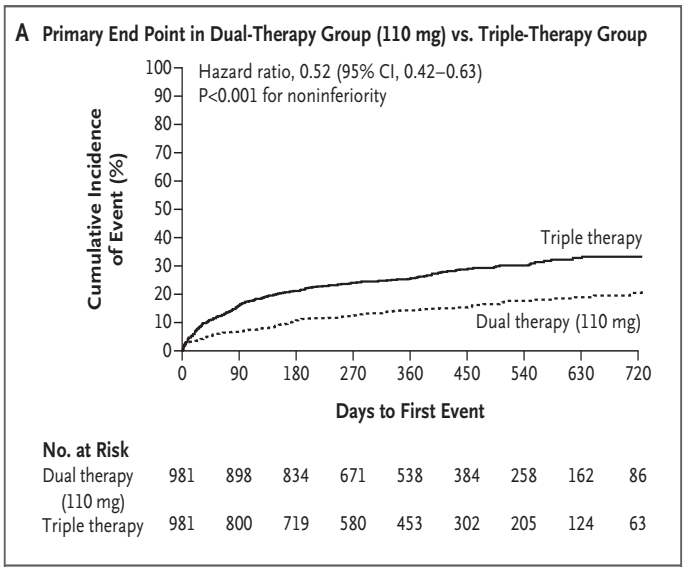
PIONEER Design



PIONEER :RRR = 41%



DUAL PCI: RRR = 48%

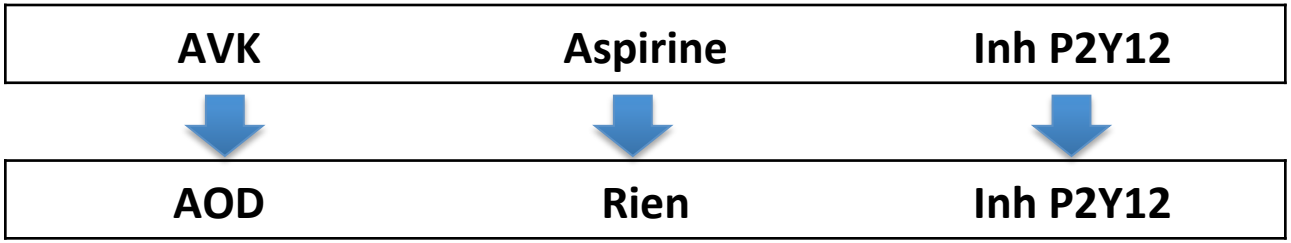


Chez le patient Coronarien stenté en FA:

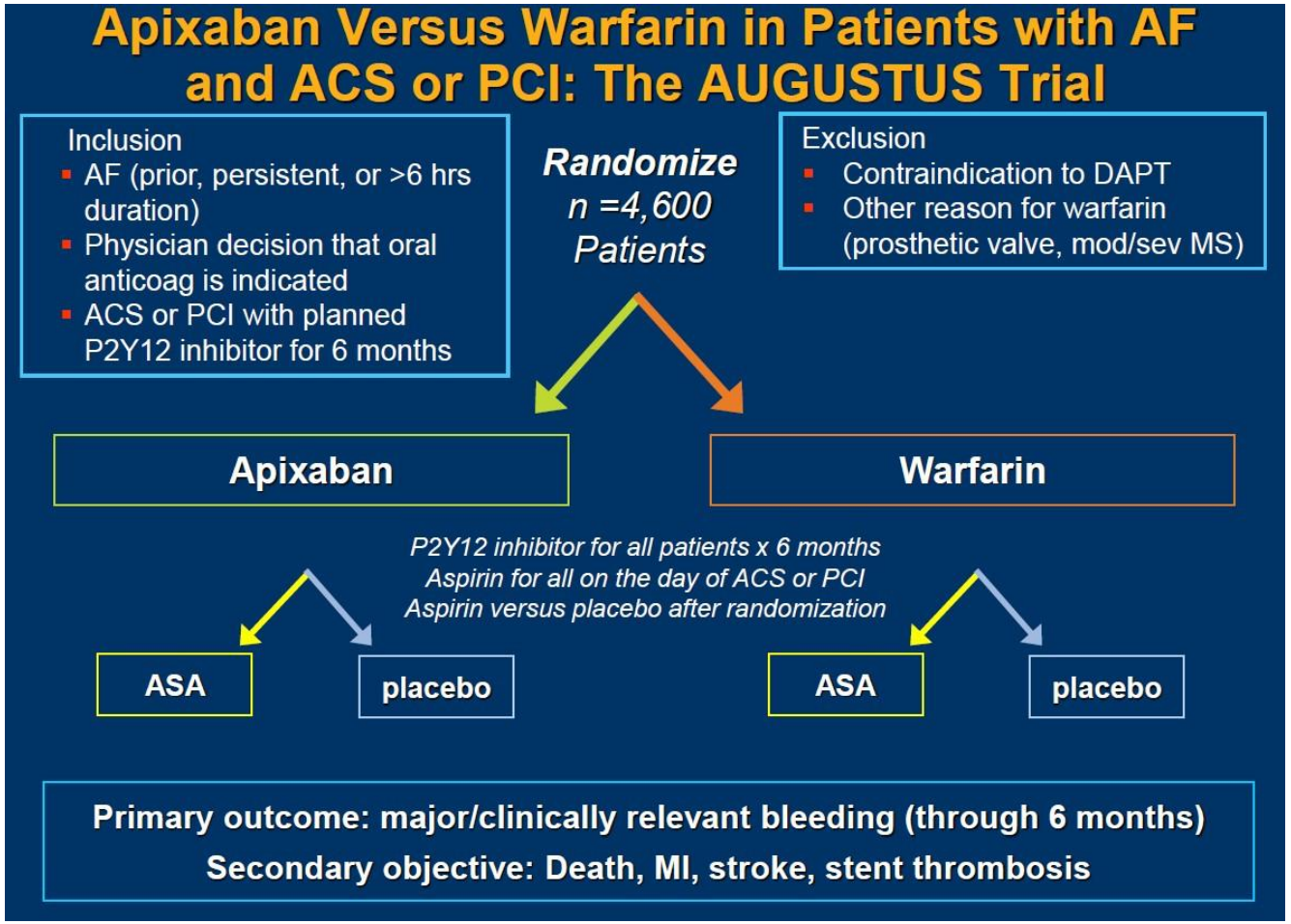
La fin de la trithérapie

AVK + Clopi + Aspirine

	Protocole	Saignements	MACE
PIONEER	Riva 15 + Clopi	- 41%	NS
DUAL PCI	Dabi 110 + inh P2Y12	- 48%	NS
AUGUSTUS	Apixaban Vs Warfarin	En cours	/
EVOLVE-AF	Idem DUAL PCI	En cours	/



AUGUSTUS


Apixaban Versus Warfarin in Patients with AF and ACS or PCI: The AUGUSTUS Trial
Inclusion
AF (prior, persistent, or >6 hrs duration)
Physician decision that oral anticoag is indicated
ACS or PCI with planned P2Y12 inhibitor for 6 months
Randomize
n =4,600
Patients
Exclusion
Contraindication to DAPT
Other reason for warfarin (prosthetic valve, mod/sev MS)
Apixaban
Warfarin
P2Y12 inhibitor for all patients x 6 months
Aspirin for all on the day of ACS or PCI
Aspirin versus placebo after randomization
ASA
placebo
ASA
placebo
Primary outcome: major/clinically relevant bleeding (through 6 months)
Secondary objective: Death, MI, stroke, stent thrombosis

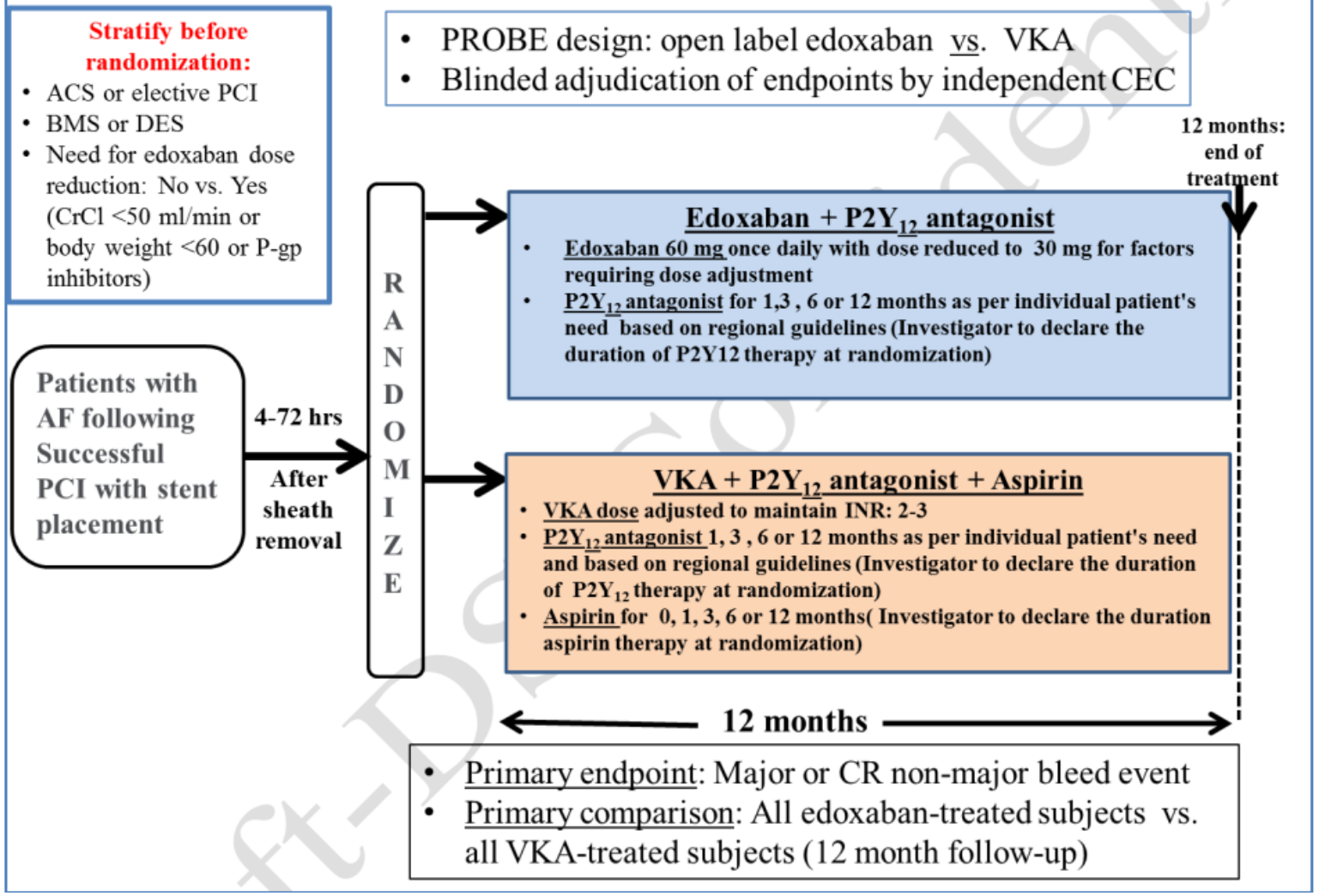
EVOLVE-AF Trial

QUINTILES

Duke Clinical Research Institute
DUKE UNIVERSITY MEDICAL CENTER

CARDIALYSIS
Clinical Trial Management - Core Laboratories

Figure 1. Schematic presentation of the study design:



Les arguments pour un AOD seul après 1 an ?

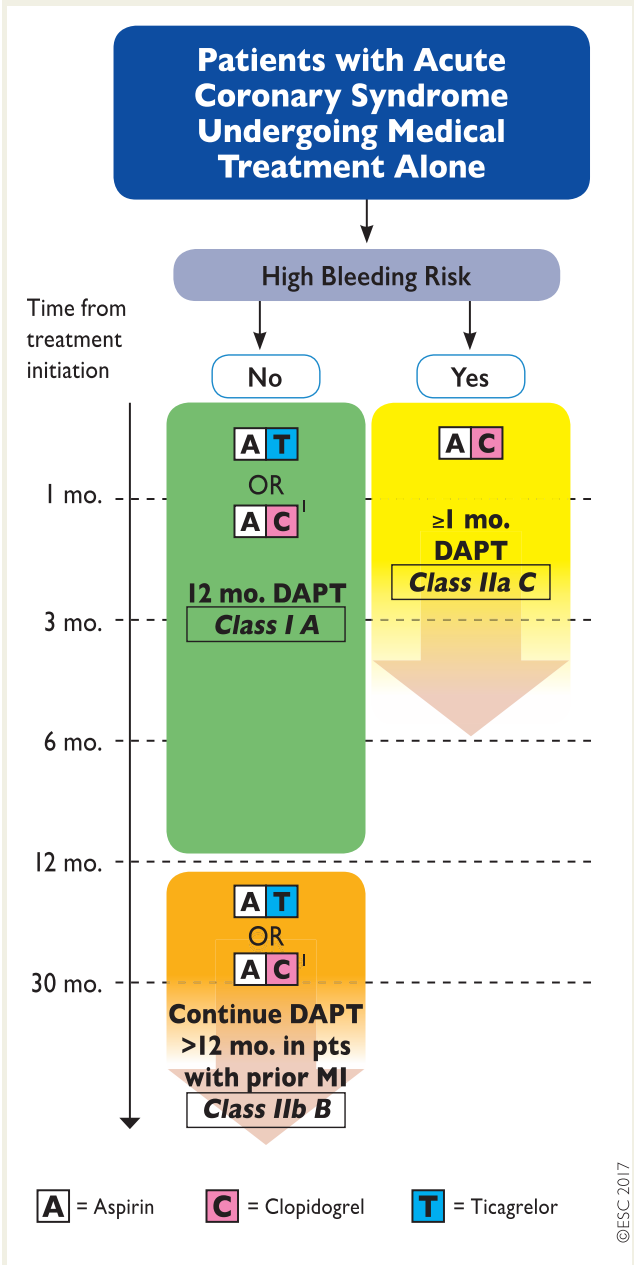
7.3 Cessation of all antiplatelet agents

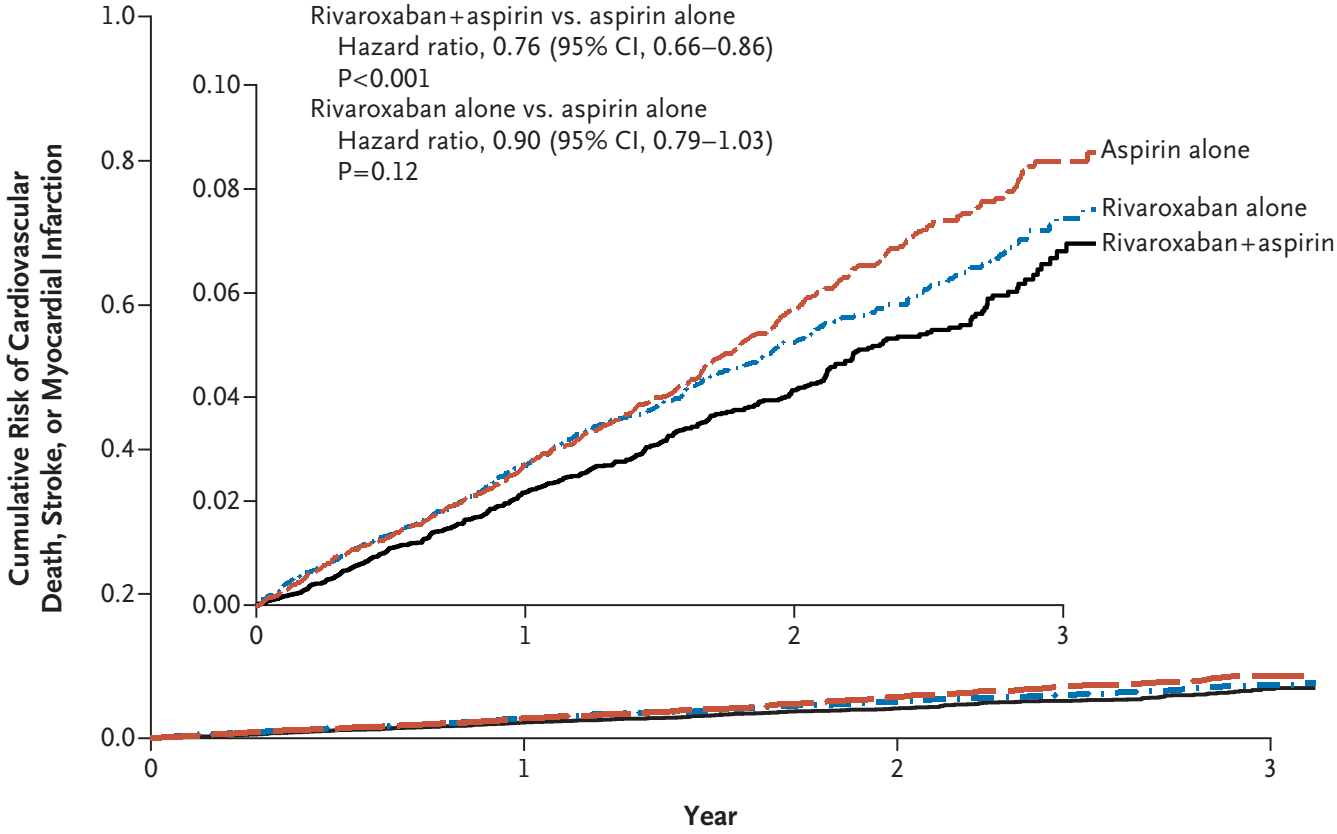
Data on the timing of cessation of any antiplatelet ag… …s requiring chronic OAC are scarce. In stabilized event-fr… …ation of an… antiplatelet agent at 1 year after stenti… …is patient n… based on studies demonstratin… …superior to… OAC + aspirin may not l… …t associated… therapy with OA… …et agent (aspi… consid… …patients at ve… …nts with mech…

Chez les patients stables après 1 an sous AVK: l'arrêt de l'aspirine est conseillé

L'association ACO + AAP (Asp oi Clopi) peut être considéré au dela d'un an chez les très haut risque /les porteurs de valves mécaniques ou les polyartériels.

Trt aprés SCA sans angioplastie





No. at Risk				
Aspirin alone	9126	7808	3860	669
Rivaroxaban alone	9117	7824	3862	670
Rivaroxaban+aspirin	9152	7904	3912	658

Figure 1. Cumulative Incidence of the Primary Efficacy Outcome among Participants Receiving Rivaroxaban plus Aspirin, Rivaroxaban Alone, or Aspirin Alone.

Peut-on arrêter l’AAP et Quand

7.3 Cessation of all antiplatelet agents

Data on the timing of cessation of any antiplatelet agents in stented patients requiring chronic OAC are scarce. In stabilized event-free patients, discontinuation of any antiplatelet agent at 1 year after stenting is encouraged in this patient population based on studies demonstrating that OACs alone are superior to aspirin post-ACS, and OAC + aspirin may not be more protective but associated with excess bleeding.[198] Dual therapy with OAC and one antiplatelet agent (aspirin or clopidogrel) may be considered beyond 1 year in patients at very high risk of coronary events as defined in *Table 5*[34] and in patients with mechanical prosthesis and atherosclerotic disease.

7.4 Type of anticoagulants

PIONEER AF-PCI is the only randomized study comparing VKAs and NOACs in patients with AF undergoing PCI for ACS or for stable CAD (i.e. patients who have an indication to receive DAPT).[191] However, in this study, two non-approved rivaroxaban regimens for AF patients were tested and a low (i.e. 15 mg *q.d.*) or very low (i.e. 2.5 mg *b.i.d.*) rivaroxaban dose in combination with a single $P2Y_{12}$ inhibitor or DAPT was compared to VKA plus DAPT, respectively. The study was underpowered for ischaemic endpoints. Therefore, no conclusion can be made on the advantages and limitations of each OAC as compared to others. However, there was an excess of stroke events in the 2.5 mg *b.i.d.* rivaroxaban arm in combination with 6-month DAPT as compared to VKA and 6-month DAPT (6 vs. 0 events; $P = 0.02$).

In the four phase III NOAC AF trials, no interactions were demonstrated between treatment effect and outcome according to prior coronary status (ACS vs. no ACS), and it is likely that the benefit of NOAC over VKA is preserved in CAD patients with AF.[199–202] At least, this was the case among patients exposed to antiplatelet therapy. There is no strong evidence for choosing one NOAC over another. Dabigatran is the only NOAC that has been tested in a phase III trial at reduced daily regimen (i.e. 110 mg *b.i.d.*) and for which non-inferiority vs. warfarin was shown.[199] Although lower doses of other NOACs (i.e. apixaban 2.5 mg *b.i.d.* or edoxaban 30 mg *o.d.*) might be considered to reduce bleeding risk, these dosages have been evaluated only in a subset of patients in the phase III trials based on prespecified dosing algorithms. Their benefit in stroke prevention in patients with a normal renal function is uncertain. Three ongoing large-scale outcome studies are evaluating combinations of NOACs or VKAs with antiplatelet therapy in AF patients undergoing stent-PCI (NCT02164864, NCT02415400, and NCT02866175). Various dose regimens of NOAC, different types of $P2Y_{12}$ inhibitors, and different exposure times are being evaluated.

$P2Y_{12}$ inhibitor selection and timing *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
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

$P2Y_{12}$ inhibitor selection and timing *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
Ticagrelor or prasugrel on top of aspirin may be considered instead of clopidogrel in stable CAD patients undergoing PCI, taking into account the ischaemic (e.g. high SYNTAX score, prior stent thrombosis, location and number of implanted stents) and bleeding (e.g. according to PRECISE-DAPT) risks.	IIb	C
In NSTE-ACS patients in whom coronary anatomy is not known, it is not recommended to administer prasugrel.	III	B

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(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Switching between oral $P2Y_{12}$ inhibitors

ESC European Society of Cardiology

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

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Plein de bonnes raisons pour arrêter prématurément un essai...

Différence convaincante entre les traitements comparés

Aucune chance d'avoir une différence entre les traitements

Pas d'événement

Nouvelles informations rendant l'essai obsolète

Toxicité trop forte

Recrutement trop lent

Faible qualité des données

Observance au traitement trop faible

Ressources trop faibles ou diminuées

Démotivation

Efficacité du traitement ?
➔ Arrêt pour efficacité

Aucune chance de conclure ?
➔ Arrêt pour futilité

Patients exposés à un risque toxique ?
➔ Arrêt pour sécurité

Bon déroulement de l'essai ?
➔ Mesures correctrices

Diapo D Pérol

Dual antiplatelet therapy duration in patients with acute coronary syndrome treated with percutaneous coronary intervention

ESC
European Society of Cardiology

Recommendations	Class	Level
In patients with ACS treated with coronary stent implantation, DAPT with a $P2Y_{12}$ inhibitor on top of aspirin is recommended for 12 months unless there are contra-indications such as excessive risk of bleeding (e.g. PRECISE-DAPT ≥25).	I	A
In patients with ACS and stent implantation who are at high-risk of bleeding (e.g. PRECISE-DAPT ≥25), discontinuation of $P2Y_{12}$ inhibitor therapy after 6 months should be considered.	IIa	B
In patients with ACS treated with bioresorbable vascular scaffolds, DAPT for at least 12 months should be considered.	IIa	C

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Dual antiplatelet therapy duration in patients with acute coronary syndrome undergoing medical therapy management

ESC European Society of Cardiology

Recommendations	Class	Level
In patients with ACS who are managed with medical therapy alone and treated with DAPT, it is recommended to continue $P2Y_{12}$ inhibitor therapy (either ticagrelor or clopidogrel) for 12 months.	I	A
Ticagrelor is recommended over clopidogrel, unless the bleeding risk outweighs the potential ischaemic benefit.	I	B
In patients with medically managed ACS who are at high-risk of bleeding (e.g. PRECISE-DAPT ≥25), DAPT for at least 1 month should be considered.	IIa	C

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(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Dual antiplatelet therapy duration in patients with acute coronary syndrome undergoing medical therapy management *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
In patients with prior MI at high ischaemic risk who are managed with medical therapy alone and have tolerated DAPT without a bleeding complication, treatment with DAPT in the form of ticagrelor 60 mg *b.i.d.* on top of aspirin for longer than 12 months and up to 36 months may be considered.	IIb	B
In patients with prior MI not treated with coronary stent implantation who have tolerated DAPT without a bleeding complication and who are not eligible for treatment with ticagrelor, continuation of clopidogrel on top of aspirin for longer than 12 months may be considered.	IIb	C
Prasugrel is not recommended in medically managed ACS patients.	III	B

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

Dual antiplatelet therapy duration in patients with indication for oral anticoagulation

ESC
European Society of Cardiology

Recommendations	Class	Level
It is recommended to administer periprocedurally aspirin and clopidogrel in patients undergoing coronary stent implantation.	I	C
In patients treated with coronary stent implantation, triple therapy with aspirin, clopidogrel and OAC should be considered for 1 month, irrespective of the type of stent used.	IIa	B
Triple therapy with aspirin, clopidogrel and OAC for longer than 1 month and up to 6 months should be considered in patients with high ischaemic risk due to ACS or other anatomical/procedural characteristics, which outweigh the bleeding risk.	IIa	B
Dual therapy with clopidogrel 75 mg/day and OAC should be considered as an alternative to 1-month triple antithrombotic therapy in patients in whom the bleeding risk outweighs the ischaemic risk.	IIa	A

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

Dual antiplatelet therapy duration in patients with indication for oral anticoagulation *(continued)*

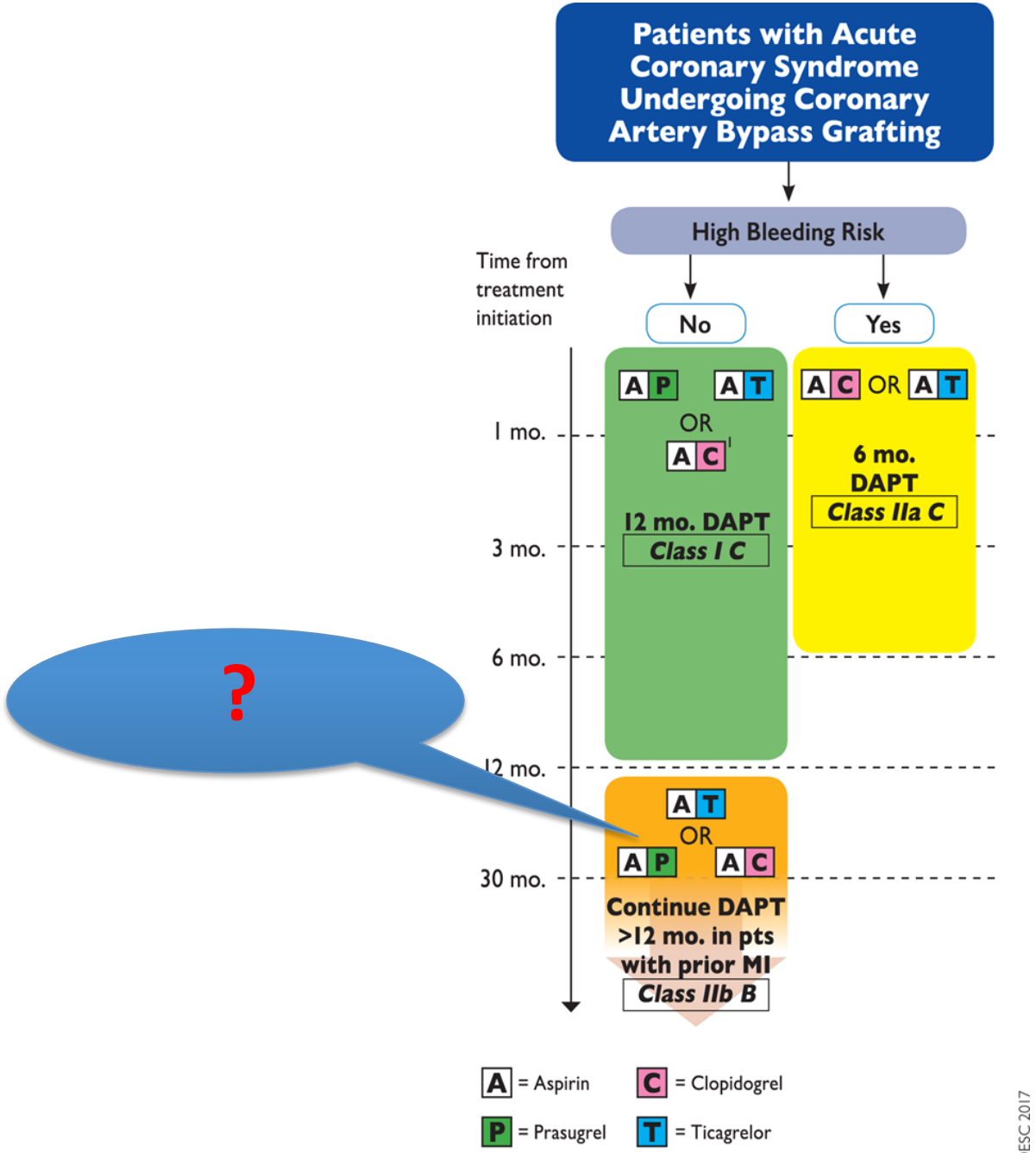
ESC European Society of Cardiology

Recommendations	Class	Level
Discontinuation of antiplatelet treatment in patients treated with OAC should be considered at 12 months.	IIa	B
In patients with an indication for VKA in combination with aspirin and/or clopidogrel, the dose intensity of VKA should be carefully regulated with a target INR in the lower part of the recommended target range and a time in the therapeutic range >65–70%.	IIa	B
When a NOAC is used in combination with aspirin and/or clopidogrel, the lowest approved dose effective for stroke prevention tested in AFib trials should be considered.	IIa	C
When rivaroxaban is used in combination with aspirin and/ or clopidogrel, rivaroxaban 15 mg *q.d.* may be used instead of rivaroxaban 20 mg *q.d.*	IIb	B
The use of ticagrelor or prasugrel is not recommended as part of triple antithrombotic therapy with aspirin and OAC.	III	C

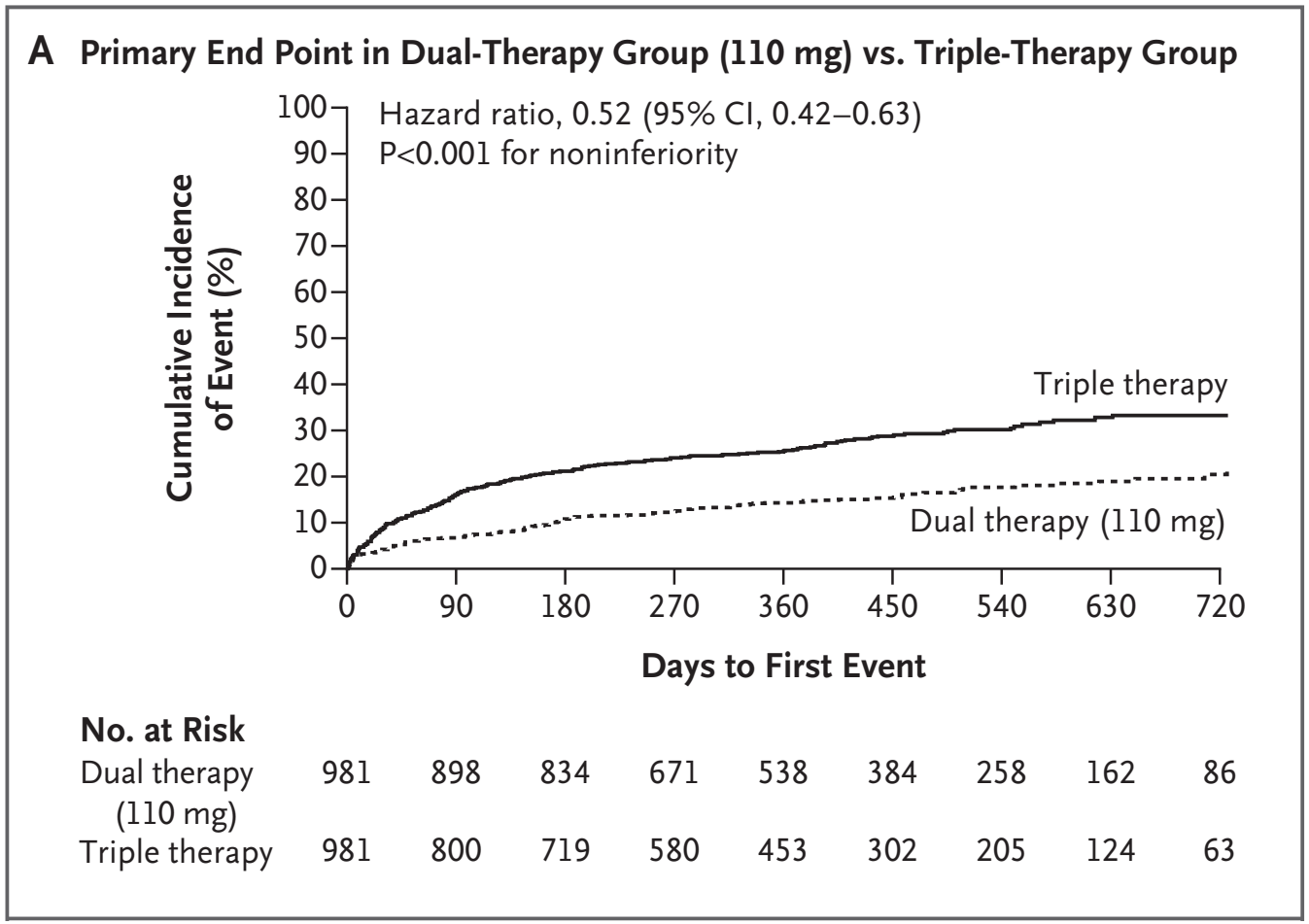
2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Recommendations	Class[a]	Level[b]
In patients with stable CAD treated with coronary stent implantation, DAPT consisting of clopidogrel in addition to aspirin is generally recommended[c] for 6 months, irrespective of the stent type.[100,101,104,126–130]	I	A
Irrespective of the intended DAPT duration, DES[c] is the preferred treatment option.[129–132]	I	A
In patients with stable CAD considered at high bleeding risk (e.g. PRECISE-DAPT ≥25), DAPT for 3 months[d] should be considered.[105,106]	IIa	B
In patients with stable CAD treated with drug-coated balloon, DAPT for 6 months should be considered.[122,124,133]	IIa	B
In patients with stable CAD treated with bioresorbable vascular scaffolds, DAPT for at least 12 months should be considered.	IIa	C
In patients with stable CAD who have tolerated DAPT without a bleeding complication and who are at low bleeding but high thrombotic risk, continuation of DAPT with clopidogrel for >6 months and ≤30 months may be considered.[26,107–109]	IIb	A
In patients with stable CAD in whom 3-month DAPT poses safety concerns, DAPT for 1 month[e] may be considered.	IIb	C

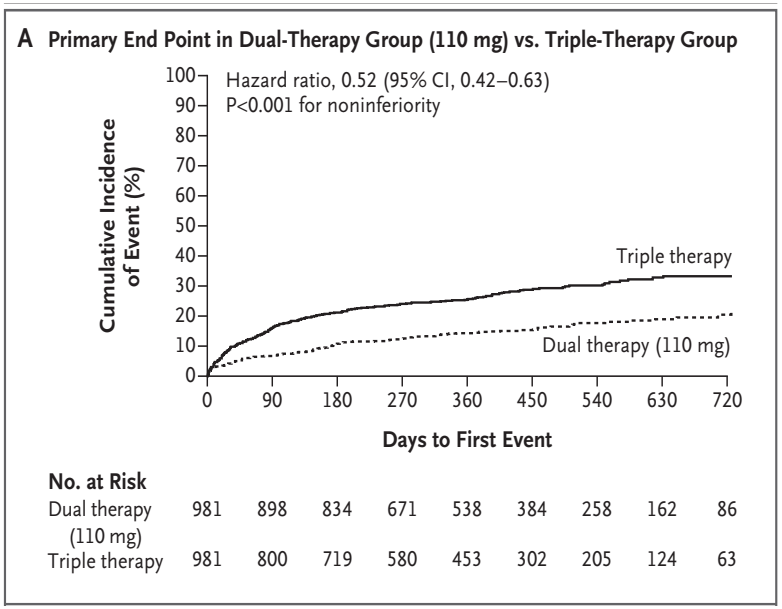
Recommendations	Class[a]	Level[b]
In patients with ACS treated with coronary stent implantation, DAPT with a $P2Y_{12}$ inhibitor on top of aspirin is recommended for 12 months unless there are contraindications such as excessive risk of bleeding (e.g. PRECISE-DAPT ≥25).[20,23,40]	I	A
In patients with ACS and stent implantation who are at high risk of bleeding (e.g. PRECISE-DAPT ≥25), discontinuation of $P2Y_{12}$ inhibitor therapy after 6 months should be considered.[13,18,143]	IIa	B
In patients with ACS treated with bioresorbable vascular scaffolds, DAPT for at least 12 months should be considered.	IIa	C
In patients with ACS who have tolerated DAPT without a bleeding complication, continuation of DAPT for longer than 12 months may be considered.[26,139]	IIb	A
In patients with MI and high ischaemic risk[c] 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.[29,115,142]	IIb	B


Patients with Acute Coronary Syndrome Undergoing Coronary Artery Bypass Grafting
High Bleeding Risk
Time from treatment initiation
No
Yes
A P
A T
OR
A C
12 mo. DAPT
Class I C
A C OR A T
6 mo. DAPT
Class IIa C
1 mo.
3 mo.
6 mo.
12 mo.
30 mo.
?
A T
OR
A P
A C
Continue DAPT >12 mo. in pts with prior MI
Class IIb B
A = Aspirin
C = Clopidogrel
P = Prasugrel
T = Ticagrelor

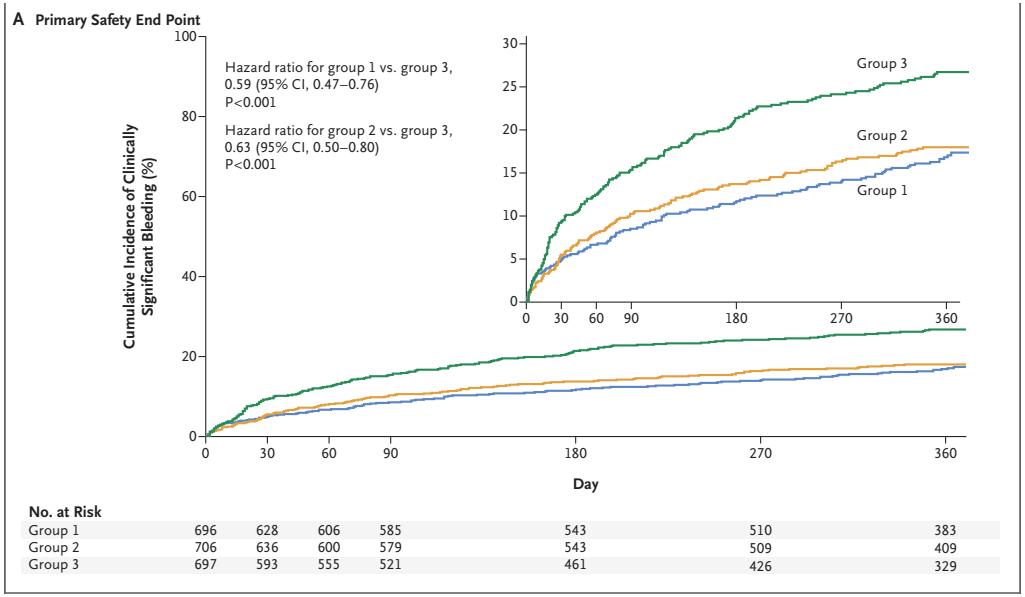
DUAL PCI: RRR = 48%



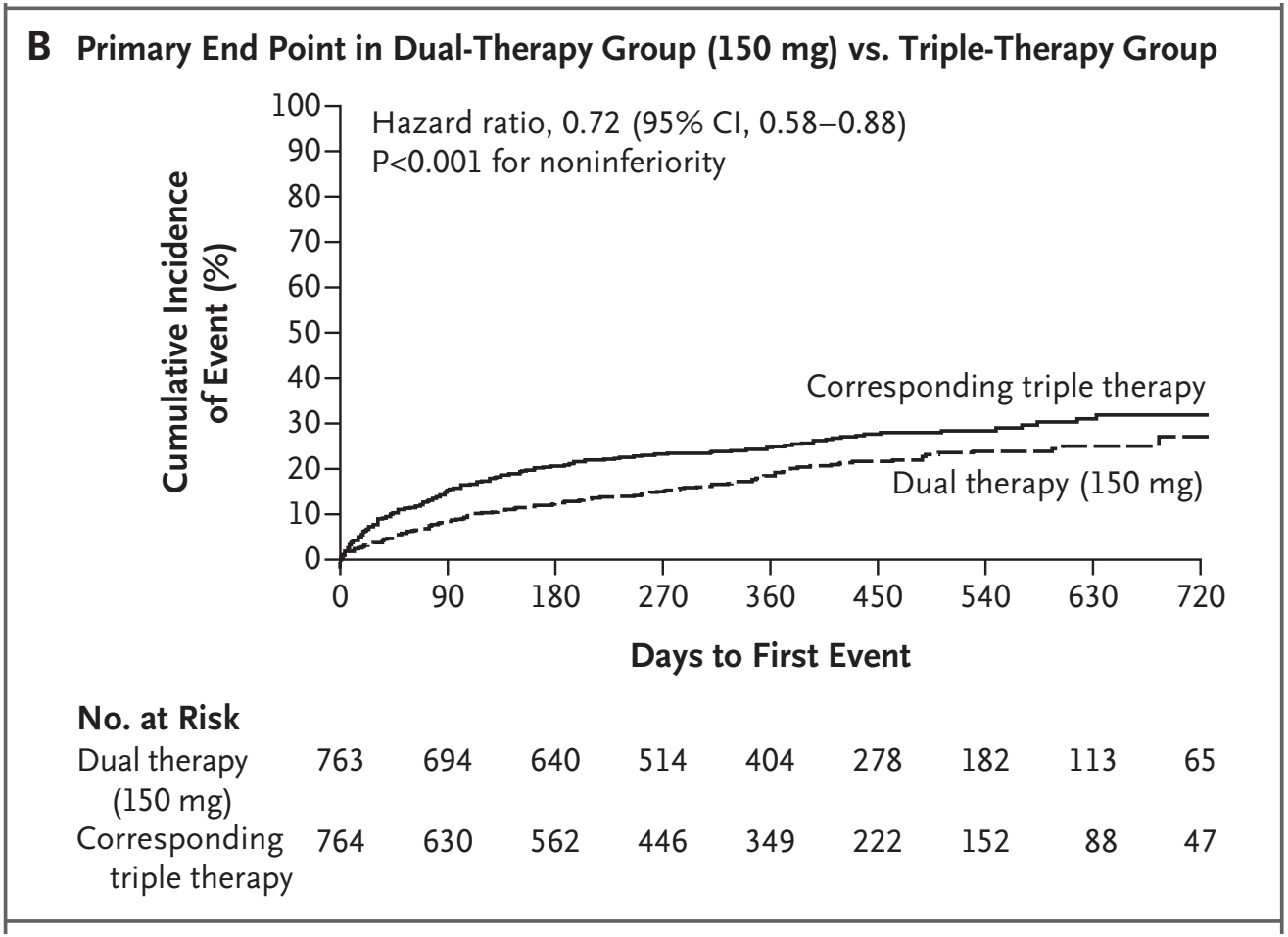
DUAL PCI: RRR = 48%



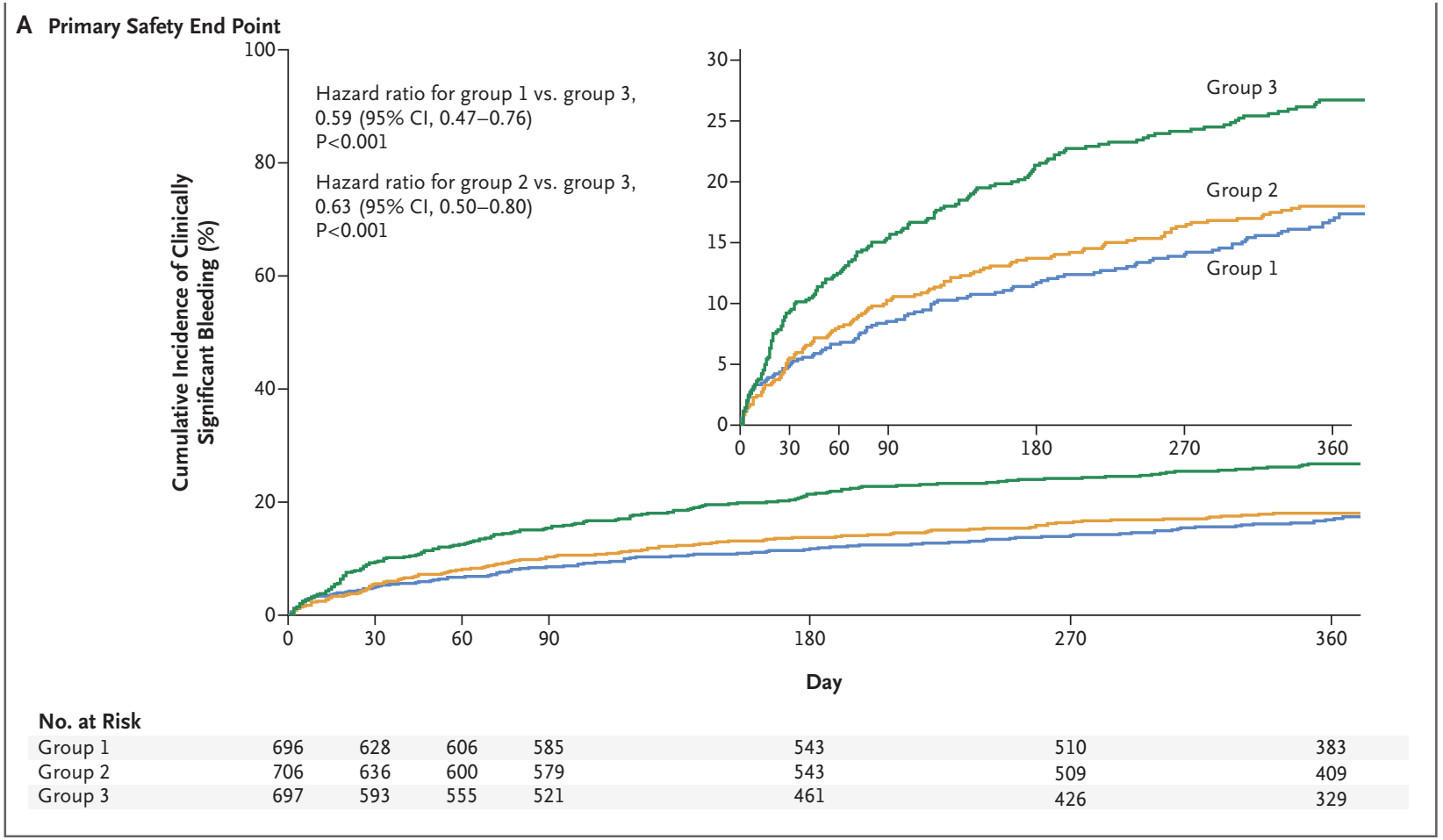
PIONEER :RRR = 41%



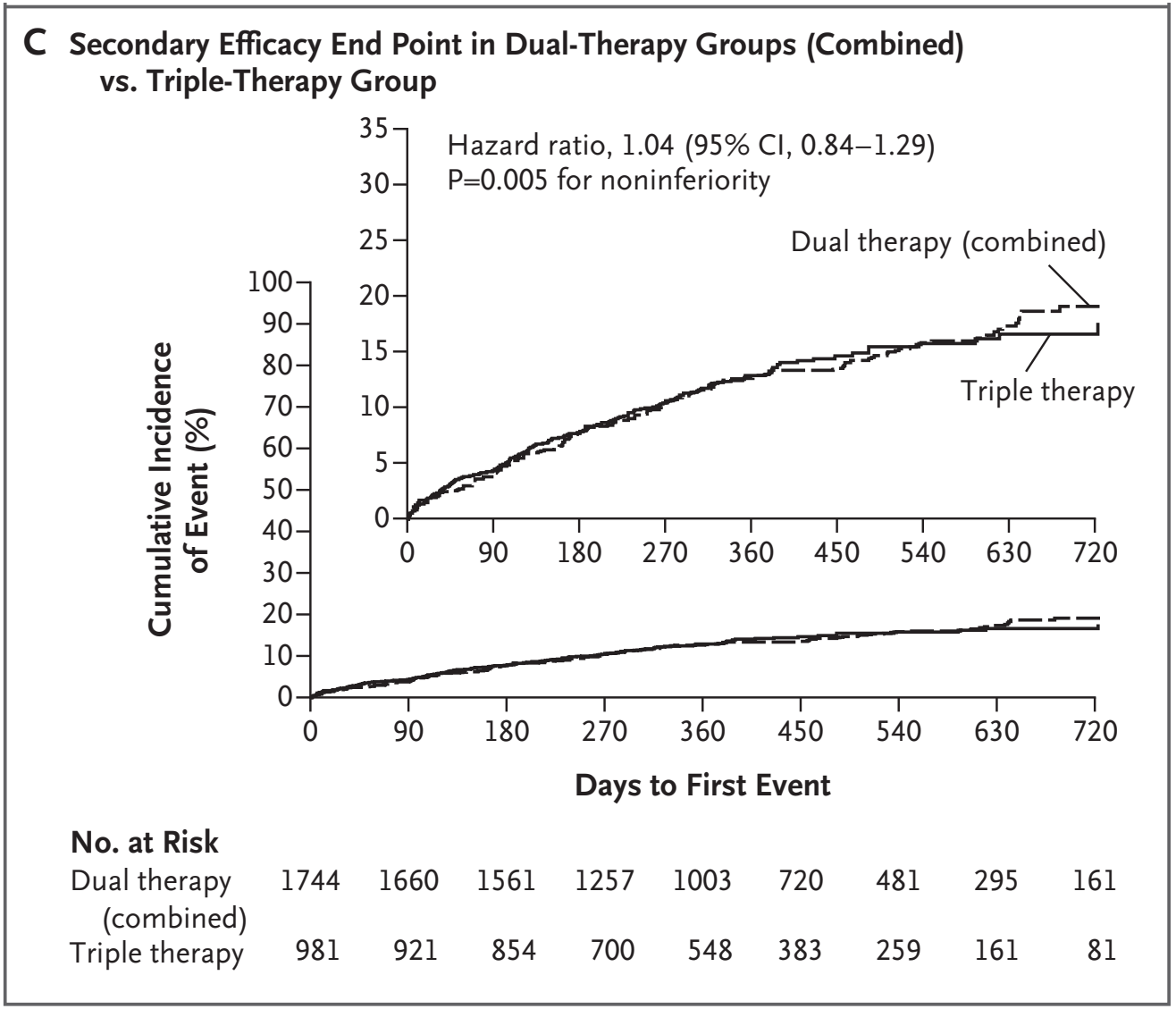
DUAL PCI: bras 150



PIONEER :RRR = 41%



Dual PCI: secondary end point



PIONEER: secondary End point

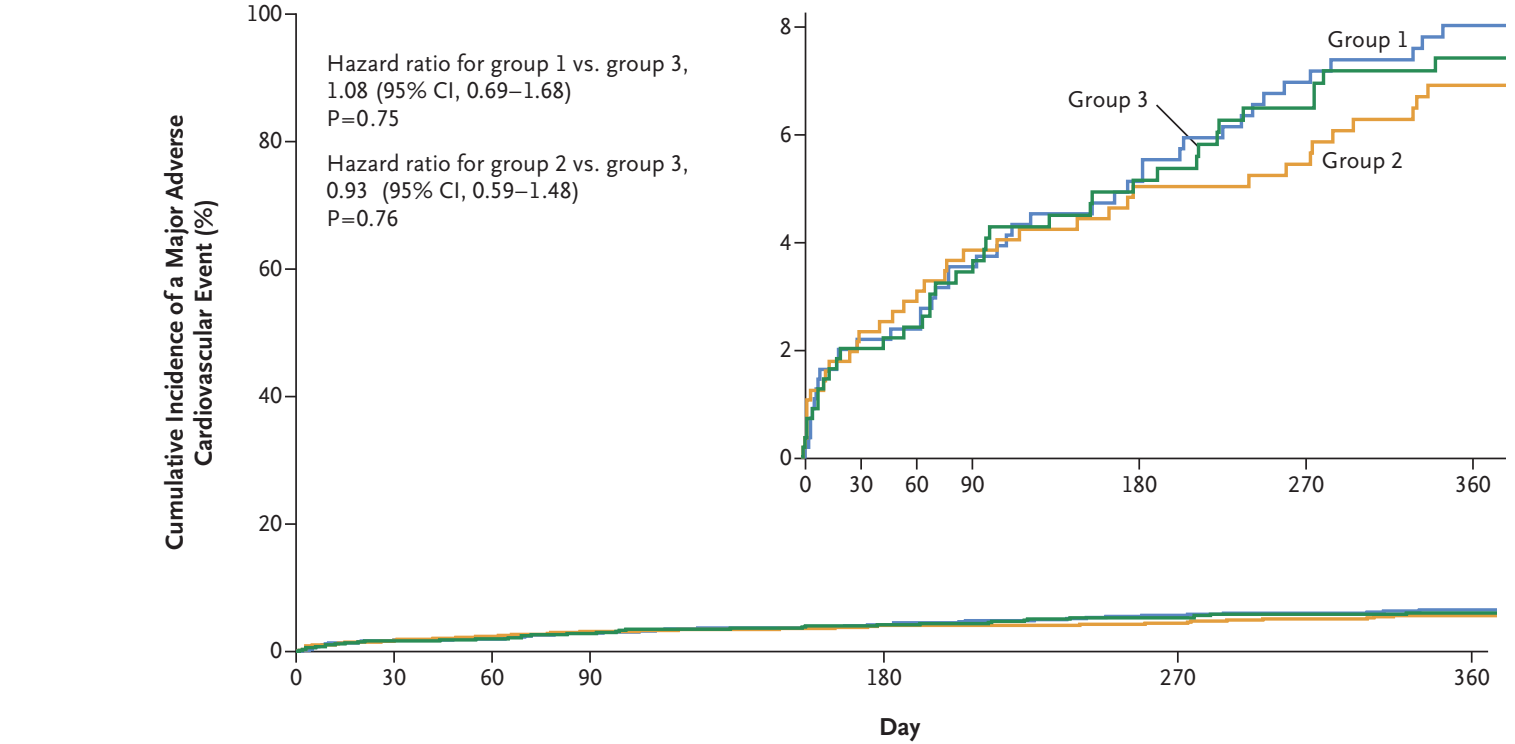


Table 3. Cumulative Incidence of Secondary Efficacy End Points, with Stratification According to Intended Duration of DAPT.*

Cohort and End Point	Group 1	Group 2	Group 3	Group 1 vs. Group 3		Group 2 vs. Group 3	
	No. of Participants with Events (Kaplan–Meier Event Rate)			Hazard Ratio (95% CI)	P Value	Hazard Ra[illegible]	[illegible]alue
All participants — no.	694	704	695				
Major adverse cardiovascular event	41 (6.5)	36 (5.6)	36 (6.0)	1.08 (0.69–1.68)			
Death from cardiovascular causes	15 (2.4)	14 (2.2)	11 (1.9)	1.29 [illegible]			
Myocardial infarction	19 (3.0)	17 (2.7)	21 (3.5)				
Stroke	8 (1.3)	10 (1.5)					
Stent thrombosis	5 (0.8)						
Major adverse cardiovascular event or stent thrombosis	41 [illegible]						
Participants assigned to DAPT for 1 mo — no.							
Major adverse cardiovascular event						[illegible].36–3.84)	0.79
Death from cardiovascular causes						0.96 (0.13–6.80)	0.97
Myocardial infarction						2.93 (0.30–28.16)	0.33
Stroke						0.65 (0.11–3.91)	0.64
Stent thrombosis						1.97 (0.18–21.74)	0.57
Major adverse cardiovascular event or stent thrombosis			5 (5.2)			1.17 (0.36–3.84)	0.79
Participants assigned to DAPT for 6 mo — no.		248	243				
Major adverse cardiovascular event		16 (7.0)	9 (4.3)			1.72 (0.76–3.88)	0.19
Death from cardiovascular causes		6 (2.8)	4 (1.9)			1.45 (0.41–5.12)	0.57
Myocardial infarction		7 (3.0)	6 (2.9)			1.13 (0.38–3.37)	0.82
Stroke		6 (2.7)	0				0.02
Stent thrombosis		4 (1.7)	1 (0.4)			3.91 (0.44–35.02)	0.19
Major adverse cardiovascular event or stent thrombosis		16 (7.0)	9 (4.3)			1.72 (0.76–3.40)	0.19
Participants assigned to DAPT for 12 mo — no.		348	340				
Major adverse cardiovascular event		14 (4.5)	22 (7.4)			0.57 (0.29–1.11)	0.10
Death from cardiovascular causes		6 (1.9)	5 (1.7)			1.08 (0.33–3.55)	0.89
Myocardial infarction		7 (2.3)	14 (4.8)			0.44 (0.18–1.10)	0.07
Stroke		2 (0.6)	4 (1.3)			0.46 (0.08–2.51)	0.36
Stent thrombosis		0	2 (0.8)				0.10
Major adverse cardiovascular event or stent thrombosis		14 (4.5)	22 (7.4)			0.57 (0.29–1.11)	0.10

PIONEER

Le nb d'AVC dans le bras Riva 15 + Clopi

vs

chez ceux sous Riv 2.5 + DAPT pd 6 mois est >

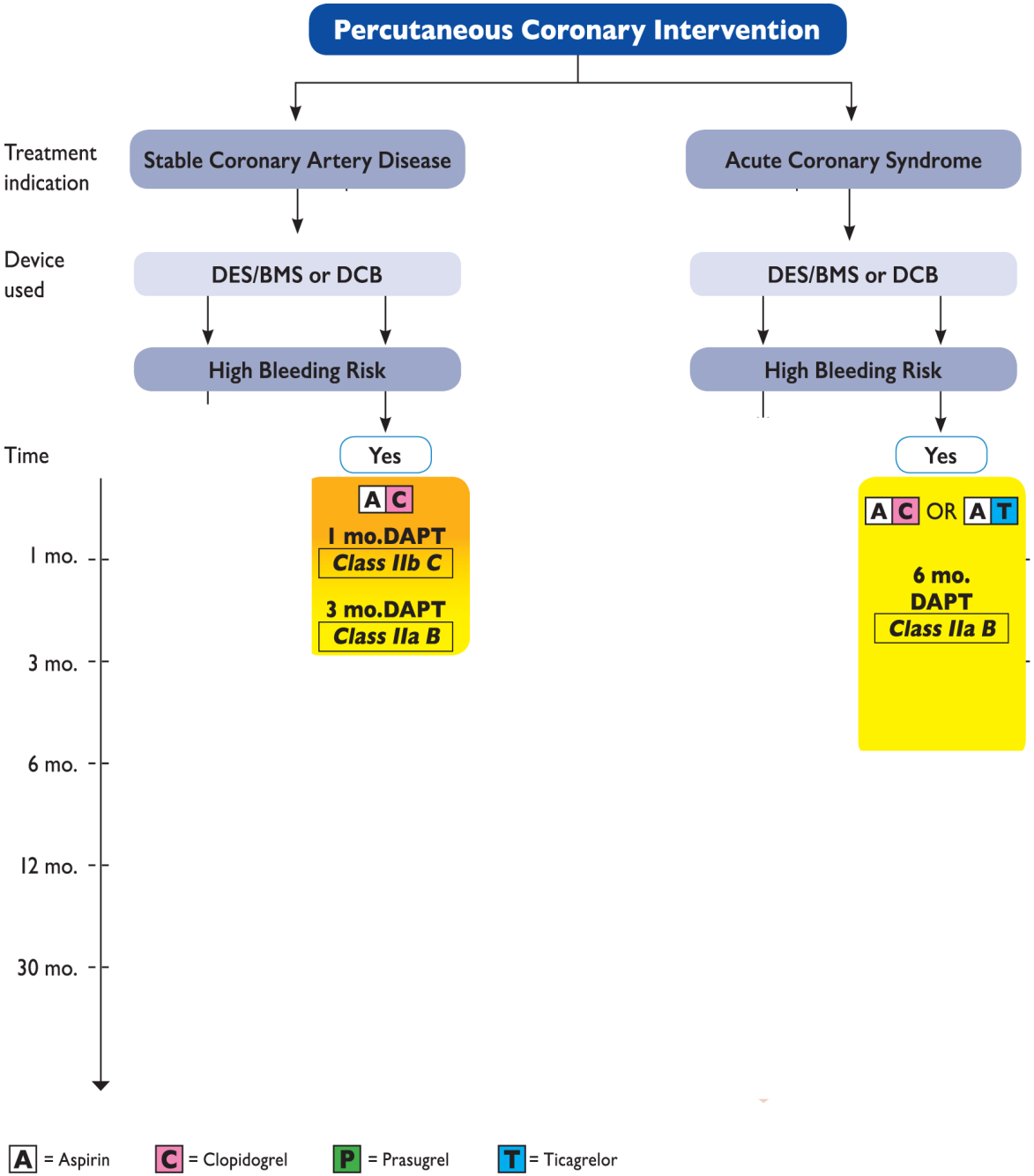
À celui de la trithérapie

Table 1. Baseline Patient Characteristics and Inclusion Criteria.*

Variable	Drug-Coated Stent (N=1221)	Bare-Metal Stent (N=1211)
Baseline characteristics		
Age — yr	75.7±9.4	75.7±9.3
Female sex — no. (%)	364 (29.8)	374 (30.9)
Body-mass index†	27.5±4.8	27.2±4.6
Diabetes — no./total no. (%)	414/1217 (34.0)	391/1210 (32.3)
Hypertension — no./total no. (%)	952/1219 (78.1)	961/1208 (79.6)
Hypercholesterolemia — no./total no. (%)	742/1197 (62.0)	746/1189 (62.7)
STEMI — no. (%)	57 (4.7)	48 (4.0)
NSTEMI — no. (%)	273 (22.4)	281 (23.2)
Unstable angina — no. (%)	177 (14.5)	193 (15.9)
Stable CAD — no. (%)	714 (58.5)	689 (56.9)
Multivessel disease — no./total no. (%)	755/1201 (62.9)	738/1198 (61.6)
Previous myocardial infarction — no./total no. (%)	237/1211 (19.6)	258/1203 (21.4)
Previous PCI — no./total no. (%)	270/1215 (22.2)	265/1208 (21.9)
Previous CABG — no./total no. (%)	115/1217 (9.4)	122/1209 (10.1)
Congestive heart failure — no./total no. (%)	175/1212 (14.4)	150/1211 (12.4)
Atrial fibrillation — no./total no. (%)	424/1215 (34.9)	418/1209 (34.6)
Previous stroke — no./total no. (%)	132/1212 (10.9)	110/1208 (9.1)
Peripheral vascular disease — no./total no. (%)	190/1208 (15.7)	190/1201 (15.8)
Chronic obstructive lung disease — no./total no. (%)	131/1207 (10.9)	141/1202 (11.7)
CRUSADE score‡	34.1±0.4	34.6±0.4
Inclusion criteria — no. (%)§		
Age ≥75 yr	788 (64.5)	776 (64.1)
Oral anticoagulation planned to continue after PCI	448 (36.7)	431 (35.6)
Hemoglobin <11 g/liter or transfusion within 4 wk before randomization	185 (15.2)	194 (16.0)
Platelet count <100,000/mm³	20 (1.6)	18 (1.5)
Hospital admission for bleeding in previous 12 mo	46 (3.8)	33 (2.7)
Stroke in previous 12 mo	15 (1.2)	24 (2.0)
Previous intracerebral hemorrhage	14 (1.1)	19 (1.6)
Severe chronic liver disease	11 (0.9)	10 (0.8)
Creatinine clearance <40 ml/min	219 (17.9)	245 (20.2)
Cancer in previous 3 yr¶	119 (9.7)	120 (9.9)
Planned major surgery in next 12 mo	187 (15.3)	211 (17.4)
Glucocorticoids or NSAID planned for >30 days after PCI	38 (3.1)	34 (2.8)
Expected nonadherence to >30 days of dual antiplatelet therapy	41 (3.4)	47 (3.9)

Les patients de cette étude sont loins d'être rares

- 76 ans
- Angor stable dans 58% cas.
- 36% avaient un trt AC au long cours prévisionnel
- 3% avaient saigné dans les 12 mois.


Percutaneous Coronary Intervention
Treatment indication
Stable Coronary Artery Disease
Acute Coronary Syndrome
Device used
DES/BMS or DCB
DES/BMS or DCB
High Bleeding Risk
High Bleeding Risk
Time
Yes
Yes
A C
1 mo.DAPT
Class IIb C
3 mo.DAPT
Class IIa B
A C OR A T
6 mo.
DAPT
Class IIa B
1 mo.
3 mo.
6 mo.
12 mo.
30 mo.
A = Aspirin
C = Clopidogrel
P = Prasugrel
T = Ticagrelor

Dual antiplatelet therapy duration and related stent choices in patients with stable coronary artery disease treated with percutaneous coronary intervention

ESC European Society of Cardiology

Recommendations	Class	Level
	I	A
	I	A
In patients with stable CAD considered at high bleeding risk (e.g. PRECISE-DAPT ≥25), DAPT for 3 months should be considered*.	IIa	B
	IIa	B

*:The evidence supporting this recommendation comes from two studies where zotarolimus-eluting Endeavour sprint stent has been investigated in conjunction with a 3-month DAPT regimen.

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(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

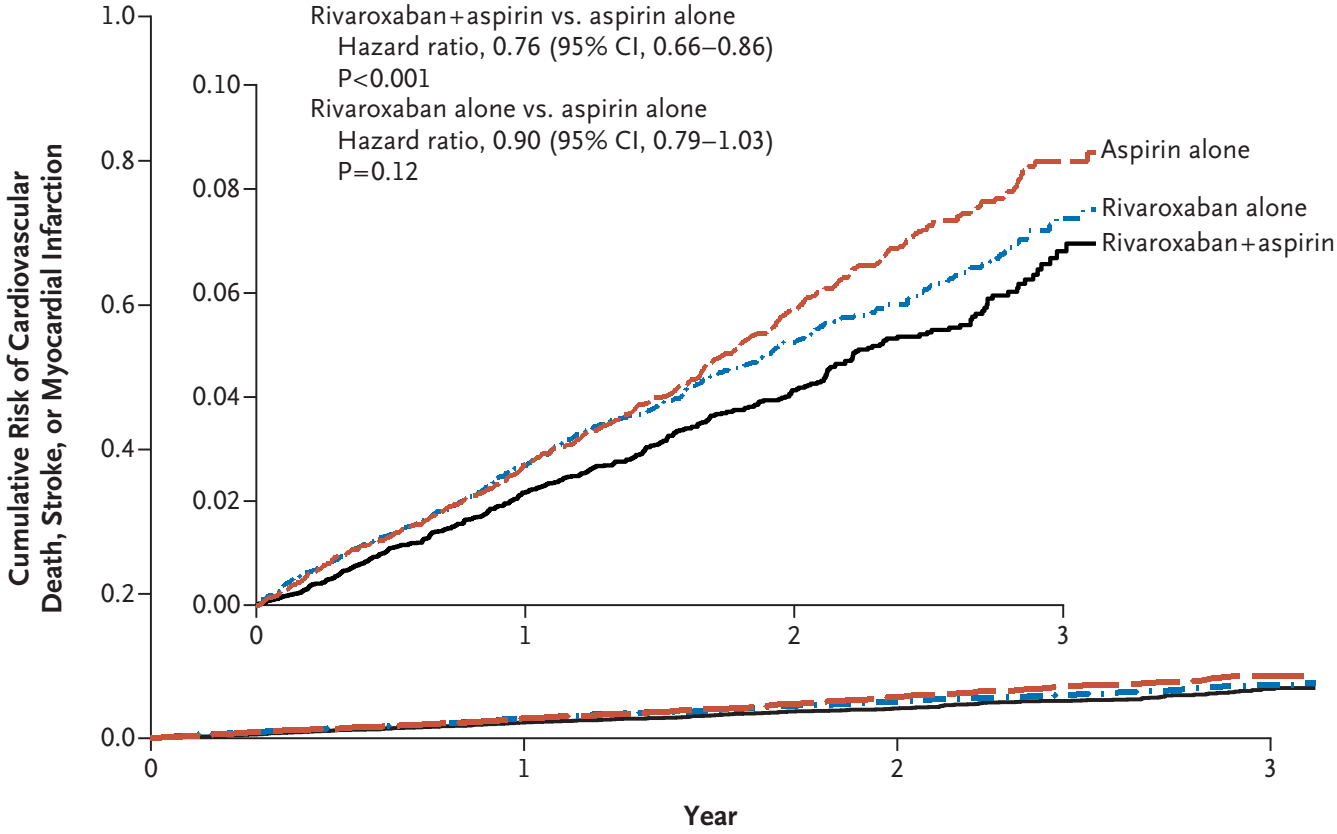
Dual antiplatelet therapy duration and related stent choices in patients with stable coronary artery disease treated with percutaneous coronary intervention *(continued)*

ESC European Society of Cardiology

Recommendations	Class	Level
	IIa	C
	IIb	A
In patients with stable CAD in whom 3-month DAPT poses safety concerns, DAPT for 1 month may be considered*.	IIb	C

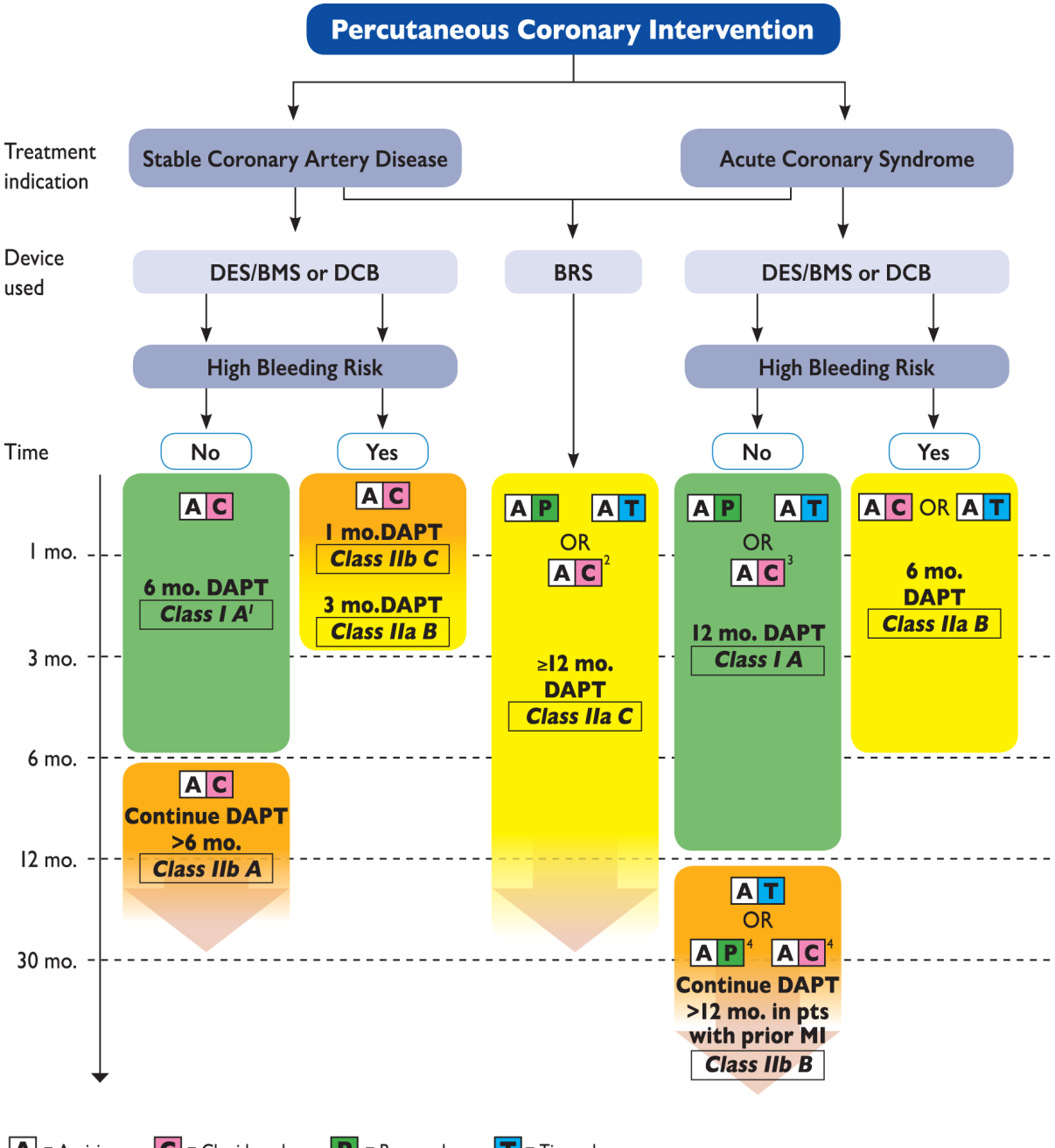
*;1-month DAPT after implantation of zotarolimus-eluting Endeavour sprint stent or drug coated stent reduced risks of reintervention, myocardial infarction and inconsistently of stent thrombosis compared to bare-metal stent under similar DAPT duration. It is unclear if this evidence applies to other contemporary DES.

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



No. at Risk				
Aspirin alone	9126	7808	3860	669
Rivaroxaban alone	9117	7824	3862	670
Rivaroxaban+aspirin	9152	7904	3912	658

Figure 1. Cumulative Incidence of the Primary Efficacy Outcome among Participants Receiving Rivaroxaban plus Aspirin, Rivaroxaban Alone, or Aspirin Alone.


Percutaneous Coronary Intervention
Treatment indication
Stable Coronary Artery Disease
Acute Coronary Syndrome
Device used
DES/BMS or DCB
BRS
DES/BMS or DCB
High Bleeding Risk
High Bleeding Risk
Time
No
Yes
No
Yes
1 mo.
3 mo.
6 mo.
12 mo.
30 mo.
A C
6 mo. DAPT
Class I A1
A C
1 mo.DAPT
Class IIb C
3 mo.DAPT
Class IIa B
A P
A T
OR
A C2
≥12 mo. DAPT
Class IIa C
A P
A T
OR
A C3
12 mo. DAPT
Class I A
A C OR A T
6 mo. DAPT
Class IIa B
A C
Continue DAPT >6 mo.
Class IIb A
A T
OR
A P4
A C4
Continue DAPT >12 mo. in pts with prior MI
Class IIb B
A = Aspirin
C = Clopidogrel
P = Prasugrel
T = Ticagrelor