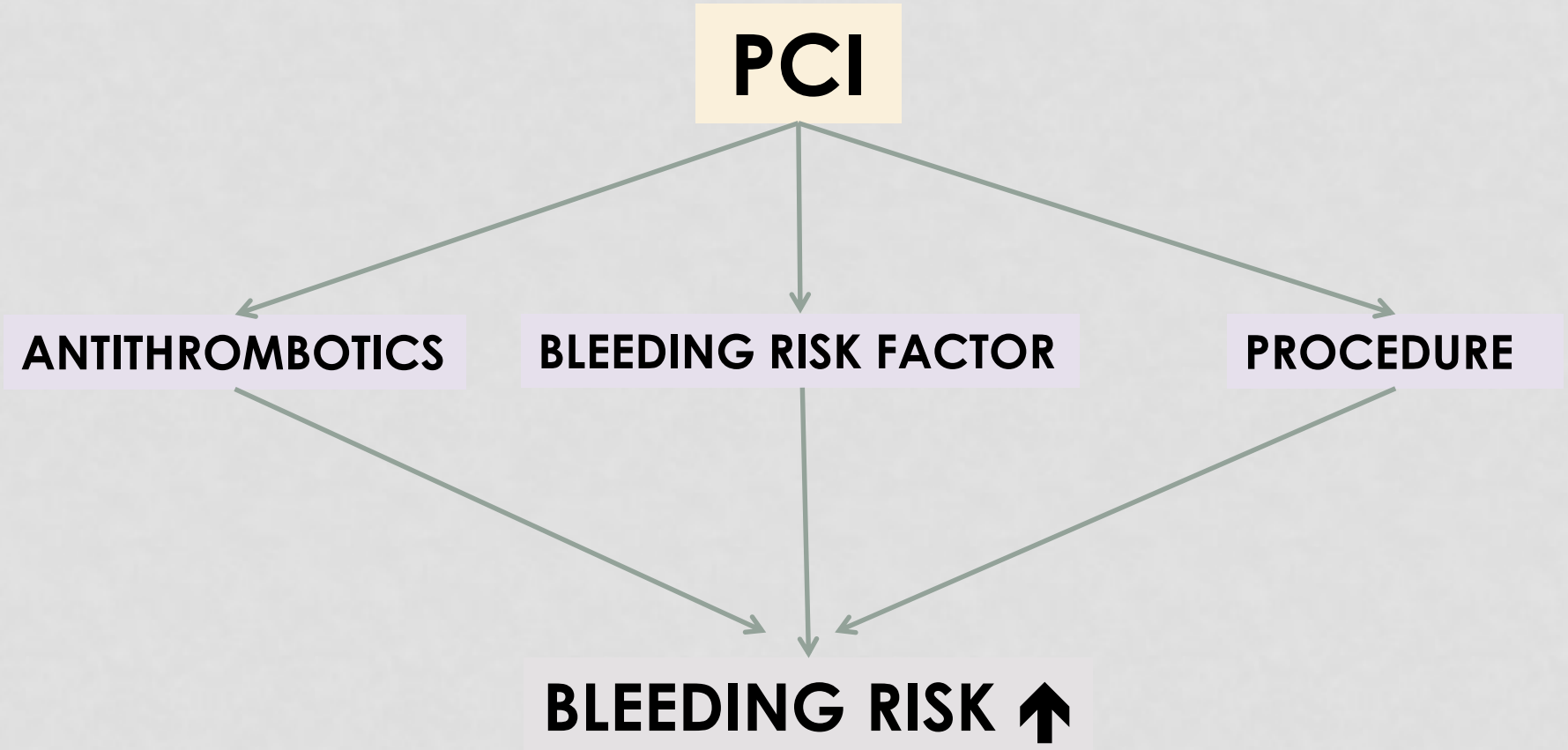
MINIMIZING AND MANAGEMENT OF PCI-RELATED BLEEDING

NGUYEN CUU LOI, MD. FSCAI
Vice-President, Vietnam Society of Interventional Cardiology


PCI
ANTITHROMBOTICS
BLEEDING RISK FACTOR
PROCEDURE
BLEEDING RISK ↑

PCI-related Antithrombotics

Antiplatelets	+	Parenteral anticoagulation	±	Thrombo -lytics	±	OAC
Aspirin + P2Y12 Inhibitors ± GPIIB/IIIA inhibitors		UFH **or** Enoxaparine		Streptokinase **or** Alteplase Reteplase Tenecteplase		AVK **or** NOAC

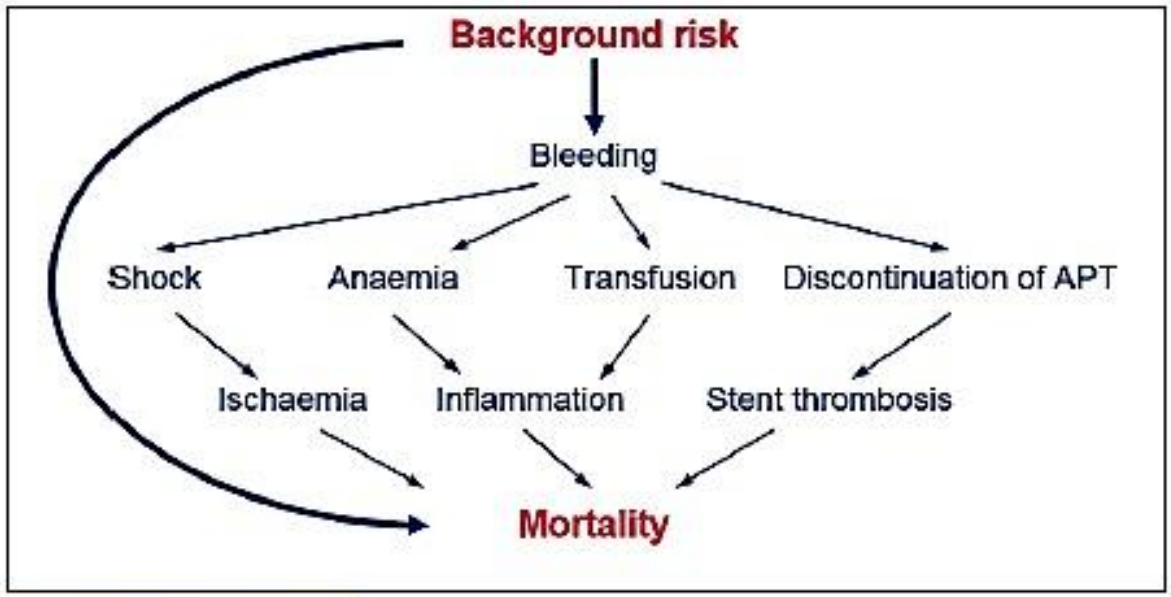
Personal bleeding risks

- History of prior bleeding
- Female
- Advanced age
- Low body weight
- Chronic kidney disease
- Diabetes mellitus
- Anemia
- Concurrent Steroid or NSAID treatment

AHA/ACC Guideline 2016

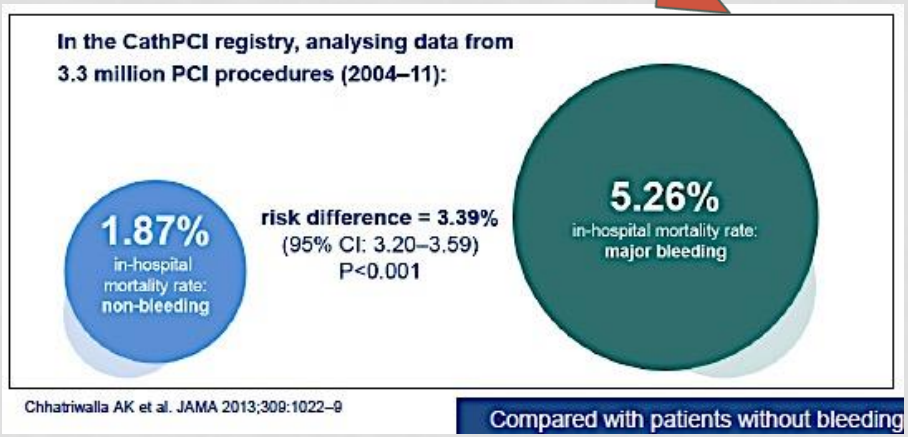
Procedural technical aspects

- Difficult hemostasis arterial access
  (Femoral artery, brachial artery)
- Large size catheter (> 6F)
- Manual compression



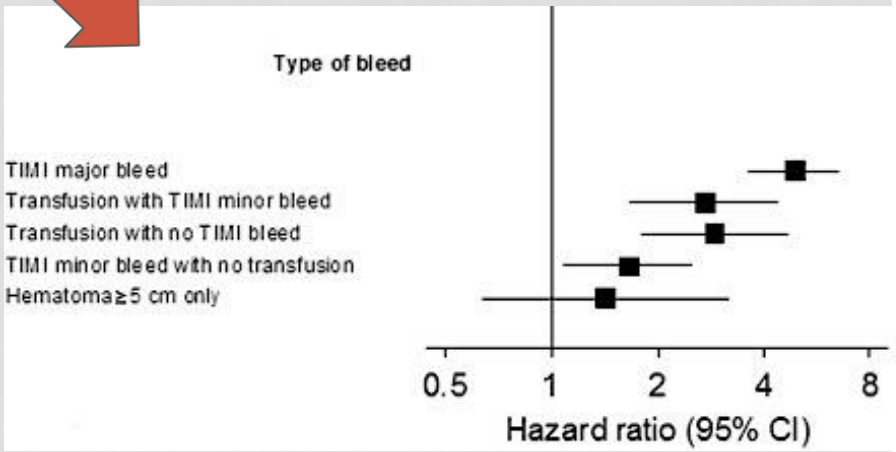
nts who experience

Steg et al. Eur Heart J 2011;32:1854–64



Chhatriwalla AK et al. JAMA 2013;309:1022–9

Compared with patients without bleeding



Independent Hazard of the occurrence of different types of major bleed within 30 days on subsequent mortality within 1 year

PCI-related bleeding

Prevention >>> Treatment

Stratification of bleeding risk

Before PCI

PCI Risk Assessment Tool

http://scaiscientificsessions.org/PCIRiskWeb2/PCIRiskWeb2.htm

Patient Name:	
MRN:	
DOB:	
Age:	
Sex:	
Height (cm):	
Weight (kg):	
Race:	
Admission Source:	
Health Insurance:	

History and Risk Factors

Hypertension:	No
Prior Heart Failure:	No
Prior PCI:	No
Prior CABG:	No
Currently on Dialysis:	No
Cerebrovascular Disease:	No
Peripheral Arterial Disease:	No
Chronic Lung Disease:	No
Diabetes Mellitus:	No
Hemoglobin (g/dL):	
Serum Creatinine (mg/dL):	

Clinical Evaluation

CAD Presentation:	No Sx, No angina (within 14 days)
CCS Angina Class (last 2 weeks):	No ischemic symptoms
NYHA Heart Failure Class (last 2 weeks):	No Heart Failure
Cardiogenic Shock within 24 hrs:	No
Cardiac Arrest within 24 hrs:	No

Procedural Details

IABP:	No
PCI Status:	
LVEF:	
Cardiogenic Shock at start of PCI:	No
Primary Arterial Access:	
≥2 vessels with ≥70% DS:	No
Number of lesions treated:	1
Stent use:	

Predicted Outcomes

Show Inputs

In-hospital mortality (NCDR)	0.0%	☐
In-hospital bleeding (NCDR)	1.3%	☐
In-hospital femoral complications (DELTA)		☐
In-hospital AKI (NCDR)	Odds ratio=0.5 vs. a healthy 50 yo	☐
In-hospital dialysis (NCDR)	Odds ratio=1.0 vs. a healthy 50 yo	☐
1-year TVR (MassDAC) *(Target Vessel Revascularization)*		☐
30-day Readmission (MassDAC)	<9%	☐

After PCI

Duration of Dual AntiPlatelet Therapy (DAPT)

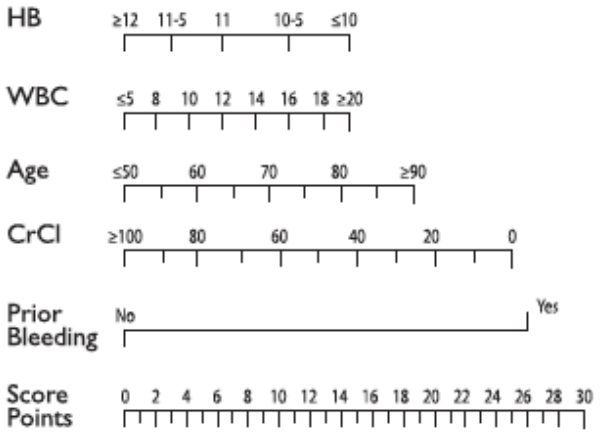
Clinical and Procedural Factors Associated With Increased Ischemic Risk (Including Stent Thrombosis) or Increased Bleeding Risk

Increased Ischemic Risk/Risk of Stent Thrombosis (favor longer-duration DAPT)	**Increased Bleeding Risk** (favor shorter-duration DAPT)
Increased ischemic risk · Advanced age · ACS presentation · Multiple prior MIs · Extensive CAD · Diabetes mellitus · CKD ***Increased risk of stent thrombosis*** · ACS presentation · Diabetes mellitus · LV EF < 40% · First-generation drug-eluting stent · Stent undersizing · Stent underdeployment · Small stent diameter · Greater stent length · Bifurcation stents · In-stent restenosis	· History of prior bleeding · OAC therapy · Female sex · Advanced age · Low body weight · CKD · Diabetes mellitus · Anemia · Chronic steroid or NSAID therapy

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

Duration of DAPT

Table 3 Risk scores validated for dual antiplatelet therapy duration decision-making

	PRECISE-DAPT score[18]	DAPT score[15]	
Time of use	At the time of coronary stenting	After 12 months of uneventful DAPT	
DAPT duration strategies assessed	Short DAPT (3–6 months) vs. Standard/long DAPT (12–24 months)	Standard DAPT (12 months) vs. Long DAPT (30 months)	
Score calculation[a]		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 dual antiplatelet therapy in coronary artery disease developed in collaboration with EACTS

P2Y12 Inhibitor Monotherapy versus Dual Antiplatelet Therapy in Patients Undergoing Percutaneous Coronary Intervention

The SMART-CHOICE randomized, open-label, noninferiority trial

ACC.19 Late-Breaking Clinical Trials

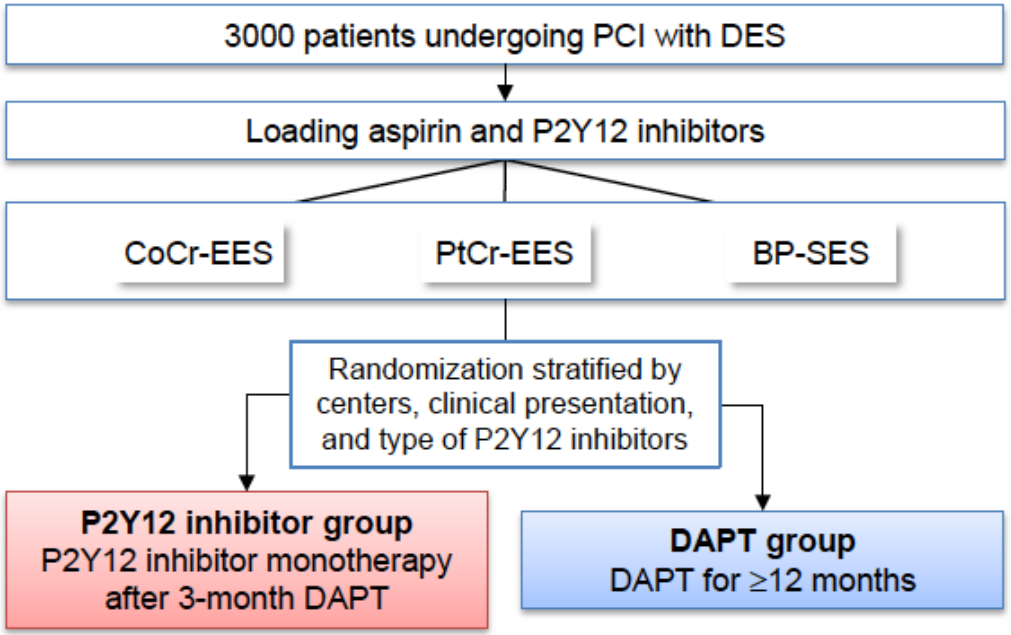
Joo-Yong Hahn, MD/PhD

On the behalf of SMART-CHOICE trial investigators

Aim: *To compare the efficacy and safety of clopidogrel monotherapy versus aspirin plus P2Y12 antagonist following 3-month of DAPT in patients undergoing PCI with DES.*

Study design

A prospective, multicenter, randomized, open-label, noninferiority trial

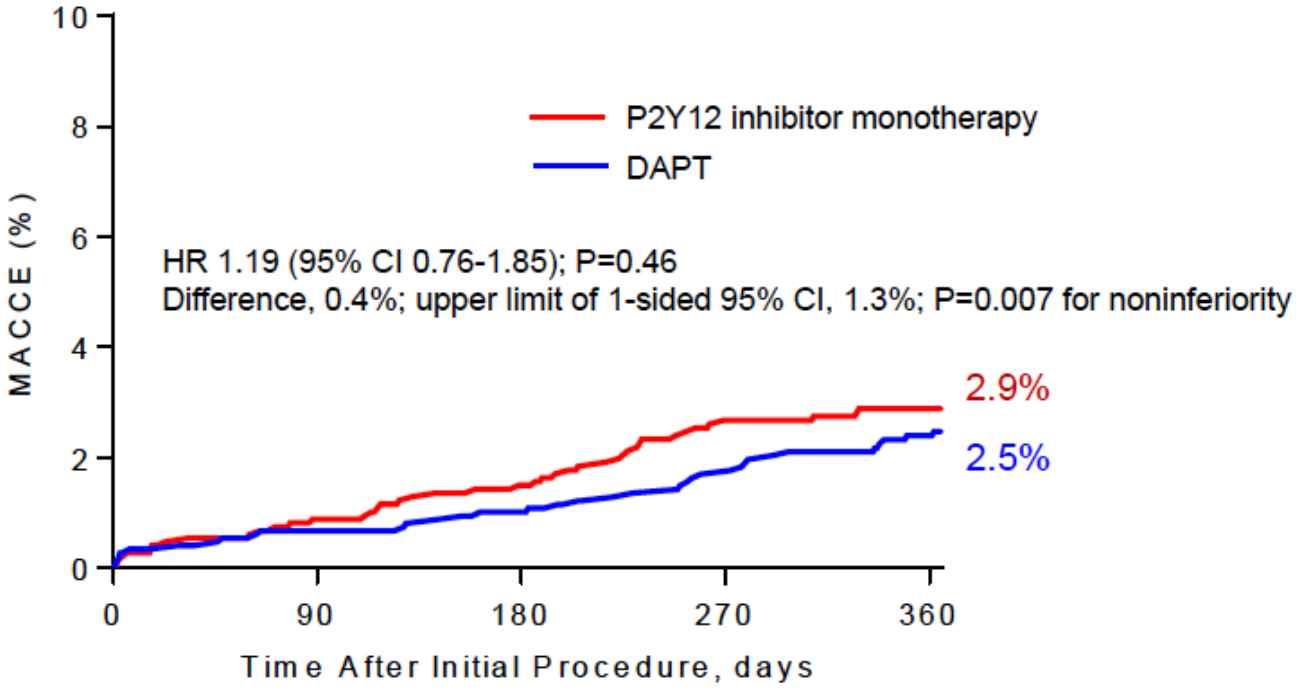


- CoCr-EES: cobalt-chromium everolimus eluting stent (Xience series)
- PtCr-EES: platinum-chromium everolimus-eluting stent (Promus series and Synergy)
- BP-SES: bioresorbable polymer- sirolimus-eluting stent (Orsiro)

Primary endpoint: 12-month MACCE

ClinicalTrials.gov NCT02079194

Primary end point (MACCE)



No. at risk					
DAPT	1498	1471	1454	1436	1220
P2Y12 inhibitor	1495	1456	1430	1402	1202

* MACCE = A composite of all-cause death, myocardial infarction, or stroke

Clinical outcomes at 12 months

Outcome	P2Y12 inhibitor monotherapy (n=1495)	Dual antiplatelet therapy (n=1498)	HR (95% CI)	P Value
MACCE	42 (2.9%)	36 (2.5%)	1.19 (0.76-1.85)	0.46
Death	21 (1.4%)	18 (1.2%)	1.18 (0.63-2.21)	0.61
Myocardial infarction	11 (0.8%)	17 (1.2%)	0.66 (0.31-1.40)	0.28
Cerebrovascular accident	11 (0.8%)	5 (0.3%)	2.23 (0.78-6.43)	0.14
Death or myocardial infarction	31 (2.1%)	32 (2.2%)	0.98 (0.60-1.61)	0.94
Cardiac death	11 (0.8%)	13 (0.9%)	0.86 (0.38-1.91)	0.70
Cardiac death or myocardial infarction	22 (1.5%)	27 (1.9%)	0.83 (0.47-1.45)	0.50
Stent thrombosis	3 (0.2%)	2 (0.1%)	1.51 (0.25-9.02)	0.65
Bleeding BARC type 2-5	28 (2.0%)	49 (3.4%)	0.58 (0.36-0.92)	0.02
Major bleeding	12 (0.8%)	14 (1.0%)	0.87 (0.40-1.88)	0.72
Net adverse clinical and cerebral events	65 (4.5%)	81 (5.6%)	0.81 (0.58-1.12)	0.20

Major bleeding was defined as BARC type 3-5 bleeding.
Net adverse clinical and cerebral events were defined as MACCE plus BARC type 2-5 bleeding.

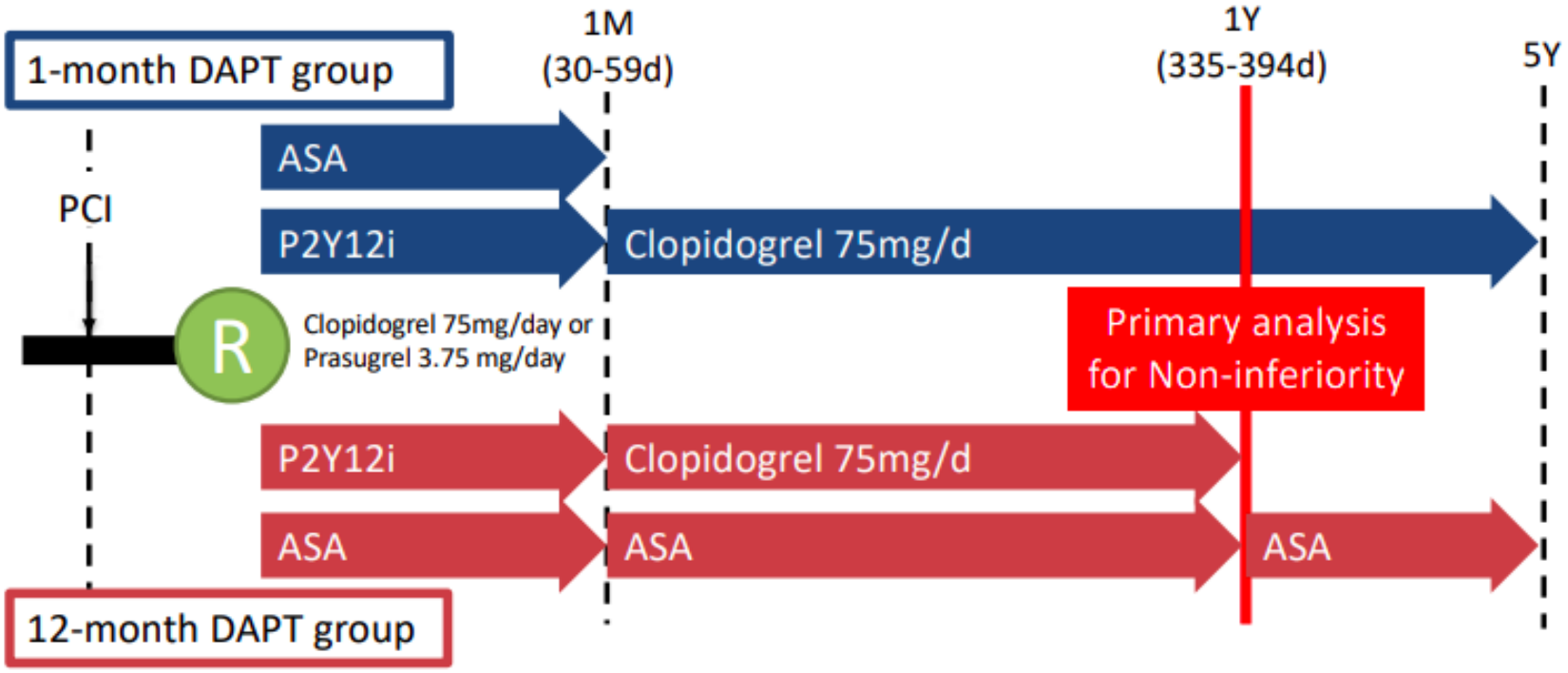
One-Month Dual Antiplatelet Therapy Followed by Clopidogrel Monotherapy versus Standard 12-Month Dual Antiplatelet Therapy with Clopidogrel After Drug-Eluting Stent Implantation:

Hirotoshi Watanabe

Takenori Domei, Takeshi Morimoto, Hiroki Shiomi, Masahiro Natsuaki, Toshiaki Toyota, Kensuke Takagi, Yoshiki Hata, Satoru Suwa, Mamoru Nanasato, Masanobu Ohya, Masahiro Yagi, Takafumi Yokomatsu, Mitsuru Abe, Kenji Ando, Kazushige Kadota, Ken Kozuma, Yoshihiro Morino, Yuji Ikari, Kengo Tanabe, Koichi Nakao, Kazuya Kawai, Yoshihisa Nakagawa, and Takeshi Kimura,
on behalf of STOPDAPT-2 investigators

STOPDAPT-2:

Prospective multicenter open-label randomized trial comparing 1-month versus 12-month DAPT after CoCr-EES implantation with limited exclusion criteria.



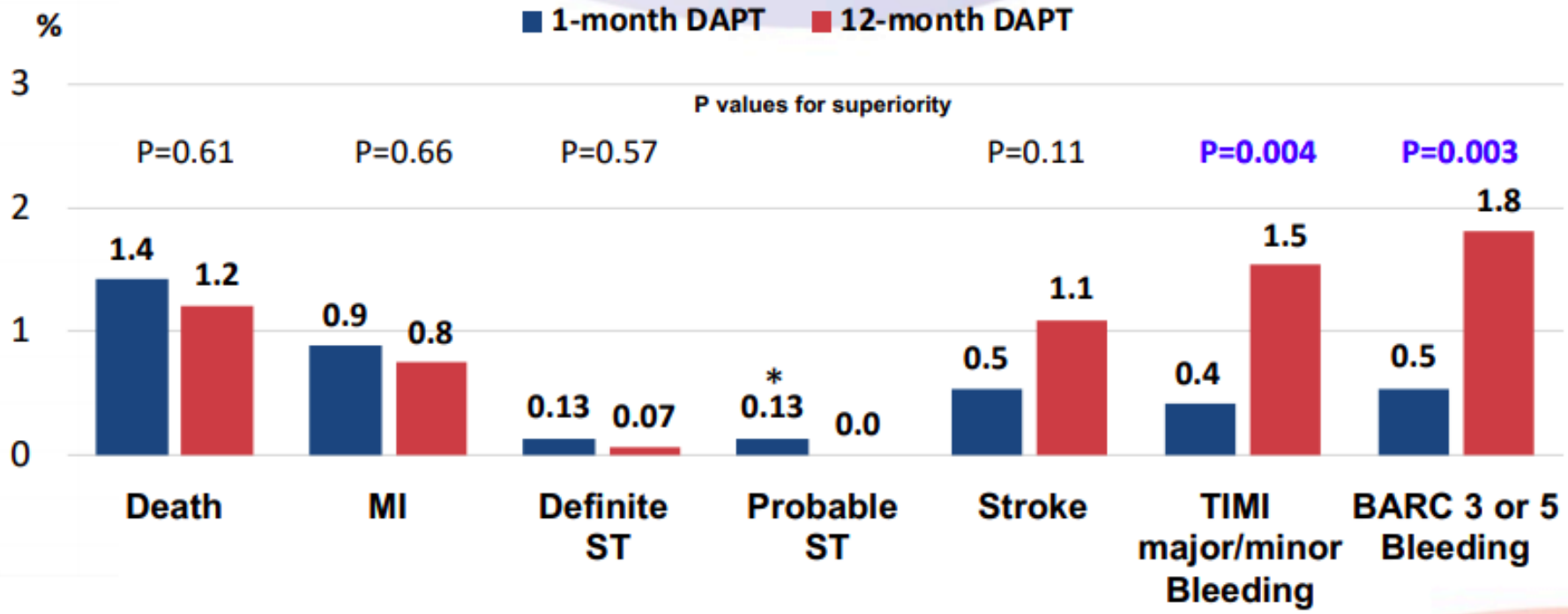
IVUS - guided and - controlled

STOPDAPT-2

Baseline Clinical Characteristics

	1-month DAPT N=1500	12-month DAPT N=1509
Age, years	68.1±10.9	69.1±10.4
Men	79%	77%
ACS	38%	39%
STEMI	19%	18%
Stable CAD	62%	61%
Diabetes	39%	38%
Severe CKD (eGFR<30ml/min/m^2)	6%	6%
Prior MI	14%	13%
Prior PCI	34%	35%
CREDO-Kyoto thrombotic risk score		
High; Intermediate; Low	8%; 21%; 71%	8%; 24%; 68%
CREDO-Kyoto bleeding risk score		
High; Intermediate; Low	7%; 27%; 66%	7%; 27%; 66%

Clinical Outcomes at 1 year



* 2 cases of probable ST (undefined death) in the 1-month DAPT group occurred before discontinuing DAPT at 1-month

Others…

EVOLVE short DAPT: solo Aspirine after 3-month DAPT in elderly pts.

TWILIGHT: solo Ticagrelor after 3-month DAPT

Onyx ONE: only 1 month DAPT with polymer-free DES

Triple Therapy
(DAPT + OAC)

PCI /
- *AF with indication of OAC,*
- *Moderate-severe mitral stenosis,*
- *Mechanic valve*

Pre-PCI Considerations

1. ***Assess the need for PCI:***
Does the patient really need a stent ?
The 2017 appropriate use criteria (AUC) for PCI

2. ***Assess the risk of stroke:***
Long-term OAC is recommended for CHA2DS2-VASc > 2 in men and > 3 in women.

3. ***Assess the risk of bleeding:***
A HAS-BLED score of >3 is associated with a high bleeding risk but is not a reason to withhold anticoagulation.

Modifiable and non-modifiable risk factors for bleeding in anticoagulated patients with AF

Modifiable bleeding risk factors:
Hypertension (especially when systolic blood pressure is >160 mmHg)
Labile INR or time in therapeutic range <60% in patients on vitamin K antagonists
Medication predisposing to bleeding, such as antiplatelet drugs and non-steroidal anti-inflammatory drugs
Excess alcohol (≥8 drinks/week)
Potentially modifiable bleeding risk factors:
Anaemia
Impaired renal function
Impaired liver function
Reduced platelet count or function

Non-modifiable bleeding risk factors:
Age (>65 years) (≥75 years)
History of major bleeding
Previous stroke
Dialysis-dependent kidney disease or renal transplant
Cirrhotic liver disease
Malignancy
Genetic factors
Biomarker-based bleeding risk factors:
High-sensitivity troponin
Growth differentiation factor-15
Serum creatinine/estimated CrCl

European Heart Journal - doi:10.1093/eurheartj/ehw210

Shortening and downgrading Triple therapy

ISAR-TRIPLE: Study Organization

TEST HYPOTHESES:

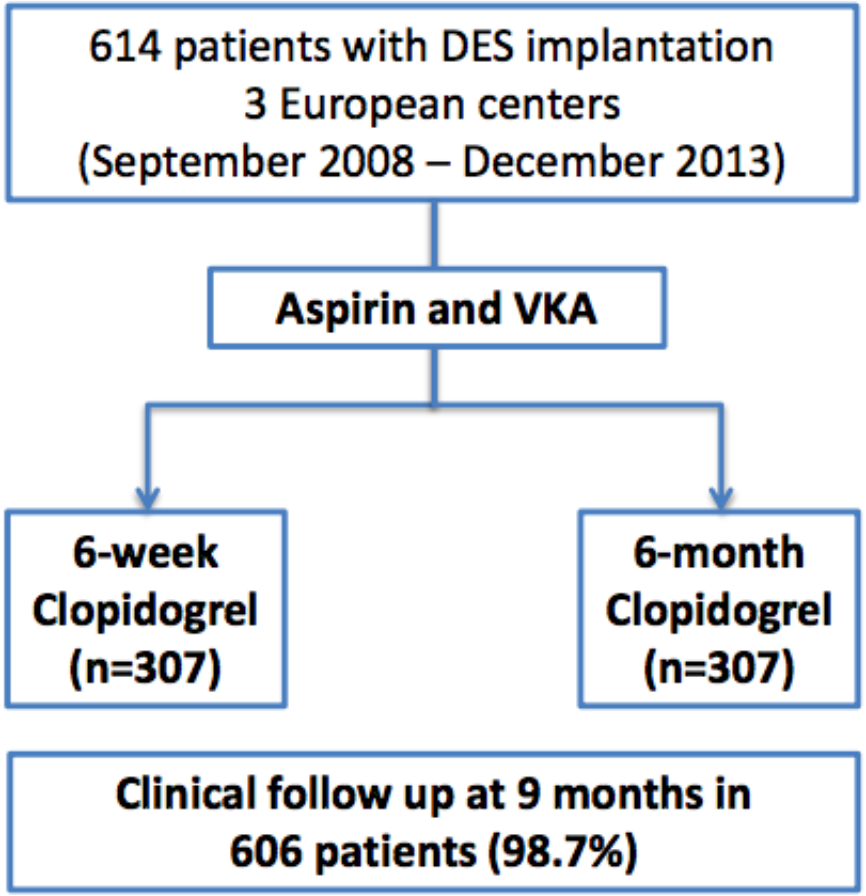
6-week superior to 6-month therapy; Primary Endpoint 10%, Risk reduction 60% with 6-week therapy; Power = 80%, alpha = 0.05; 283 patients per group

PRIMARY ENDPOINT:

- Death, myocardial infarction, definite stent thrombosis, stroke or TIMI major bleeding at 9 months

SECONDARY ENDPOINTS:

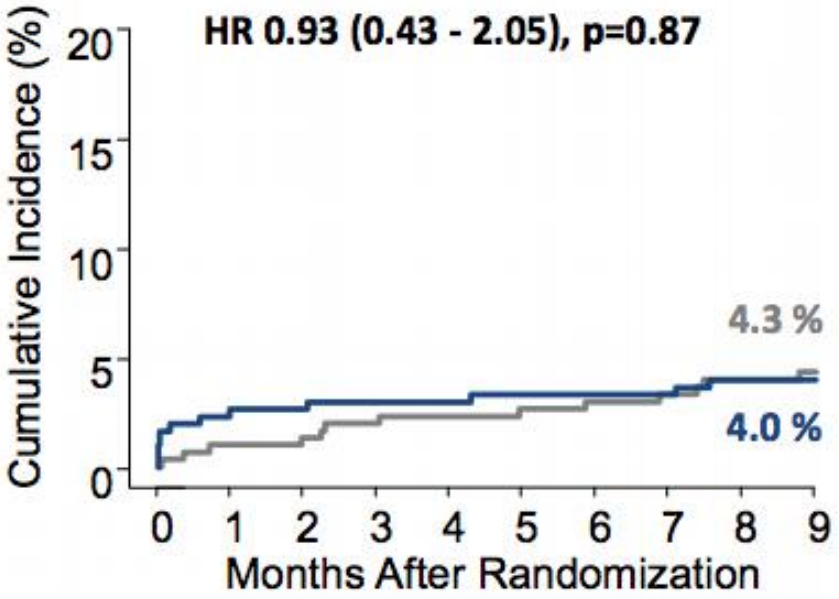
- Ischemic complications: Cardiac death, myocardial infarction, definite stent thrombosis or ischemic stroke
- Bleeding complications (TIMI major)



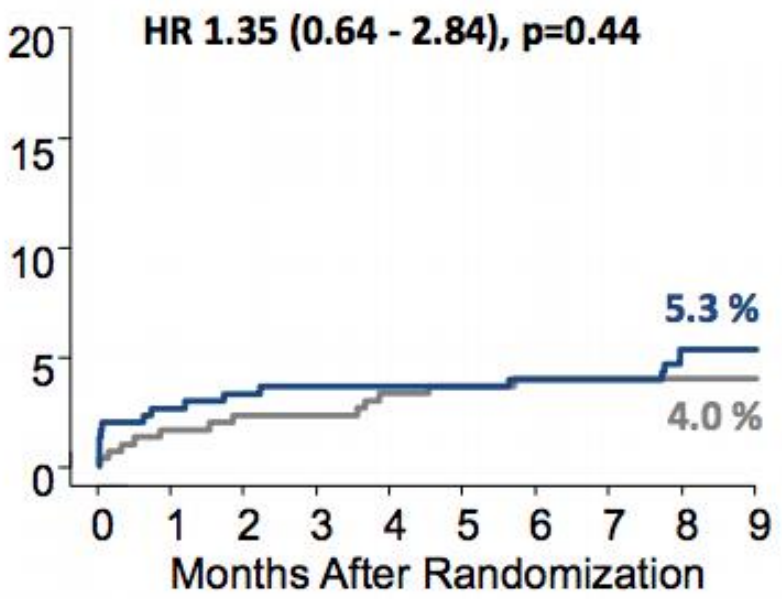
VKA: Vitamin K Antagonist

Secondary Endpoints

Cardiac death, myocardial infarction, stent thrombosis or ischemic stroke

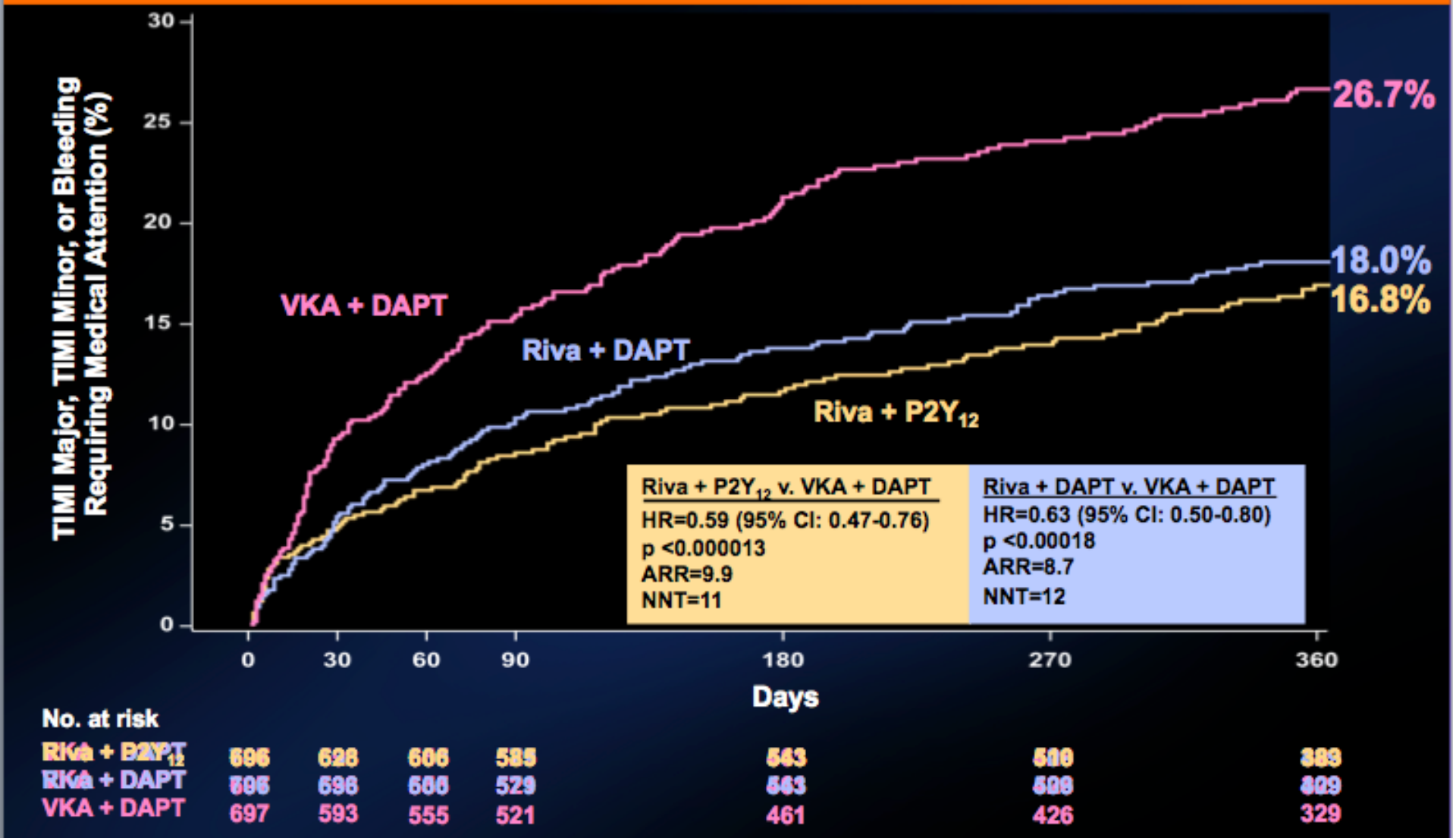


TIMI major bleeding



6-month group
6-week group

Kaplan-Meier Estimates of First Occurrence of Clinically Significant Bleeding Events



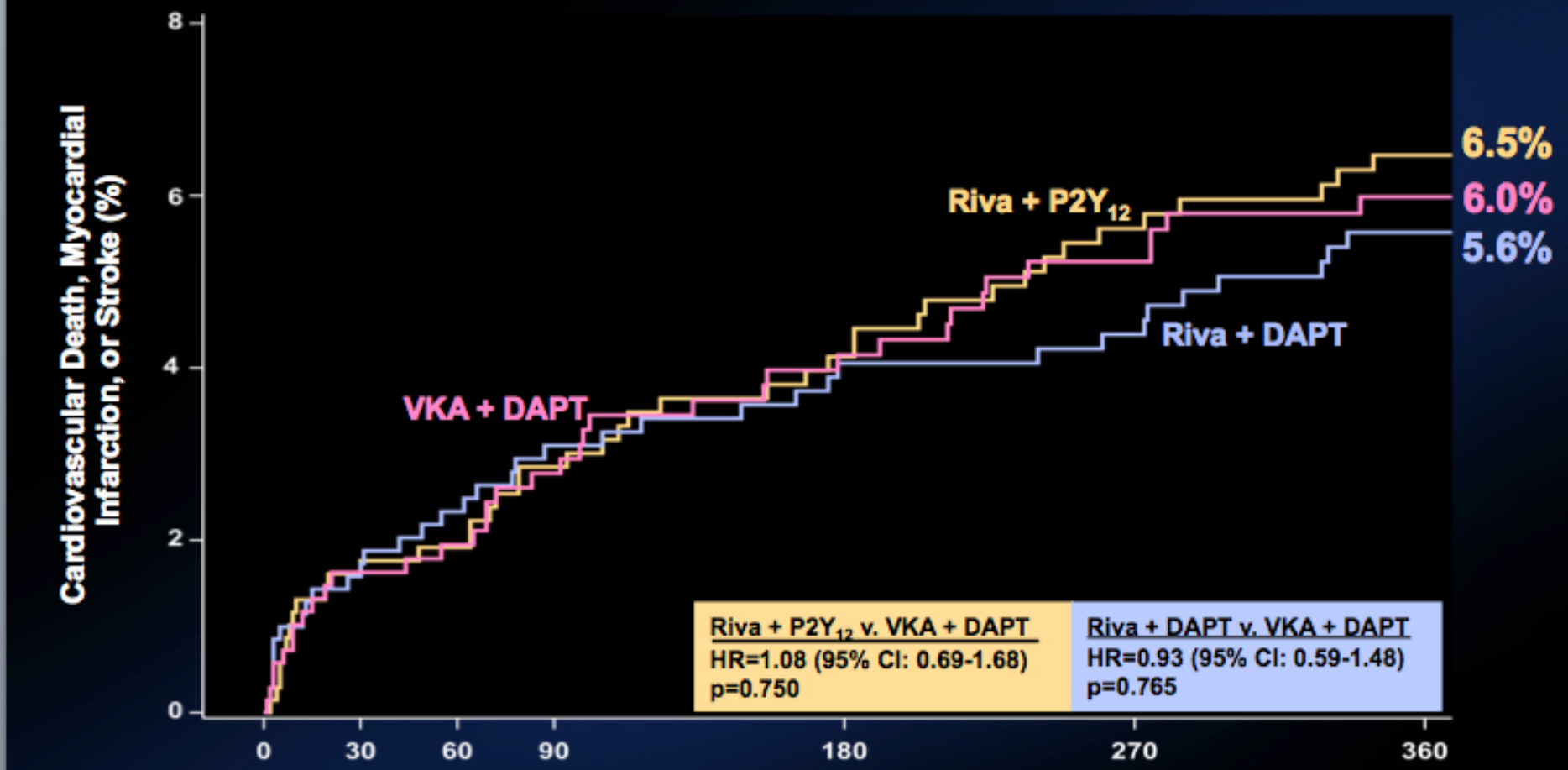
No. at risk

Riva + P2Y12	696	628	606	585	543	510	383
Riva + DAPT	696	596	566	529	463	409	309
VKA + DAPT	697	593	555	521	461	426	329

Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Clinically significant bleeding is the composite of TIMI major, TIMI minor, and BRMA.
Hazard ratios as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Log-Rank P-values as compared to VKA group are based on the (stratified, only for Overall, 2.5 mg BID/15 mg QD comparing VKA) two-sided log rank test.

Gibson et al. AHA 2016

Kaplan-Meier Estimates of First Occurrence of CV Death, MI or Stroke



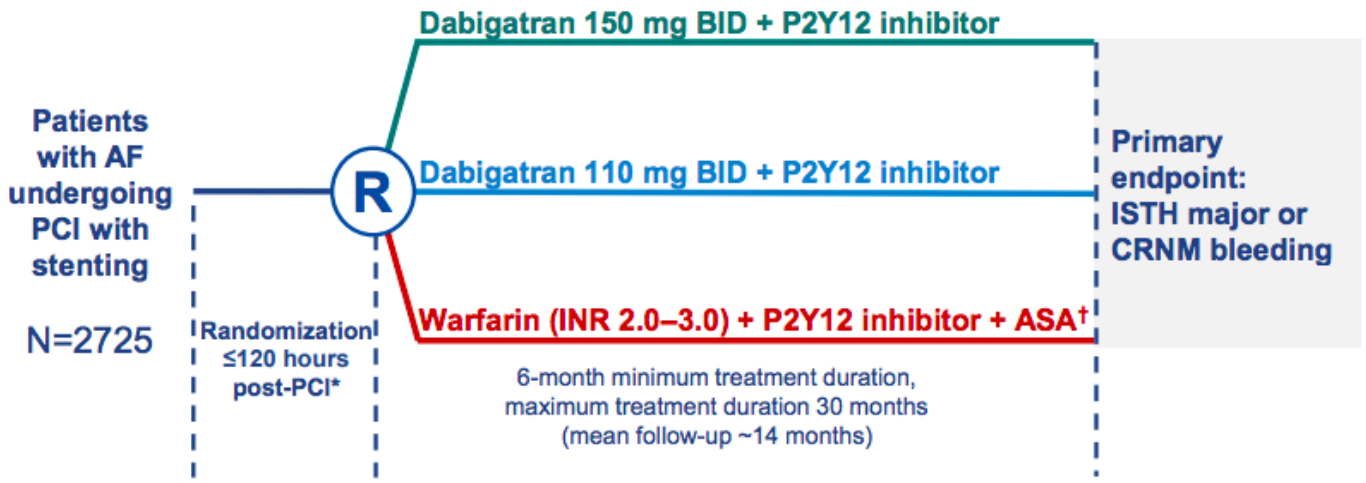
No. at risk							
Riva + $P2Y_{12}$	694	648	633	621	590	562	430
Riva + DAPT	704	662	640	628	596	570	457
VKA + DAPT	695	635	607	579	543	514	408

Treatment-emergent period: period starting after the first study drug administration following randomization and ending 2 days after stop of study drug.
Composite of adverse CV events is composite of CV death, MI, and stroke.
Hazard ratios as compared to VKA group are based on the (stratified, only for the Overall, 2.5 mg BID/15 mg QD comparing VKA) Cox proportional hazards model.
Log-Rank P-values as compared to the VKA group are based on the (stratified, only for Overall, 2.5 mg BID/115 mg QD comparing VKA) two-sided log rank test.
6 Subjects were excluded from all efficacy analyses because of violations in Good Clinical Practice guidelines

Gibson et al. AHA 2016

RE-DUAL PCI tested the safety and efficacy of 2 regimens of dual therapy with dabigatran without ASA vs triple therapy with warfarin

RE-DUAL PCI was a multicentre, randomized, open-label trial

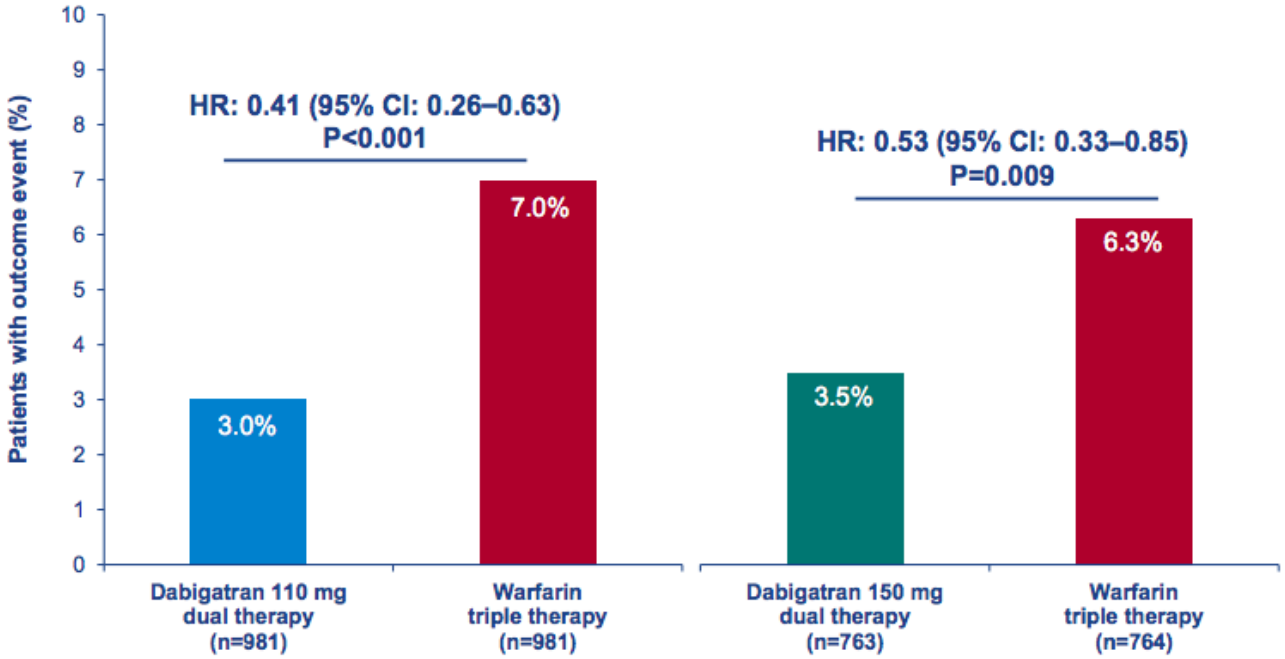


Primary endpoint was time to first ISTH major or clinically relevant non-major bleeding event

Composite efficacy Endpoint: Time to first event of death, TE event (MI, stroke, systemic embolism) and unplanned revascularization

Cannon et al. Clin Cardiol 2016; Cannon et al. N Engl J Med

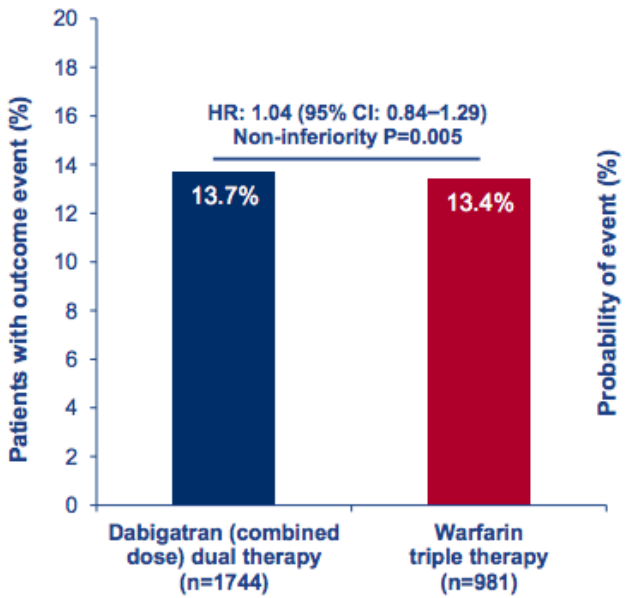
TIMI major or minor bleeding: significantly lower rate for dabigatran dual therapy

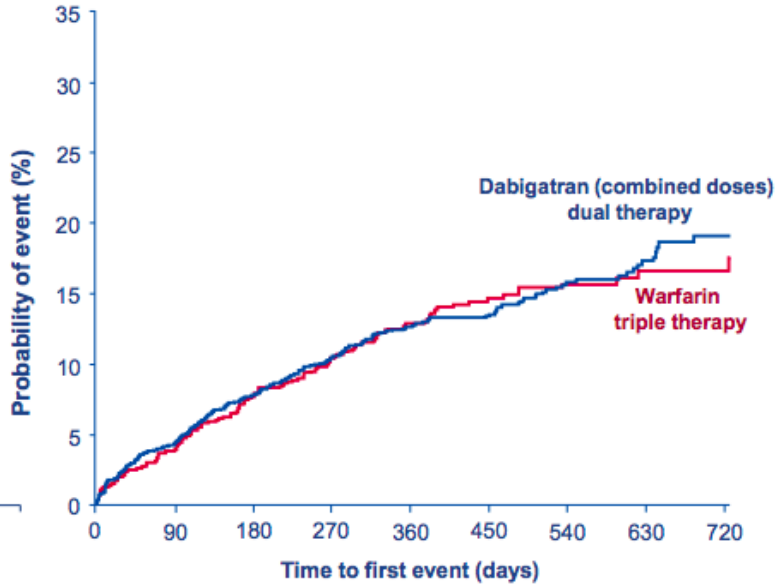


TIMI major bleeding definition: fatal, ICH, clinically overt bleeding with fall in Hb ≥5 g/dL; TIMI minor bleeding definition: Clinically overt bleeding (including imaging), resulting in Hb drop of 3 to <5 g/dL; TIMI, Thrombolysis in Myocardial Infarction; Cannon et al. N Engl J Med 2017

Dabigatran dual therapy was non-inferior to warfarin triple therapy in the composite efficacy endpoint

Composite endpoint of death or thromboembolic event (MI, stroke or systemic embolism) or unplanned revascularization (PCI/CABG)

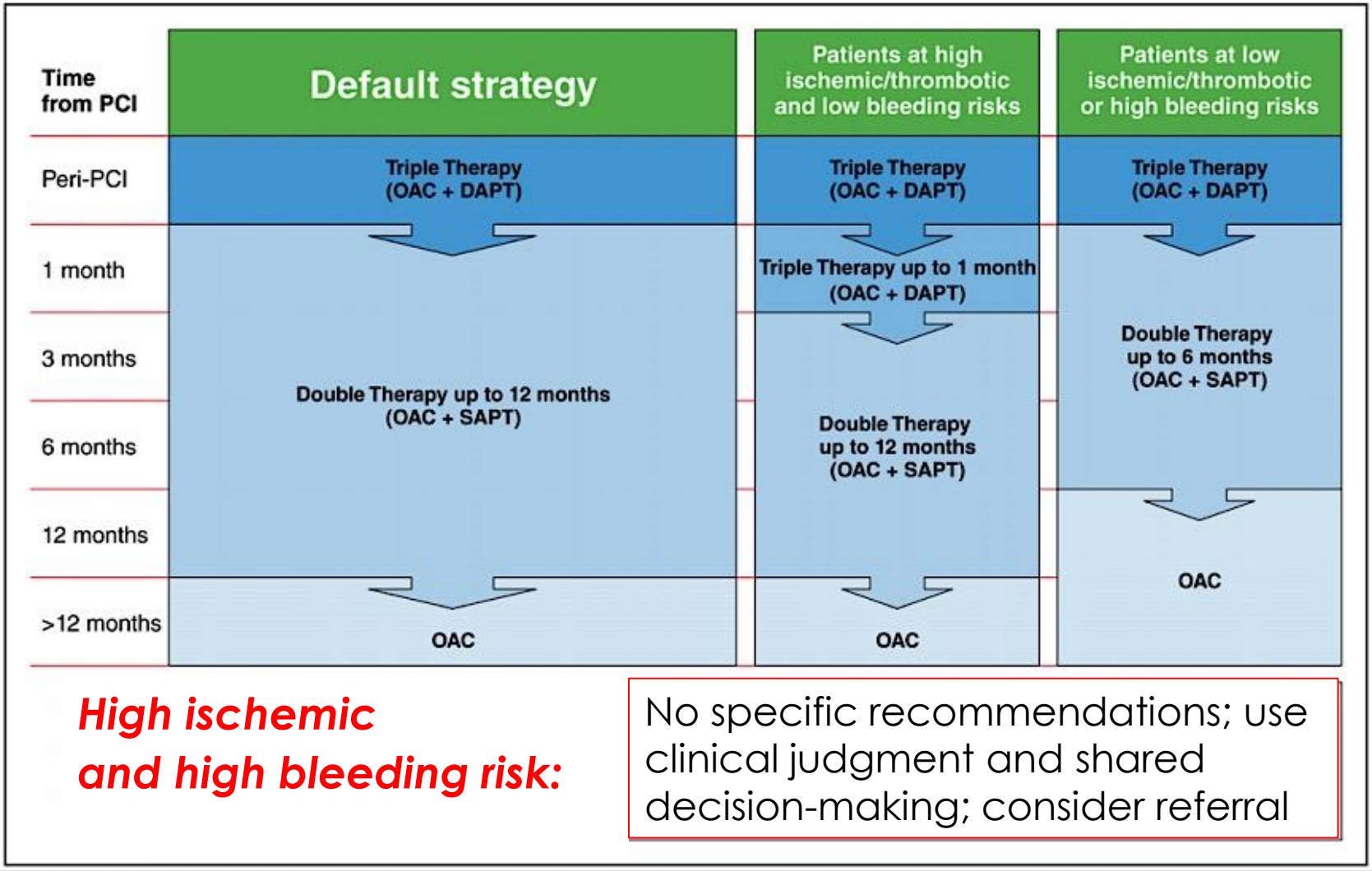




CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; Cannon et al. N Engl J Med 2017; Cannon et al ESC 2017

C. Considerations After PCI

Antithrombotic therapy in patients with AF undergoing PCI treated with OAC



High ischemic and high bleeding risk:

No specific recommendations; use clinical judgment and shared decision-making; consider referral

2018 North American expert consensus update.

2018 North American expert consensus update.

C. Considerations After PCI

2) Antiplatelet agent considerations

- Most patients enrolled in recent studies were taking Clopidogrel.
- Prasugrel and Ticagrelor should not be used as a component of Triple therapy *(Class III-harm / 2017 ESC guidelines)*.
- Aspirin dose should typically not exceed 81 mg.

Cesar Jara and Jayant Bagai. Tips for Management of Patients Who Require Oral Anticoagulation for Atrial Fibrillation and Post-PCI Antiplatelet Therapy. SCAI-QIT Tips, June 17.2019.

2018 North American expert consensus update.

C. Considerations After PCI

3) Anticoagulant considerations

- No role of withholding OAC in patients with AF post-PCI and treating them with just DAPT.
- Both ESC guidelines and NAEC recommend DOAC instead of warfarin if no contraindication.
- DOACs are not approved for "valvular AF," which is AF in the presence of a mechanical heart valve or moderate-to-severe mitral stenosis.
- Reasonable to continue Warfarin if tolerable or if CrCl < 30 ml/min. INR should be 2-2.5.

Cesar Jara and Jayant Bagai. Tips for Management of Patients Who Require Oral Anticoagulation for Atrial Fibrillation and Post-PCI Antiplatelet Therapy. SCAI-QIT Tips, June 17.2019.

Combination with Proton Pump Inhibitors (PPI)

Summary and Synthesis of Guideline, Expert Consensus Documents, and Comprehensive Review Article Recommendations on the ***Management of Patients Treated With Triple Therapy***

- Assess ischemic and bleeding risks using validated risk predictors (e.g., CHA2DS2-VASc, HAS-BLED)
- Keep triple therapy duration as short as possible; dual therapy only (oral anticoagulant and clopidogrel) may be considered in select patients
- Consider a target INR of 2.0–2.5 when warfarin is used
- Clopidogrel is the P2Y12 inhibitor of choice
- Use low-dose (≤100 mg daily) aspirin
- **PPIs should be used in patients with a history of gastrointestinal bleeding and are reasonable to use in patients with increased risk of gastrointestinal bleeding**

Measures to minimize bleeding while on DAPT

Recommendations		
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 DAPTc is recommended.	I	B
Routine platelet function testing to adjust antiplatelet therapy before or after elective stenting is not recommended	III	A

2017 ESC focused update on DAPT in coronary artery disease

Interaction between PPI and P2Y12 inhibitors

- Only between Omeprazol, Esomeprazol and Clopidogrel
- Study results not consistent

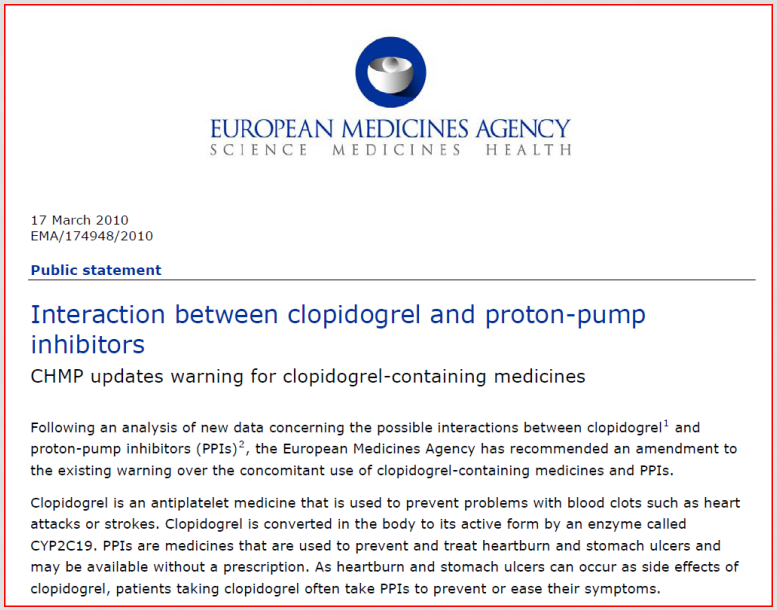
FDA 10. OCT 2010

- With regard to the proton pump inhibitor (PPI) drug class, this recommendation applies ***only to omeprazole and not to all PPIs***. Not all PPIs have the same inhibitory effect on the enzyme (CYP 2C19) that is crucial for conversion of Plavix into its active form.

- **Pantoprazole** (Protonix) may be an alternative PPI for consideration. It is a weak inhibitor of CYP2C19 and has less effect on the pharmacological activity of Plavix than omeprazole.

EMA MARCH 17, 2010

...there are no solid grounds to extend the warning to other PPIs. The class warning for all PPIs has been replaced with a warning stating that **only the concomitant use of clopidogrel and omeprazole or esomeprazole should be discouraged.**



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

17 March 2010
EMA/174948/2010

Public statement

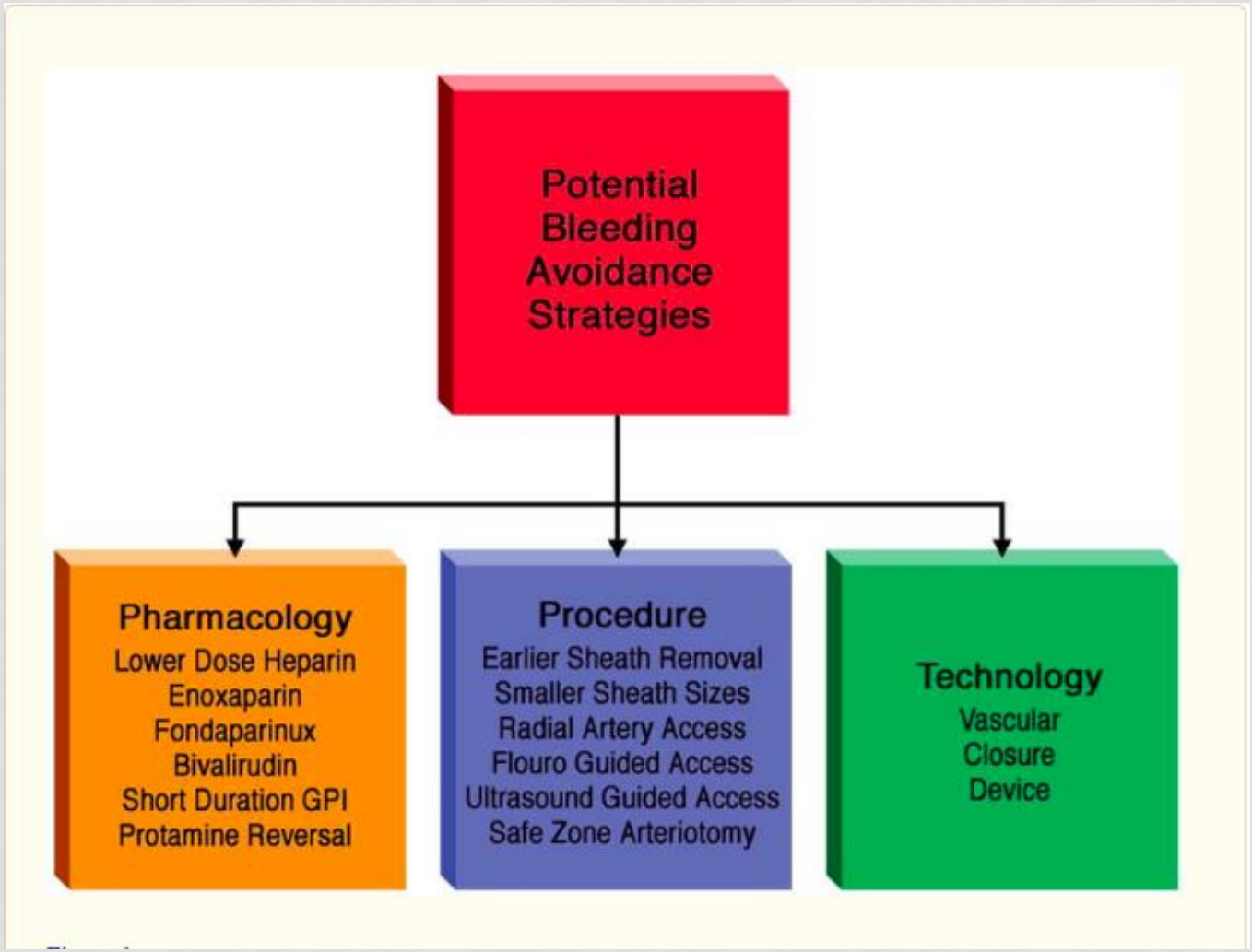
Interaction between clopidogrel and proton-pump inhibitors

CHMP updates warning for clopidogrel-containing medicines

Following an analysis of new data concerning the possible interactions between clopidogrel[1] and proton-pump inhibitors (PPIs)[2], the European Medicines Agency has recommended an amendment to the existing warning over the concomitant use of clopidogrel-containing medicines and PPIs.

Clopidogrel is an antiplatelet medicine that is used to prevent problems with blood clots such as heart attacks or strokes. Clopidogrel is converted in the body to its active form by an enzyme called CYP2C19. PPIs are medicines that are used to prevent and treat heartburn and stomach ulcers and may be available without a prescription. As heartburn and stomach ulcers can occur as side effects of clopidogrel, patients taking clopidogrel often take PPIs to prevent or ease their symptoms.

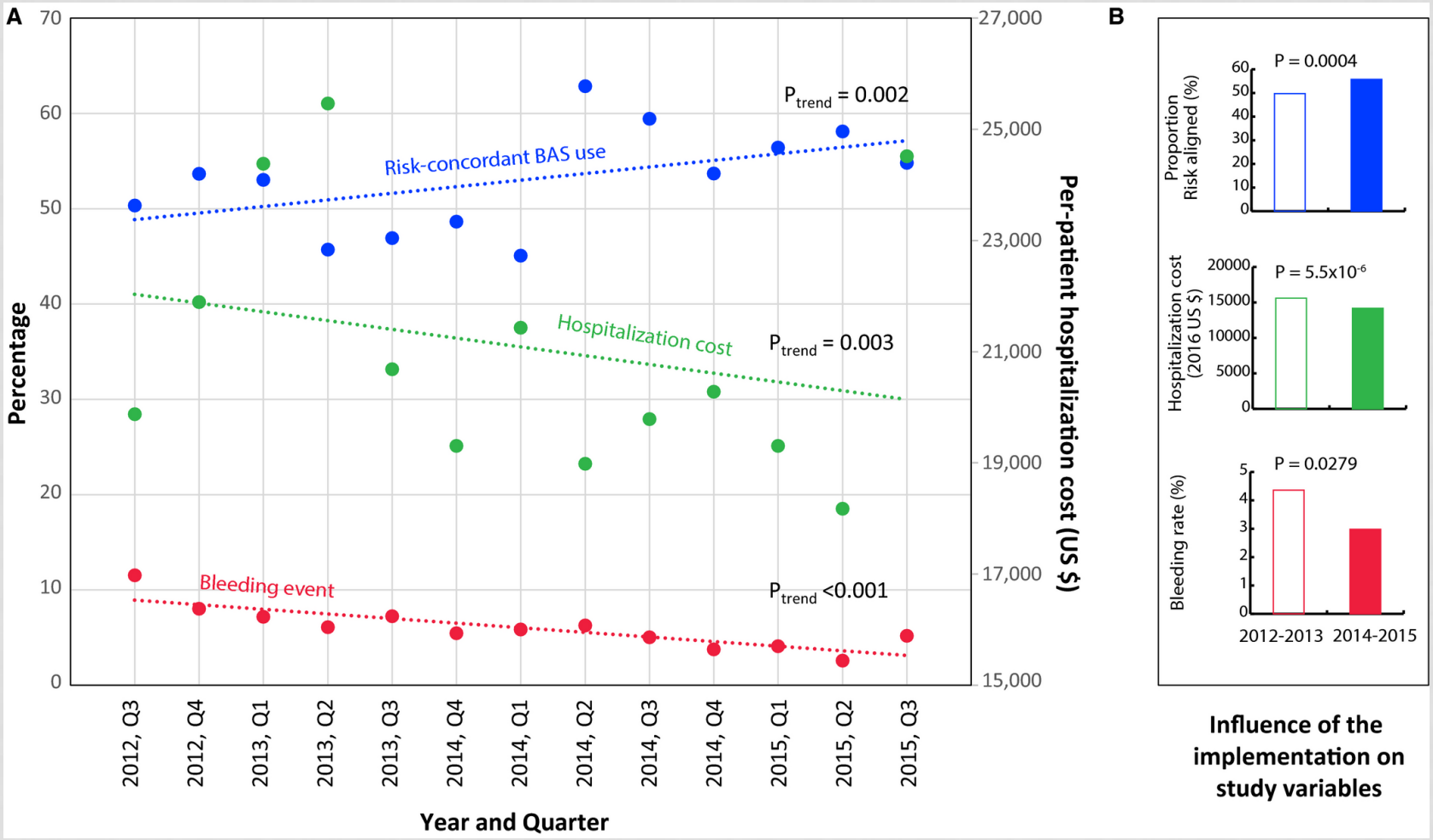
Bleeding Avoidance Strategies (BAS)



Potential improvements in bleeding complications may be related to procedural, pharmacologic and technology changes occurring over the past two decades.

J Am Coll Cardiol. 2011 Jun 28; 58(1): 1–10.

Trends in risk-concordant use of bleeding avoidance strategies (BAS), bleeding rates, and hospitalization costs



Journal of the American Heart Association. 2018;7:e008551

Management of post-PCI bleeding

Management of post-PCI bleeding

	Appearance	DAPT	OAC	Others
TRIVIAL	- Skin ecchimosis, self-resolving epistasis, small conjunctival bleeding	- Continue	- Continue or skip one dose	No
MILD	- Not self-resolving epistasis, moderate conj. bleeding, - Genitourinary or gastroint. bleeding, mild hemoptysis w. no significant blood loss	- Continue - Consider shortening - Switch to less potent P2Y12(-).	- Triple → Dual w. Clopidogrel	PPI
MODERATE ↓> 3g Hb	genitourinary or gastroint. bleeding with significant blood loss but hemodynamically stable	- Stop and → SAPT (P2Y12 inh.). - Consider shortening - Switch to less potent P2Y12(-).	- Discontinue or reversal unless high thrombotic risk - Down to Dual w. Clopidogrel - Dual → Single w.OAC	PPI

Management of post-PCI bleeding

Class	Appearance	DAPT	OAC	Others
SEVERE >5g Hb	- Genitourinary or gastroint. bleeding with significant blood loss but hemodynamically stable	- Stop and → SAPT (P2Y12 inh.) - Stop all antithrombotics if bleeding persists - Shortening and switch to less potent P2Y12(-).	- Discontinue or reversal unless high thrombotic risk - Restart w. Dual (Clopidogrel + OAC) - Or switch Dual → Single w.OAC	- PPI - RBC transfusion (Hb < 8) - Surgery or endoscopy
LIFE-THREATENING	- Massive genitourin., respir, or gastroint. bleeding . with hemodynamic unstability, - Active intracranial, spinal or intraocular.	- Discontinue all antithrombotics - Restart SAPT with P2Y12(-)	- Stop and reverse	- Fluid - RBC - Platelet - PPI - Surgery or Endoscopy

Antidote of NOAC

I	B-NR	3. **Idarucizumab is recommended for the reversal of dabigatran in the event of life-threatening bleeding or an urgent procedure (S4.3-2).** **NEW**: New evidence has been published about idarucizumab to support LOE B-NR.
IIa	B-NR	4. **Andexanet alfa can be useful for the reversal of rivaroxaban and apixaban in the event of life-threatening or uncontrolled bleeding (S4.3-3, S4.3-4).** **NEW**: New evidence has been published about andexanet alfa to support LOE B-NR.

2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

Idarucizumab (PRAXBIND)

Monoclonal antibody binds and inactivates dabigatran.

(a) Last dose taken within <12 hours (with normal renal function)

(b) Significantly abnormal PTT and/or thrombin time (especially thrombin time >25 seconds)

Dose

- A total of 5 grams is usually sufficient. This is typically provided as two separate 2.5-mg doses

- However, for patients with an unusually high level dabigatran (e.g. new-onset renal failure with drug accumulation), there is a possibility that additional doses might be needed.

Josh Farkas. Anticoagulant reversal. In: Internet Book of Critical Care (IBCC). February 11, 2017

Andexanet Alfa

- Specifically designed as a reversal agent for Xa-inhibitors.

- Clinical data is limited, and this agent is insanely expensive.

- Many hospitals have chosen not to include this agent in their formularies.

Josh Farkas. Anticoagulant reversal. In: Internet Book of Critical Care (IBCC). February 11, 2017

Two dosing regimens:

- Low-dose regimen: 400-mg IV bolus at 30 mg / min, followed by a 2-hour IV infusion at 4 mg / min.

- High dose: 800-mg IV bolus at 30 mg / min, followed by a 2-hour IV infusion at 8 mg per minute

Table 2 Dosing Recommendations for Andexanet Alfa

FXa Inhibitor	Last FXa Inhibitor Dose	Last FXa Inhibitor Dose < 8 Hours Prior/Unknown	Last FXa Inhibitor Dose ≥ 8 Hours Prior
Rivaroxaban	≤ 10 mg	low dose	low dose
Rivaroxaban	> 10 mg / unknown	high dose	low dose
Apixaban	≤ 5 mg	low dose	low dose
Apixaban	> 5 mg / unknown	high dose	low dose

REVERSAL OF AVK

- Vitamin K lowers INR faster than withholding warfarin alone; however, it has not been clearly demonstrated that vitamin K treatment does lower the risk of major hemorrhage.

- A dose of 1-2.5mg vitamin K1 reduces the range of INR from 5.0-9.0 to 2.0-5.0 within 24-48 hours, and for an INR >10.0, a dose of 5mg may be more appropriate.

- Vitamin K is less effective for acenocoumarol or phenprocoumon than warfarin.

- The absolute risk of thromboembolism associated with overcorrection appears to be ***in the same range*** as the risk of bleeding due to over-anticoagulation.

Am J Cardiovasc Drugs. 2004;4(1):43-55.

warfarin: urgent reversal

- The most important intervention to reverse warfarin is vitamin K.
- 10 mg IV, as soon as possible (***infused over 30 minutes***).
- FFP or PCC will work only for ~8 hours.
- Vitamin K will do the job after the FFP/PCC wears off. It takes Vitamin K 6-12 hours to start working

Josh Farkas. Anticoagulant reversal. In: Internet Book of Critical Care (IBCC). February 11, 2017

Reversal of Heparin given via bolus

- Heparin given within <30 minutes : 1 mg protamine per 100 units heparin
- Heparin given 30-60 minutes ago : 0.5-0.75 mg protamine per 100 units heparin
- Heparin given 60-120 minutes ago : 0.375-0.5 mg protamine per 100 units heparin
- Heparin given 2-6 hours ago : 0.25-0.375 mg protamine per 100 units heparin

Josh Farkas. Anticoagulant reversal. In: Internet Book of Critical Care (IBCC). February 11, 2017

Reversal of heparin infusion

1 mg protamine per 100 units of heparin which the patient has received **over the last two hours.**

Josh Farkas. Anticoagulant reversal. In: Internet Book of Critical Care (IBCC). February 11, 2017

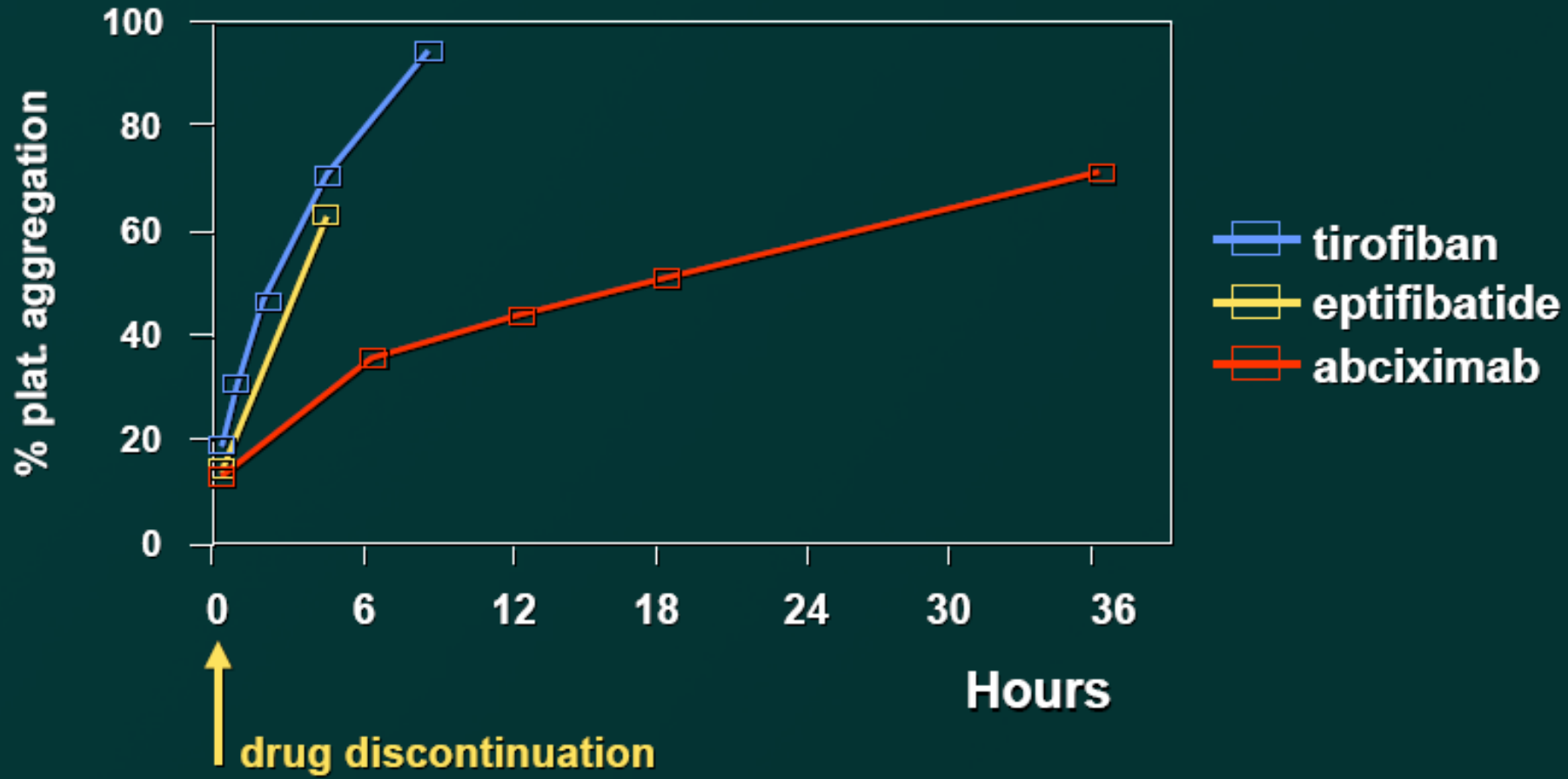
Reversal of Enoxaparine

- **Enoxaparin within <8 hours:** 1 mg protamine per 1 mg enoxaparin. If bleeding continues, may give additional 0.5 mg protamine per mg enoxaparin.
- **Enoxaparin given 8-12 hours previously:** 0.5 mg protamine per 1 mg enoxaparin.
- **Enoxaparin given >12 hours previously:** Protamine less likely to be beneficial.

Josh Farkas. Anticoagulant reversal. In: Internet Book of Critical Care (IBCC). February 11, 2017

GPIIb/IIIa Inhibitors

Reversibility of Platelet Inhibition



ACUTE AND SEVERE GPIIB/IIIA-RELATED THROMBOCYTOPENIA

- Rate < 1%
- Abxicimab > Tirofiban > Eptifibatide
- Platelets < 20K
- Discontinue drug (and Heparine), repeat platelet counting
- Management:
  - ***Abxicimab***: infusion of 1 platelet unit

    (Long biological half-life: 6-12 hours)
  - ***Eptifibatid, Tirofiban***: repeat platelet counting after 4-6h

    (Intermediate plasma half-life: 2 - 2,5 hours)

- Target: platelet > 20K
- Always check platelet counting before using GPIIB/IIIA

CONCLUSIONS

- ❖ Bleeding is the most common complication relating to PCI ***(procedure, antithrombotics…)***

- ❖ Some of treatment strategies for bleeding make the outcome worse ***(discontinuation of antithrombotics, transfusion…)***

- ✧ Careful evaluation Thrombosis / Bleeding risk before PCI,
- ✧ Application of Bleeding Avoidance Strategy during PCI
- ✧ Shortening and downgrading combination of antithrombotic therapy

… potentially improve PCI-related bleeding comlications

Thank you for your attention