Le mieux est l'ennemi du bien

ou quand trop devient moins pour les traitements anti-thrombotiques chez les patients avec Mcas et indication d'anticoagulation

- Dr Jean-Marc Raymond
  - Juin 2021

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Conflits d'intérêts

Conférencier et comité consultatif : Servier et Alliance BMS/Pfizer – 2011 - 2021

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Objectif

- Définir les facteurs qui influencent les évènements dans une population avec indication d'ACO et MCAS
- Définir et connaître la durée optimale du traitement anti-thrombotique lors du traitement invasif coronarien avec et sans ACO
- Revisiter les dernières recommandations canadiennes
  - les données ayant permis leur rédaction en ce qui a trait à l'utilisation des ACOD en association avec les anti-plaquettaires

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Cas Clinique SCA

- Homme 75 ans,
- FR de la MCAS: HTA, dyslipidémie, DT2, surcharge pondérale,
- ATCD: hypothyroïdie, HDB avec exérèse de polypes il y à 2 ans, fibrillation auriculaire paroxystique sous DOAC,
- Admis pour STEMI antéro-latéral traité par angioplastie primaire avec implantation de trois EEMs (IVA et D1). Reperfusion complète, flot TIMI 3.

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Cas Clinique SCA

- Examen physique normal,
- Hb 121, Plaquettes 240
- Creat 112, eGFR 45, HbA1c 6.9%
- ETT: dysfonction segmentaire avec HK modérée antéro-latérale et akininésie apicale. FE 40%,

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Selon les recommandations canadiennes, la meilleure combinaison antithrombotique pour ce patient serait?

1. AAS 80 mg ID x 1 mois + Ticagrelor 90 mg BID + coumadin
2. Ticagrelor 90 mg BID + coumadin
3. AAS 80 mg ID x 1 mois + Ticagrelor 90 mg BID + Rivaroxaban 15 mg ID
4. AAS 80 mg ID x 3 mois + clopidogrel 75 mg ID + apixaban 2.5 mg BID
5. AAS 80 mg ID x 1 mois + clopidogrel 75 mg ID + apixaban 5 mg BID

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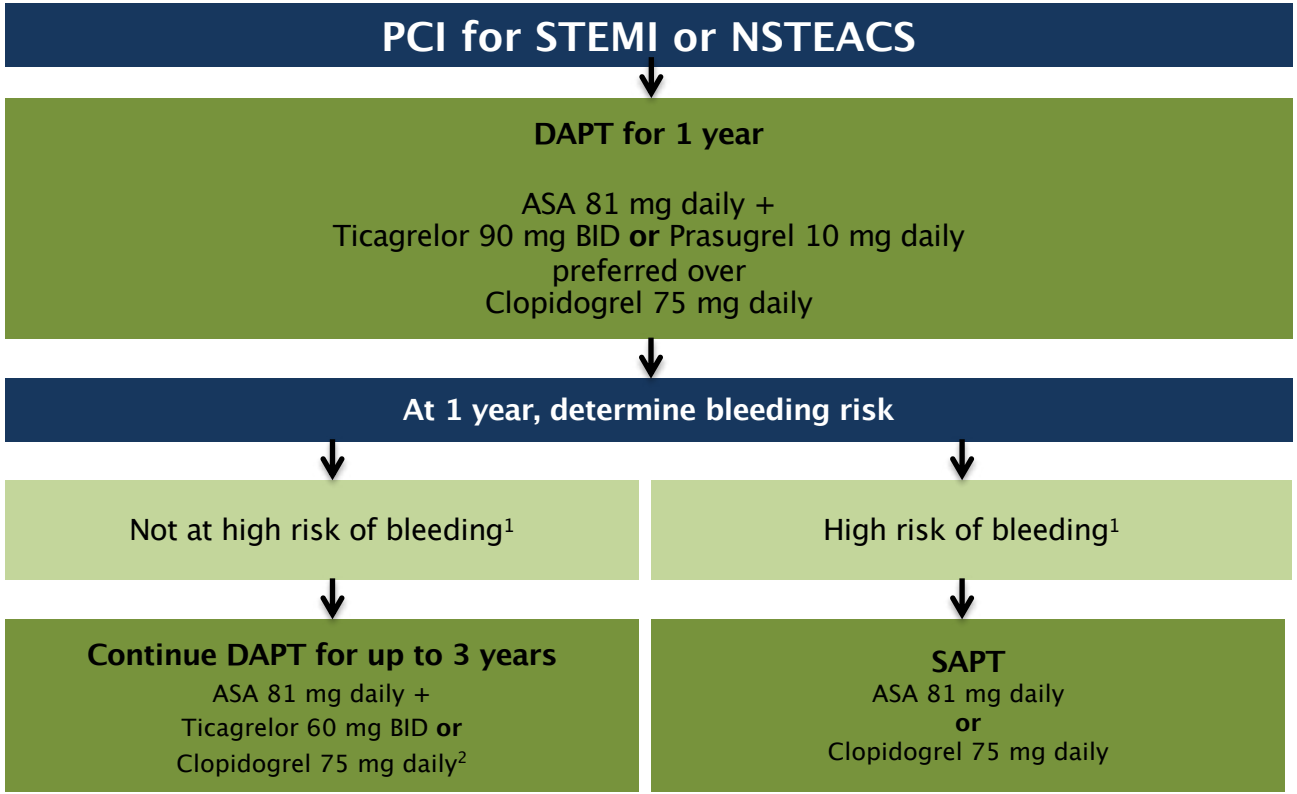

1 Factors associated with increased bleeding risk include: need for OAC in addition to DAPT, advanced age (> 75 years), frailty, anemia with hemoglobin < 110 g/dL, chronic renal failure (creatinine clearance < 40 mL/min), low body weight (< 60 kg), hospitalization for bleeding within last year, prior stroke/intracranical bleed, regular need for NSAIDS or prednisone

2 Instead of ticagrelor or clopidogrel, prasugrel 5–10 mg daily is also an option (weak recommendation)

Strong recommendation

Weak recommendation

Canadian Journal of Cardiology 34 (2018) 214-233

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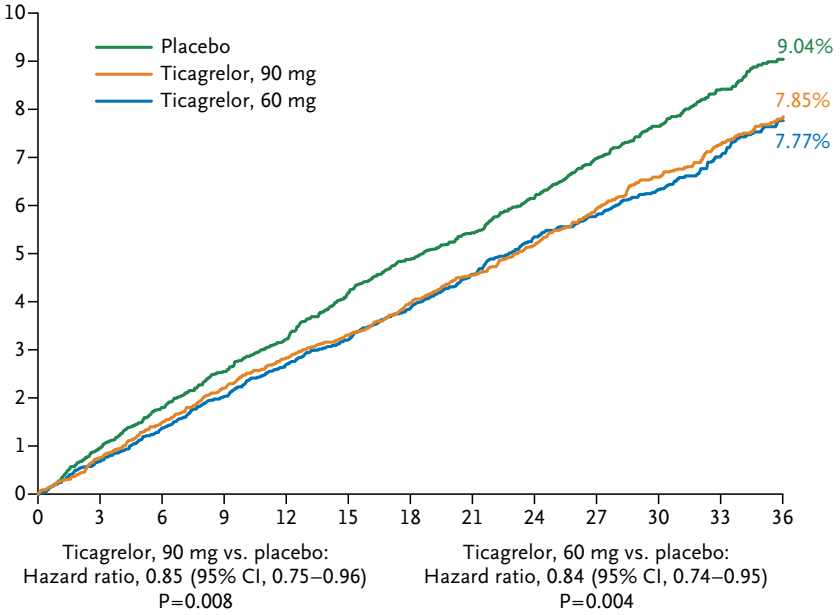
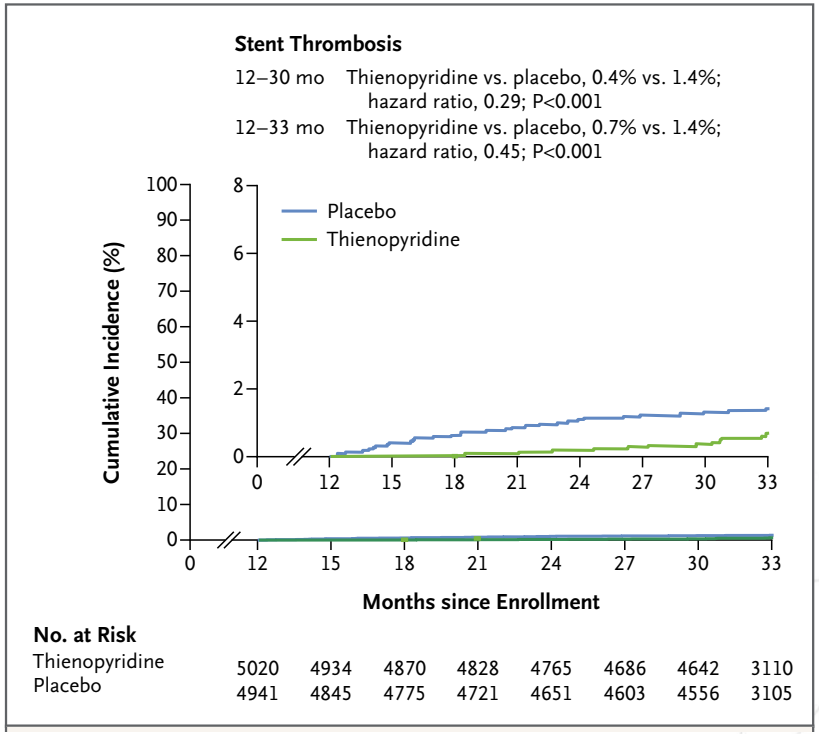
DAPT LONG TERME?





Bonaga and al, Pegasus-Timi 54, NEJM 2015
Mauri and al, Dapt study, NEJM 2014

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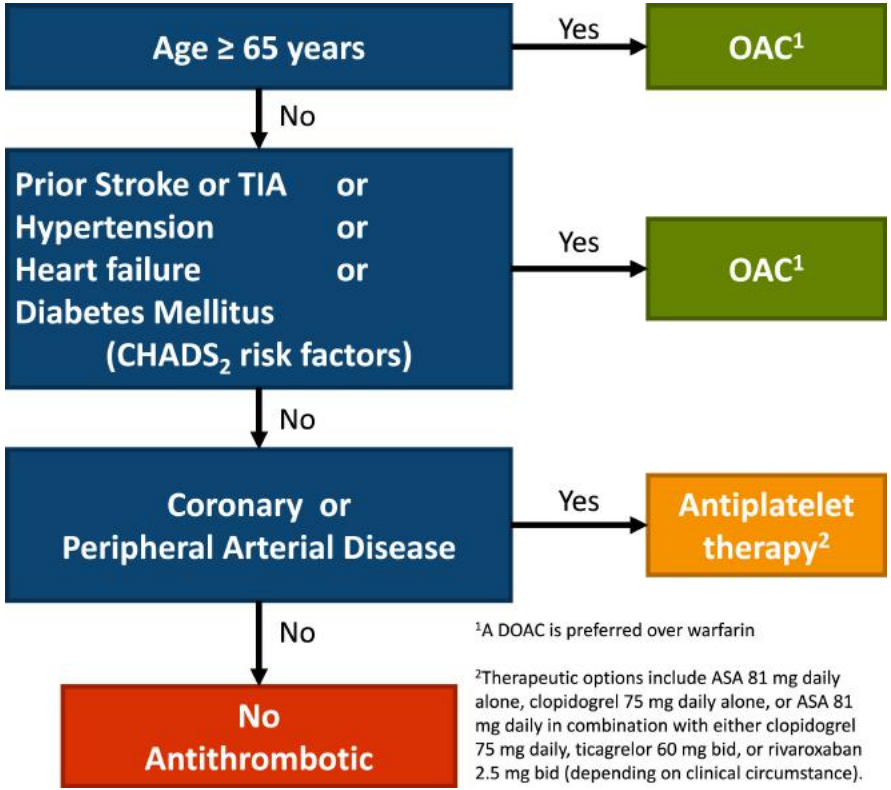

Canadian Journal of Cardiology 34 (2018) 1374-1395

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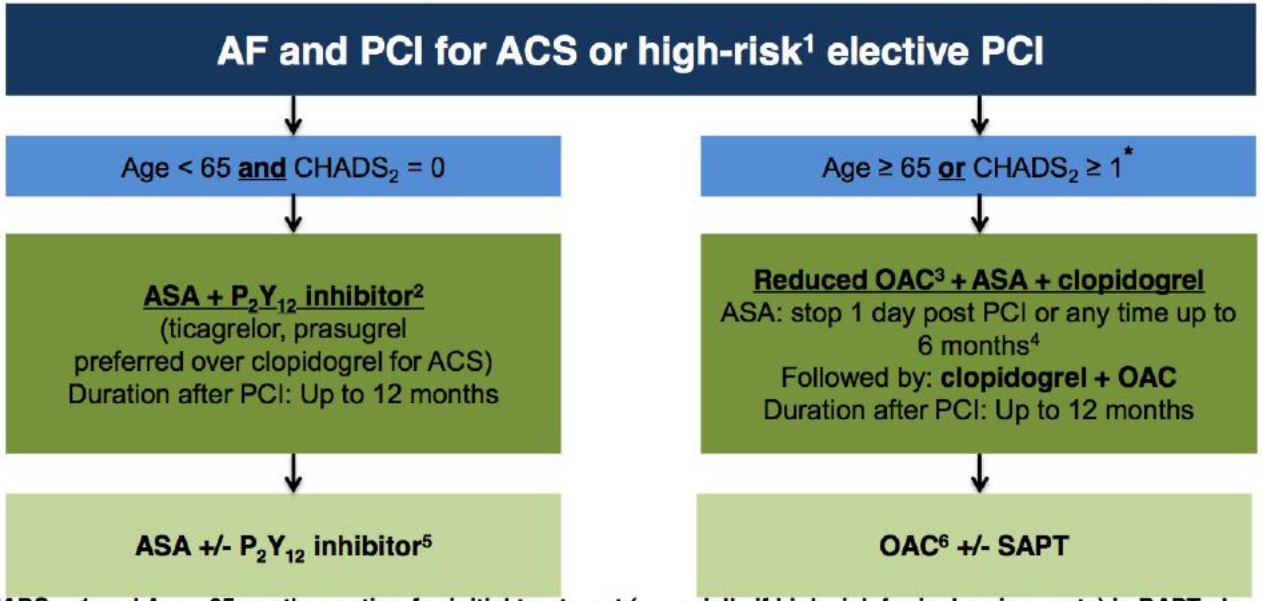
2018 CCS/CAIC Focused Update of the Guidelines for the Use of Antiplatelet Therapy



***If $CHADS_2$ =1 and Age< 65 another option for initial treatment (especially if high-risk for ischemic events) is DAPT alone using ASA+ticagrelor or ASA+prasugrel, similar to the recommendation for the $CHADS_2$=0 patient**

1. A PCI is considered high-risk based on clinical and angiographic features such as: diabetes, prior ACS, chronic renal dysfunction (creatinine clearance < 60 mL/min), prior stent thrombosis, current smoker, multi-vessel coronary artery disease, multiple stents implanted, complex bifurcation lesion, total stent length > 60 mm, chronic total occlusion intervention or bioabsorbable vascular scaffold implantation.
2. Ticagrelor and prasugrel are recommended in ACS patients, whereas clopidogrel is recommended for elective PCI.
3. Regimens evaluated in the context of triple therapy include rivaroxaban 2.5 mg BID or warfarin. If warfarin is to be used, recommended INR target is 2.0-2.5. OAC options evaluated in the context of a dual pathway strategy include rivaroxaban 15 mg daily (plus clopidogrel) or dabigatran 110 mg/150 mg BID (plus clopidogrel).
4. DAPT will have been started as part of ACS management or prior to high risk elective PCI. ASA may be discontinued as early as the day following PCI or it can be continued longer term (eg. 1, 3 or maximum 6 months after PCI). The timing of when to discontinue ASA will vary, depending on the individual patient's ischemic and bleeding risk.
5. A P_2Y_{12} inhibitor can be added to ASA if high-risk clinical or angiographic features of ischemic events and low risk of bleeding.
6. The dose of OAC beyond 1 year after PCI should be standard stroke prevention doses as per the CCS Atrial Fibrillation Guidelines. Single antiplatelet therapy with either ASA or clopidogrel may be added to OAC if high-risk clinical or angiographic features of ischemic events and low risk of bleeding.

Canadian Journal of Cardiology 34 (2018) 214-233

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JACC Journals

From: Triple Therapy for Atrial Fibrillation and Percutaneous Coronary Intervention: A Contemporary Review

J Am Coll Cardiol. 2014;64(12):1270-1280. doi:10.1016/j.jacc.2014.06.1193

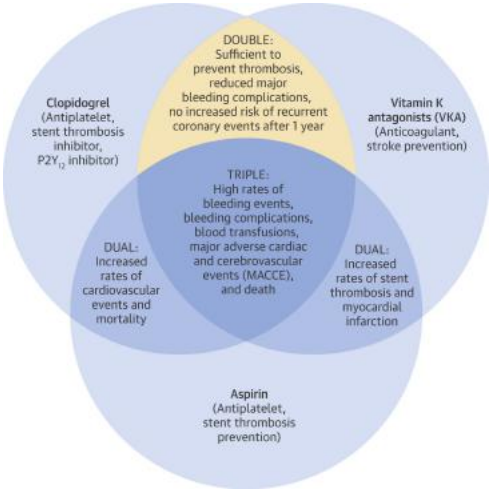

Figure Legend:

Double and Triple Antiplatelet Therapy Risks in AF and PCI

Patients with atrial fibrillation (AF) who undergo percutaneous coronary intervention (PCI): combining antiplatelet and anticoagulant therapies in search of an optimal equilibrium in between bleeding risk on the one hand and thrombotic and thromboembolic risk on the other.

The WOEST Trial: First randomised trial comparing two regimens with and without aspirin in patients on oral anticoagulant therapy undergoing coronary stenting

Willem Dewilde, Tom Oirbans, Freek Verheugt, Johannes Kelder, Bart De Smet, Jean-Paul Herrman, Tom Adriaenssens, Mathias Vrolix, Antonius Heestermans, Marije Vis, Saman Rasoul, Kaioum Sheikjoesoef, Tom Vandendriessche, Carlos Van Mieghem, Kristoff Cornelis, Jeroen Vos, Guus Brueren, Nicolien Breet and Jurriën ten Berg

The WOEST Trial= **W**hat is the **O**ptimal antiplat**E**let and anticoagulant therapy in patients with oral anticoagulation and coronary **S**ten**T**ing (clinicaltrials.gov NCT00769938)

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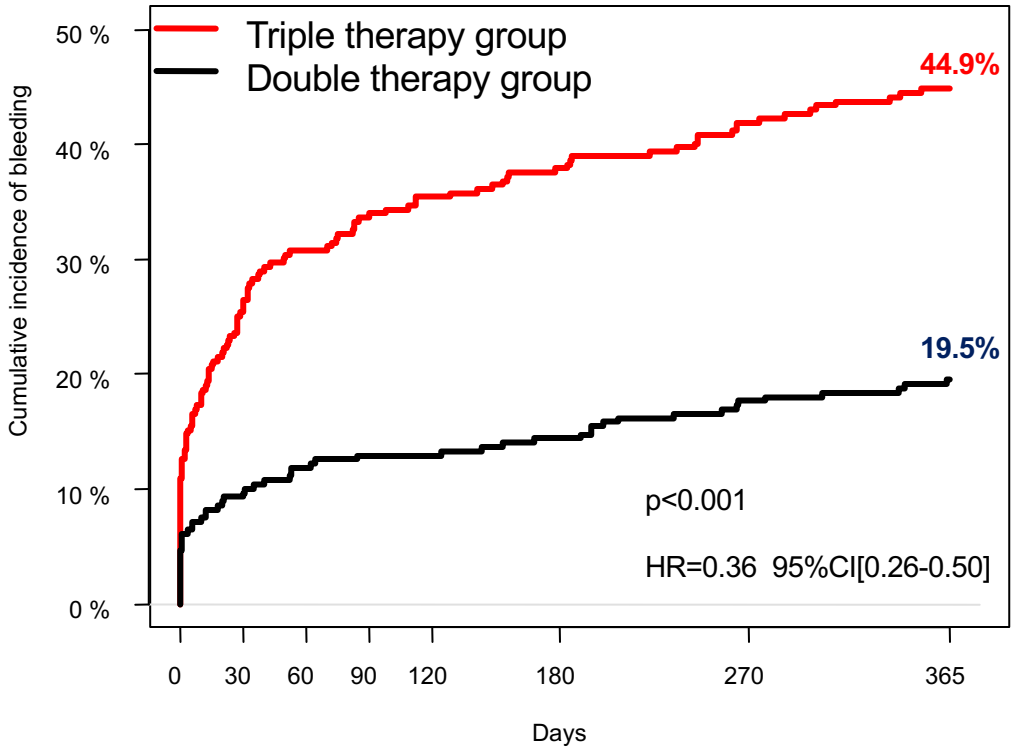
Primary Endpoint: Total number of TIMI bleeding events



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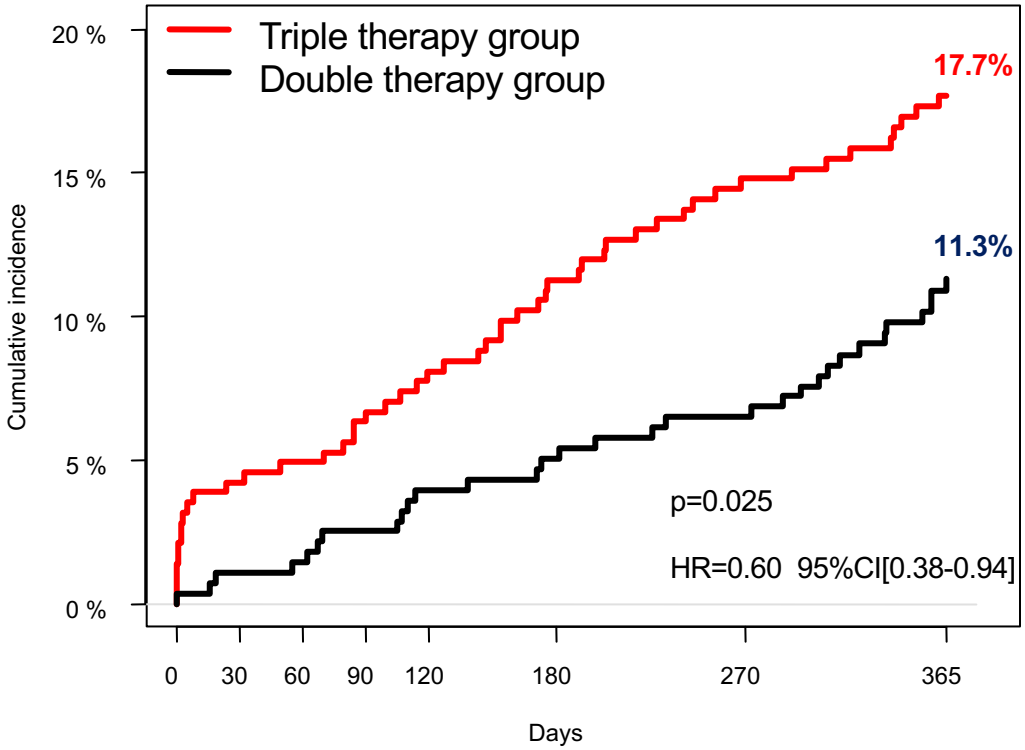
Secondary Endpoint (Death, MI,TVR, Stroke, ST)



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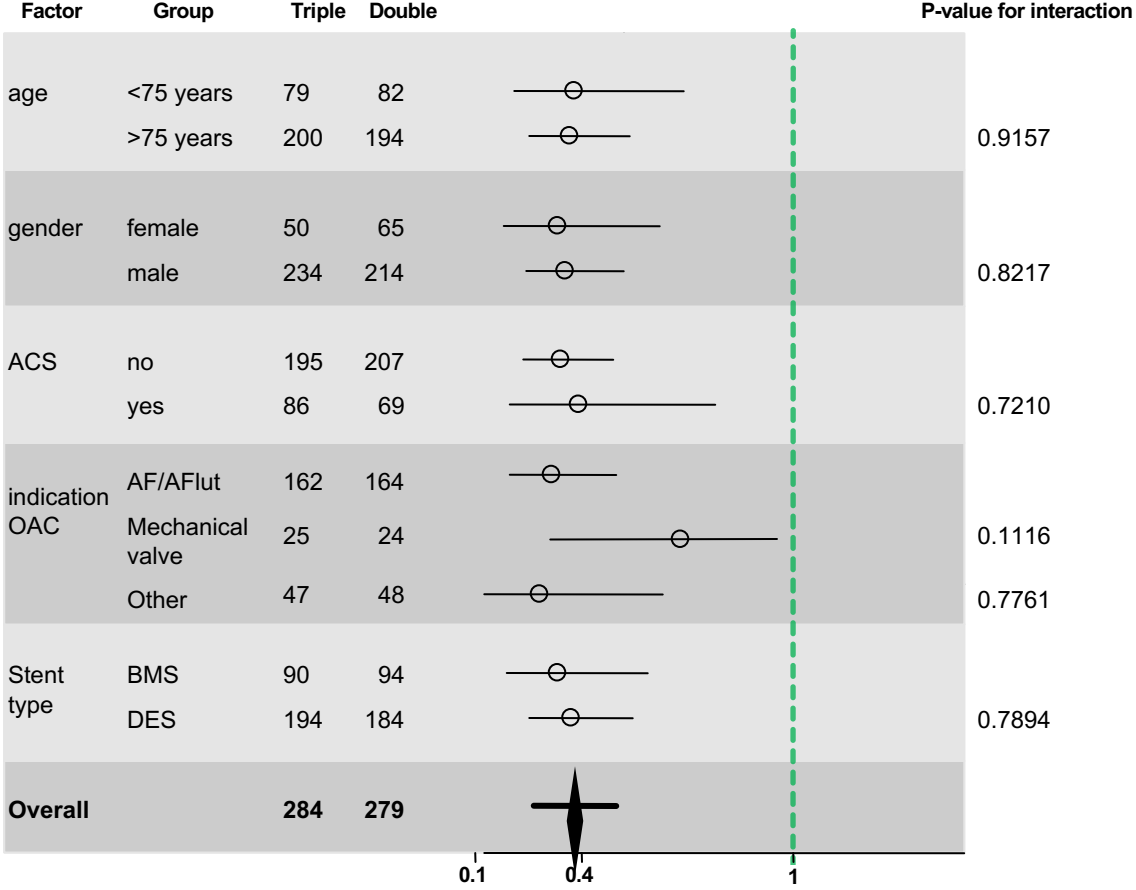
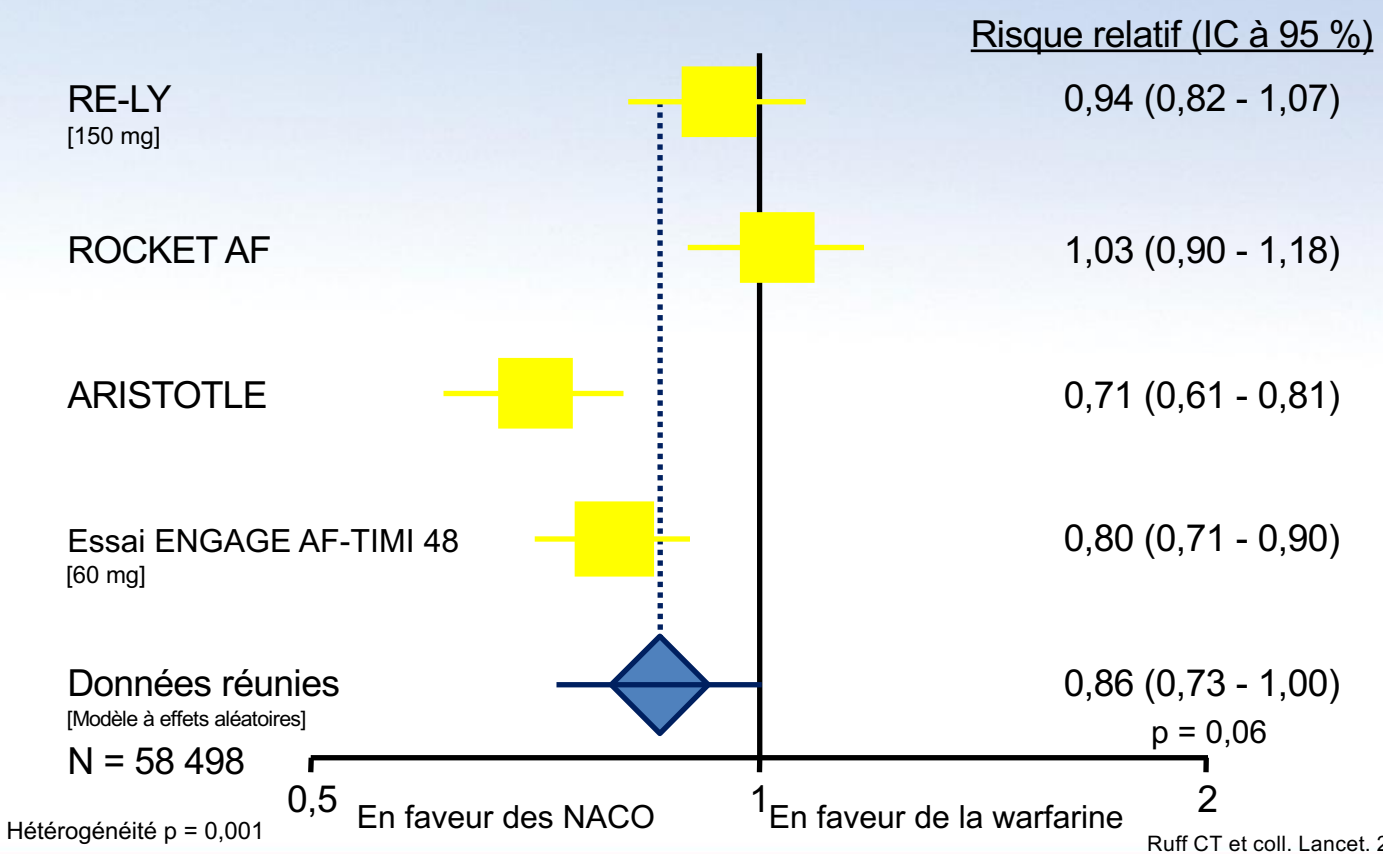
WOEST

Forest plot of primary endpoint Hazard Ratios

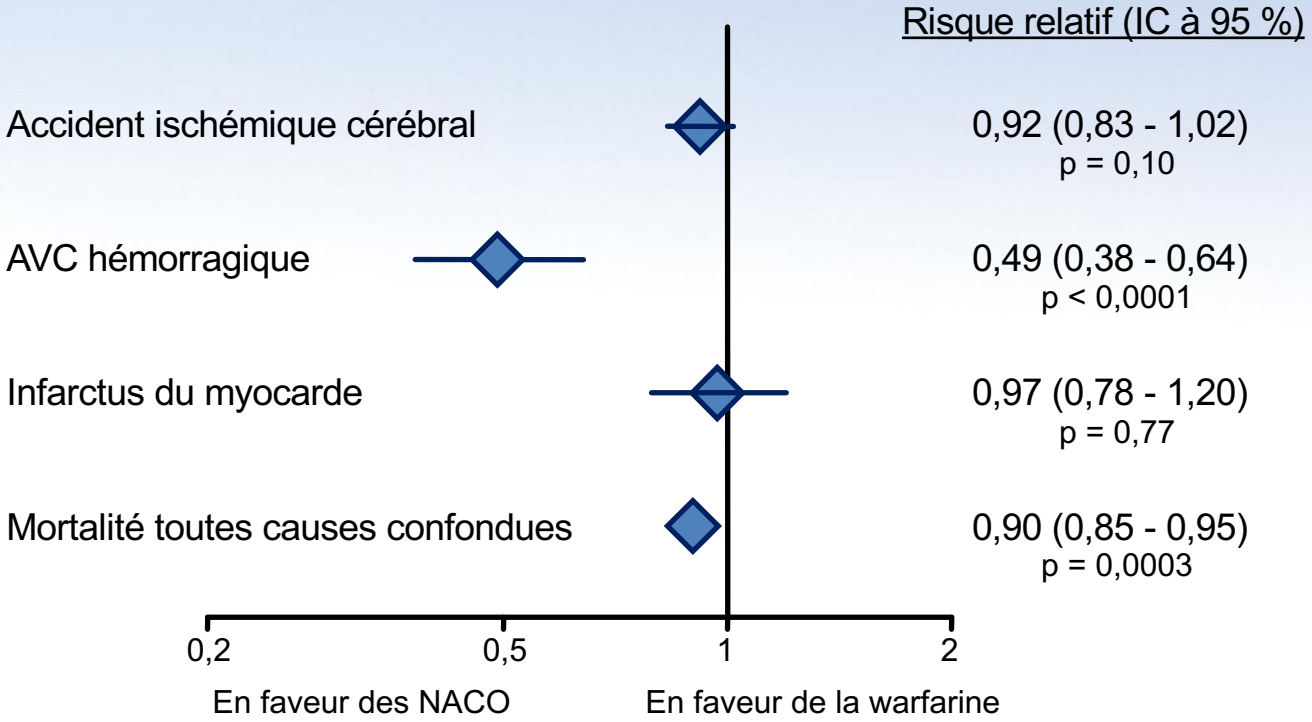


Tous les NACO : Hémorragie majeure



Ruff CT et coll. Lancet. 2013.

Critères secondaires d'évaluation de l'efficacité



Hétérogénéité p = n.s. pour tous les résultats cliniques

Ruff CT et coll. Lancet. 2013.

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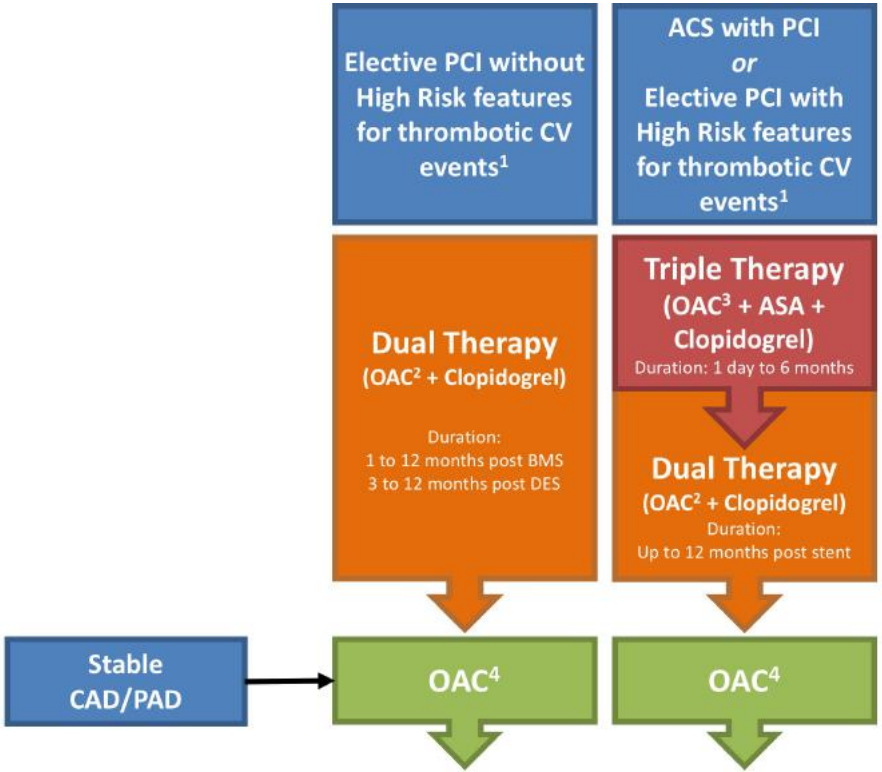
CCS AF Guidelines – CAD/PAD + CHADS-65 = 0



Andrade et al, Guide directrice FA, Canadian Journal of Cardiology 2020

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Randomized Trials of NOACs Following PCI

Drug	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Trial	RE-DUAL	PIONEER	AUGUSTUS	ENTRUST-PCI
Key Inclusion	**AF + PCI (elective or not)**	**AF + PCI (elective or not) + stent**	**AF + ACS and/or PCI**	**AF + PCI + stent**
Key exclusion	Recent use of fibrinolytics, stroke or major bleeding within 1 month, CrCl < 30 ml/min	History of stroke or TIA, GI bleed within 12 months, CrCl < 30 ml/min	History of ICH, ongoing bleeding, coagulopathy, CrCl < 30 ml/min	Stroke within 2 weeks, known bleeding diathesis, CrCl < 15 ml/min
Studied regimens	**110mg + P2Y12 150mg + P2Y12 War (INR 2-3) + DAPT**	**15mg + P2Y12 2.5mg + DAPT War (INR 2-3) + DAPT**	**5mg + P2Y12 War (INR 2-3) + P2Y12 5mg + DAPT War (INR 2-3) + DAPT**	**60mg + P2Y12 VKA + DAPT**
ASA duration in DAPT arm (protocol)	**1 month in bare-metal stent, 3 months in drug-eluting stent**	**1, 6 or 12 months**	**6 months**	**Risk-based: 30 days to 12 months**
Time from event (or PCI) to randomisation	**Between 6h and 120h (actual time not available)**	**within 72h of sheath removal (actual time not available)**	**within 14 days of ACS or PCI (mean 6.6 days; median 6 days)**	**Between 4h and 5 days (median 45.1h)**
Primary endpoint	time to first ISTH major or CRNM bleeding event	% of participants with TIMI clinically significant bleeding or bleed requiring medical attention	time to first ISTH major or CRNM bleeding at 6 months (ISTH)	Time to first ISTH major or CRNM bleeding event
Primary endpoint population	ITT	ITT	ITT	ITT
Timing of primary	**minimum 6 months, event-driven**	**12 months**	**6 months**	**12 months**
Main efficacy outcome	MI, stroke, SE, D, unplanned revasc	CV death, MI, stroke	D or hospitalization; D or ischemic event	composite of CV death, stroke, SEE, MI or definite stent thrombosis
Adjudication	Blinded	Blinded	Blinded	Blinded
Enrollment	2725	2124	4614	1506
TTR in VKA arm	Mean 64%	Mean 65%	Mean 56% (median 59%)	Mean 60% (median 63.1%)

Adapted from Capodanno D, DJ. Dual antithrombotic therapy for atrial fibrillation and PCI. Lancet 2019; published online Sept 3. http://dx.doi.org/10.1016/ S0140-6736(19)31954-3.

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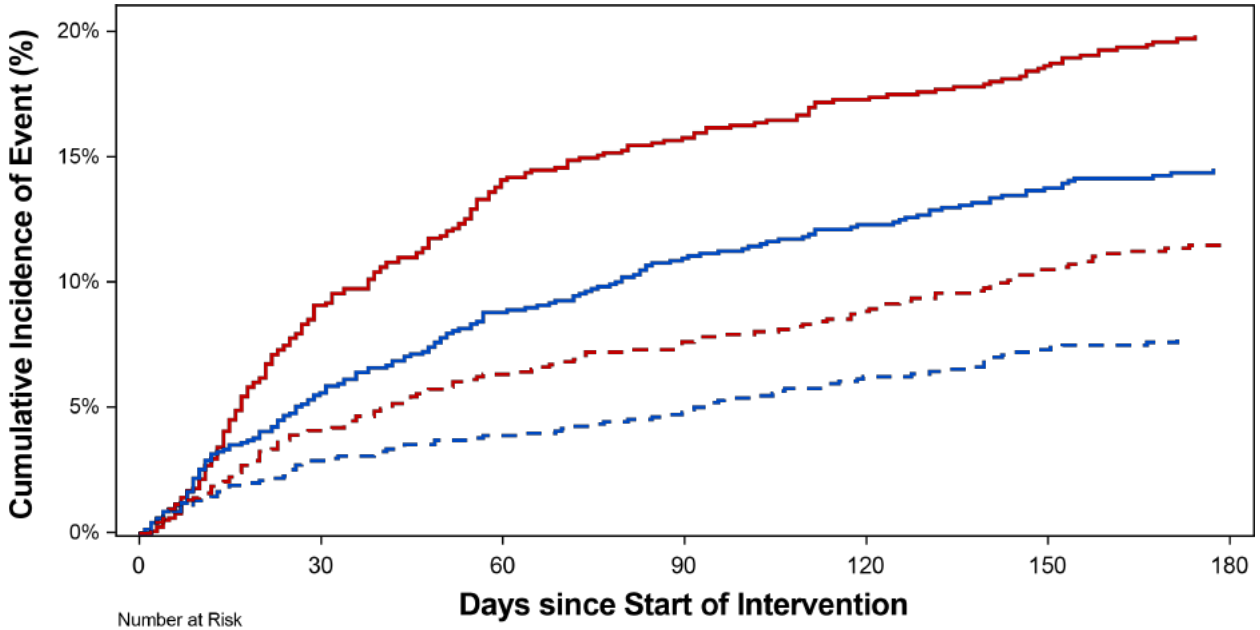
Major / CRNM Bleeding (Augustus)



Number at Risk							
Apixaban and Aspirin	1145	1036	975	937	903	880	485
Apixaban and Placebo	1143	1075	1044	1007	975	947	536
VKA and Aspirin	1123	962	881	838	800	776	467
VKA and Placebo	1126	1007	947	917	883	851	528

VKA + Aspirin (18.7%)

Apixaban + Aspirin (13.8%)

VKA + Placebo (10.9%)

Apixaban + Placebo (7.3%)

Apixaban + Placebo vs. VKA + Aspirin: 11.4% absolute risk reduction (NNT=9)

Lopes RD, et al. N Engl J Med 2019; 380:1509-1524DOI: 10.1056/NEJMoa1817083

Et si notre patient avait un SCA avec une atteinte coronarienne non significative et traitée médicalement, quel serait le meilleur traitement antithrombotique?

1. DOAC seul
2. DOAC + DTAP x 1mois puis STAP
3. DOAC + DTAP x 3 mois puis STAP
4. DOAC + STAP

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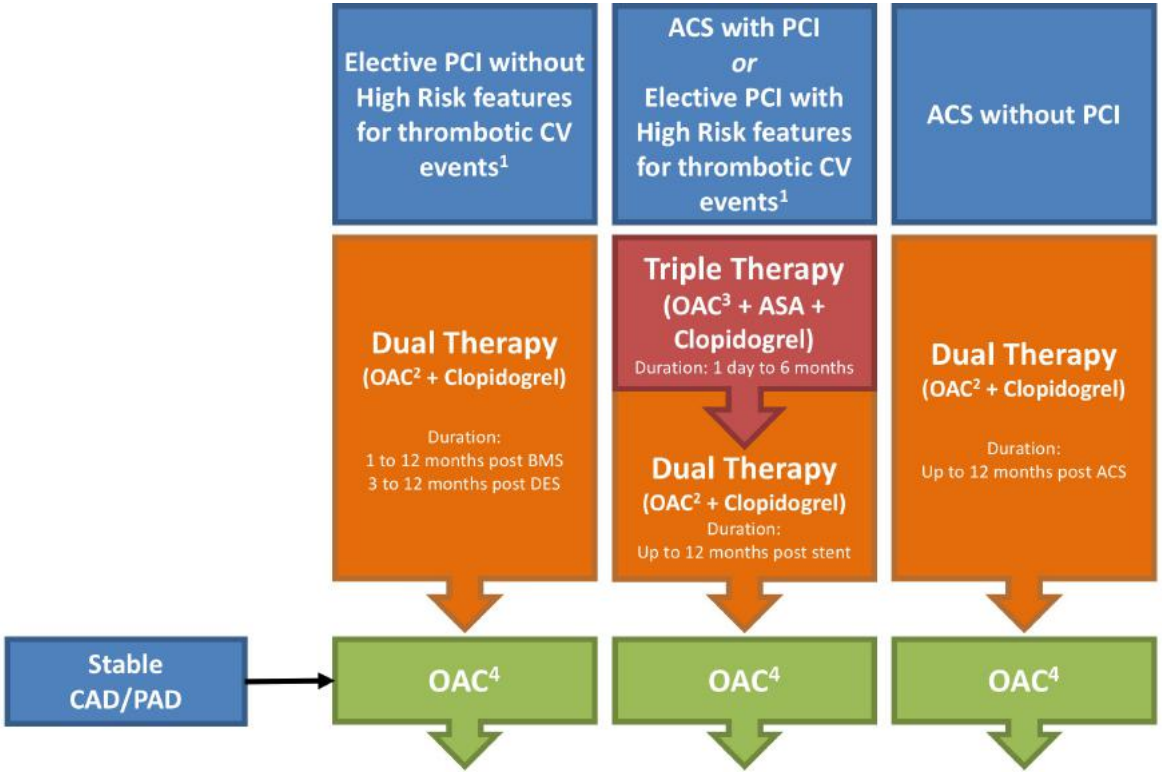
CCS AF Guidelines – CAD/PAD + CHADS-65 = 0



Andrade et al, Guide directrice FA, Canadian Journal of Cardiology 2020

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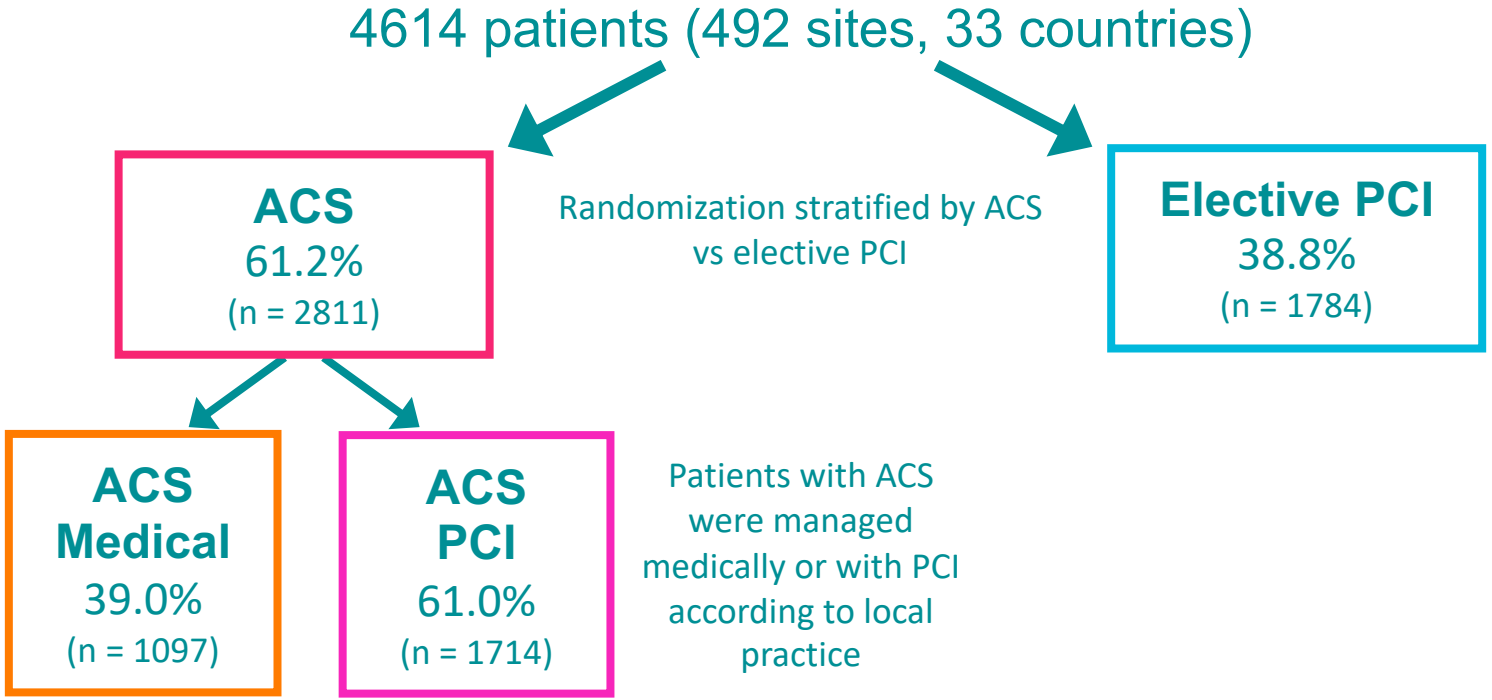
Patient Allocation (Augustus)



19 pts with missing information about ACS and PCI

Windecker S et al. Oral presentation at TCT 2019, September 25th to 29th, San Francisco, CA, USA.

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Baseline Characteristics

	ACS Medical n = 1097	ACS PCI n = 1714	Elective PCI n = 1784
Age, median (25^{th}, 75^{th}), years	70 (64, 77)	71 (64.0, 77.3)	71 (65, 77)
Female	39%	27%	25%
Diabetes mellitus	32%	35%	41%
Creatinine clearance, median (25^{th}, 75^{th}), mL/min	72 (54, 91)	76 (57, 96)	76 (59, 98)
Heart failure	57%	39%	38%
CHA_2DS_2-VASc score, median (25^{th}, 75^{th})	4 (3, 5)	4 (3, 5)	4 (3, 5)
HAS-BLED score, median (25^{th}, 75^{th})	2 (2, 3)	2 (2, 3)	3 (2, 3)
Prior OAC	48%	42%	57%
$P2Y_{12}$ inhibitor			
Clopidogrel	98%	90%	93%
Prasugrel	0.2%	1.7%	1.2%
Ticagrelor	2.1%	8.7%	6.3%
Number of days to randomization, median (25^{th}, 75^{th})	9 (6, 12)	5 (3, 9)	5 (2, 9)

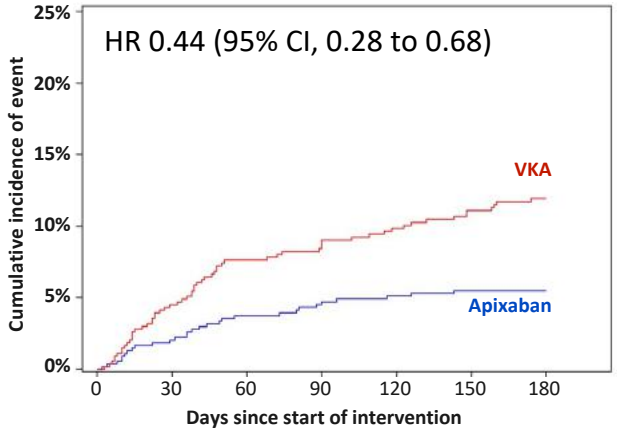
ACS, acute coronary syndrome; CHA_2DS_2-VASc, congestive heart failure, hypertension, age ≥ 75 (2 points), diabetes, stroke/transient ischemic attack (2 points), vascular disease, age 65 to 74, and sex (female); HAS-BLED, hypertension, abnormal renal or liver function, previous stroke/transient ischemic attack, bleeding, labile international normalized ratio, elderly, drugs or alcohol; OAC, oral anticoagulation; PCI, percutaneous intervention.

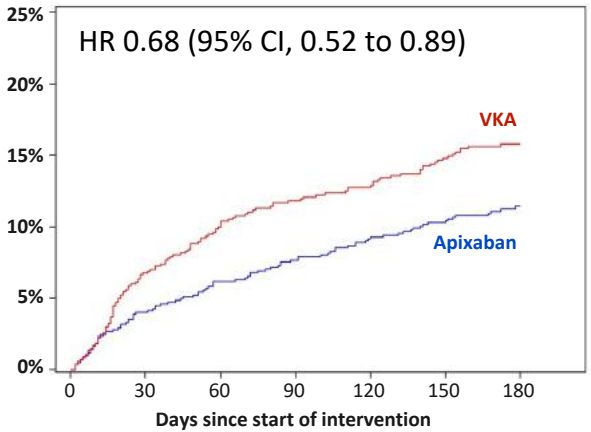
Windecker S et al. Oral presentation at TCT 2019, September 25^{th} to 29^{th}, San Francisco, CA, USA.

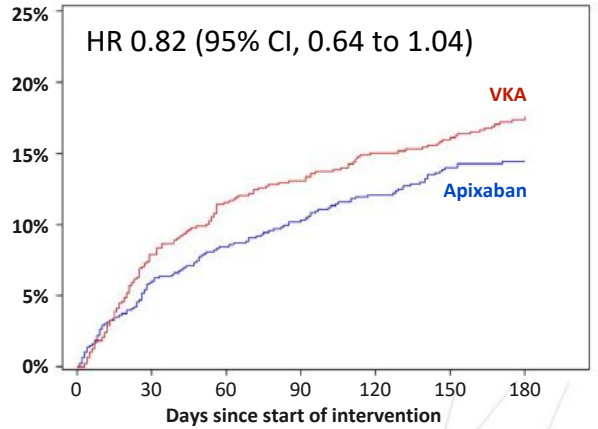
Primary Endpoint: ISTH Major* or CRNM Bleeding Apixaban vs VKA (Augustus)

ACS Medical	ACS PCI	Elective PCI
n = 1097	n = 1714	n = 1784

P for Interaction (ACS medical, ACS PCI, elective PCI) = **0.052**





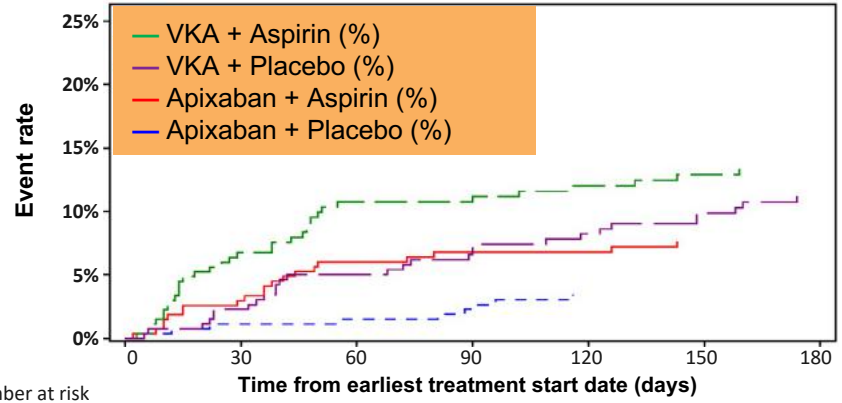


Windecker S et al. Oral presentation at TCT 2019, September 25th to 29th, San Francisco, CA, USA.

ACS Medical (Augustus)

ISTH Major/CRNM Bleeding

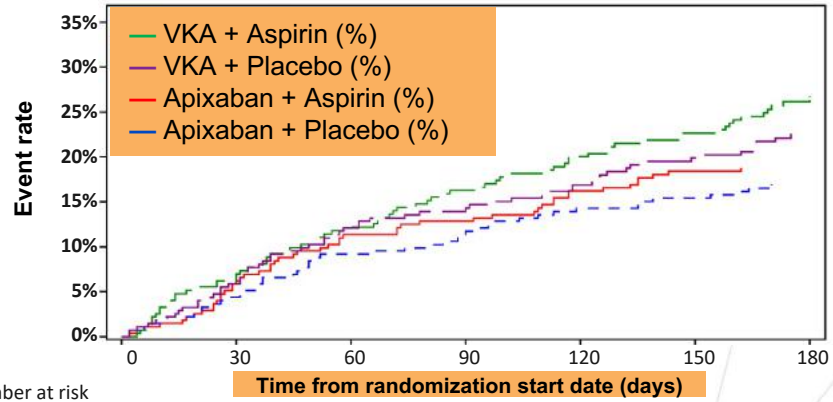
Apixaban + Placebo vs VKA + Aspirin:
10% absolute risk reduction (NNT = 10)



Number at risk							
Apixaban + ASA	273	256	241	237	233	228	134
Apixaban + placebo	273	264	256	251	246	244	155
VKA + ASA	272	243	220	212	201	197	131
VKA + placebo	273	254	241	234	223	217	139

Death/Hospitalization

Apixaban + Placebo vs VKA + Aspirin:
10% absolute risk reduction (NNT = 10)



Number at risk							
Apixaban + ASA	273	257	240	235	226	220	127
Apixaban + placebo	274	261	248	241	233	230	147
VKA + ASA	274	254	237	224	214	206	128
VKA + placebo	276	257	239	234	225	217	138

Windecker S et al. Oral presentation at TCT 2019, September 25th to 29th, San Francisco, CA, USA.

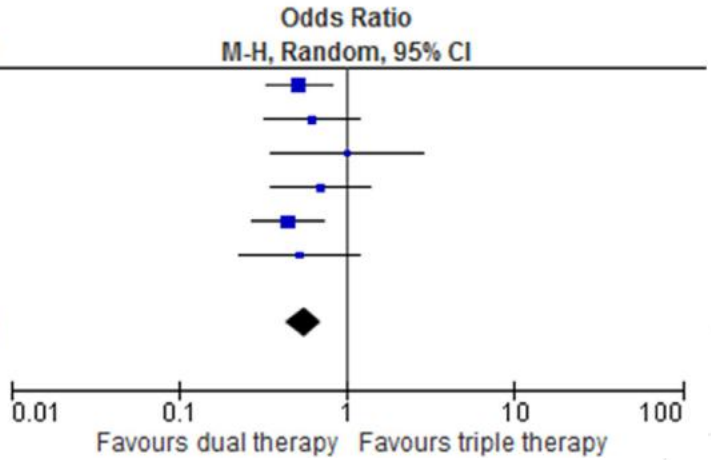
Méta analyse des différentes études SCA et FA

Major bleeding

Study or Subgroup	Dual therapy Events	Total	Triple therapy Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
AUGUSTUS	29	2279	55	2277	30.7%	0.52 [0.33, 0.82]
ENTRUST AF-PCI	15	751	24	755	14.8%	0.62 [0.32, 1.19]
ISAR TRIPLE	7	307	7	307	5.6%	1.00 [0.35, 2.89]
PIONEER AF-PCI	14	696	20	697	13.2%	0.69 [0.35, 1.39]
RE-DUAL PCI	30	1744	37	981	26.5%	0.45 [0.27, 0.73]
WOEST	9	297	16	284	9.1%	0.52 [0.23, 1.20]
Total (95% CI)		**6074**		**5301**	**100.0%**	**0.55 [0.43, 0.71]**
Total events	104		159			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.56$, $df = 5$ ($P = 0.77$); $I^2 = 0\%$

Test for overall effect: $Z = 4.62$ ($P < 0.00001$)



Elisabetta Ricottini and al, European Journal of Internal Medecine 2020

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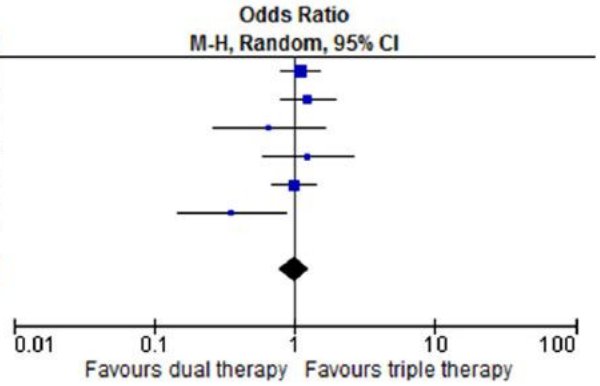
A. All-cause mortality

Study or Subgroup	Dual therapy Events	Total	Triple therapy Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
AUGUSTUS	79	2279	72	2277	29.0%	1.10 [0.79, 1.52]
ENTRUST AF-PCI	45	751	37	755	20.6%	1.24 [0.79, 1.93]
ISAR TRIPLE	8	307	12	307	7.1%	0.66 [0.27, 1.63]
PIONEER AF-PCI	16	696	13	697	10.0%	1.24 [0.59, 2.59]
RE-DUAL PCI	85	1744	48	981	26.1%	1.00 [0.69, 1.43]
WOEST	7	297	18	284	7.3%	0.36 [0.15, 0.87]
Total (95% CI)		**6074**		**5301**	**100.0%**	**0.99 [0.76, 1.28]**
Total events	240		200			

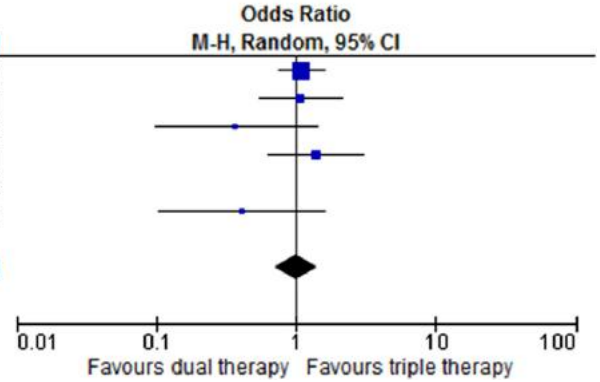
Heterogeneity: Tau² = 0.03; Chi² = 7.47, df = 5 (P = 0.19); I² = 33%
Test for overall effect: Z = 0.10 (P = 0.92)



B. Cardiovascular mortality

Study or Subgroup	Dual therapy Events	Total	Triple therapy Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
AUGUSTUS	58	2279	53	2277	49.6%	1.10 [0.75, 1.60]
ENTRUST AF-PCI	17	751	16	755	20.9%	1.07 [0.54, 2.13]
ISAR TRIPLE	3	307	8	307	6.4%	0.37 [0.10, 1.40]
PIONEER AF-PCI	15	696	11	697	16.9%	1.37 [0.63, 3.01]
RE-DUAL PCI	0	0	0	0		Not estimable
WOEST	3	297	7	284	6.2%	0.40 [0.10, 1.58]
Total (95% CI)		**4330**		**4320**	**100.0%**	**0.99 [0.70, 1.41]**
Total events	96		95			

Heterogeneity: Tau² = 0.03; Chi² = 4.72, df = 4 (P = 0.32); I² = 15%
Test for overall effect: Z = 0.04 (P = 0.97)



Elisabetta Ricottini and al, European Journal of Internal Medecine 2020

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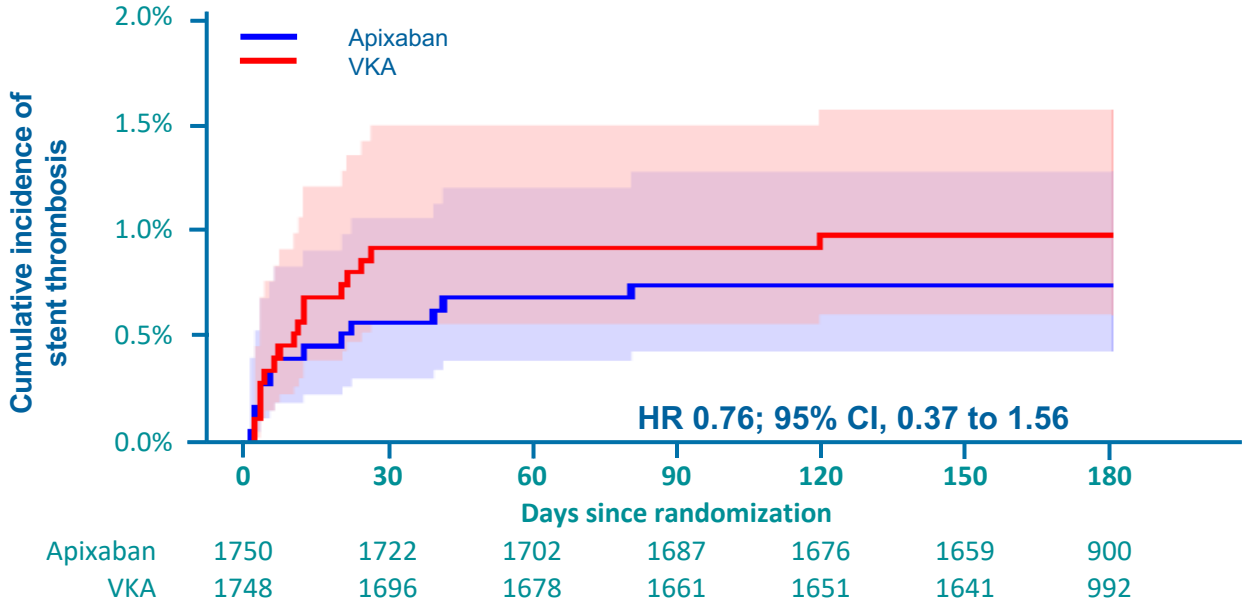
Ischemic Outcomes: Aspirin vs Placebo

Endpoint	Aspirin (n = 2307)	Placebo (n = 2307)	HR (95% CI)
Death/Ischemic Events (%)	6.5	7.3	0.89 (0.71 to 1.11)
Death (%)	3.1	3.4	0.91 (0.66 to 1.26)
CV Death (%)	2.3	2.5	0.92 (0.63 to 1.33)
Stroke (%)	0.9	0.8	1.06 (0.56 to 1.98)
Myocardial Infarction (%)	2.9	3.6	0.81 (0.59 to 1.12)
Definite or Probable Stent Thrombosis (%)	0.5	0.9	0.52 (0.25 to 1.08)
Urgent Revascularization (%)	1.6	2.0	0.79 (0.51 to 1.21)
Hospitalization (%)	25.4	23.4	1.10 (0.98 to 1.24)

CI, confidence interval; CV, cardiovascular; HR, hazard ratio; VKA, vitamin K antagonist.

Lopes RD et al. Oral presentation at ACC 2019, 16-18 March, New Orleans, LA, USA, late breaking clinical trial 405-08.

Results: Definite/Probable Stent Thrombosis - Apixaban Versus VKA



Summary

- The number (proportion) of patients with definite/probable stent thrombosis at 6 months was 13 (0.74%) for apixaban and 17 (0.97%) for VKA (HR, 0.76; 95% CI 0.37 to 1.56).

For all patients, $P2Y_{12}$ inhibitor use was planned for at least 6 months.

Coadministration of apixaban with antiplatelet agents increases the risk of bleeding.[2,3]

CI, confidence interval; HR, hazard ratio; SmPC, summary of product characteristics; VKA, vitamin K antagonist.

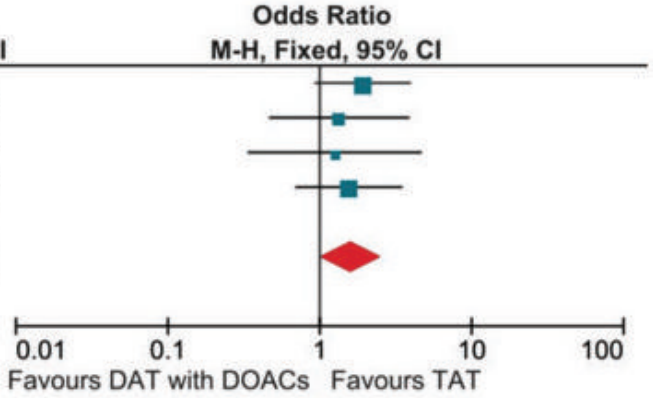
1. Lopes RD et al. *Circulation*. 2020;141:781-783; 2. Apixaban Product monograph: https://pdf.hres.ca/dpd_pm/00053440.PDF accessed September 2020; 3. Apixaban SmPC available at www.ema.europa.eu/en/medicines/human/EPAR/eliquis#product-information-section accessed August 2020.

Stent thrombosis

Study or Subgroup	DAT with DOACs Events	Total	TAT Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
AUGUSTUS	21	2307	11	2307	35.3%	1.92 [0.92, 3.99]
ENTRUST-AF-PCI	8	751	6	755	19.2%	1.34 [0.46, 3.89]
PIONEER AF-PCI	5	694	4	695	12.8%	1.25 [0.34, 4.69]
RE-DUAL PCI	22	1744	8	981	32.7%	1.55 [0.69, 3.50]
Total (95% CI)		**5496**		**4738**	**100.0%**	**1.60 [1.02, 2.52]**
Total events	56		29			

Heterogeneity: $Chi^2 = 0.47$, $df = 3$ ($P = 0.92$); $I^2 = 0\%$

Test for overall effect: $Z = 2.04$ ($P = 0.04$)



Galli and al, Europace 2019

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Cas #2

- Claudette Jean
- 72 ans
- Comptable retraitée
- Quand ne joue pas au Scrabble et Catan avec ses petits-enfants.
  - Danse le Kompa jusqu'au petite heures du matin

Claudette---Anamnèse

- DB
  - Bien contrôlé avec Metformin
- Hypertension
  - (tension artérielle (TA) : 162/92) (prend actuellement du Coversyl, Biso et de la nifédipine XL)
- MCAS
  - NSTEMI il y a 10 mois
  - PCI sur TC et D1.(DES)
  - Cd petite et grêle
  - Aucun sy d’angine depuis sa dilatation

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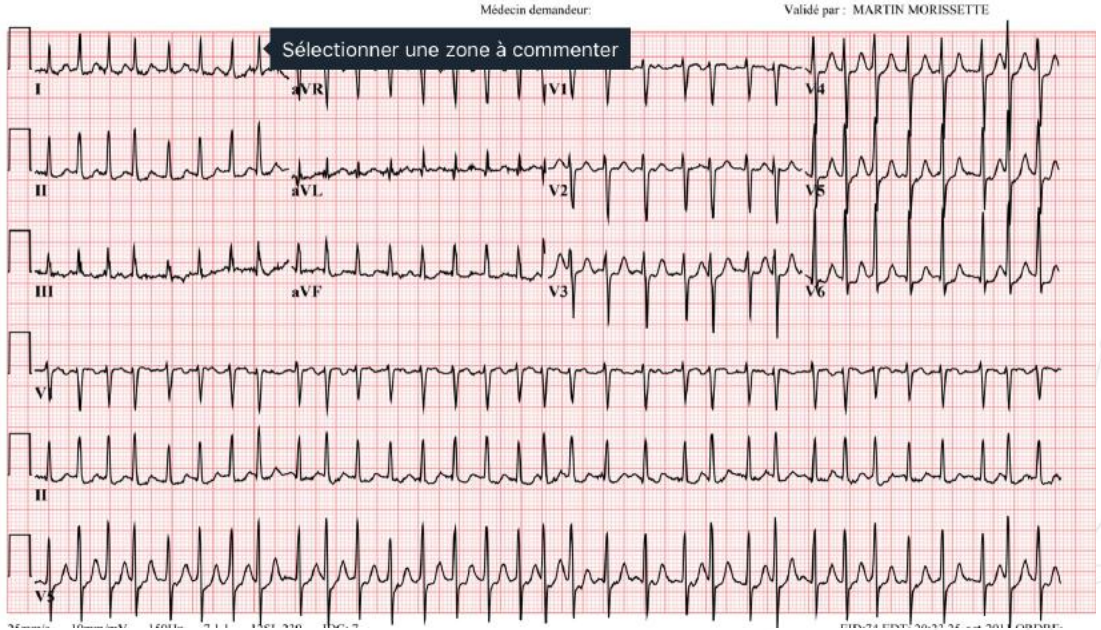
Claudette---Anamnèse

- Lors de sa dernière visite annuelle pour un examen physique, elle s’est plaint d'épisodes intermittents de palpitations
- Symptômes associés : dyspnée à l'effort, Fatigue

- Hier soir, visite à l’urgence
  - Même symptômes



Claudette---Anamnèse

- Laboratoire
  - Formule sanguine, électrolytes, créatinine (et taux de filtration glomérulaire estimé, ou TFGe), TSH (thyroid stimulating hormone) et épreuves de la fonction hépatique : tous normaux
- Échocardiographie
  - Légère dilatation de l'oreillette gauche
  - Légère hypertrophie ventriculaire gauche
  - Fonction systolique ventriculaire gauche normale
  - trace régurgitation mitrale et tricuspidienne
  - Volume de l'oreillette gauche : 33 mL/m^2

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Médication

- Ticagrelor 90 mg po bid.
- Asa 80 mg po die
- Metformin 850mg po bid
- Coversyl 8 mg po die
- Nifedipine 90mg po die.
- Bisoprolol 1,25 débuté depuis palpitatons.

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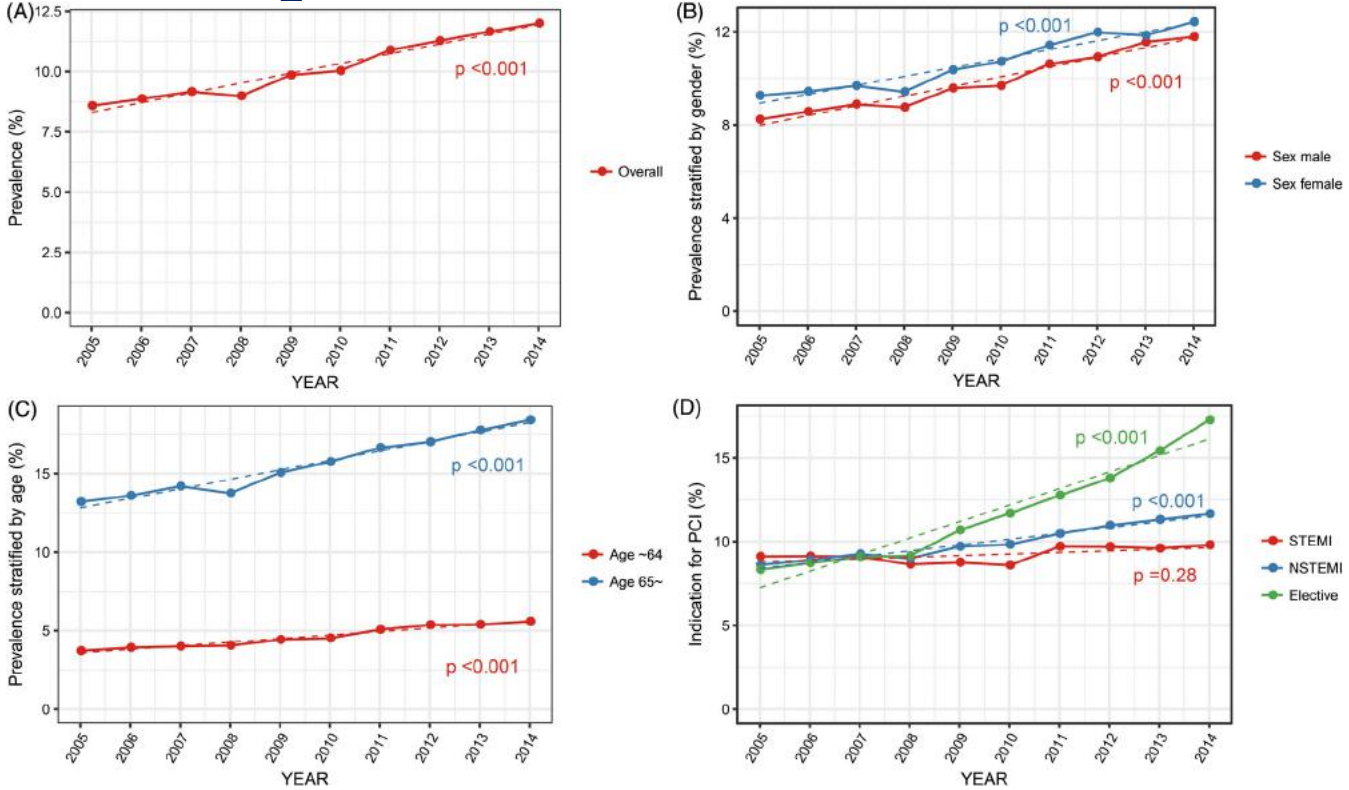
Questions 2

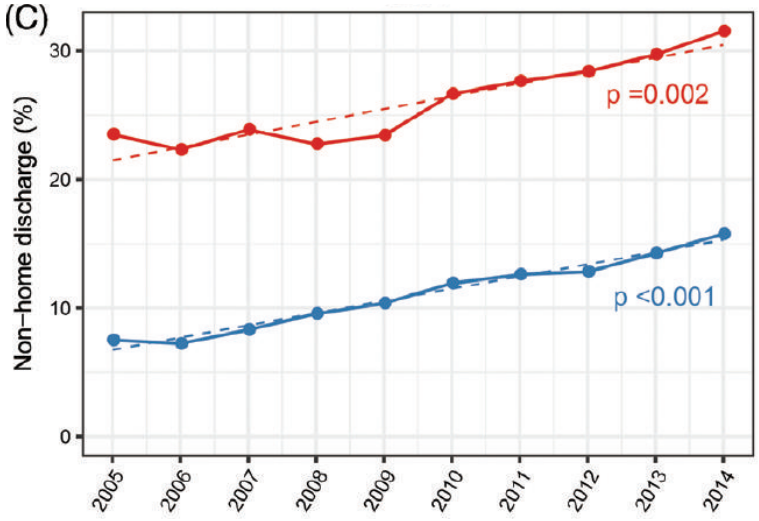
- Quelle est sa meilleure protection anti-thombotique considérant son risque thombotique et de saignements?
  - 1. Continuer Ticagrelor et ASA sur 3 ans et réévaluer par la suite
  - 2. Compléter Ticagrelor et ASA ad 12 mois, et changer par la suite pour un DOAC seul
  - 3.La mettre sous un DOAC à dose prouvé pour les avc avec plus ou moins du Clopidogrel et envisager dc le Cloplidogrel a 12 mois.
  - 4. Coumadin seul.
  - 5. La mettre sous Ticagrelor, ASA et un DOAC

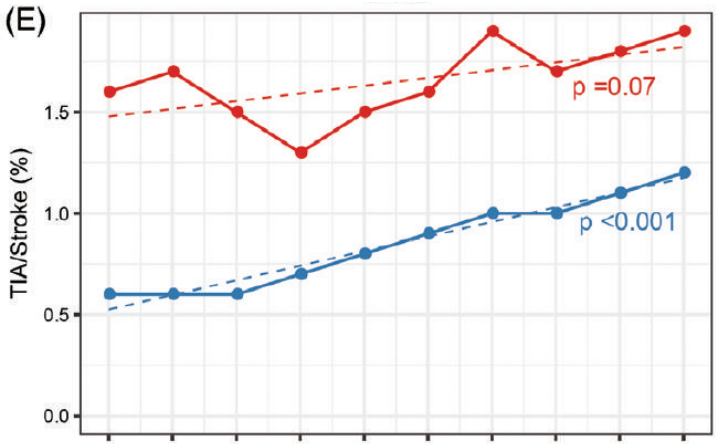
PCI chez pt avec FA

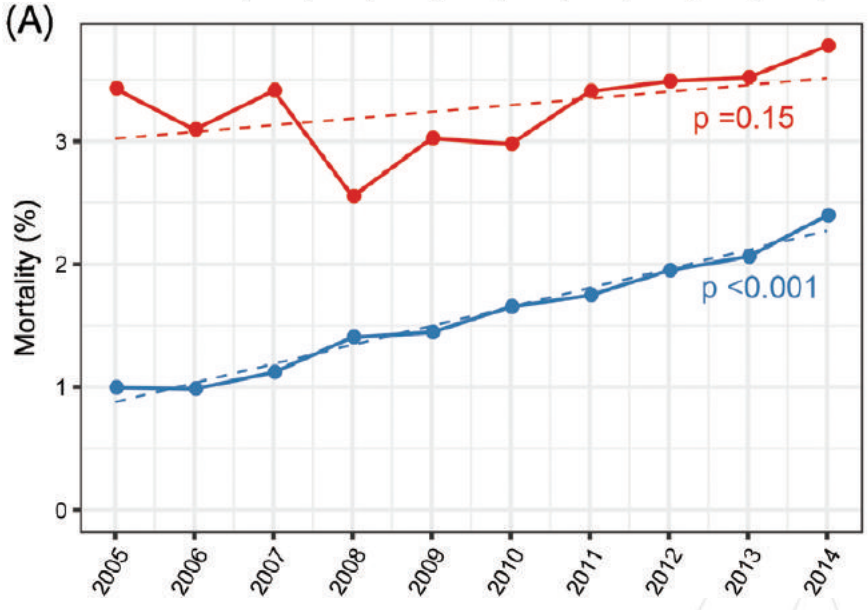


Morita and al, Clinical Cardiology 2019

PCI chez pt avec FA

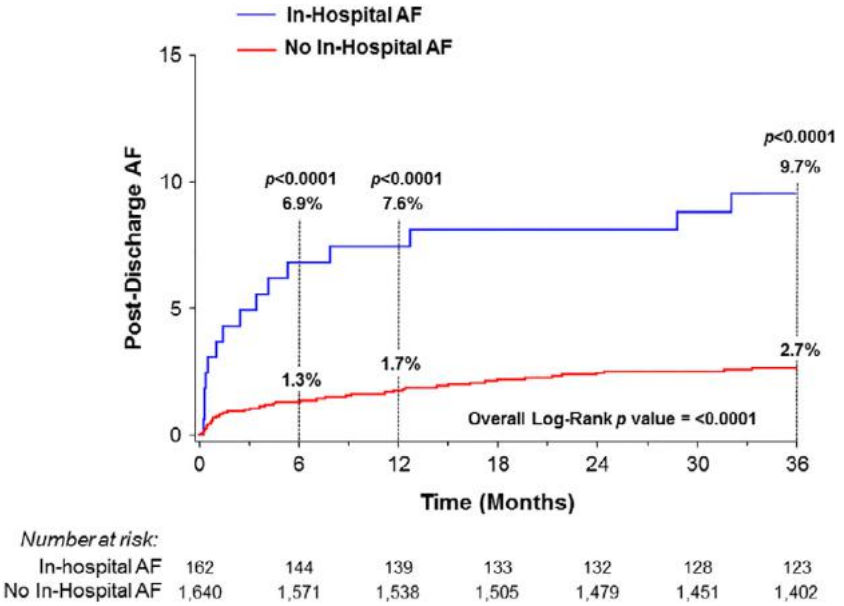


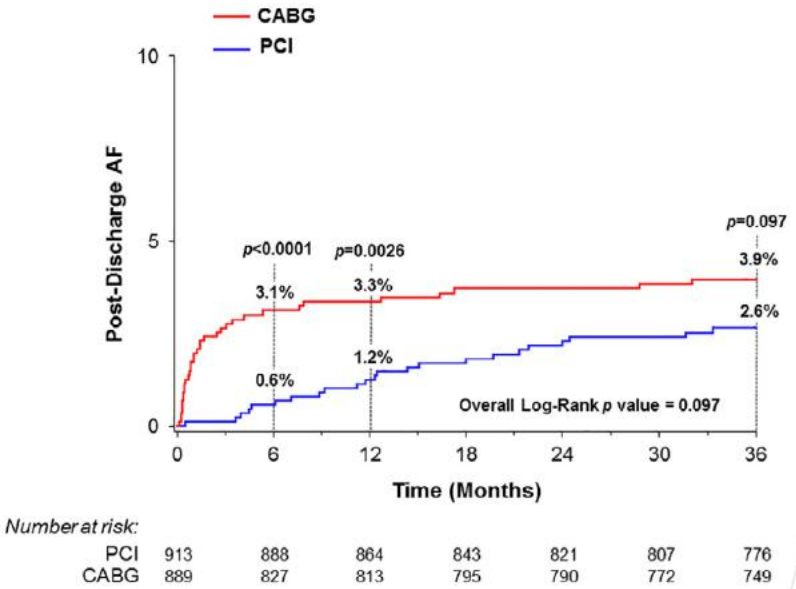




Morita and al, Clinical Cardiology 2019

Excel: à l'intérieur...





Kosmidou, Stones and al, The American Journal of Cardiology

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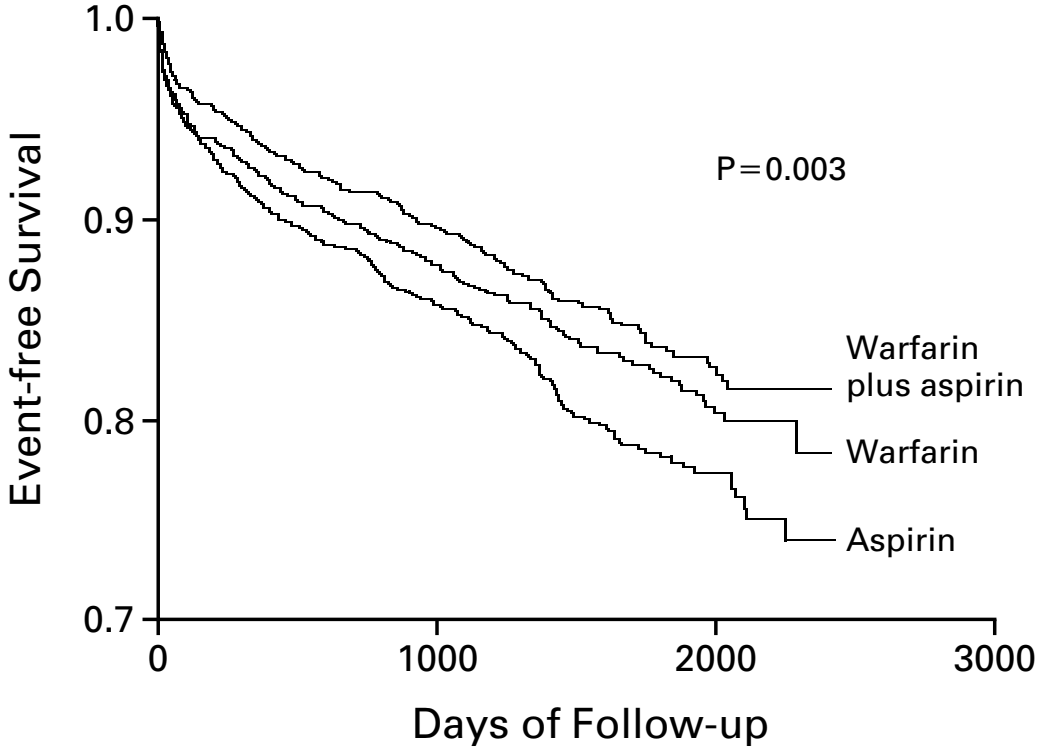
Post infarctus, pas de fa. Waris 2



Hurlen al, NEJM 2002 and

Figure 1. Event-free Survival Curves for the Composite End Point of Death, Nonfatal Reinfarction, and Thromboembolic Stroke.

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Post infarctus, pas de fa. Waris 2

TABLE 5. NONFATAL BLEEDING COMPLICATIONS ACCORDING TO TREATMENT GROUP.

COMPLICATION	ASPIRIN	WARFARIN	ASPIRIN PLUS WARFARIN
		no. of patients	
Major bleeding			
Cerebral	1	5	3
Gastrointestinal	6	18	21
Urinary	—	2	—
Muscle or skin	—	1	—
Other	1	7	4
Total	8	33	28
Minor bleeding			
Nose or airways	7	20	30
Gastrointestinal	18	30	45
Urinary	7	24	27
Muscle or skin	—	8	16
Other	7	21	15
Total	39	103	133

Hurlen al, NEJM 2002 and

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Antithrombotic Therapy for Atrial Fibrillation with Stable Coronary Disease

Satoshi Yasuda, M.D., Ph.D., Koichi Kaikita, M.D., Ph.D., Masaharu Akao, M.D., Ph.D., Junya Ako, M.D., Ph.D., Tetsuya Matoba, M.D., Ph.D., Masato Nakamura, M.D., Ph.D., Katsumi Miyauchi, M.D., Ph.D., Nobuhisa Hagiwara, M.D., Ph.D., Kazuo Kimura, M.D., Ph.D., Atsushi Hirayama, M.D., Ph.D., Kunihiko Matsui, M.D., M.P.H., and Hisao Ogawa, M.D., Ph.D., for the AFIRE Investigators*

Satoshi Yasuda, Nejm 2019

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Table 1. Characteristics of the Patients at Baseline (Modified Intention-to-Treat Population).*

Characteristic	Rivaroxaban Monotherapy (N=1107)	Combination Therapy (N=1108)
Age — yr	74.3±8.3	74.4±8.2
<75 yr — no. (%)	525 (47.4)	527 (47.6)
≥75 yr — no. (%)	582 (52.6)	581 (52.4)
Male sex — no. (%)	875 (79.0)	876 (79.1)
Body-mass index†	24.5±3.7	24.5±3.7
Current smoker — no. (%)	146 (13.2)	146 (13.2)
Diabetes — no. (%)	461 (41.6)	466 (42.1)
Previous stroke — no. (%)	148 (13.4)	175 (15.8)
Previous myocardial infarction — no. (%)	384 (34.7)	393 (35.5)
Previous PCI — no. (%)	781 (70.6)	783 (70.7)
Type of stent — no./total no. (%)		
Drug-eluting	500/723 (69.2)	477/721 (66.2)
Bare-metal	171/723 (23.7)	171/721 (23.7)
Both types	19/723 (2.6)	36/721 (5.0)
Unknown	33/723 (4.6)	37/721 (5.1)
Previous CABG — no. (%)	125 (11.3)	127 (11.5)
Type of atrial fibrillation — no. (%)		
Paroxysmal	596 (53.8)	580 (52.3)
Persistent	164 (14.8)	175 (15.8)
Permanent	347 (31.3)	353 (31.9)
Creatinine clearance		
Mean — ml/min	62.8±25.7	61.7±24.0
Distribution — no./total no. (%)		
<30 ml/min	54/1053 (5.1)	60/1039 (5.8)
30 to <50 ml/min	300/1053 (28.5)	293/1039 (28.2)
≥50 ml/min	699/1053 (66.4)	686/1039 (66.0)

Satoshi Yasuda, Nejm 2019

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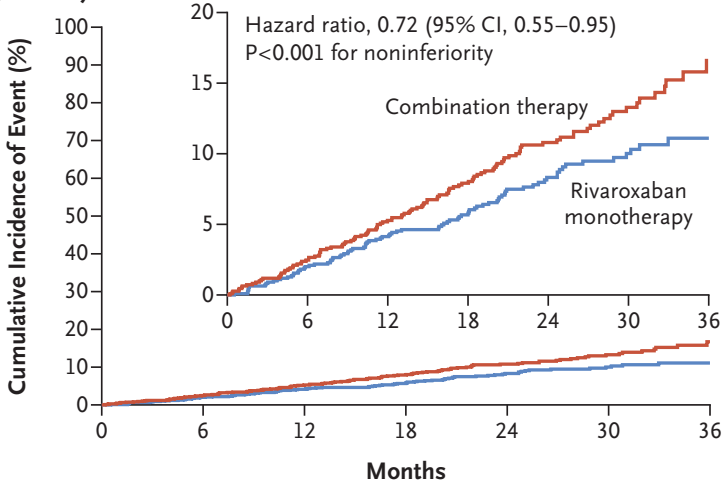
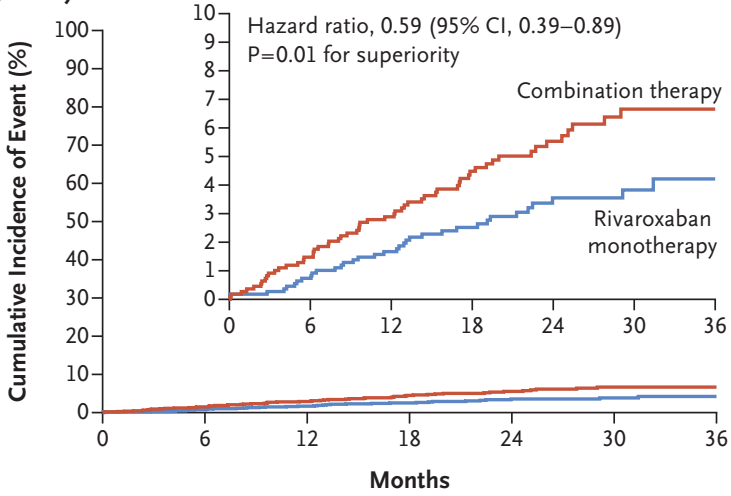
A Primary Efficacy End Point



No. at Risk							
Combination therapy	1108	1057	962	754	499	292	80
Rivaroxaban monotherapy	1107	1071	984	774	518	309	89

B Primary Safety End Point



No. at Risk							
Combination therapy	1099	1055	962	750	506	294	80
Rivaroxaban monotherapy	1099	1074	994	786	526	312	89

Satoshi Yasuda, Nejm 2019

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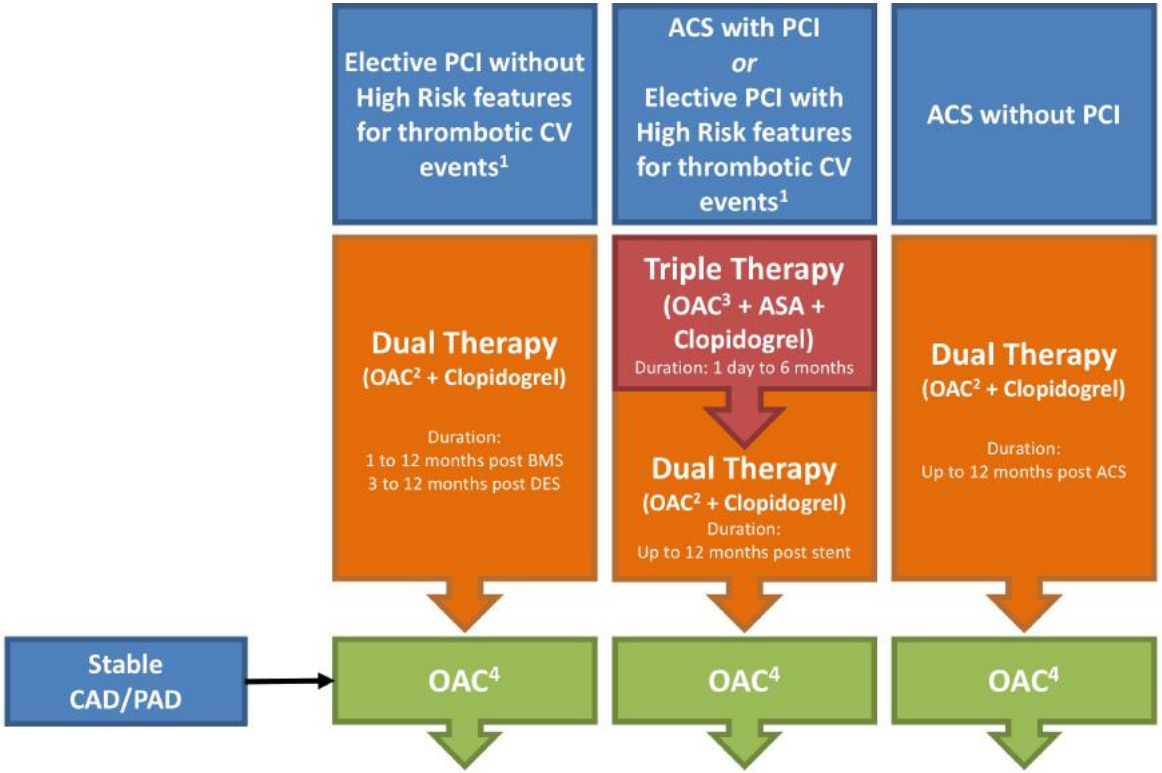
CCS AF Guidelines – CAD/PAD + CHADS-65 = 0



Andrade et al, Guide directrice FA, Canadian Journal of Cardiology 2020

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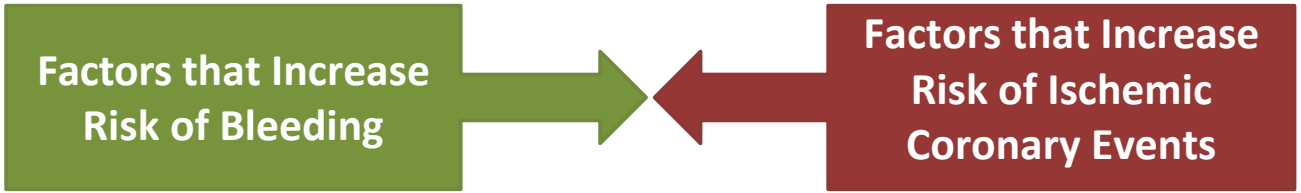
Figure S7 (Figure 2 from 2018 Update): Risk factors associated with an increased risk of bleeding, and an increased risk of ischemic coronary outcomes (recurrent MI, stent thrombosis)



- **Patient Factors**
  - Age (> 65 years)
  - Low body weight (< 60 kg)
  - Hypertension
  - History of bleeding (esp. within 1y)
  - Prior Stroke or intracranial bleed
  - Combined OAC and antiplatelet use
  - Concomitant NSAID or prednisone use
  - Excess alcohol consumption
  - Abnormal liver function
  - CKD (eGFR < 60 mL/min)
  - Anemia (hemoglobin <110 g/L)
  - Labile INR (TTR <60%)

- **Patient Factors**
  - Diabetes mellitus treated with OHG or insulin
  - Current smoker
  - CKD (eGFR < 60 mL/min)
  - Prior ACS
  - Prior stent thrombosis
- **Clinical Presentation**
  - ACS (STEMI, NSTEMI, UA)
- **Angiographic factors**
  - Multi-vessel disease
  - Multiple (≥ 3) stents implanted
  - Stenting of a bifurcation lesion
  - Total stent length > 60 mm
  - Left main or proximal LAD stenting
  - Chronic occlusion intervention
  - Bioabsorbable vascular scaffold

Andrade, Verma, Macle and al, CJC online Supplement 2019

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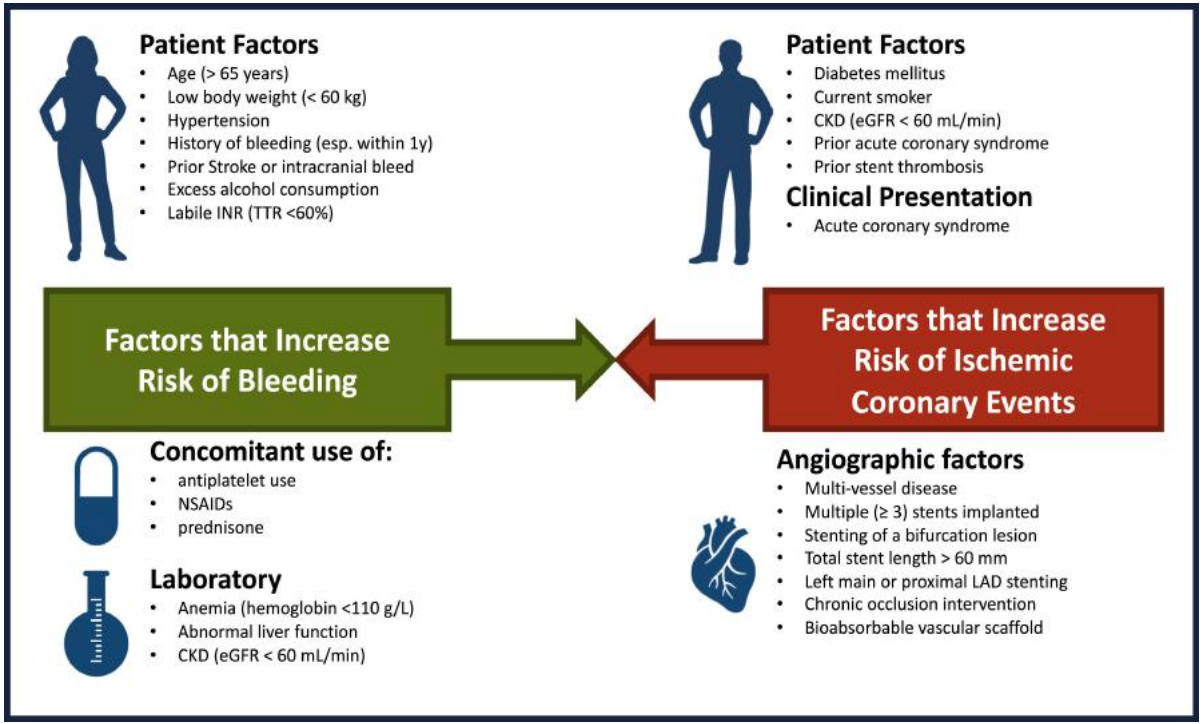

Andrade, Verma, Macle and al, CJC online Supplement 2019

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Conclusion

- FA et MCAS sont des entités qui coexistent fréquemment
- Favoriser des doses connues pour la prévention des AVC
- Le mieux est parfois l'ennemi du bien
- Se souvenir que l'ASA peut être utile au début surtout si anatomie complexe.
- Toujours soupeser le risque de saignement et de thrombose

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