SSVQ Société des sciences vasculaires du Québec
Chef de file en santé vasculaire.

FA et SCA (traitée médicalement ou invasivement) & FA et MCAS stable

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18 Septembre 2020

CRCHUM RESEARCH CENTRE

CENTRE CARDIOVASCULAIRE DU CHUM

Université de Montréal

CHUM

Conflits d'intérêts

- **Subvention de recherche:** Miltenyi Biotec, Astra-Zeneca, Abbott Vasculaire

- **Honoraires de conférencier et aviseur:** Astra-Zeneca, Boehringer Ingelheim, Pfizer, Bayer, Servier, Abbott Vasculaire, Sanofi, Amgen et Novartis

OBJECTIFS

- **Gérer l'anticoagulation dans le contexte d'un centre avec hémodynamie.**

- **Adapter l'anticoagulation dans un centre périphérique sans traitement invasif.**

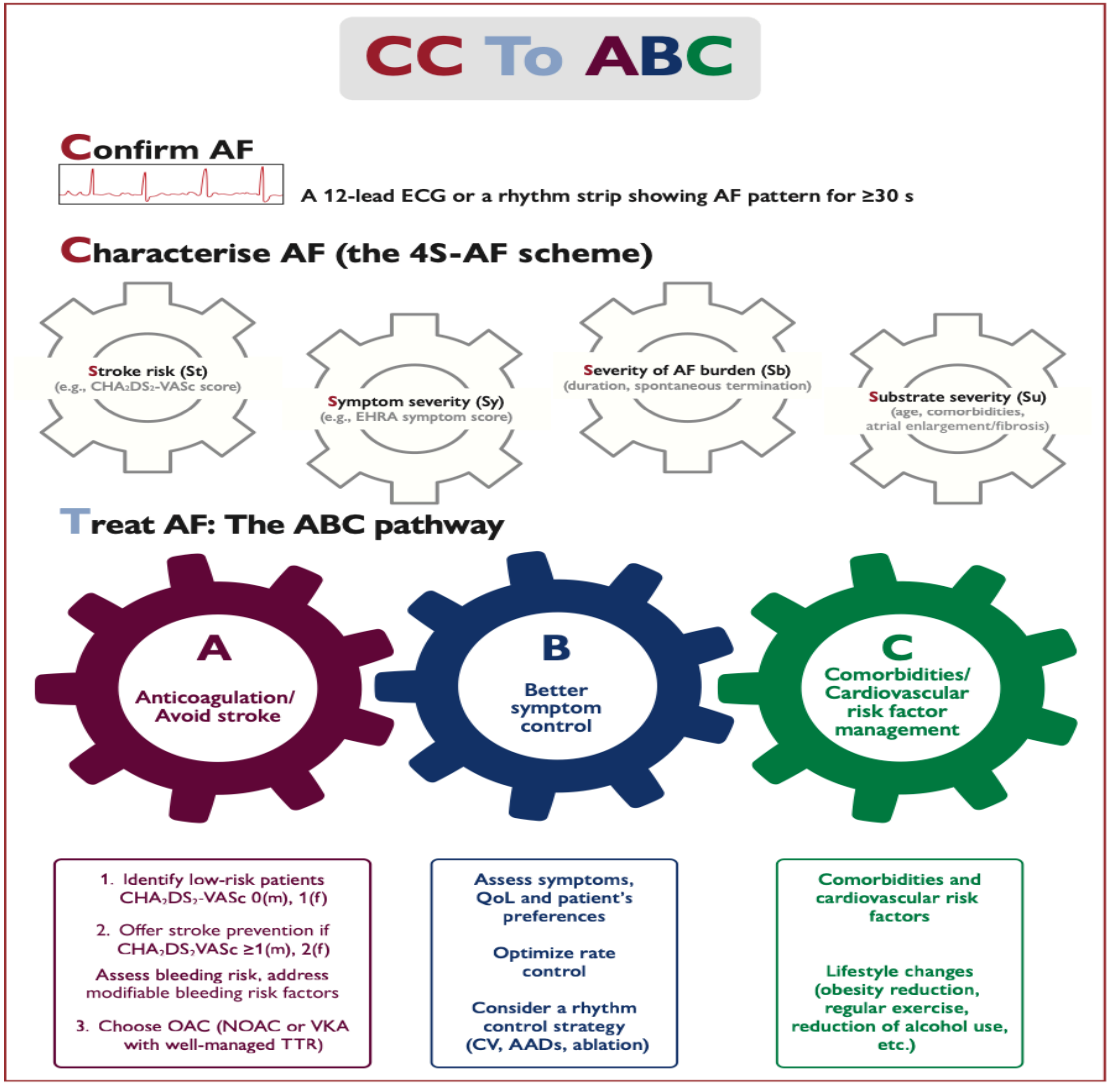
- **Prescrire judicieusement l'anticoagulation en bureau lorsque la MCAS est stabilisée.**

L'impact de la FA au Canada

- On estime qu'environ 350 000 Canadiens sont atteints de FA[1].
  - La FA touchera 25 % des Canadiens de ≥ 40 ans[2].
- La FA augmente le risque d'AVC ischémique de trois à cinq fois[1,3].
  - Les AVC dus à la FA sont associés à des taux accrus de morbidité et de mortalité dans les cas d'AVC non liés à une FA[4,5].
- En présence de FA, le taux annuel d'AVC est de 4,5 %[6].
  - Environ 16 000 AVC liés à la FA par an au Canada (environ 20 % de tous les AVC[7])

1. Fondation des maladies du cœur et de l'AVC. http://www.coeuretavc.ca/coeur/conditions/fibrillation-auriculaire Consulté le 9 janvier 2017. 2. Lloyd-Jones DM, et al. Circulation 2004;110:1042–6. 3. European Heart Rhythm Association, et al. Eur Heart J 2010;31:2369-429. 4. Dulli DA, et al. Neuroepidemiology 2003;22:118-23. 5. Marini C, et al. Stroke 2005;36:1115-9. 6. [Aucun auteur cité]. Arch Intern Med 1994;154:1449-57. 7. Wolf PA, et al. Stroke 1991;22:983-8.

Approche FA - Mise à jour ESC 2020
29 août 2020



European Heart Journal, 29 août 2020. ehaa612, https://doi.org/10.1093/eurheartj/ehaa612

The "CCS Algorithm" for OAC Therapy in AF

2014 UPDATE

Age ≥ 65 — YES → **OAC***

NO

Prior Stroke/SE/TIA or Hypertension or Heart failure or Diabetes Mellitus
(CHADS$_2$ risk factors) — YES → **OAC***

NO

CAD or Arterial vascular disease
(coronary, aortic, peripheral) — YES → **ASA**

NO

No Antithrombotic

Consider and modify (if possible) all factors influencing risk of bleeding on OAC (hypertension, antiplatelet drugs, NSAIDs, excessive alcohol, labile INRs) and specifically bleeding risks for NOACs (low eGFR, age ≥ 75, low body weight)**

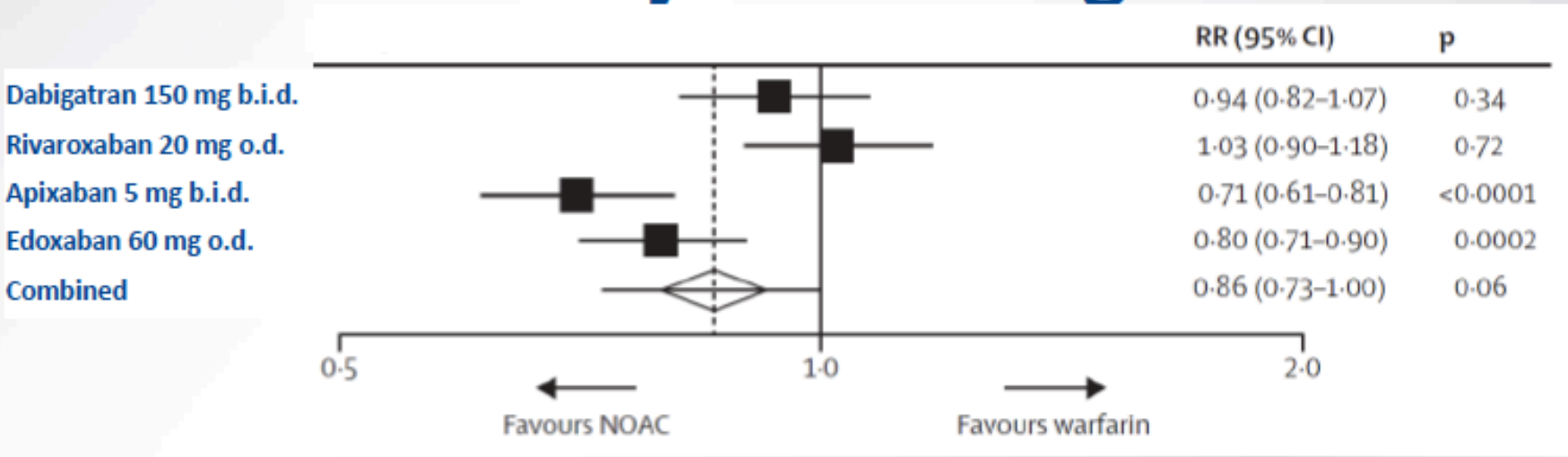
****may require lower dosing**

* We suggest that a NOAC be used in preference to warfarin for non-valvular AF.

2014 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. Can J Cardiol 2014:30(10). Pages 1114–1130 Macle L, et al. *Can J Cardiol* 2016;32:1170-85; Verma A, et al. *Can J Cardiol* 2014;30:1114-30.

New oral anticoagulants in patients with atrial fibrillation: a meta-analysis of phase III trials

Major bleeding

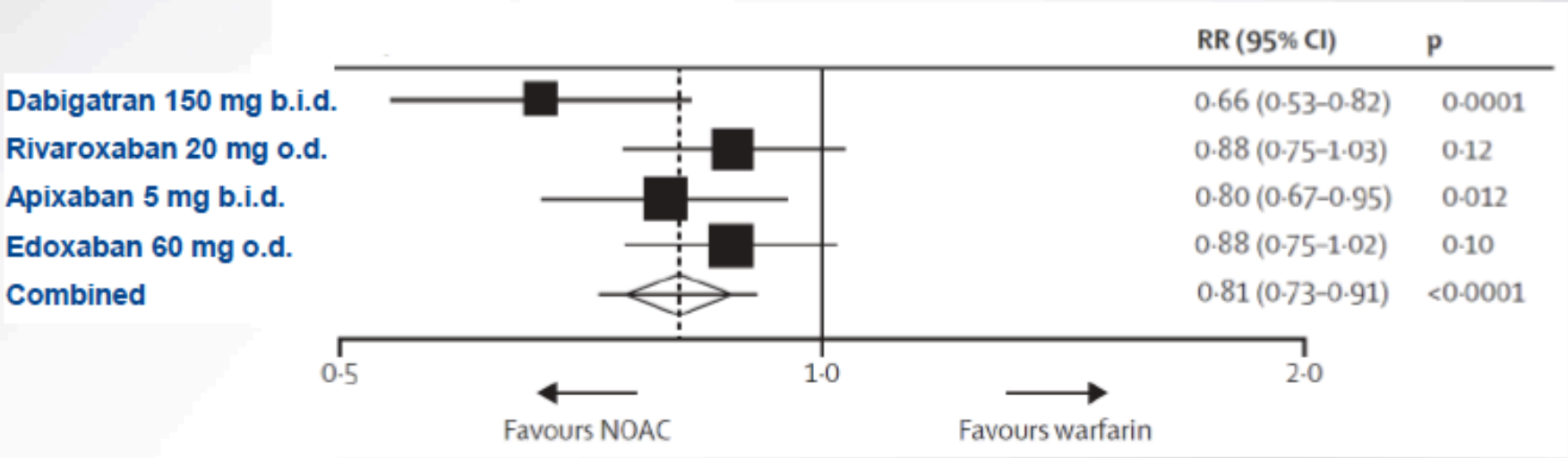


Note: Important differences between the treatments, patient demographics and trial characteristics that might affect study outcomes were not accounted for in the meta-analysis.

Ruff CT et al., Lancet 2013 Dec 3; doi: 10.1016/S0140-6736(13)62343-0

New oral anticoagulants in patients with atrial fibrillation: a meta-analysis of phase III trials

Stroke or systemic embolic events



Note: Important differences between the treatments, patient demographics and trial characteristics that might affect study outcomes were not accounted for in the meta-analysis.

Ruff CT et al., Lancet 2013 Dec 3; doi: 10.1016/S0140-6736(13)62343-0

Toutefois ….!

- Jusqu'à 30% des patients en FA anticoagulés (AVK) ont une MCAS et sont des candidats potentiels à une DTAP.

- Entre 5% to 10% des patients soumis à une implantation d'un stent nécessitent une anticoagulation.

24.9% des patients en FA enrôlés dans ARISTOTLE ont eu une PCI[1]

1. Bahit MC *et al*, *Int J Cardiol* 2013;170:215–220

COMMENT GÉRER LA FIBRILLATION AURICULAIRE EN CONTEXTE DE MALADIE CORONARIENNE?

Double ou triple thérapie:
ACo + Antiplaquettaire(s)

- Réduit le risque d'événements thrombotiques

Mais

- Augmente le risque de saignement jusqu'à 3-5 fois

Risque hémorragique

Risque thrombotique

Complication de l'image (1) :

Nouveaux inhibiteurs P2Y12 en association avec l'ACo?

Les 2 études

PLATO (ticagrelor)

&

TRITON-TIMI 38 (prasugrel)

Les patients traités par un ACo ont été exclus!

Complication de l'image (2) :

NACOs

en association avec une DAPT

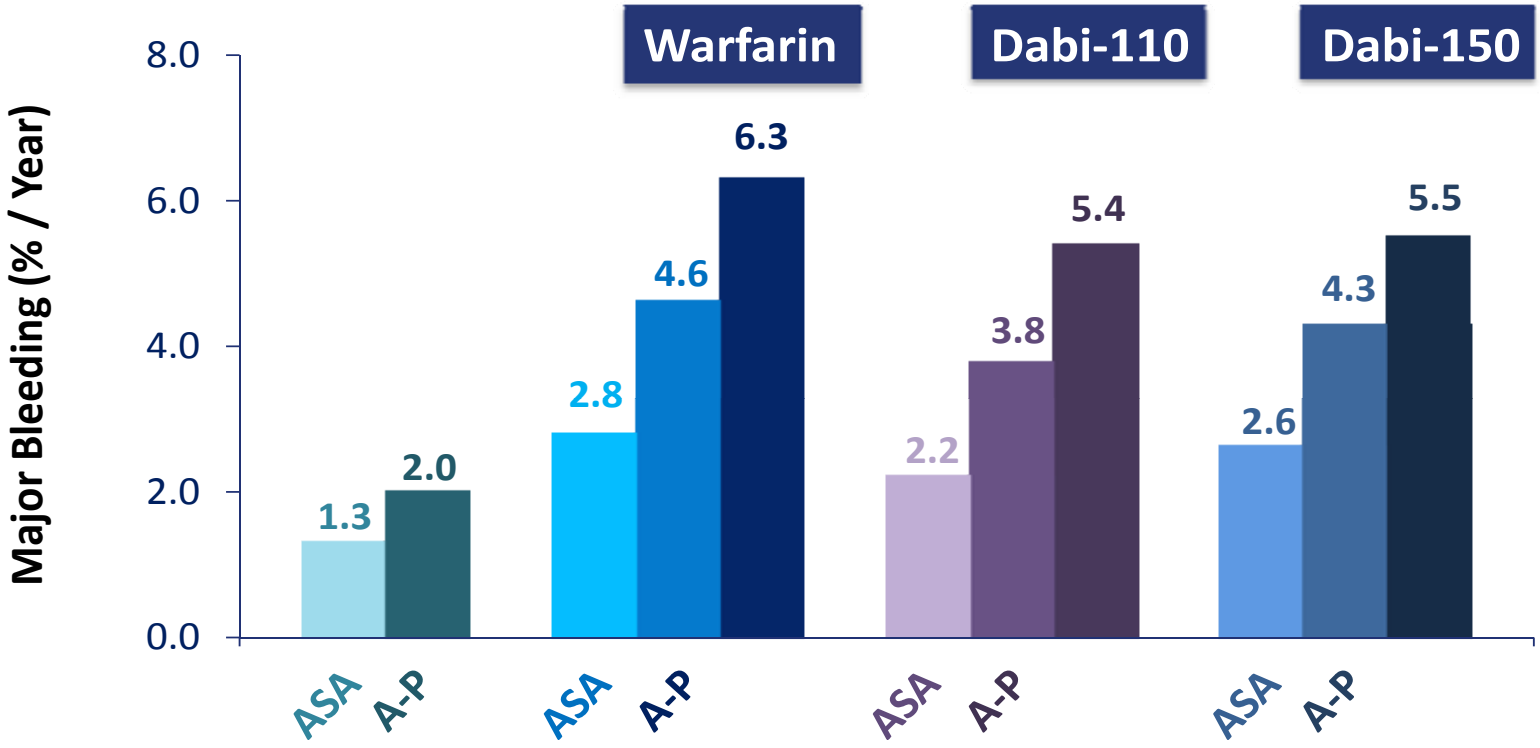
(aspirin+clopidogrel) ?

Dans toutes les études des AODs

(RELY, ROCKET-AF, ARISTOTLE & ENGAGE)

Patients sont exclus s'ils recevaient un inhibiteur P2Y12

Effet de l'ajout d'un double traitement antiplaquettaire (DAPT) à la warfarine ou à un AOD



A-P = Anti-platelet agent

Circulation 2013;127:634-40

CAS

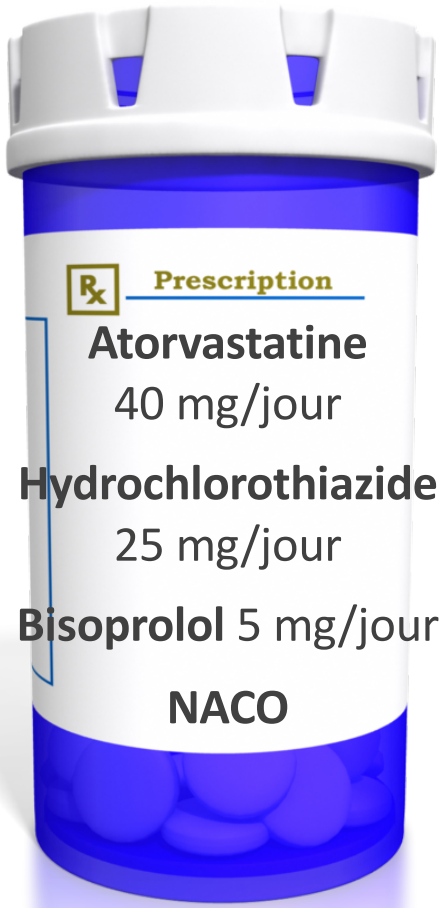
Rose : 77 ans

Antécédents :

- Hyperlipidémie
- Tabagisme (60 paquets-année → a cessé de fumer il y a 10 ans)
- Hypertension
- Fibrillation auriculaire (FA)

Apparition d'une angine stable (classe I de la SCC)

- Défaut de perfusion réversible de la paroi inférieure, d'étendue moyenne et d'intensité légère concordant avec une atteinte de la coronaire droite (sténose ≥ 50 %)



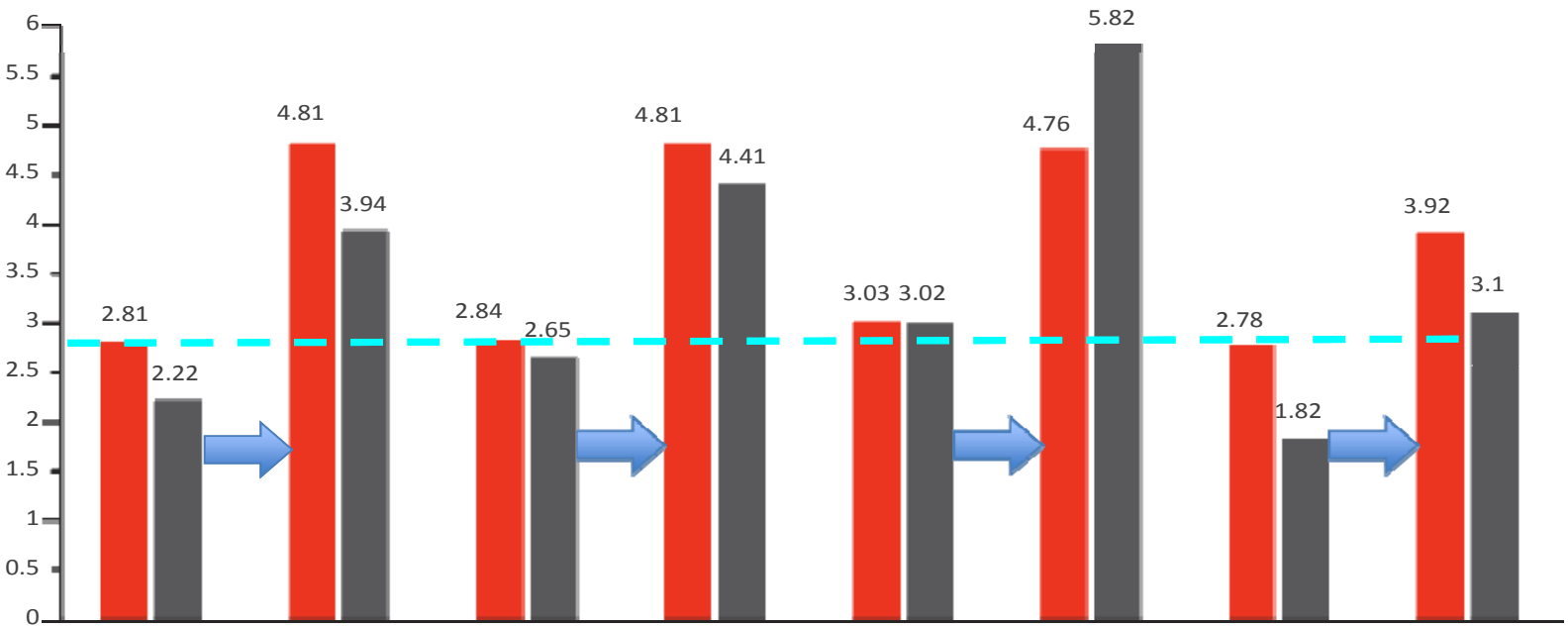
QUESTION

Ajouteriez-vous de l'AAS pour traiter sa coronaropathie stable nouvellement diagnostiquée?

A. Oui

B. Non

Comparaisons indirectes des OADs? Risque de saignement majeur / an (%) avec ou sans ASA



	RELY-110 NO ASA	RELY-110 + ASA	RELY-150 NO ASA	RELY-150 + ASA	ROCKET-AF NO ASA	ROCKET-AF + ASA	ARISTOTLE NO ASA	ARISTOTLE + ASA
WARFARIN	2.81	4.81	2.84	4.81	3.03	4.76	2.78	3.92
DOACs	2.22	3.94	2.65	4.41	3.02	5.82	1.82	3.1

Connolly SJ, et al. N Engl J Med. 2009; 361:1139–1151.
Patel MR, et al. N Engl J Med. 2011; 365:883–891.
Granger C, et al. N Eng J Med. 2011; 365:981–992

P value not available

QUESTION

Ajouteriez-vous de l'AAS pour traiter sa coronaropathie stable nouvellement diagnostiquée?

A. Oui

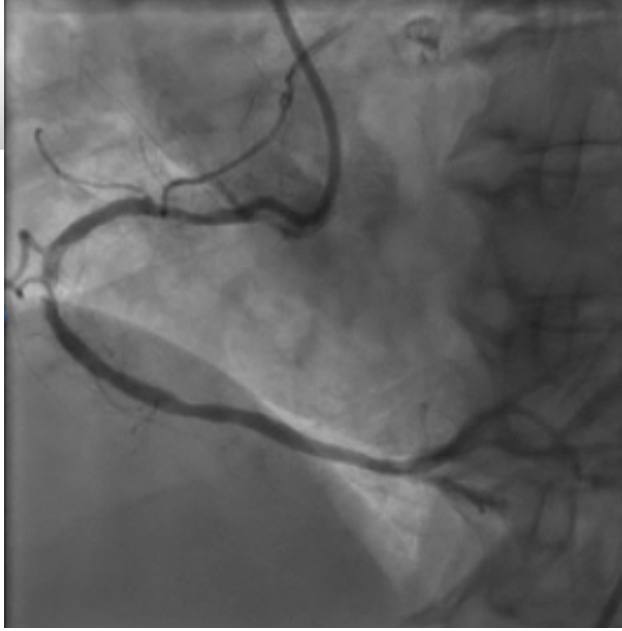
B. Non

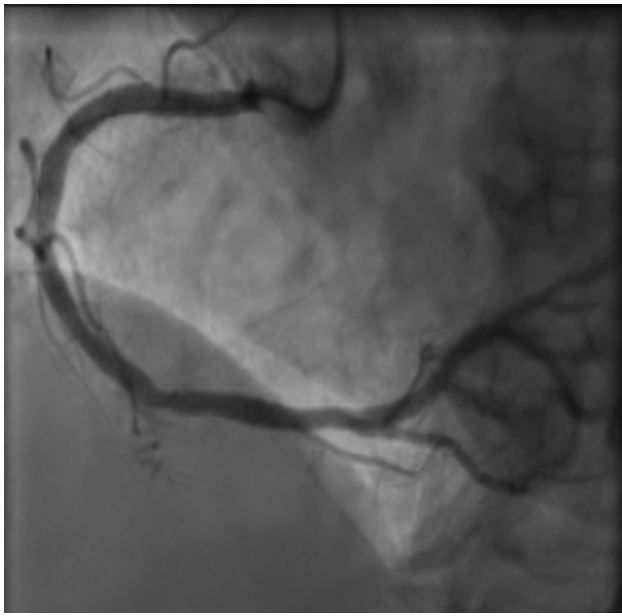
1 AN PLUS TARD

Rose : 78 ans

Admise pour un infarctus du myocarde sans élévation du segment ST (NSTEMI)

- Fonction ventriculaire gauche légèrement altérée (hypokinésie de la paroi inférieure)
- Coronarographie : sténose à 80 % de l'artère coronaire droite moyenne avec thrombus → endoprothèse à élution de médicament (EEM) de 2e génération





Gestion de l'anticoagulation périprocédurale, autant en centre ayant un labo d'hémodynamie que communautaire

Considérations

- Faut-il cesser l'anticoagulation ?
- Quand cesser ?
- Le *bridging* d'ACO est-il nécessaire ?
- Le choix de la DTAP
- Le choix de l'accès vasculaire

Gestion de l'anticoagulation périprocédurale: perspectives américaine et européenne

TABLE 1 Summary of Practical Recommendation for OAC Patients Undergoing PCI

	North American Perspective	European Perspective
Pre-procedural considerations		
Indication to PCI	Consider appropriateness.	–
Risk management	Qualitative, based on factors defining the ischemic/thrombotic and bleeding risk.	Quantitative and qualitative, based on scores and factors defining the ischemic/thrombotic and bleeding risk.
Procedural considerations		
Anticoagulation	A period of washout is always preferable (unless emergency PCI) and bridging with heparin is unnecessary (unless ACS).	Do not interrupt VKA, interrupt DOACs unless emergency PCI.
Vascular access	Prefer radial access.	Prefer radial access.
Additional intraprocedural UFH	Administer.	Administer (reduced dose if VKA, standard dose if DOACs).
Bivalirudin use	May be considered in high bleeding risk patients, particularly ACS and if femoral approach is used.	May be considered.
Use of GPIs	Limit use to selected cases at high-risk for thrombotic complications or for bail-out situations.	Do not use, except for bailout.
Use of periprocedural aspirin	Periprocedural and in-hospital.	Consider pre-treatment in most cases.
Use of periprocedural clopidogrel	Recommended.	Recommended. Pre-treatment if known coronary anatomy, emergency cases, or PCI is likely). Halved loading dose in case of VKA.
Stent selection	Prefer new-generation DES.	Prefer new-generation DES.

Gestion de l'anticoagulation périprocédurale: perspectives américaine et européenne

Table 4 Summary of the antithrombotic management differences between a VKA and NOAC in patients undergoing elective PCI

	VKA	NOAC
Periprocedural management		
Anticoagulation (see *Figure 1*)	Because of the reduced risk of bleeding, VKA should not be interrupted (or bridged with heparin).	Elective PCI • Because of the undefined intra-procedural protection against thrombotic events of NOAC, timely (12–24 h in advance, based on renal function and agent) interruption is preferred. • Depending on renal function and agent used (e.g. Dabigatran has high renal dependency for its excretion), cessation for 24–48 h may be considered. • No bridging is recommended. Emergency PCI • NOACs need not to be interrupted.
Vascular access	Because of the reduced risk of access-site bleeding complications, the radial approach should be preferred.	
Additional intra-procedural UFH	To prevent radial artery occlusion, and possibly limit the occurrence of intra-procedural thrombotic complications, UFH should be administered.	Whether NOAC is interrupted or not, UFH should be administered as per usual practice
Dose of additional intra-procedural UFH	To limit the risk of bleeding (in ongoing VKA), reduced dose (30–50 U/kg) should be given.	Standard dose UFH (70–100 U/kg) should be given
Use of bivalirudin	Because of the observation of superior safety, and possibly also efficacy, it may be considered in accordance with prescribing label.Specific data in patients on OAC are limited.	

Europace. 2019 Feb 1;21(2):192-193.doi: 10.1093/europace/euy174.

Gestion de l'anticoagulation périprocédurale: perspectives américaine et européenne

Table 4 Summary of the antithrombotic management differences between a VKA and NOAC in patients undergoing elective PCI

	VKA	NOAC
$P2Y_{12}$-receptor inhibitor	Because of potential increased risk of bleeding with prasugrel and ticagrelor in stable CAD patients on OAC, clopidogrel is generally recommended. • Consider pre-treatment with at least one antiplatelet agent in most cases. • Where coronary anatomy is known or in emergency cases, whereby a decision for PCI is likely, pre-treatment with a $P2Y_{12}$-receptor inhibitor can be considered. • Small numbers of prasugrel were used in the PIONEER-AF trial. In REDUAL-PCI, 12% were prescribed ticagrelor, which did not show excess bleeds when used with dabigatran as DAT.	
Dose of $P2Y_{12}$-receptor inhibitor	Because clopidogrel should be given in advance of PCI, 300 mg loading should generally be preferred to limit the risk of bleeding (with ongoing VKA).	Whether NOAC is interrupted or not, 300 or 600 mg loading dose should be selected as per usual practice due to limited data.
Use of GPI	Because of the observed increase in major bleeding, with no benefit in ischaemic outcomes, GPI should not be used, except for bail-out, in life-threatening situations.	Because of the observed increase in major bleeding, with no benefit in ischemic outcomes, GPI should not be use where NOACs are uninterrupted, except for bail out, in life-threatening situations.
Use of GPI as per standard practice can be made for patients on NOAC when timely discontinuation before PCI has been carried out.		

Europace. 2019 Feb 1;21(2):192-193.doi: 10.1093/europace/euy174.

Faut-il cesser l'anticoagulation avant l'ICP ?

- **OUI → Si procédure non-urgente/élective (MAJORITÉ DES CAS)**
  - **NACO**: À **cesser**
  - **AVK**: discordance entre lignes directrices américaines et européennes, mais en général à **cesser** dans notre contexte canadien

- **NON → Si procédure urgente**
  - Exemples de situation:
    - STEMI
    - NSTEMI à haut risque ou associé à une instabilité

Question

Quelle est la gestion anti-thrombotique optimale recommandée à son <u>arrivée</u> à l'hôpital (hémo ou communautaire) ?

- ASA 320 mg le premier jour, puis 80 mg die.
- Clopidogrel (300-600mg) dose de charge puis 75 mg die. **(Éviter Ticagrelor ou prasugrel)**. *<u>Attendre</u>: si suspicion de M3VX, TC, dysfonction VG et coro sera faite en dedans de 24-48h★*
- Débuter héparine IV (éviter HBPM). Éviter le bolus en dedans de 6-12h de la dernière dose du NACO. Viser PTT 50-60 sec si possible.
- Ajouter un IPP.

★Nouvelles recommandations de l'ESC (Août 2020): attendre anatomie coronarienne pour administrer P2Y12 Ib-

QUESTION

Quel schéma antithrombotique oral recommanderiez-vous pour Rose à sa sortie de l'hôpital?

A. Double thérapie antiplaquettaire (DTAP, c.-à-d. AAS + inhibiteur du récepteur de l'ADP, p. ex., le clopidogrel)

B. Anticoagulant oral (ACO, c.-à-d. warfarine ou NACO) + AAS

C. ACO + inhibiteur du récepteur de l'ADP

D. Trithérapie (DTAP + ACO)

ADP = adénosine diphosphate; NACO = nouvel anticoagulant oral

QUESTION

Pendant combien de temps Rose devrait-elle continuer de suivre le schéma antithrombotique oral qui lui a été recommandé à sa sortie de l'hôpital?

A. 1 mois
B. 3 mois
C. 6 mois
D. 12 mois
E. > 12 mois

NOMBRE DE STRATÉGIES POSSIBLES CHEZ LE PATIENT ATTEINT DE FIBRILLATION AURICULAIRE QUI SUBIT UN SCA

Dose d'AAS :	**Aucune Faible Élevée 3**	**1+8 = 9**
Durée, AAS (mois) :	**1 3 6 12 4**	**AAS**
IADP :	**Aucun Clopidogrel Prasugrel Ticagrélor 4**	**1+12 = 13**
Durée, IADP (mois) :	**1 3 6 12 4**	**IADP**
ACO :	**Aucun Warfarine Dabigatran Rivaroxaban Apixaban Edoxaban 5**	**1+10 = 11**
ACO RIN/dose :	**Faible Élevée 2**	**ACO**

- Permutations de simple, double ou triple thérapie comme traitement initial précoce (0, 1, 3, 6 mois) après un SCA : **9 x 13 x 11 = 1287**
- Permutations de simple ou double thérapie tard après le traitement initial précoce (0, 1, 3, 6 mois) après un SCA : **1287**

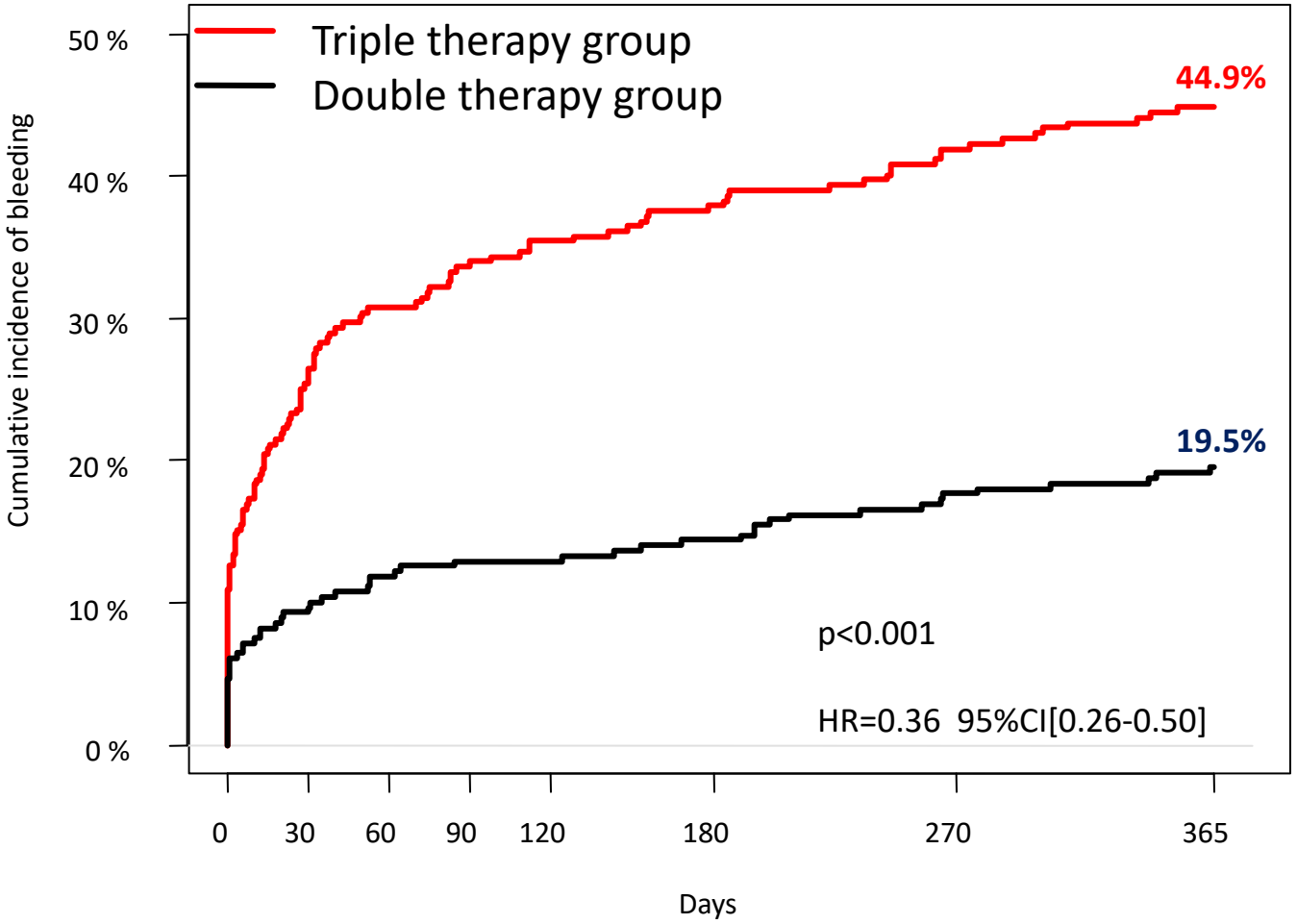
- Permutations totales possibles *au cours d'une année :* **1 656 369**

IADP = inhibiteur du récepteur de l'ADP; RIN = rapport international normalisé

Adapted from Gibson J Am Coll Cardiol 2017;69:172-75.

WOEST

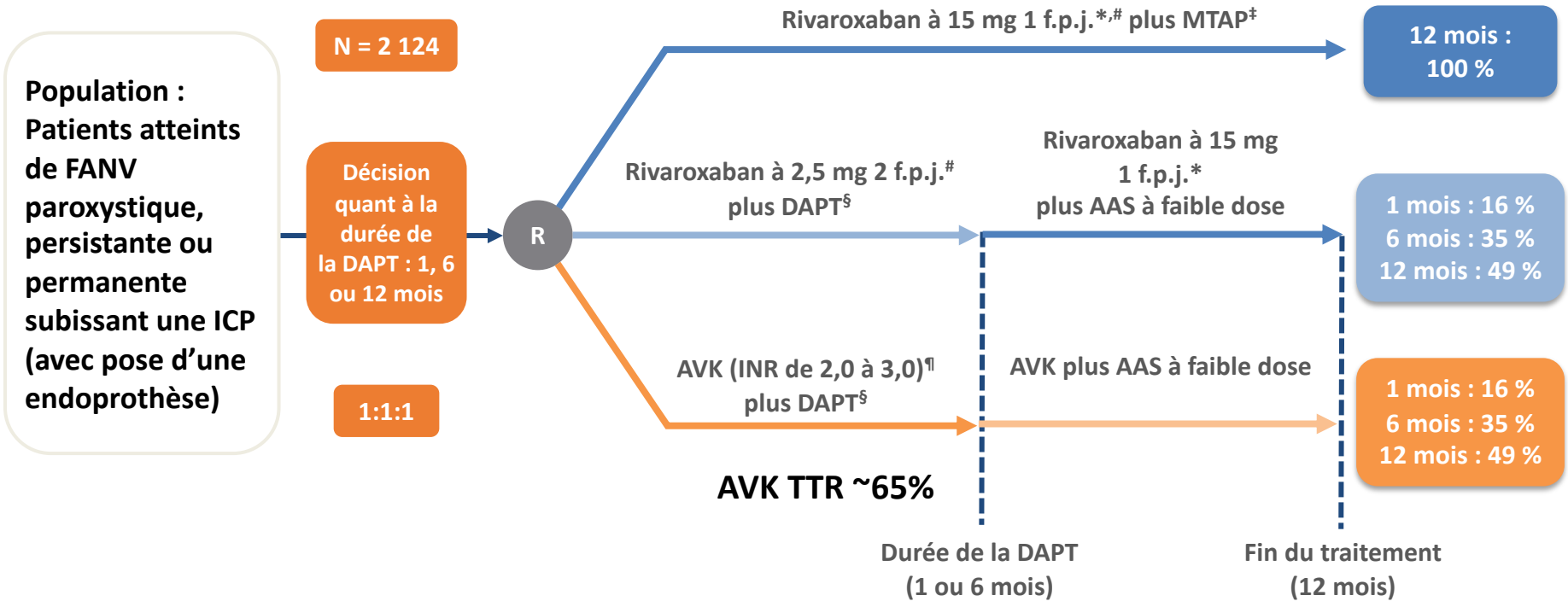
Objectif primaire: nombre total des saignements TIMI



Dewilde WJ, et al Lancet 2013; 381:1107-1115

Le rivaroxaban est le premier NACO a avoir fait l'objet d'un essai contrôlé randomisé dédié mené chez des patients atteints de FA subissant une ICP

Méthodologie : Étude ouverte de phase IIIb contrôlée et à répartition aléatoire visant à évaluer l'innocuité



* Cl_{cr} de 30 à 49 mL/min : 10 mg 1 f.p.j.; # première dose de 72 à 96 heures après le retrait de la gaine; ‡ clopidogrel (75 mg par jour) (utilisation du prasugrel ou du ticagrélor permise, mais limitée à 15 %); § AAS (75 à 100 mg par jour) plus clopidogrel (75 mg par jour) (utilisation du prasugrel ou du ticagrélor permise, mais limitée à 15 %); ¶ première dose de 12 à 72 heures après le retrait de la gaine

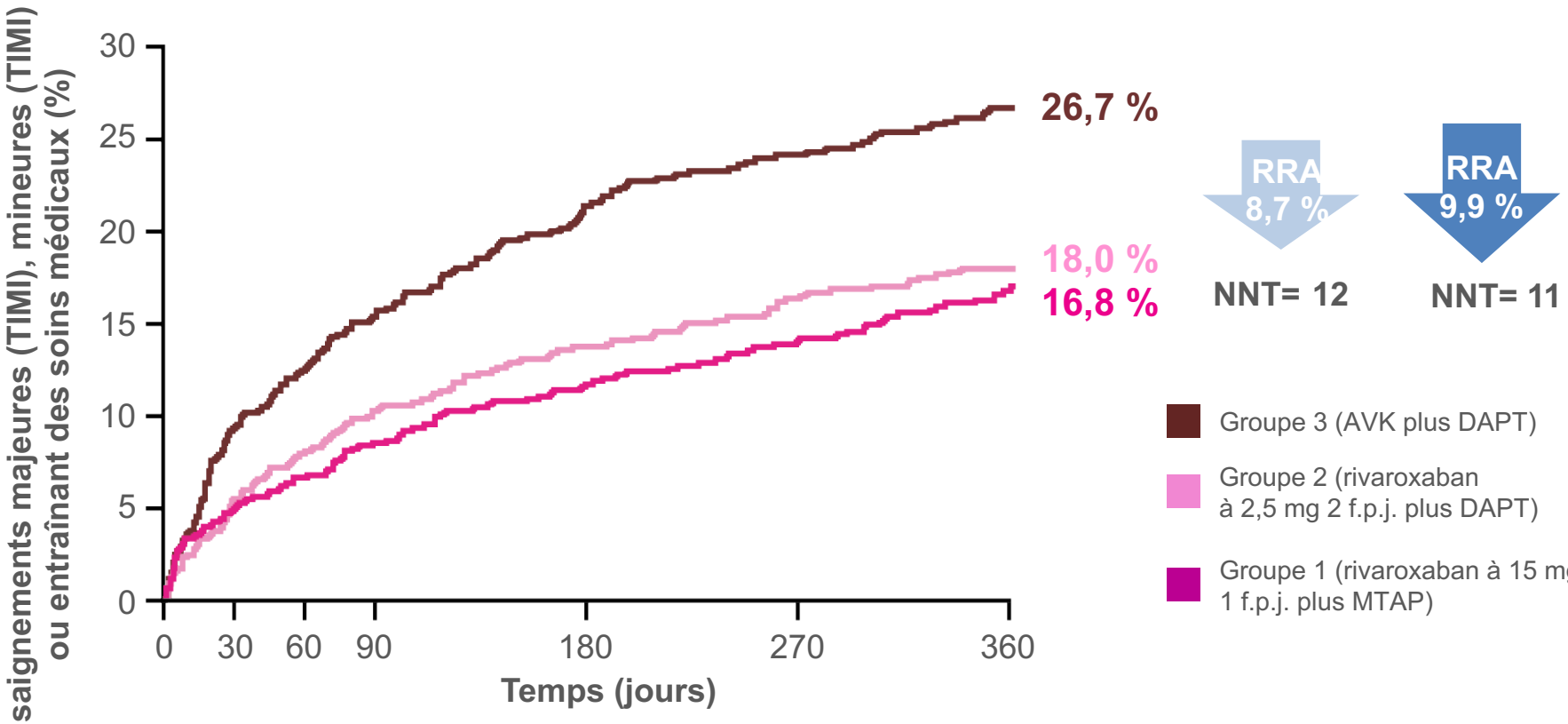
1. Janssen Scientific Affairs, LLC. 2016. https://clinicaltrials.gov/ct2/show/NCT01830543 [consulté le 10 octobre 2016];
2. Gibson CM et coll. *Am Heart J* 2015; 169: 472-478e5; 3. Gibson CM et coll. *New Engl J Med* 2016;
^doi:10.1056/NEJMoa1611594

PIONEER AF-PCI

Les 2 stratégies à base de rivaroxaban étaient associées à une amélioration significative de l'innocuité

Rivaroxaban à 15 mg 1 f.p.j. plus MTAP p/r à AVK plus DAPT : RRI = 0,59 (IC à 95 %, 0,47-0,76); p < 0,001

Rivaroxaban à 2,5 mg 2 f.p.j. plus DAPT p/r à AVK plus DAPT : RRI = 0,63 (IC à 95 %, 0,50-0,80); p < 0,001



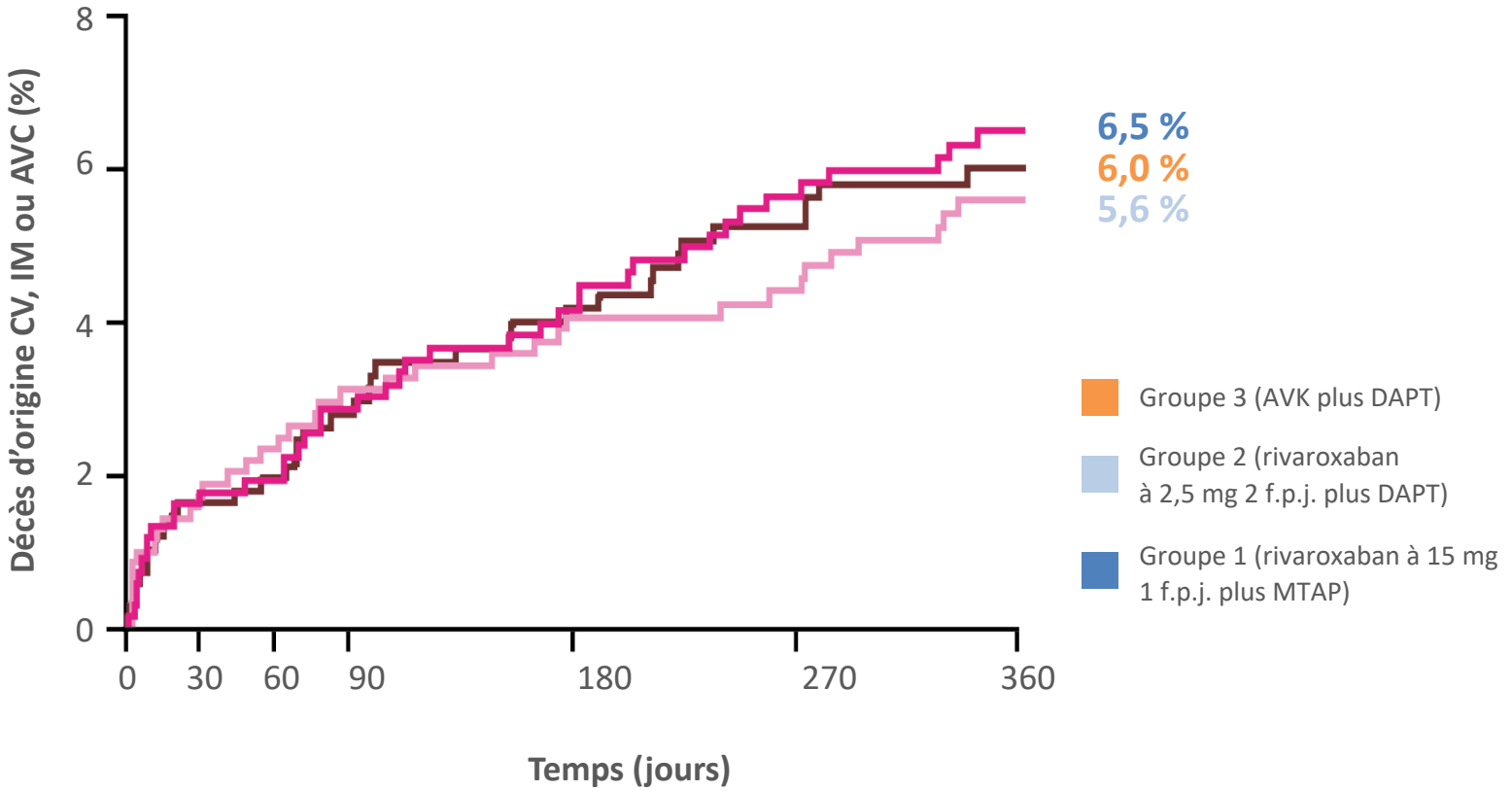
Gibson CM et coll. *New Engl J Med* 2016; doi:10.1056/NEJMoa1611594

PIONEER AF-PCI

L'efficacité des 3 stratégies thérapeutiques était comparable*

Rivaroxaban à 15 mg 1 f.p.j. plus MTAP p/r à AVK plus DAPT : RRI = 1,08 (IC à 95 %, 0,69-1,68); p = 0,750

Rivaroxaban à 2,5 mg 2 f.p.j. plus DAPT p/r à AVK plus DAPT : RRI = 0,93 (IC à 95 %, 0,59-1,48); p = 0,765

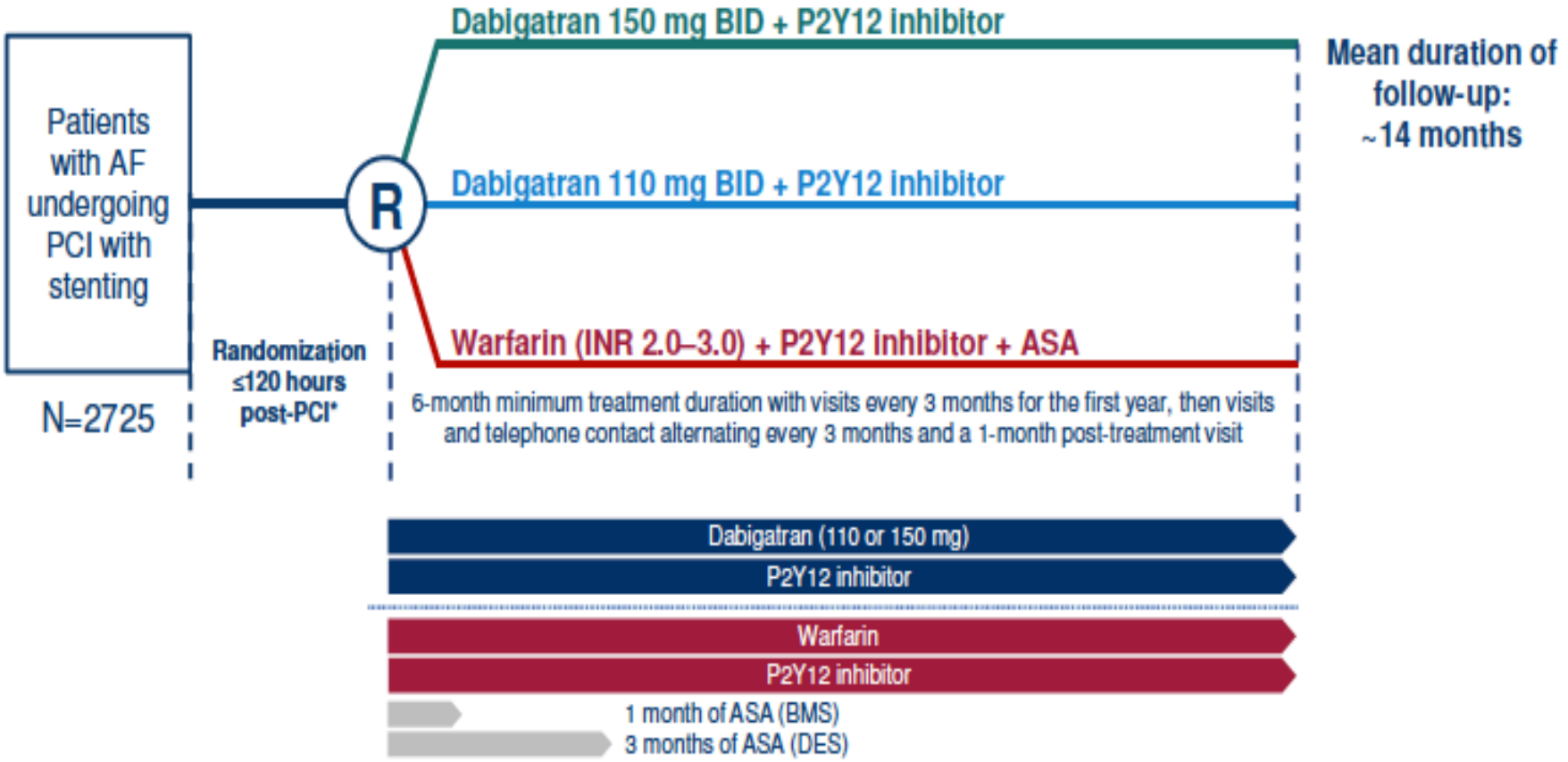


* L'essai n'avait pas la puissance nécessaire pour démontrer de manière définitive la supériorité ou la non-infériorité du rivaroxaban sur le plan des critères d'évaluation de l'efficacité.

Gibson CM et coll. New Engl J Med 2016; doi:10.1056/NEJMoa1611594

Study Design: Multicenter, randomized, open-label trial following a PROBE design

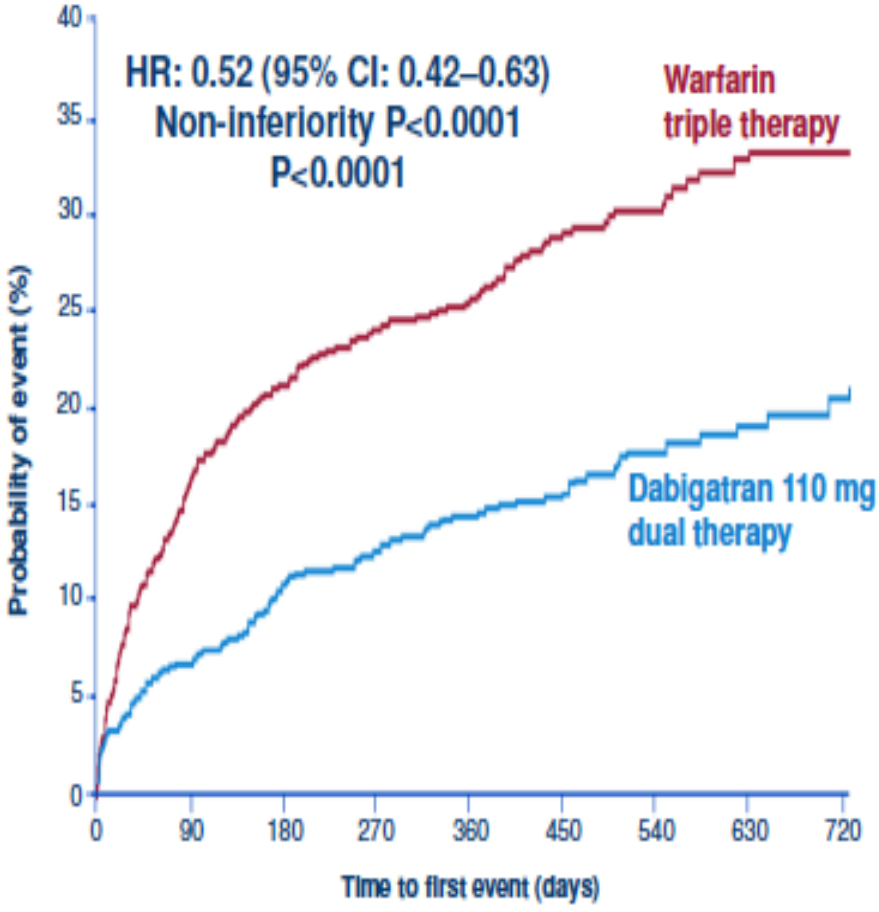
RE-DUAL PCI
Study in NVAF patients undergoing PCI

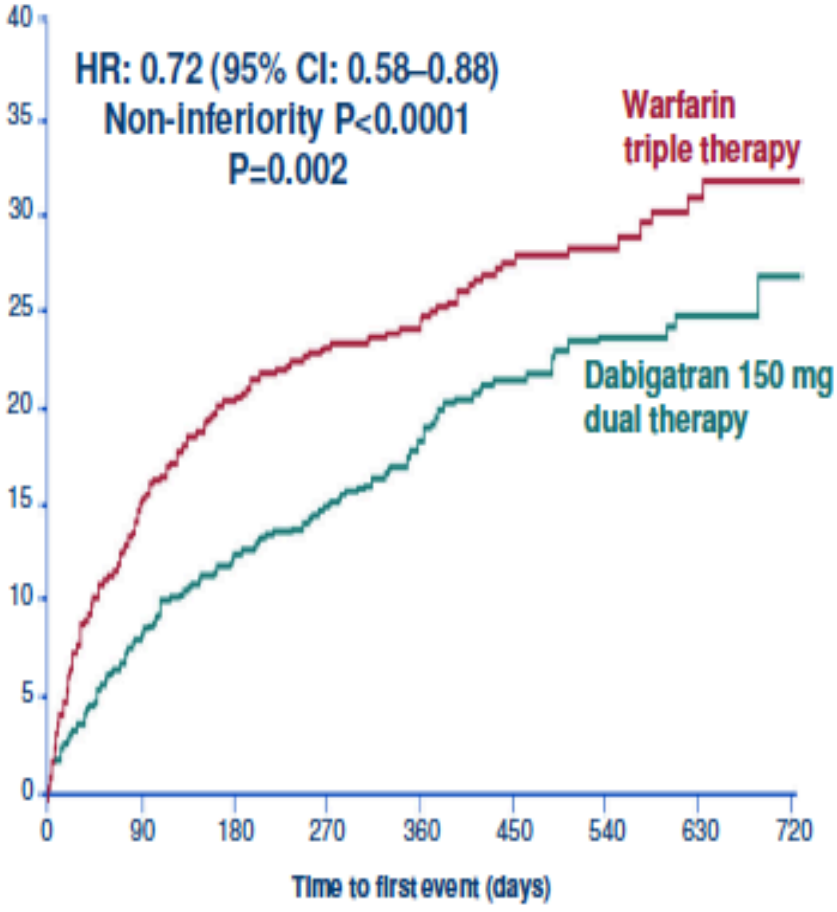


***Study drug should be administered 6 hours after sheath removal and no later than ≤120 hrs post-PCI (≤72 hrs is preferable).** PROBE, prospective, randomized, open, blinded end-point; R, randomization; BMS, bare metal stent; DES, drug-eluting stent. ClinicalTrials.gov: NCT02164864; Cannon et al. Clin Cardiol 2016

Primary Endpoint: Time to first ISTH major or clinically relevant non-major bleeding event

RE-DUAL PCI
Study in NVAF patients undergoing PCI





Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 mg vs warfarin comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≥70 in Japan and <80 or ≥80 years old elsewhere). For the dabigatran 150 mg vs warfarin comparison, an unstratified model is used, elderly patients outside the USA are excluded. Non-inferiority P value is one sided (alpha=0.025). Wald two-sided P value from (stratified) Cox proportional-hazard model (alpha=0.05)

Additional individual thromboembolic endpoints

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	Dabigatran 110 mg dual therapy (n=981) n (%)	Warfarin triple therapy (n=981) n (%)	D110 DT vs warfarin TT HR (95% CI)	D110 DT vs warfarin TT P value	Dabigatran 150 mg dual therapy (n=763) n (%)	Warfarin triple therapy (n=764) n (%)	D150 DT vs warfarin TT HR (95% CI)	D150 DT vs warfarin TT P value
All-cause death	55 (5.6)	48 (4.9)	1.12 (0.76–1.65)	0.56	30 (3.9)	35 (4.6)	0.83 (0.51–1.34)	0.44
Stroke	17 (1.7)	13 (1.3)	1.30 (0.63–2.67)	0.48	9 (1.2)	8 (1.0)	1.09 (0.42–2.83)	0.85
Unplanned revascularization	76 (7.7)	69 (7.0)	1.09 (0.79–1.51)	0.61	51 (6.7)	52 (6.8)	0.96 (0.65–1.41)	0.83
MI	44 (4.5)	29 (3.0)	1.51 (0.94–2.41)	0.09	26 (3.4)	22 (2.9)	1.16 (0.66–2.04)	0.61
Stent thrombosis	15 (1.5)	8 (0.8)	1.86 (0.79–4.40)	0.15	7 (0.9)	7 (0.9)	0.99 (0.35–2.81)	0.98

Results presented are times to event. Stent thrombosis is time to definite stent thrombosis

Duke Clinical Research Institute

Trial Design

Augustus

INCLUSION

- Atrial fibrillation (prior, persistent, >6 hr)
  - Physician decision for OAC
- Acute coronary syndrome or PCI
  - Planned $P2Y_{12}$ inhibitor for ≥6 months

Randomize
n=4600
patients

EXCLUSION

- Contraindication to DAPT
- Other reason for VKA (prosthetic valve, moderate / severe mitral stenosis)

Apixaban 5 mg BID
Apixaban 2.5 mg BID in selected patients

Open Label

VKA
(INR 2–3)

Aspirin for all on the day of ACS or PCI
Aspirin versus placebo after randomization

Aspirin — *Double Blind* — **Placebo**

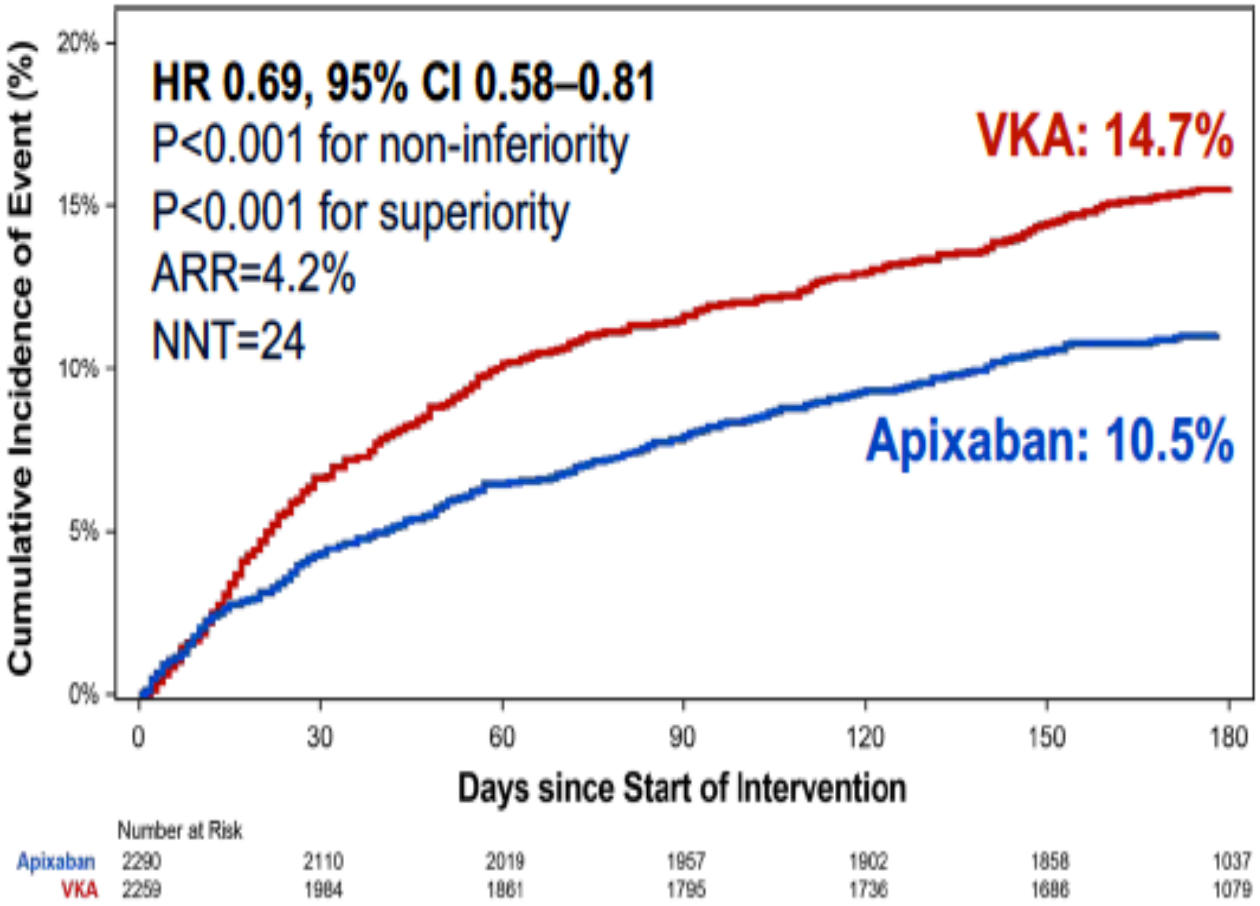
Aspirin — *Double Blind* — **Placebo**

Primary outcome: ISTH major / CRNM bleeding
Secondary outcome(s): death / hospitalization, death / ischemic events

Lopes RD, et al. Am Heart J. 2018;200:17-23.

Major / CRNM Bleeding

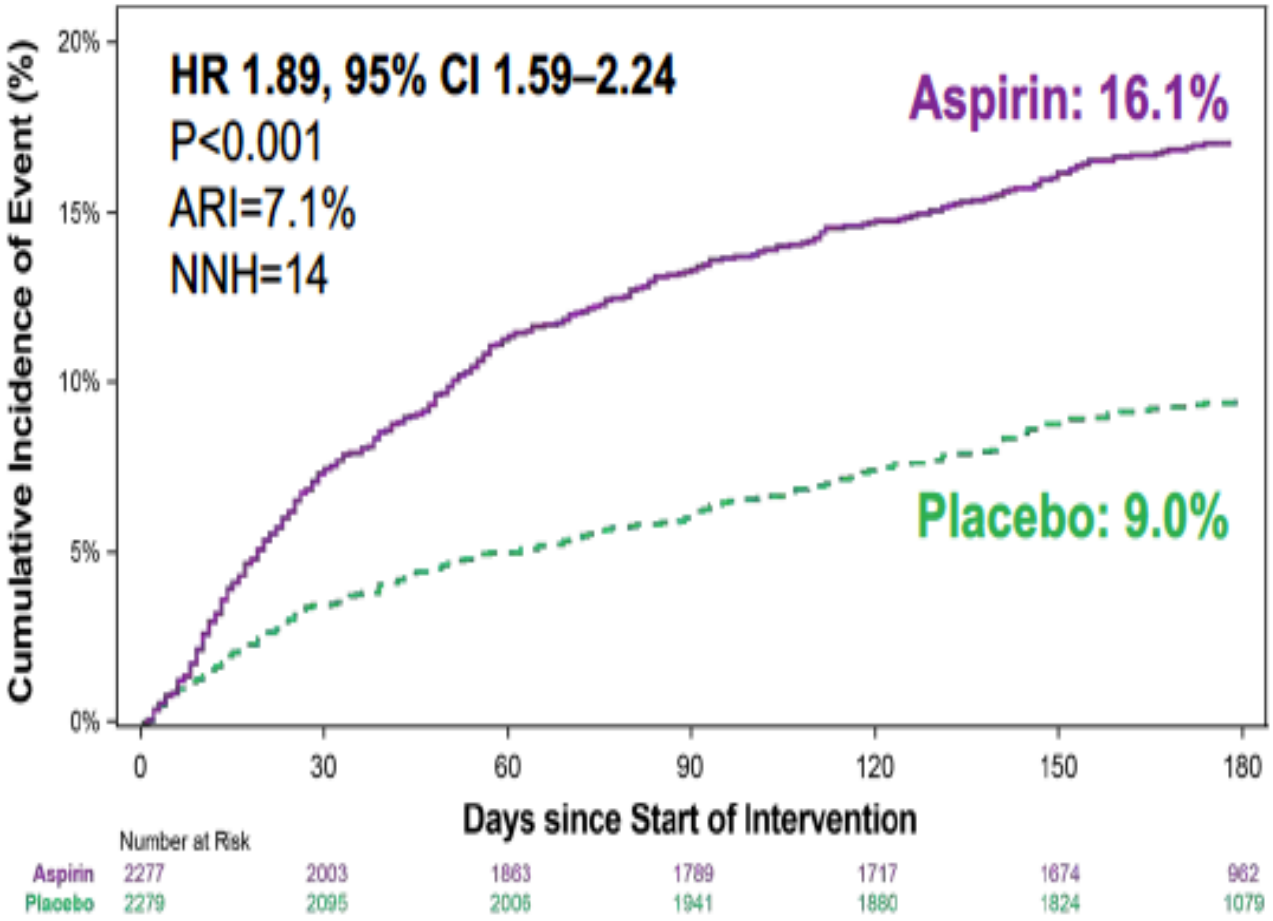
Apixaban vs. VKA



ARR: absolute risk reduction
NNT: number needed to treat

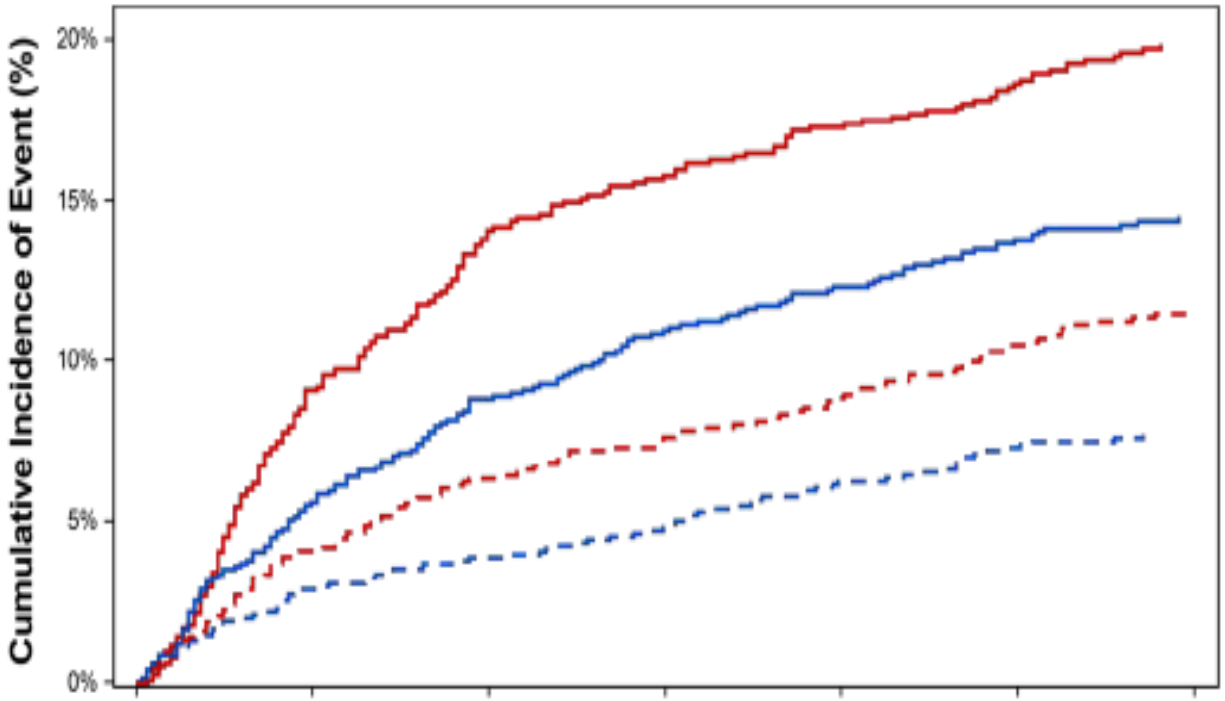
Major / CRNM Bleeding

Aspirin vs. Placebo



ARI: absolute risk increase
NNH: number needed to harm

Major / CRNM Bleeding



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%)

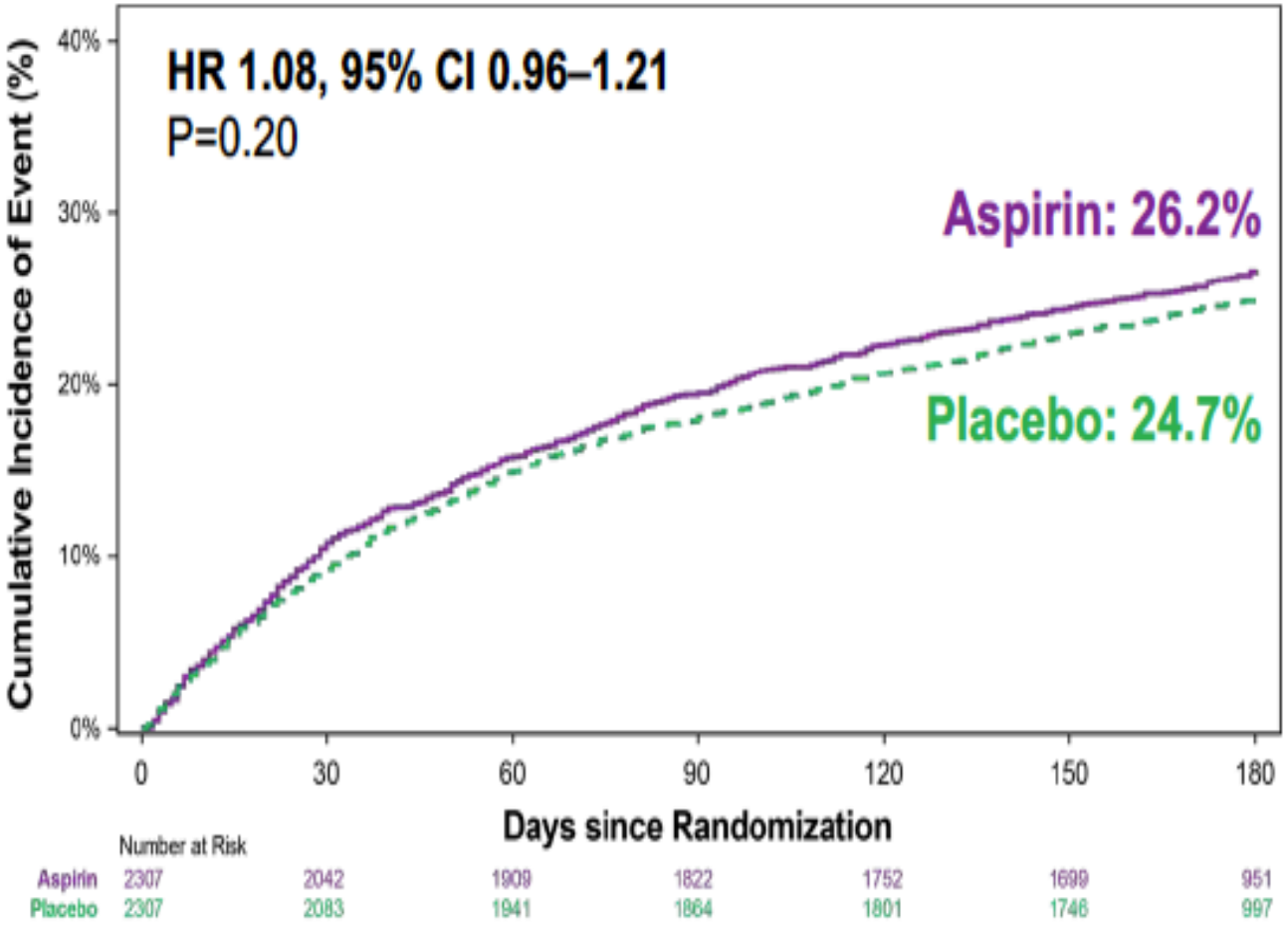
VKA + Placebo (10.9%)

Apixaban + Placebo (7.3%)

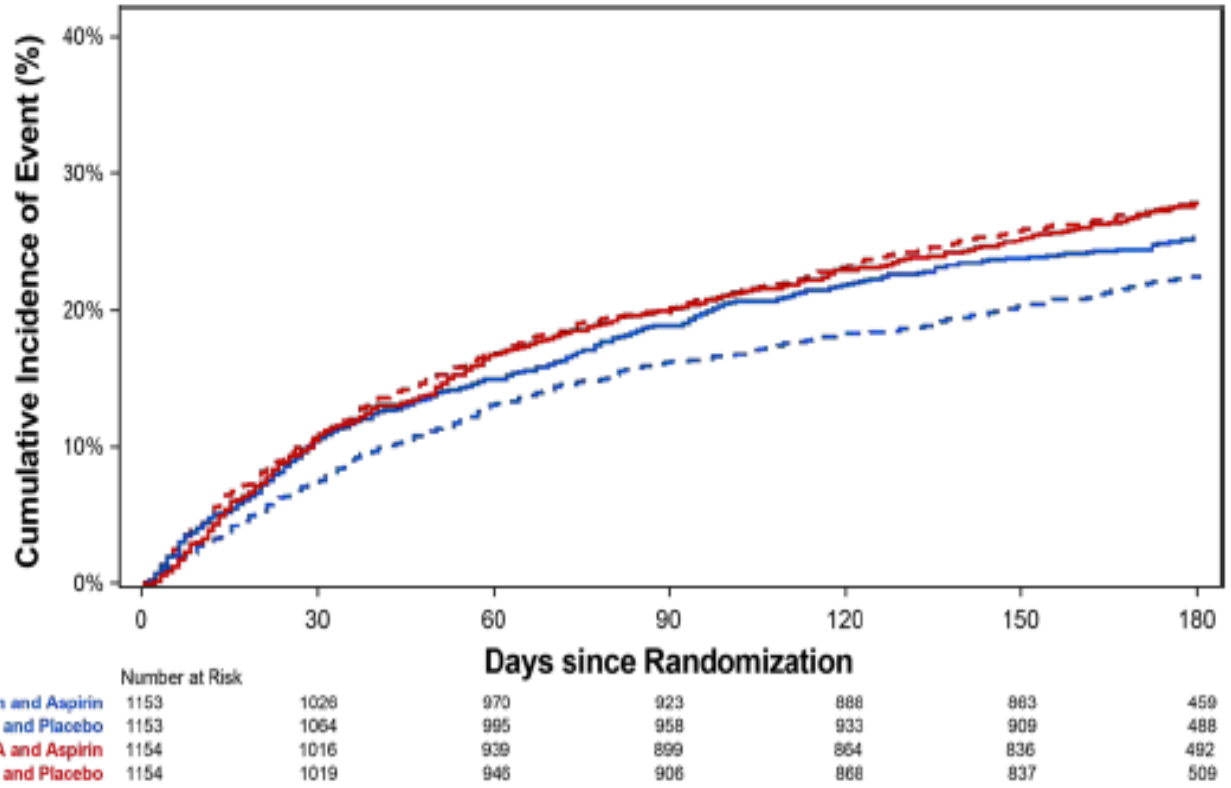
Apixaban + Placebo vs. VKA + Aspirin: 11.4% absolute risk reduction (NNT=9)

Death / Hospitalization

Aspirin vs. Placebo



Death / Hospitalization



Number at Risk

Apixaban and Aspirin	1153	1026	970	923	888	863	459
Apixaban and Placebo	1153	1064	995	958	933	909	488
VKA and Aspirin	1154	1016	939	899	864	836	492
VKA and Placebo	1154	1019	946	906	868	837	509

VKA + Aspirin (27.5%)
VKA + Placebo (27.3%)
Apixaban + Aspirin (24.9%)
Apixaban + Placebo (22.0%)

Apixaban + Placebo vs. VKA + Aspirin: 5.5% absolute risk reduction (NNT=18)

ENTRUST-AF PCI

Study Design

PROBE design: Prospective, Randomized, Open label, Blinded endpoint Evaluation in 1500 AF patients with ACS or stable CAD

Inclusion Criteria:

- *OAC indication for AF for at least 12 months*
- *Successful PCI with stent placement (goal of at least 25% ACS)*

4 hours – 5 days after sheath removal

RANDOMIZE

- *Edoxaban 60 mg/day**
  - *$P2Y_{12}$ inhibitor** (without aspirin)*
- *Vitamin K Antagonist****
  - *$P2Y_{12}$ inhibitor aspirin 1 - 12 months*****

12 m.

**Edoxaban dose reduction to 30 mg OD*
- *if CrCL≤50 ml/min*
- *BW≤60 kg*
- *certain P-gp inhibitors*

***Clopidogrel 75mg once-daily or if documented need prasugrel 5 or 10mg once-daily or ticagrelor 90mg twice-daily . Predeclared at randomization*

**** VKA, target INR 2-3*

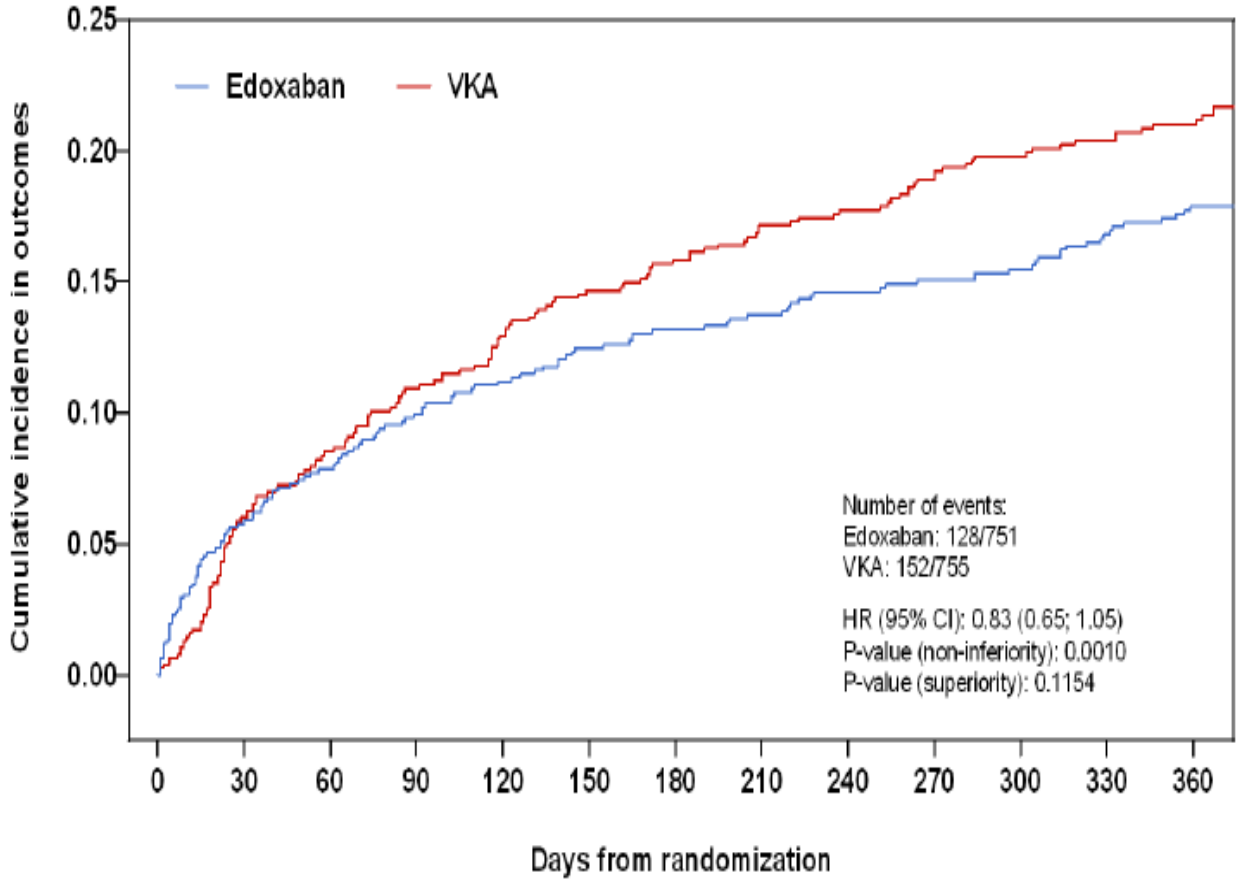
*****aspirin 100mg OD for 1-12 months guided by clinical presentation (ACS or stable CAD), $CHA_2DS\text{-}VASc_2$ and HAS_BLED*

Primary outcome:
ISTH major or clinically relevant non-major bleeding

ENTRUST-AF PCI

Primary Study Endpoint

ITT Analysis (N=1506), overall study period



Number at risk:

EDOXABAN	751	688	665	646	629	618	609	600	590	584	575	565	506
VKA	755	678	648	625	603	588	578	568	561	552	543	538	485

ENTRUST-AF PCI

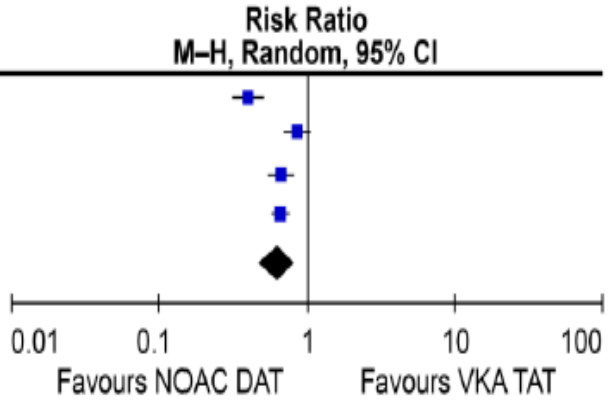
Meta-Analysis:
Comparative NOAC AF PCI trials
ISTH Major or CRNM Bleeding

ISTH Major or Clinically Relevant Non-Major Bleeding

Study or Subgroup	NOAC DAT Events	NOAC DAT Total	VKA TAT Events	VKA TAT Total	Weight	Risk Ratio M–H, Random, 95% CI
AUGUSTUS	84	1143	210	1123	23.7%	0.39 (0.31, 0.50)
ENTRUST AF-PCI	128	751	152	755	24.7%	0.85 (0.68, 1.05)
PIONEER AF-PCI	117	696	178	697	24.8%	0.66 (0.53, 0.81)
RE-DUAL PCI	305	1744	264	981	26.8%	0.65 (0.56, 0.75)
Total (95% CI)		**4334**		**3556**	**100.0%**	**0.62 (0.47, 0.81)**
Total events	634		804			

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 22.84$, df = 3 (P <0.0001); $I^2 = 87\%$

Test for overall effect: Z = 3.47 (P = 0.0005)



ENTRUST-AF PCI

Myocardial Infarction and Stent Thrombosis

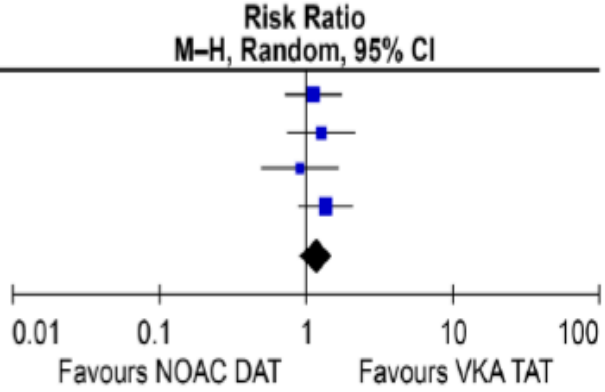
- Endpoints as defined by each of the NOAC AF PCI trials -

Myocardial Infarction

Study or Subgroup	NOAC DAT Events	Total	VKA TAT Events	Total	Weight	Risk Ratio M–H, Random, 95% CI
AUGUSTUS	38	1153	34	1154	29.3%	1.12 (0.71, 1.76)
ENTRUST AF-PCI	29	751	23	755	21.0%	1.27 (0.74, 2.17)
PIONEER AF-PCI	19	694	21	695	16.2%	0.91 (0.49, 1.67)
RE-DUAL PCI	70	1744	29	981	33.5%	1.36 (0.89, 2.08)
Total (95% CI)		**4342**		**3585**	**100.0%**	**1.18 (0.93, 1.52)**
Total events	156		107			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.25$, df = 3 (P = 0.74); $I^2 = 0\%$

Test for overall effect: Z = 1.34 (P = 0.18)

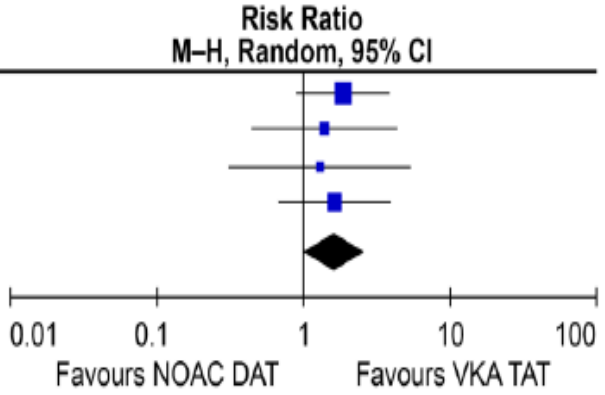


Stent Thrombosis

Study or Subgroup	NOAC DAT Events	Total	VKA TAT Events	Total	Weight	Risk Ratio M–H, Random, 95% CI
AUGUSTUS	21	1153	12	1154	40.0%	1.75 (0.87, 3.54)
ENTRUST AF-PCI	8	751	6	755	17.9%	1.34 (0.47, 3.84)
PIONEER AF-PCI	5	694	4	695	11.6%	1.25 (0.34, 4.64)
RE-DUAL PCI	22	1744	8	981	30.6%	1.55 (0.69, 3.46)
Total (95% CI)		**4342**		**3585**	**100.0%**	**1.55 (0.99, 2.41)**
Total events	56		30			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.29$, df = 3 (P = 0.96); $I^2 = 0\%$

Test for overall effect: Z = 1.92 (P = 0.06)



Question

Quel schéma antithrombotique oral recommanderiez-vous pour Rose à sa sortie de l'hôpital?

A. **Double thérapie antiplaquettaire (DTAP, c.-à-d. AAS + inhibiteur du récepteur de l'ADP, p. ex., le clopidogrel)**

B. **Anticoagulant oral (ACO, c.-à-d. warfarine ou NACO) + AAS**

C. **ACO + inhibiteur du récepteur de l'ADP**

D. **Trithérapie (DTAP + ACO)**

ADP = adénosine diphosphate; NACO = nouvel anticoagulant oral

Question

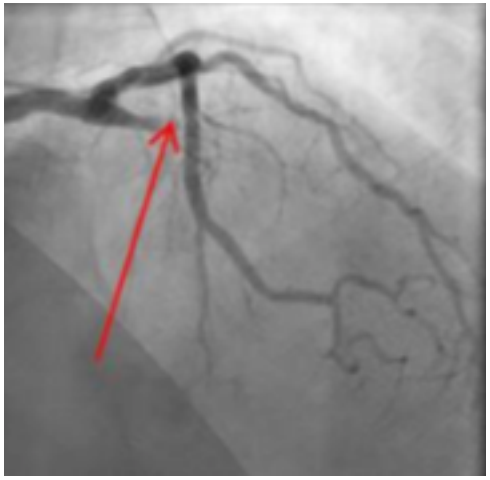
Pendant combien de temps Rose devrait-elle continuer de suivre le schéma antithrombotique oral qui lui a été recommandé à sa sortie de l'hôpital?

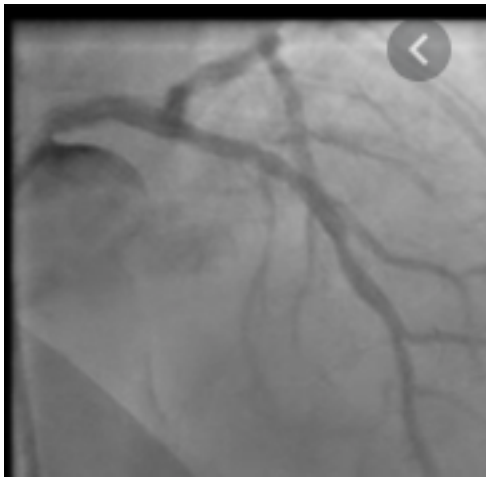
A. 1 mois
B. 3 mois
C. 6 mois
D. 12 mois
E. > 12 mois

ET SI ROSE EST EN STEMI

Rose : 78 ans

- Admise d'une façon urgente à un centre communautaire pour un STEMI ant-lat K1.
- Sera transférée pour une PCI primaire
- PCI nécessite →une endoprothèse à élution de médicament (EEM) de 2^{e} génération





Question

Quelle est la gestion anti-thrombotique optimale recommandée à son arrivée à l'hôpital (hémo ou communautaire)?

Question

Quelle est la gestion anti-thrombotique optimale recommandée à son arrivée à l'hôpital?

- **ASA 320 mg puis 80 mg die.**
- **Clopidogrel (600mg) puis 75 mg die.**
- **Bolus d'héparine au centre référant puis donner héparine IV (ou bivalirudine) per-procédure; viser un ACT entre 200-250 sec.**
- **Favoriser l'accès radial.**
- **Ajouter un IPP.**

Question

Quel schéma antithrombotique oral recommanderiez-vous pour Rose à sa sortie de l'hôpital?

A. **Double thérapie antiplaquettaire (DTAP, c.-à-d. AAS + inhibiteur du récepteur de l'ADP, p. ex., le clopidogrel)**

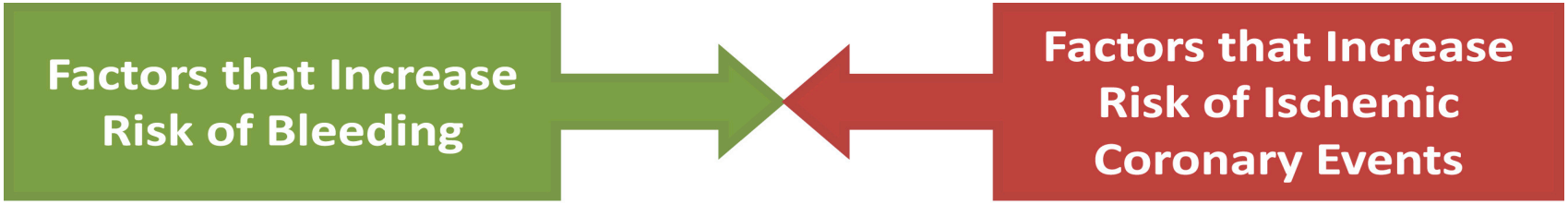
B. **Anticoagulant oral (ACO, c.-à-d. warfarine ou NACO) + AAS**

C. **ACO + inhibiteur du récepteur de l'ADP**

D. **Trithérapie: DTAP (ASA X 7 à 30J & Clopidogrel x 1an) + ACO**

ADP = adénosine diphosphate; NACO = nouvel anticoagulant oral

La balance entre le risque ischémique et le risque hémorragique en lien avec l'anticoagulation – SCC 2018



- **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%)

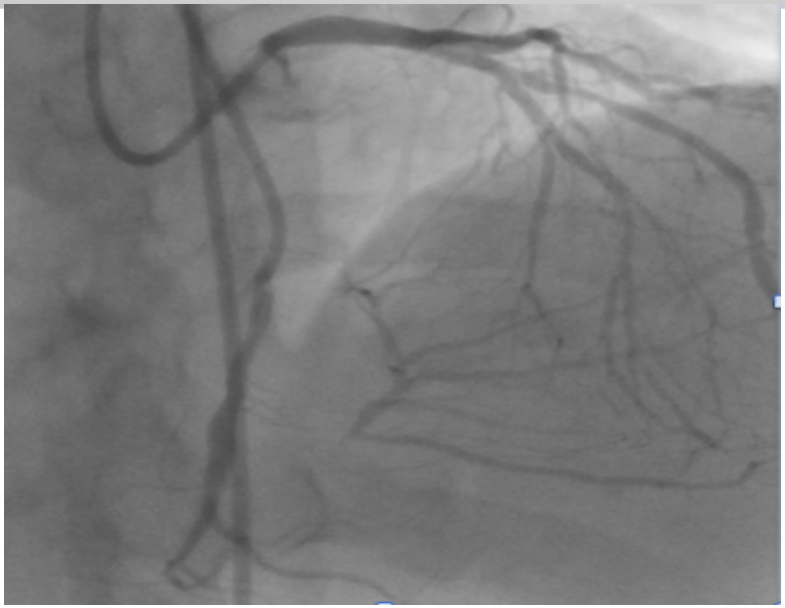
- **Patient Factors**
  - Diabetes mellitus treated with OHG or insulin
  - Current smoker
  - CKD (eGFR < 60 mL/min)
  - Prior ACS
  - Prior stent thrombosis
- **Clinical Presentation**
  - ACS (STEMI, NSTEMI, UA)
- **Angiographic factors**
  - Multi-vessel disease
  - Multiple (≥ 3) stents implanted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

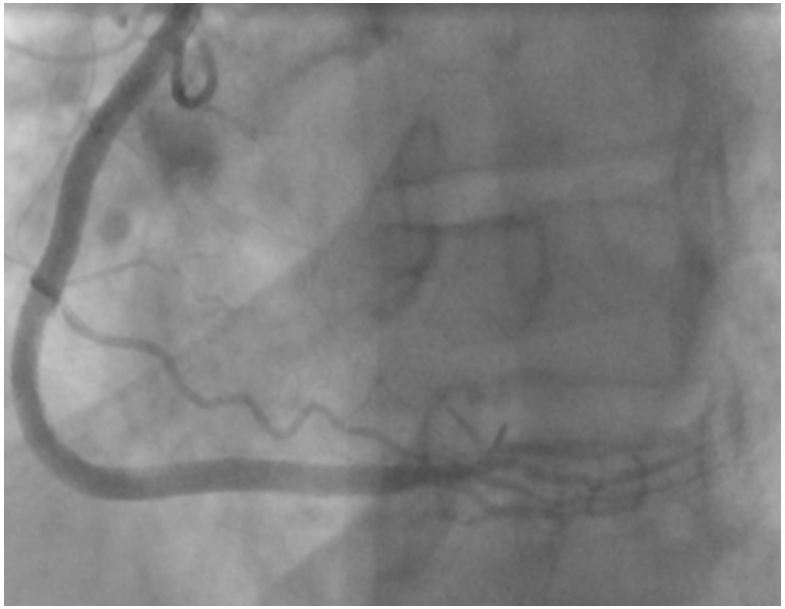
Canadian Journal of Cardiology 2018 341371-1392DOI: (10.1016/j.cjca.2018.08.026)

ET SI ROSE AVAIT UNE CTO

Rose : 78 ans

- Admise d'une façon élective pour une PCI d'une occlusion chronique de sa coronaire droite moyenne. CCS 3\4 sous triple thérapie anti-angineuse
- PCI nécessite → 3 endoprothèses à élution de médicament (EEM) de 2e génération





QUESTION

Quelle est la gestion anti-thrombotique optimale recommandée à son arrivée à l'hôpital (hemo)?

- Stop NACO 48h avant la procédure (ou plus si cl cr en bas de 30 ml/min ou Dabi)
- Stop AVK 5 jours pré-procédure. Débuter HBPM 48 h après l'arrêt de l'AVK*. Cesser HBPM le jour de la procédure.
- ASA 320 mg la veille de la procédure puis 80 mg die.
- Clopidogrel (600mg) la veille de la procédure puis 75 mg die.
- Donner héparine IV per-procédure.
- Favoriser accès radial.
- Ajouter un IPP.
- Reprendre NACO le lendemain (ou AVK avec bridge si approprié*)

*Bridge: valve mécanique, FA CHADS-VASC >5, ICT récent <3 mois, TEV <3mois (éléments cliniques à haut risque thromboembolique)

QUESTION

Quel schéma antithrombotique oral recommanderiez-vous pour Rose à sa sortie de l'hôpital?

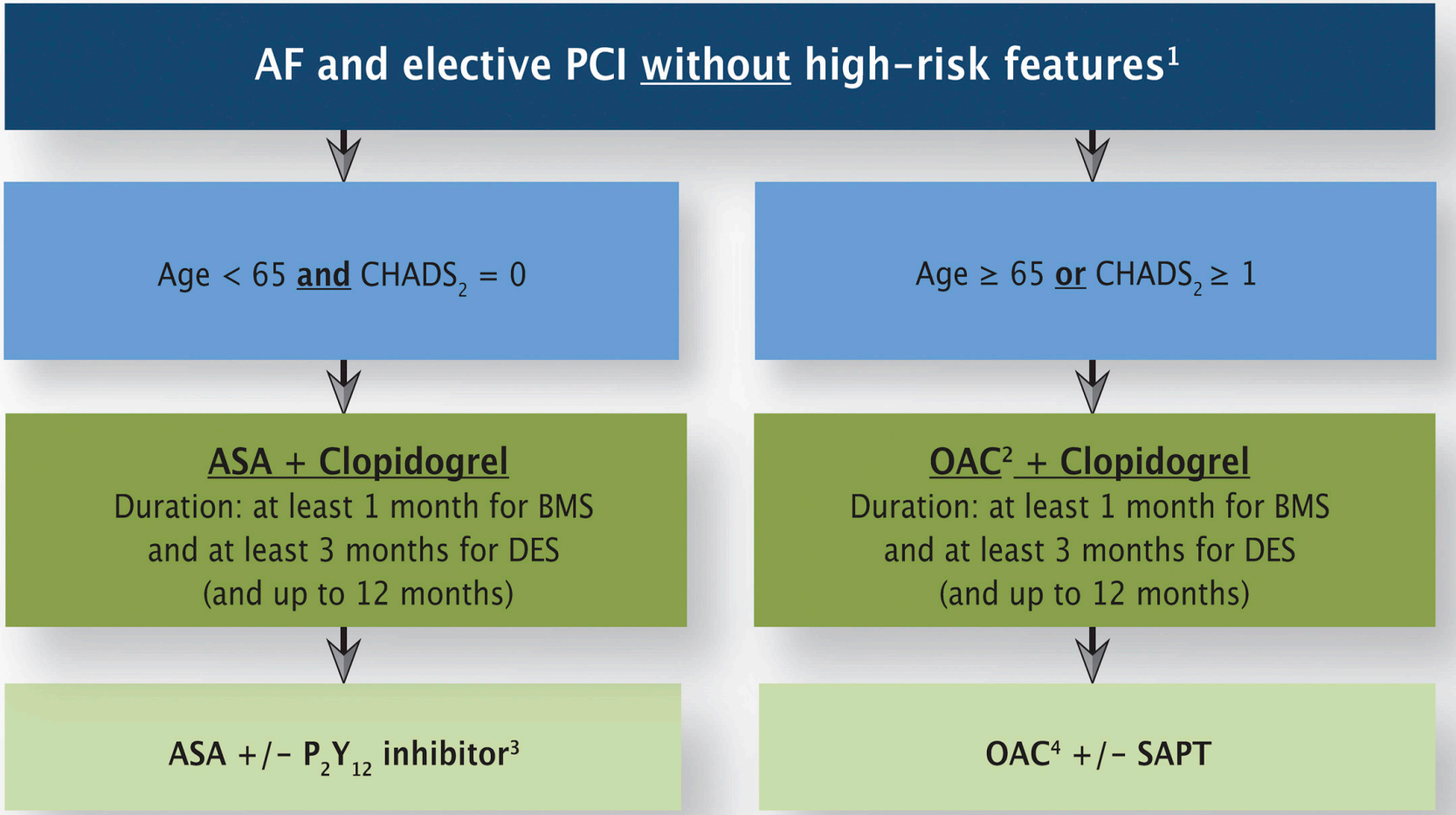
A. Double thérapie antiplaquettaire (DTAP, c.-à-d. AAS + inhibiteur du récepteur de l'ADP, p. ex., le clopidogrel)

B. Anticoagulant oral (ACO, c.-à-d. warfarine ou NACO) + AAS

C. ACO + inhibiteur du récepteur de l'AD

D. Trithérapie (DTAP + ACO)

ADP = adénosine diphosphate; NACO = nouvel anticoagulant oral



1 A PCI is considered high-risk based on clinical and angiographic features such as: diabetes mellitus, prior ACS, chronic renal dysfunction (creatinine clearance < 60 mL/min), prior stent thrombosis, current smoker, multi-vessel disease, multiple stents implanted, complex bifurcation lesion, total stent length > 60 mm, chronic total occlusion intervention or bioabsorbable vascular scaffold (BVS) implantation.

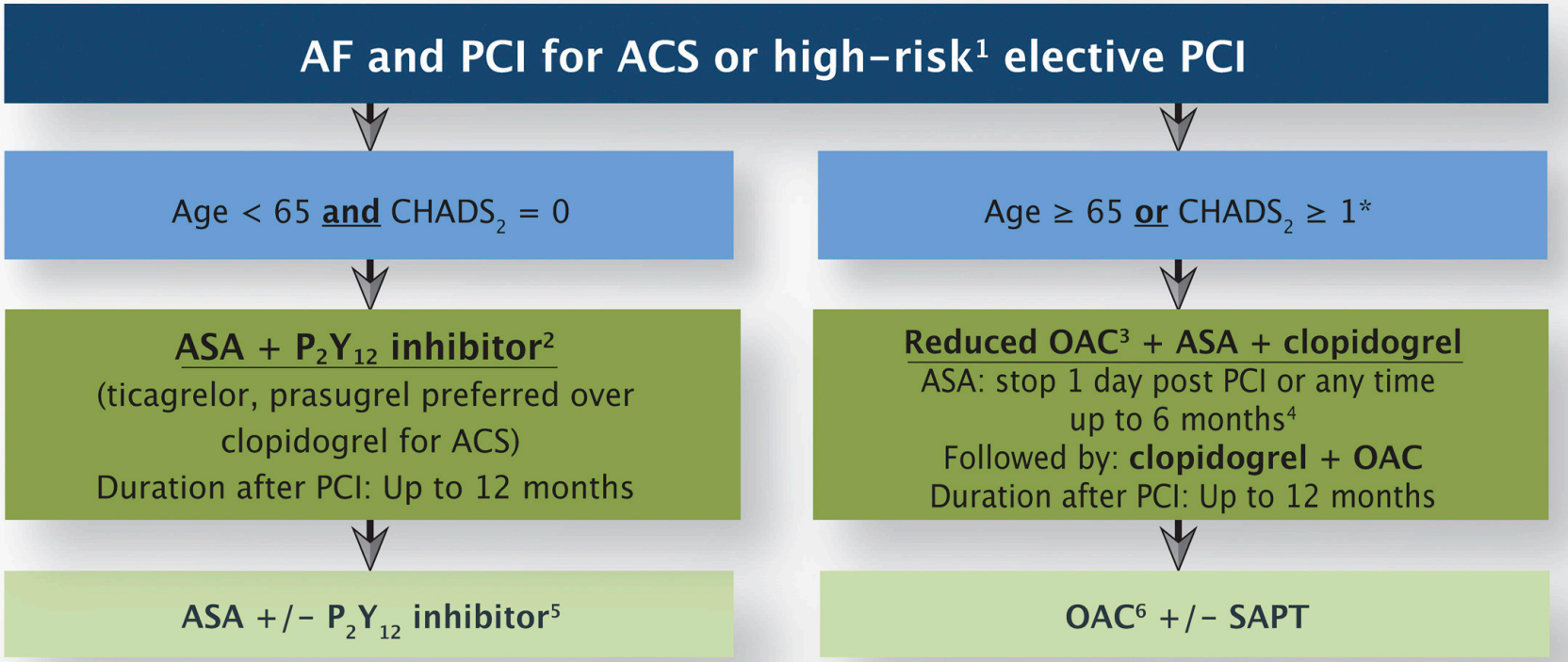
2 OAC regimens evaluated in this context include rivaroxaban 15 mg daily (10 mg in patients with renal dysfunction), dabigatran 110 mg or 150 mg BID and warfarin. If warfarin is to be used, recommended INR target is 2.0-2.5. All patients should receive a loading dose of ASA 160 mg at the time of PCI (if previously ASA naïve). Thereafter, ASA can be discontinued as early as the day following PCI.

3 Extended treatment with a P2Y12 inhibitor can be added to ASA if high-risk clinical or angiographic features of ischemic events develop and low risk of bleeding.

4 The dose of OAC beyond the initial period of antithrombotic therapy (up to a 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 develop and low risk of bleeding.

AF: atrial fibrillation; ASA: acetylsalicylic acid; BMS: bare-metal stent; DES: drug-eluting stent; OAC: oral anticoagulant; PCI: percutaneous coronary intervention; SAPT: single antiplatelet therapy

Canadian Journal of Cardiology 2018 34, 214-233



***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 P2Y12 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.

AF: atrial fibrillation; ACS: acute coronary syndrome; ASA: acetylsalicylic acid; OAC: oral anticoagulant; PCI: percutaneous coronary intervention; DAPT: dual antiplatelet therapy; SAPT: single antiplatelet therapy

Canadian Journal of Cardiology 2018 34, 214-233

QUESTION

Quel schéma antithrombotique oral recommanderiez-vous pour Rose à sa sortie de l'hôpital?

A. Double thérapie antiplaquettaire (DTAP, c.-à-d. AAS + inhibiteur du récepteur de l'ADP, p. ex., le clopidogrel)

B. Anticoagulant oral (ACO, c.-à-d. warfarine ou NACO) + AAS

C. ACO + inhibiteur du récepteur de l'AD

D. Trithérapie (DTAP + ACO)

ADP = adénosine diphosphate; NACO = nouvel anticoagulant oral

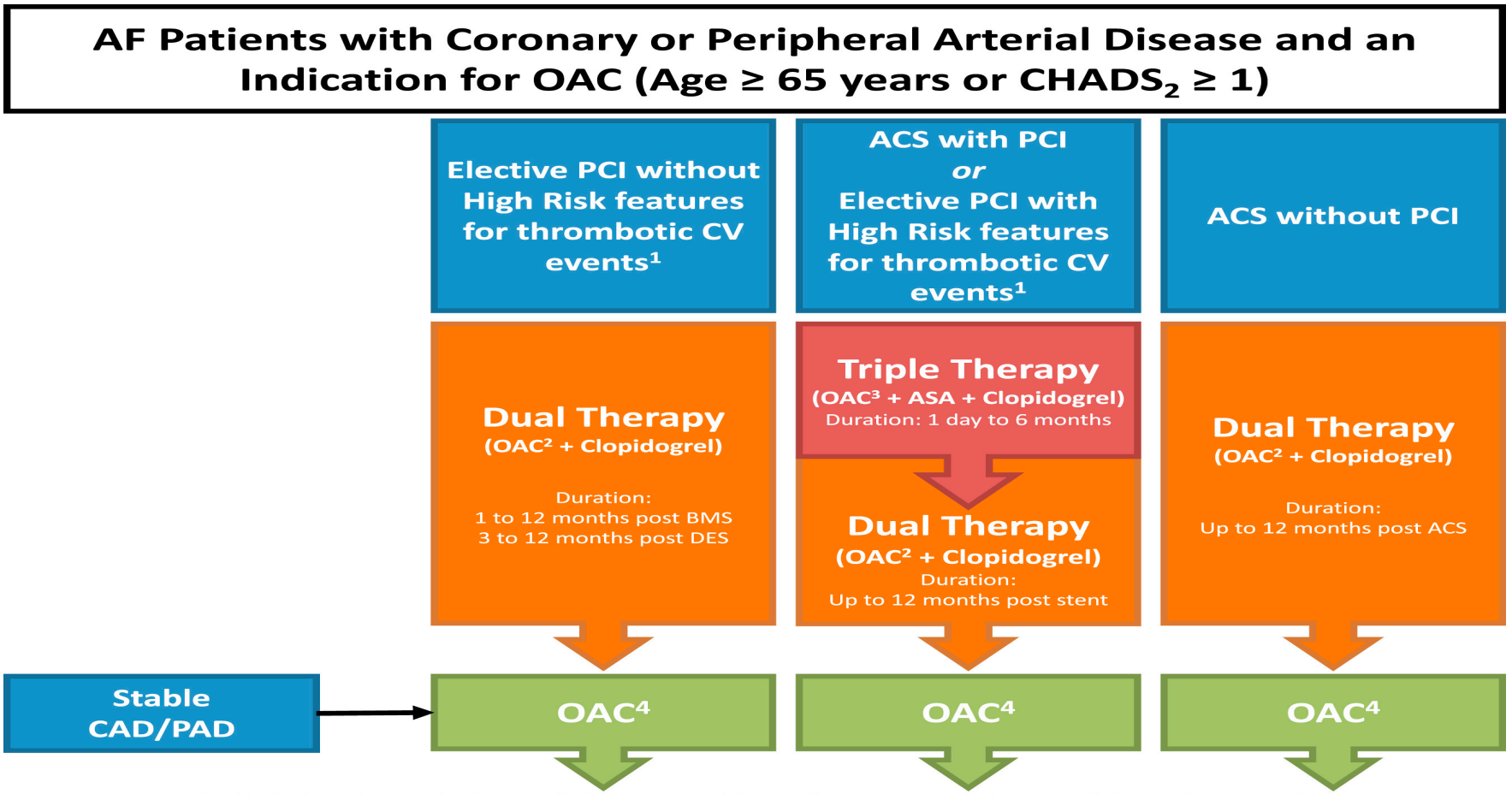
QUESTION

Quel schéma antithrombotique oral recommanderiez-vous pour Rose à sa sortie de l'hôpital?

- **ASA x 1 mois (max), Plavix x 1 an, NACO (*dose réduite**** pour la durée de la triple thérapie puis NACO peut être augmenté à la pleine dose si cliniquement approprié en plus d'un IPP.**

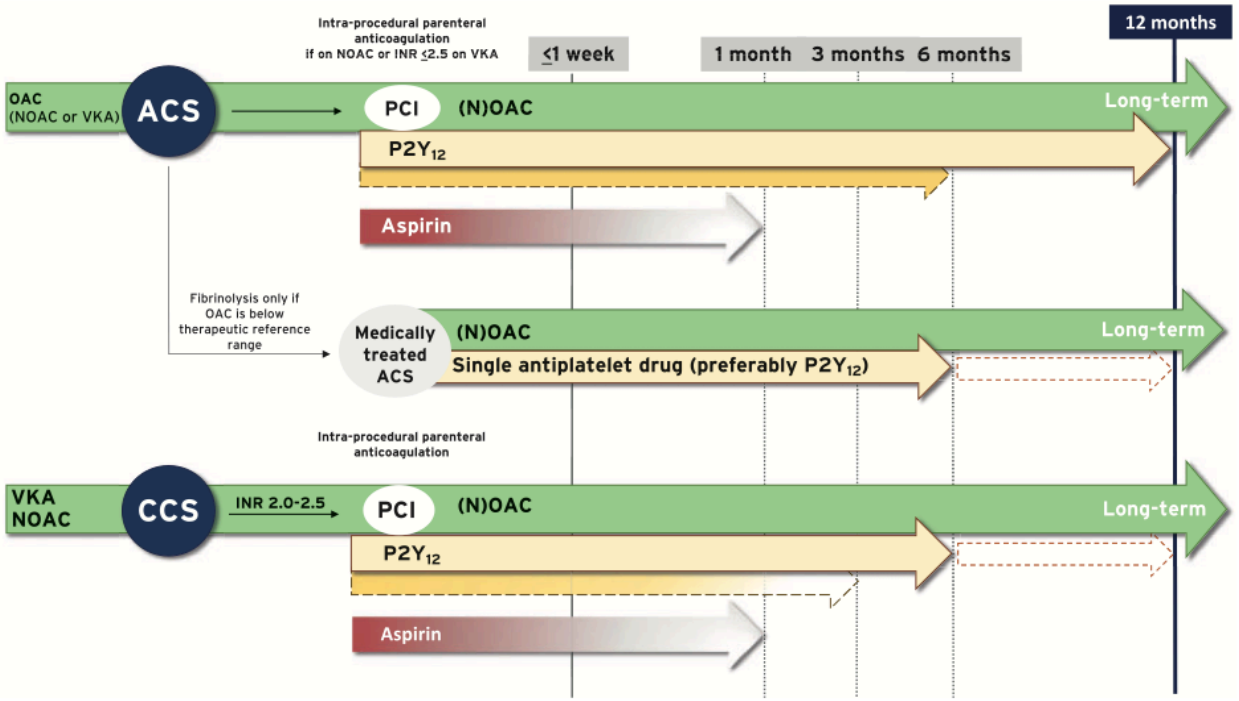
*Si risque élevé des complications hémorragiques
NACO = nouvel anticoagulant oral

Gestion du traitement antithrombotique selon les recommandations de la SCC - 2018



Canadian Journal of Cardiology 2018 34, 214-233

Mise à jour de la Société Européenne de Cardiologie: lignes directrices de la gestion de la FA (Août 2020): Cas de patients avec SCA ou SCC



THROMBOTIC RISK FACTORS

- Diabetes mellitus requiring therapy
- Prior ACS/recurrent myocardial infarction
- Multivessel CAD
- Concomitant PAD
- Premature CAD (occurring at age of <45 y) or accelerated CAD (new lesion within 2 years)
- CKD (eGFR <60 mL/min)
- Clinical presentation (ACS)
- Multivessel stenting
- Complex revascularisation (left main stenting, bifurcation lesion stenting, chronic total occlusion intervention, last patent vessel stenting)
- Prior stent thrombosis on antiplatelet treatment
- Procedural factors (stent expansion, residual dissection, stent length, etc.)

BLEEDING RISK FACTORS

- Hypertension
- Abnormal renal or liver function
- Stroke or ICH history
- Bleeding history or bleeding diathesis (e.g., anaemia with haemoglobin <110 g/L)
- Labile INR (if on VKA)
- Elderly (>65 years)
- Drugs (concomitant OAC and antiplatelet therapy, NSAIDs), excessive alcohol consumption

STRATEGIES TO REDUCE BLEEDING ASSOCIATED WITH PCI

- Radial artery access
- PPIs in patients taking DAPT who are at increased risk of bleeding (e.g., the elderly, dyspepsia, gastro-oesophageal reflux disease, Helicobacter pylori infection, chronic alcohol use)
- Non–administration of unfractionated heparin in patients on VKA with INR >2.5
- Pre-treatment with aspirin only, add a $P2Y_{12}$ inhibitor when coronary anatomy is known or if STEMI
- GP IIb/IIIa inhibitors only for bailout or periprocedural complications
- Shorter duration of combined antithrombotic therapy

Eur Heart J. 2020 Aug 29;ehaa612. doi: 10.1093/eurheartj/ehaa612. Online ahead of print.

Mise à jour de la Société Européenne de Cardiologie: lignes directrices de la gestion de la FA (Août 2020)

Recommendations for patients with AF and an ACS, PCI, or CCS[1068]

General recommendations for patients with AF and an indication for concomitant antiplatelet therapy	Class[a]	Level[b]
In AF patients eligible for NOACs, it is recommended to use a NOAC[c] in preference to a VKA in combination with antiplatelet therapy.[1079,1081]	I	A
In patients at high bleeding risk (HAS-BLED ≥3), rivaroxaban 15 mg o.d. should be considered in preference to rivaroxaban 20 mg o.d. for the duration of concomitant single or DAPT, to mitigate bleeding risk.[1080]	IIa	B
In patients at high bleeding risk (HAS-BLED ≥3), dabigatran 110 mg b.i.d. should be considered in preference to dabigatran 150 mg b.i.d. for the duration of concomitant single or DAPT, to mitigate bleeding risk.[1079]	IIa	B
In AF patients with an indication for a VKA in combination with antiplatelet therapy, the VKA dosing should be carefully regulated with a target INR of 2.0 - 2.5 and TTR>70%.[1094,1095,1104,1105]	IIa	B
Recommendations for AF patients with ACS		
In AF patients with ACS undergoing an uncomplicated PCI, early cessation (≤1 week) of aspirin and continuation of dual therapy with an OAC and a $P2Y_{12}$ inhibitor (preferably clopidogrel) for up to 12 months is recommended if the risk of stent thrombosis[d] is low or if concerns about bleeding risk[e] prevail over concerns about risk of stent thrombosis,[d] irrespective of the type of stent used.[1090,1092–1095]	I	B
Triple therapy with aspirin, clopidogrel, and an OAC[f] for longer than 1 week after an ACS should be considered when risk of stent thrombosis[d] outweighs the bleeding risk,[e] with the total duration (≤1 month) decided according to assessment of these risks, and the treatment plan should be clearly specified at hospital discharge.	IIa	C
Recommendations in AF patients with a CCS undergoing PCI		
After uncomplicated PCI, early cessation (≤1 week) of aspirin and continuation of dual therapy with OAC for up to 6 months and clopidogrel is recommended if the risk of stent thrombosis[d] is low or if concerns about bleeding risk[e] prevail over concerns about risk of stent thrombosis,[d] irrespective of the type of stent used.[1076,1078–1081]	I	B
Triple therapy with aspirin, clopidogrel, and an OAC[f] for longer than 1 week should be considered when risk of stent thrombosis[d] outweighs the bleeding risk,[e] with the total duration (≤1 month) decided according to assessment of these risks, and the treatment plan should be clearly specified at hospital discharge.	IIa	C

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Conclusion (1)

- Chez les patients atteints de FA, les NACOs ont fait leurs preuves d'efficacité et de sécurité.
- Les ÉRC sont là pour nous guider sur la prise en charge des patients en FA et MCAS (stable, post ACS ou post PCI).
- Attention pour la comparaison entre les agents: les études sont différentes dans leurs critères d'inclusion/exclusion, design, taille d'échantillon, durée de suivi..

Conclusion (2)

- Double thérapie réduit les saignements et n'augmente pas les complications ischémiques
- ASA à cesser dans les plus brefs délais post PCI (selon risque complications coronariennes ischémiques/ thrombotiques)
- La gestion de l'anticoagulation péri-procédurale doit se faire selon une démarche algorithmique claire tenant compte des risques thrombotique et hémorragique du patient.