Cas clinique FA et SCA

Dr Belhameche

GHEF

CNCH 2018

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

74 ans

FR : HTA .

Dyslipidémie.

Tabagisme sevré.

ATCD: - Carcinome epidermoide en 1999(Uvuloplastie et amygdalectomie) RX et CH.

- Thyroïdectomie partielle en 2001 pour nodule toxique.

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

- PM pour MRA en 2004 .
- Néoplasie du colon en 2007 (hemicolectomie gauche et chimiothérapie) .
- Cardiopathie ischémique avec un IDM latéral sur une occlusion de la CX proximale pris en charge par ATL primaire.

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Bilan

- Facteurs de risque maitrisés.
- PM réglé en mode VVIR du fait de la permanence de la FA.
- FEVG 45% (séquelle latérale a type d'hypokinésie).

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.
2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Traitement

- Previscan (INR stable entre 2 et 3).
- Detensiel 10 mg.
- Ramipril 5 mg.
- Aldactazine 25mg.
- Crestor 5mg.

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.
2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Histoire

- Consulte pour dyspnée et oppression thoracique.
- Examen clinique quelques râles sibilants aux bases.
- ECG non contributif car EE.
- Troponine 150 µg/l .

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.
2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Coronarographie

Resténose sub-occlusive de la CX proximale ATL plus stent actif

Dose de charge aspirine(500mg) et plavix (300mg).

Traitement de sortie

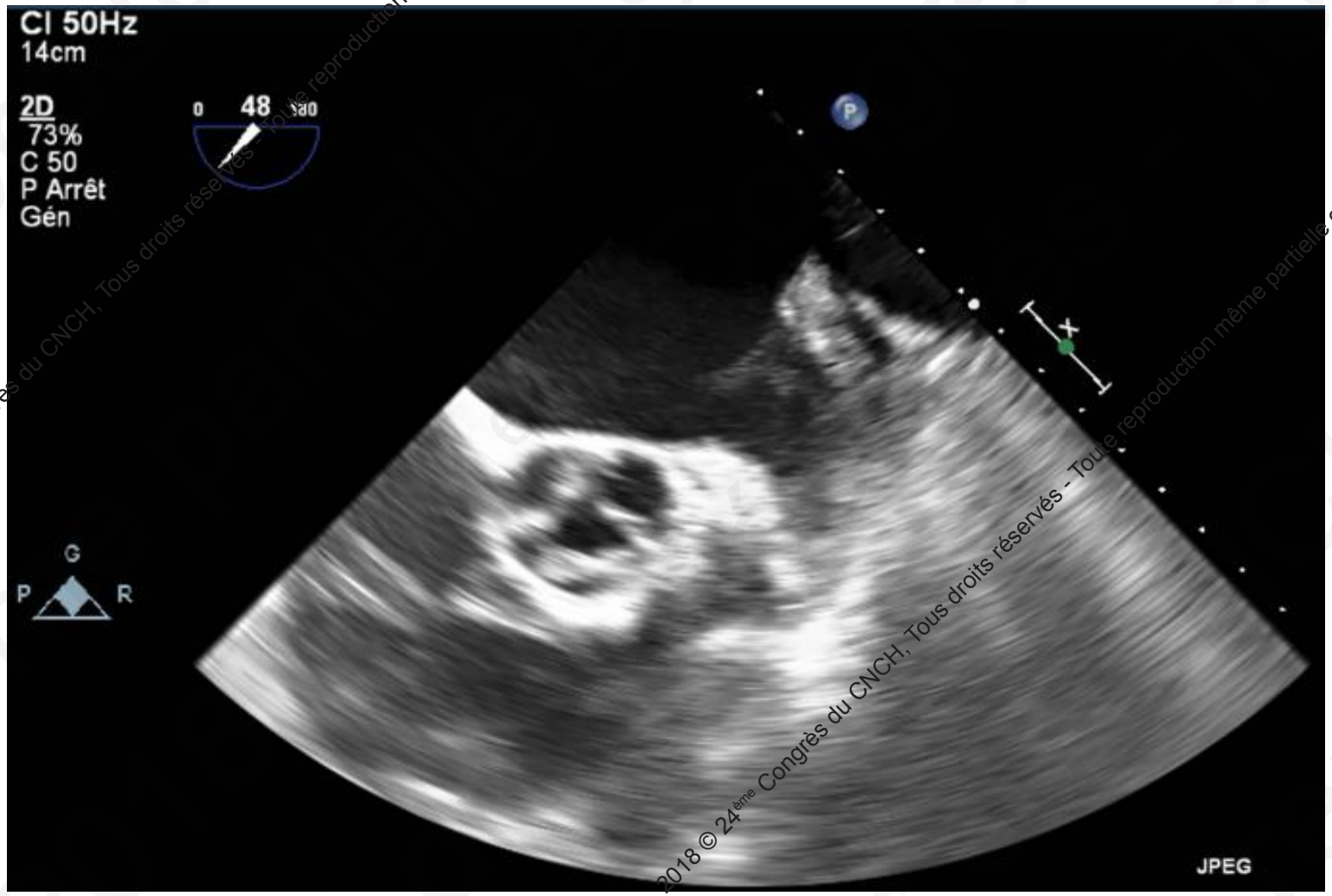
- Previscan.
- Aspegique 100mg.
- Plavix 75 mg.
- Detensiel 10mg.
- Ramipril 5mg
- Crestor 5mg.
- Aldactazine 25mg.

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Evolution

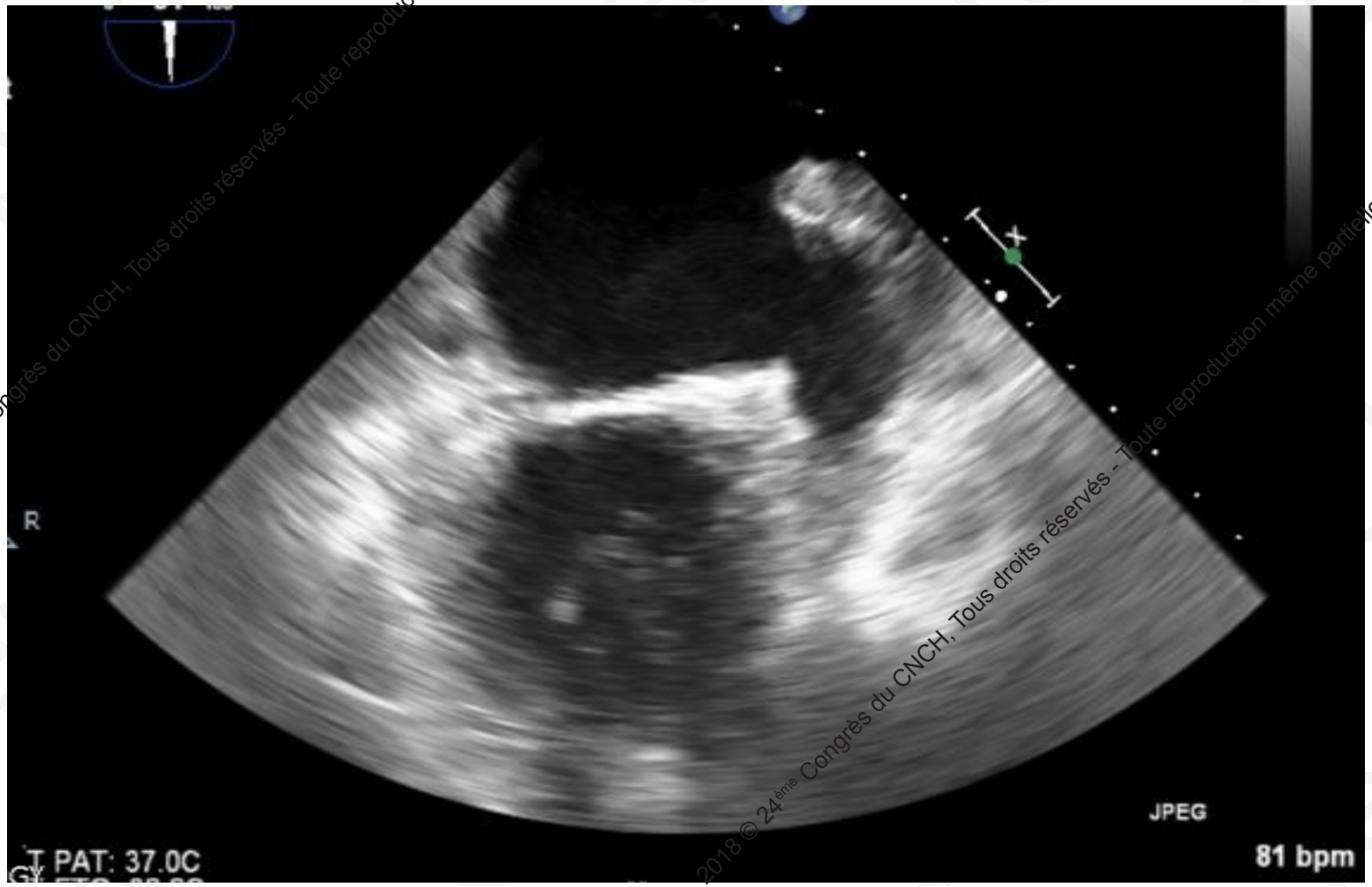
- 1 mois hémorragie digestive sévère ayant nécessité une transfusion (Polype tubuleux dysplasique).
- Arrêt triple thérapie et mis sous bithérapie AVK Aspégic , persistance du saignement.
- Arrêt de la bithérapie pendant 1mois mis sous AVK seul mais les INR sont labiles.
- Consulte pour hémiparésie mains droite et aphasie transitoire (Scanner en faveur d'un AVC minime et ETO thrombus intra auriculaire.

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.
2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.



- Mise sous Xarelto 15mg et Plavix 75 mg.
- A nouveau hémorragie digestive.
- Arrêt du Xarelto et Aspegic et remise sous AVK seul.
- INR labiles et à 3 mois persistance du thrombus intra auriculaire.

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

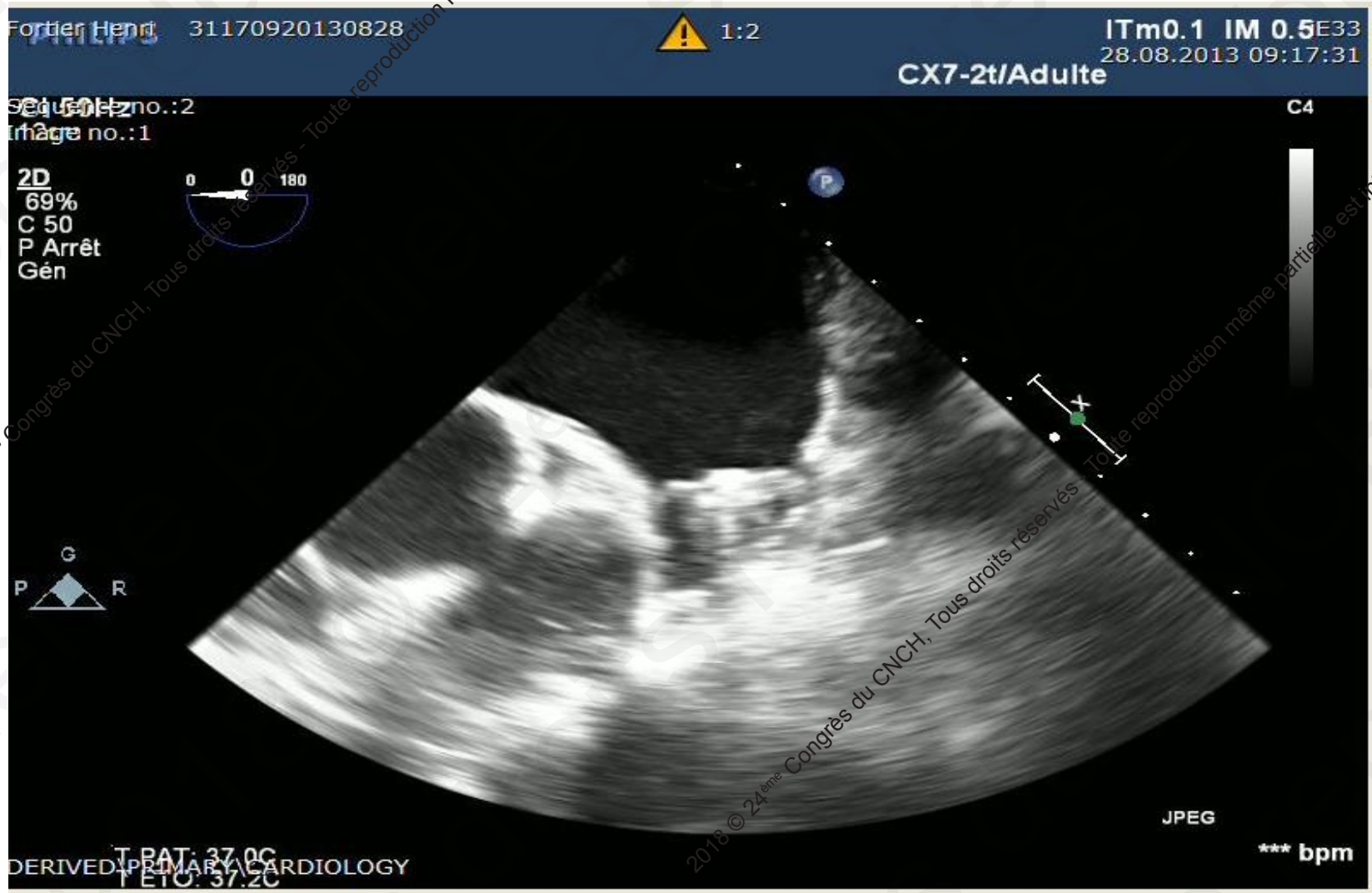


2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Quel traitement ?

- AOD
- Poursuite AVK.
- Bithérapie: antiagrégant (A-P ou autre).
- Bithérapie AVK- AA.
- Bithérapie AOD- AA.
- Fermeture Auricule?? (Thrombus intra auriculaire)

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.



Quelles sont les données des études

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Etudes FA/ SCA

- Problème récurent en cardiologie +++
- Entre 20 et 45% de patients en FA sont coronariens selon les séries
- Entre 25 et 40% des patients sous AOD et aspirine ou AAP
- 5 à 8 % des patients bénéficiant d'une ATL sont en FA
- Facteurs de risques communs et pathologies parfois intriqués

The AFFIRM Investigators. *Am Heart J* 2002;143:991–1001; 2. Capodanno D *et al*, *Circ Cardiovasc Interv* 2014;7:113–124; Kralev S *et al*, *PLoS One* 2011;6:e24964; 4. Bahit MC *et al*, *Int J Cardiol* 2013;170:215–220

AF, atrial fibrillation; ASA, acetylsalicylic acid; NOAC, non-vitamin K antagonist oral anticoagulant; NVAF, non-valvular atrial fibrillation; PCI, percutaneous coronary intervention; VKA, vitamin K antagonist

Lip et al. Thromb Haemost 2010;103:13-28;

Lip et al. Eur Heart J 2014;35:3155-79;

Goto et al. Am J Cardiol 2014;114:70-8

Certitudes

- Prévention thromboembolique repose sur les <u>ANTICOAGULANTS</u>
- AAP efficacité moindre
- Risque hémorragique comparable

Etude BAFTA :

anticoagulant (AVK) vs aspirine chez le sujet > 75 ans:

- Etude randomisée, > 480 patients /bras
- **SUPERIORITE des AC** en prévention des AVC ischémiques
- Risque hémorragique **COMPARABLE**

	aspirine	AVK	
AVC i + embolies	**48**	**24**	**p=0.003**
Hémorragies	**25**	**25**	

BAFTA Study Lancet 2007; 370-493-503

Introduction

Etude active W (2006)

Randomisée, 6600 patients

ASA + clopidogrel vs AVK

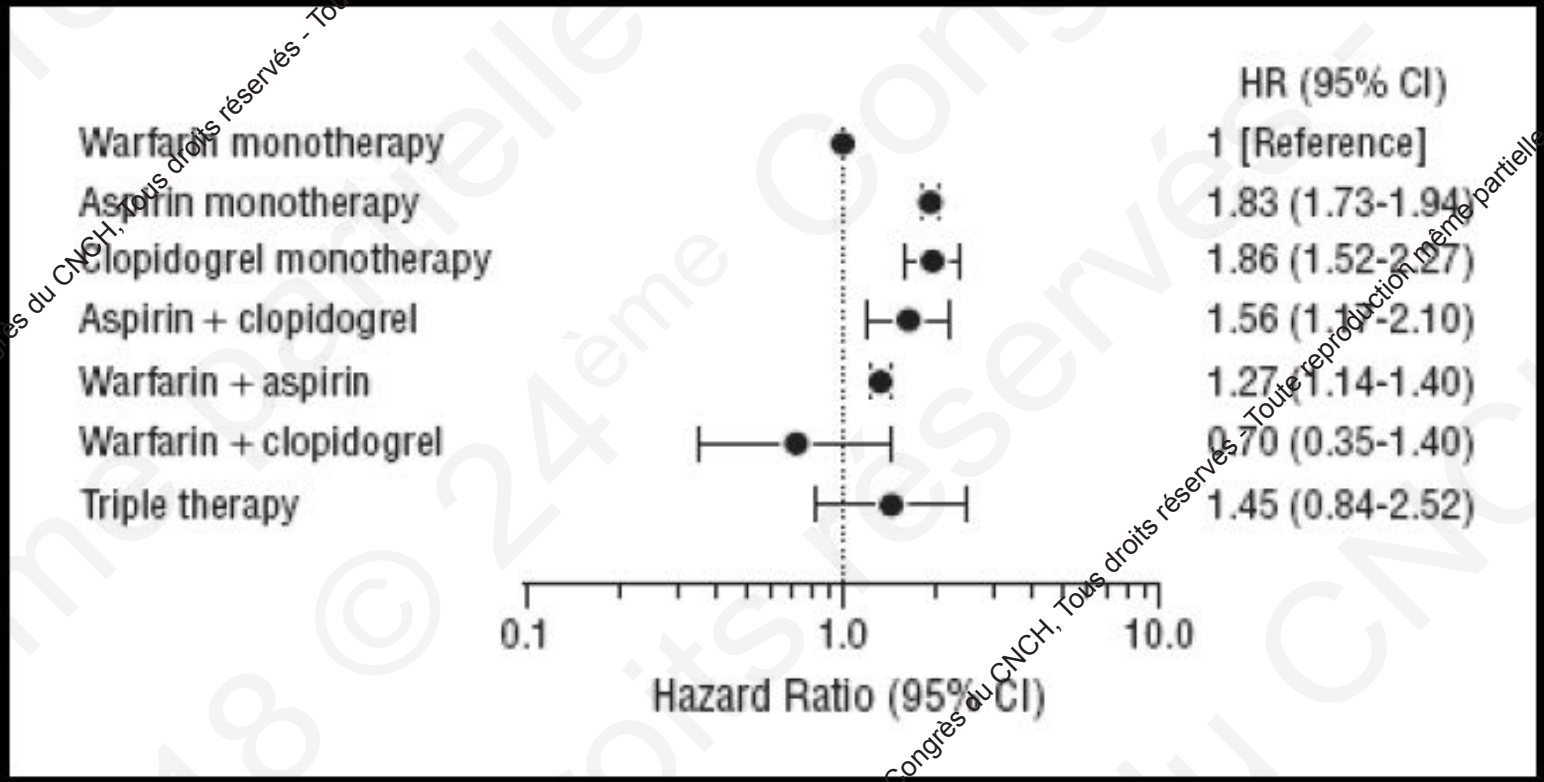
Supériorité des AVK

Critère	Clopidogrel +ASA	Warfarine	RR	p
AVC	5,64	3,63	1,45	0,0002
Saignements	2,4	2,2	1,06	0,67

Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial.
ACTIVE Writing Group of the ACTIVE Investigators., Connolly S, Pogue J, Hart R, Pfeffer M, Hohnloser S, Chrolavicius S, Pfeffer M, Hohnloser S, Yusuf S.
Lancet. 2006 Jun 10;367(9526):1903-12.

Ischaemic stroke associated with warfarin, aspirin and clopidogrel in patients with AF

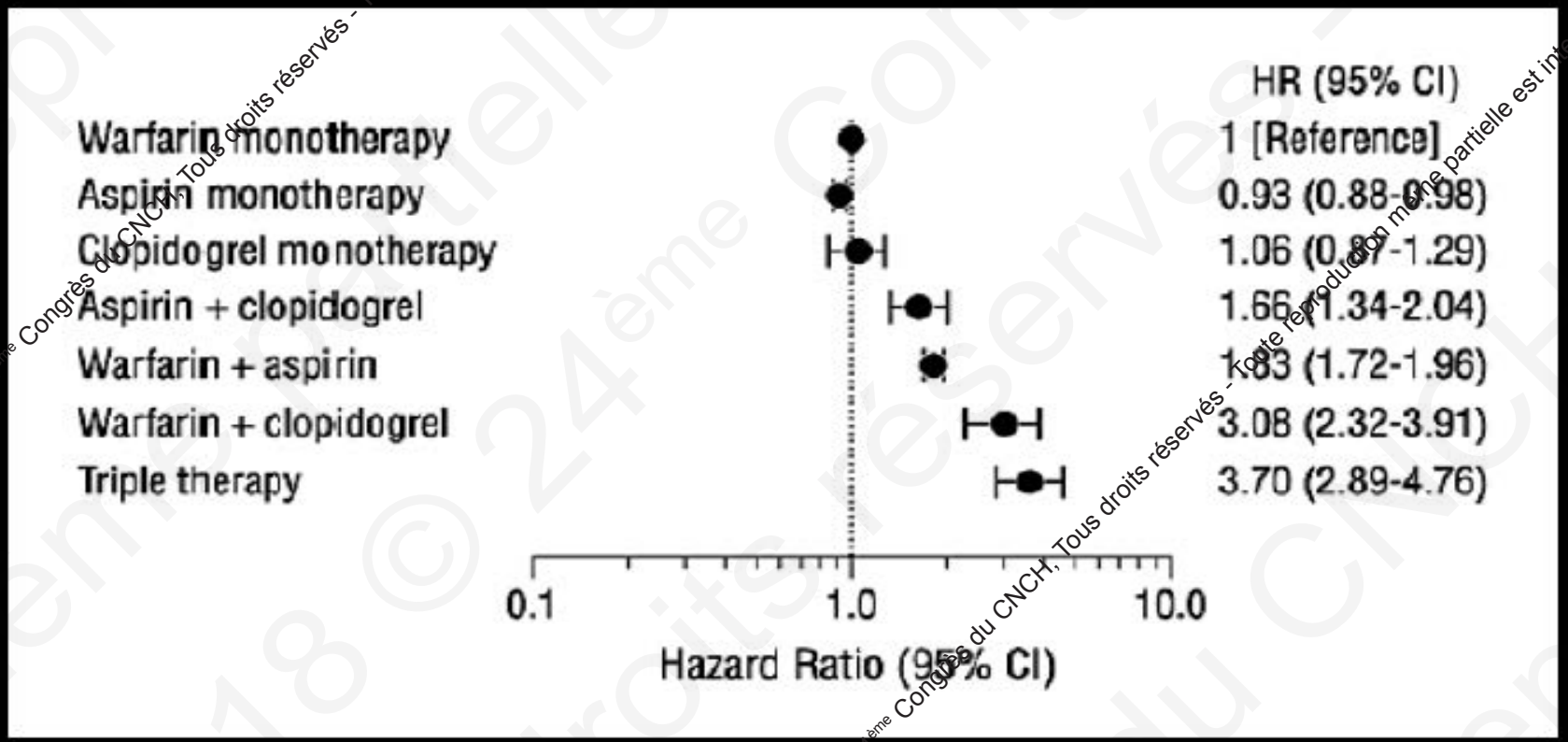
n = 82854



Hansen et al. Arch Int Med 2010; 170: 1433-1441

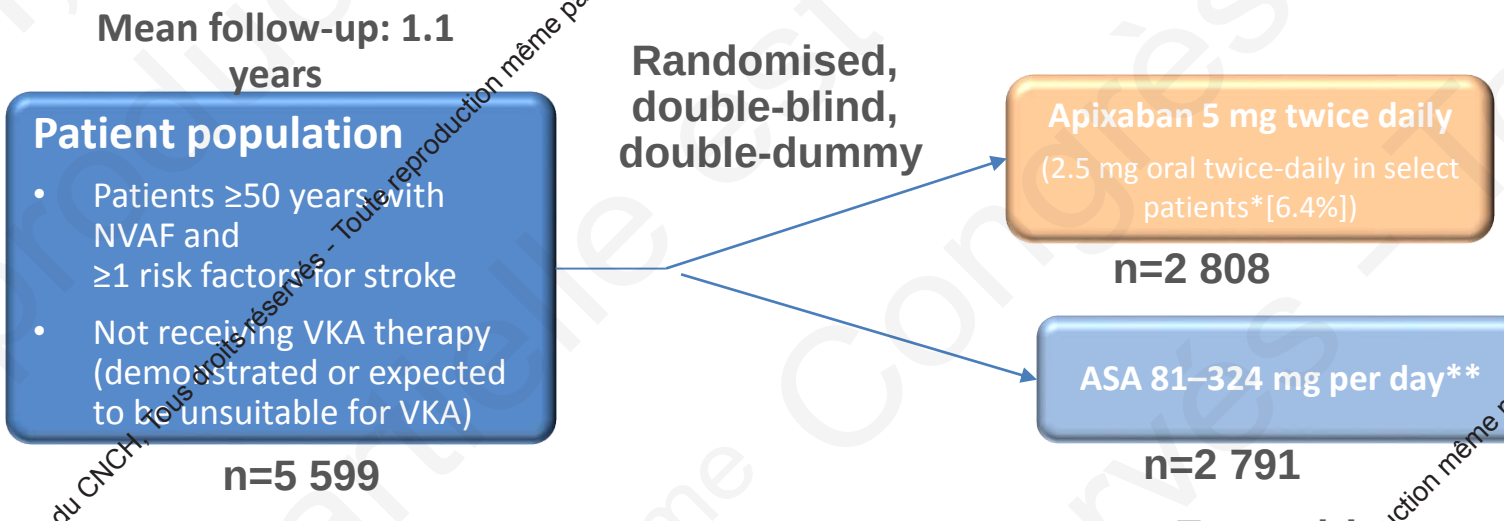
Bleeding associated with warfarin, aspirin and clopidogrel in patients with AF

n = 82854



Hansen et al. Arch Int Med 2010; 170: 1433-1441

AVERROES: Study design[1,2]



The primary objective of the trial was to determine if apixaban was superior to ASA for the prevention of the composite outcome of stroke or systemic embolism

- Primary efficacy outcome: stroke or systemic embolism
- Primary safety outcome: major bleeding

*Patients with ≥2 of the following: age ≥80 years, weight ≤60 kg, serum creatinine ≥1.5 mg/dL (133 µmol/L)

**The selection of an ASA dose of 81, 162, 243, or 324 mg was at the discretion of the investigator with 91% of subjects receiving either an 81 mg (64%) or 162 mg (27%) dose at randomisation.

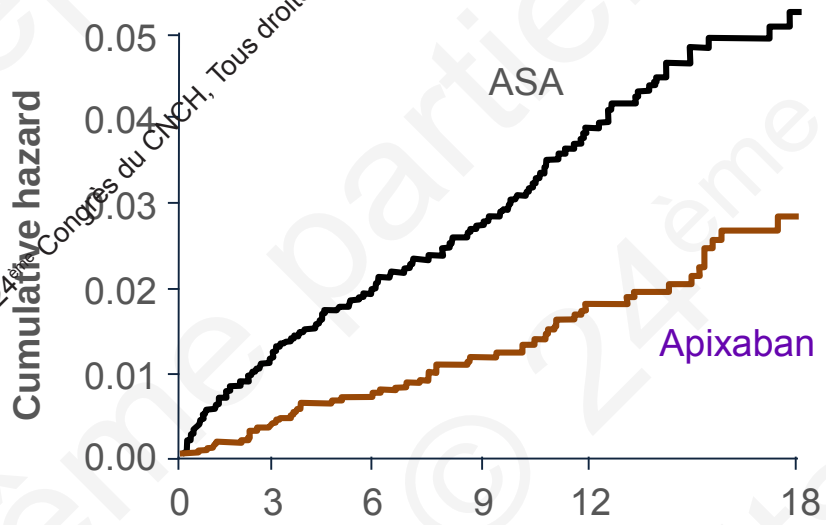
ASA, acetylsalicylic acid

1. Apixaban SmPC 2014
2. Connolly *et al. N Engl J Med* 2011;364:806-17

AVERROES: Apixaban reduces stroke or systemic embolism without increased major bleeding vs. ASA

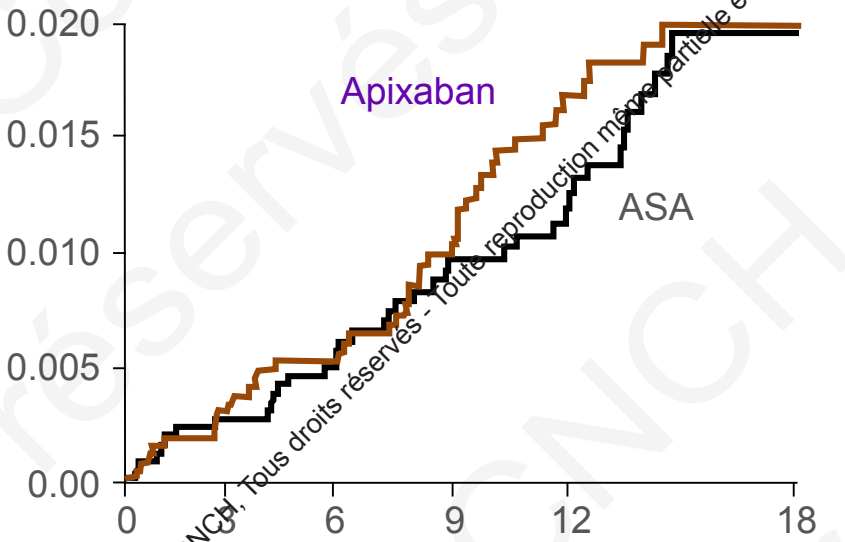
Stroke or systemic embolism (primary efficacy outcome)

HR with apixaban: 0.45
(95% CI: 0.32–0.62)
P<0.001 for superiority



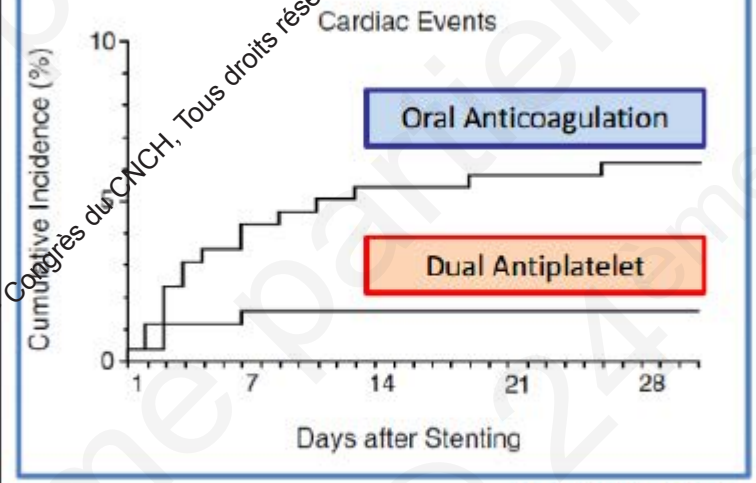
Major bleeding (primary safety outcome)

HR with apixaban: 1.13
(95% CI: 0.74–1.75)
P=0.57



Connolly *et al. N Engl J Med* 2011;364:806-17

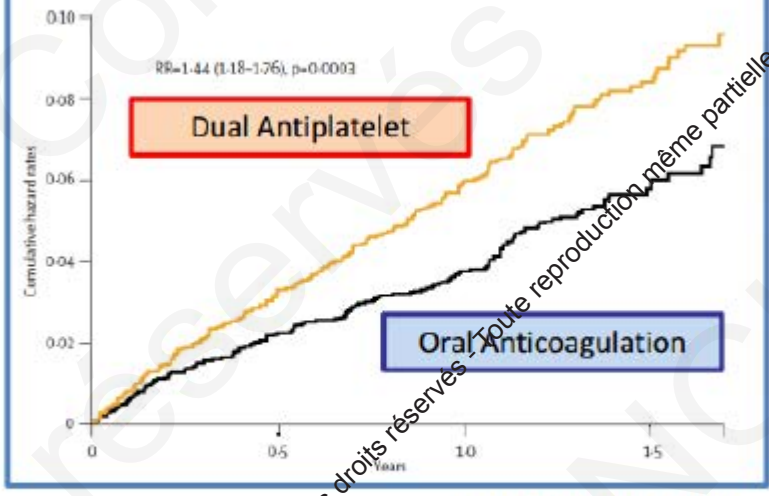
Coronary stent implantation



ISAR, NEJM 1996

+

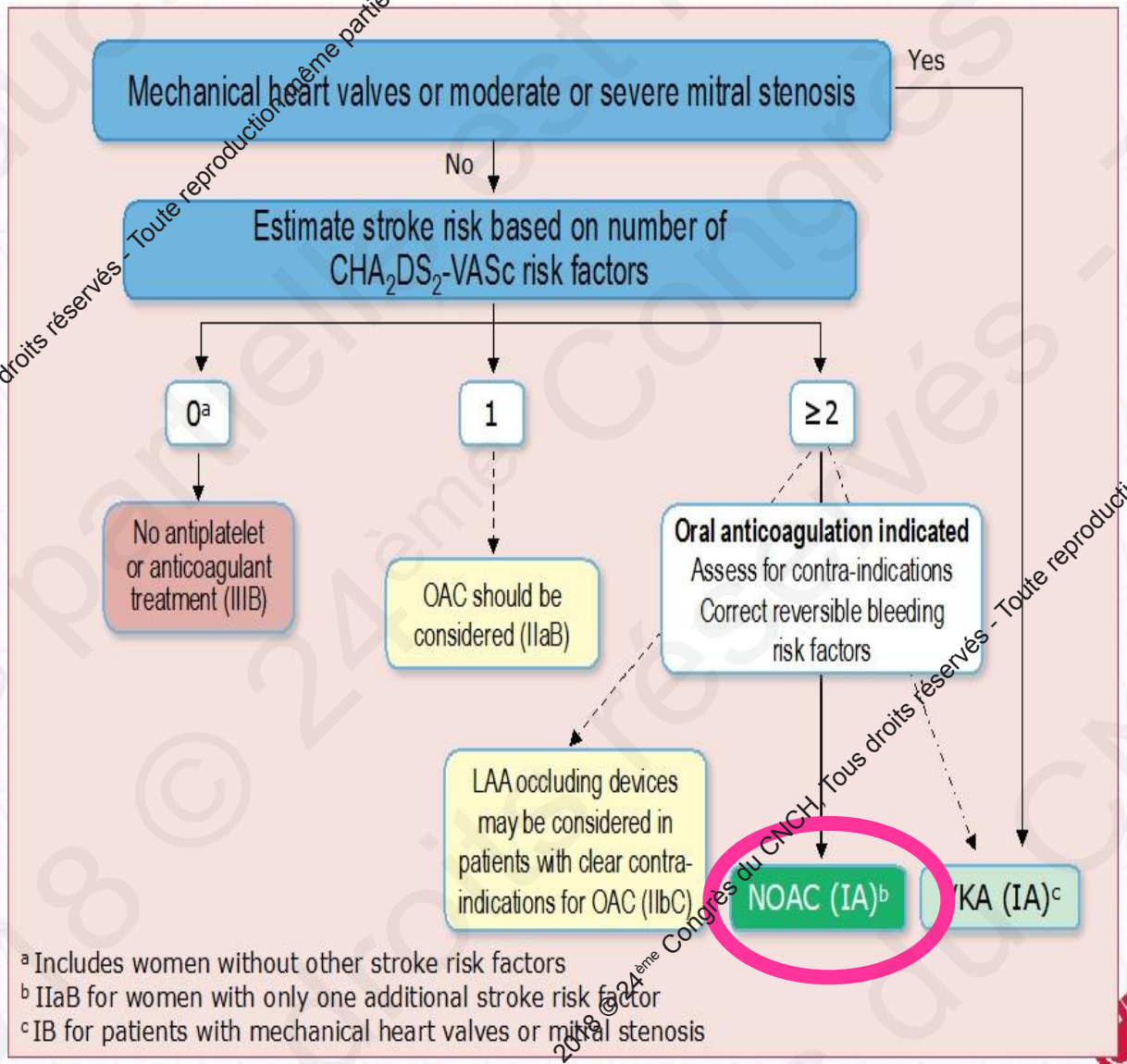
Atrial fibrillation



ACTIVE-W Lancet 2006

= Dual Antiplatelet + Oral Anticoagulation

AOD recommandés en 1ère intention



www.escardio.org/guidelines
European Heart Journal - doi:10.1093/eurheartj/ehw210
EUROPEAN SOCIETY OF CARDIOLOGY®

Quelles sont les questions posées en cas de SCA

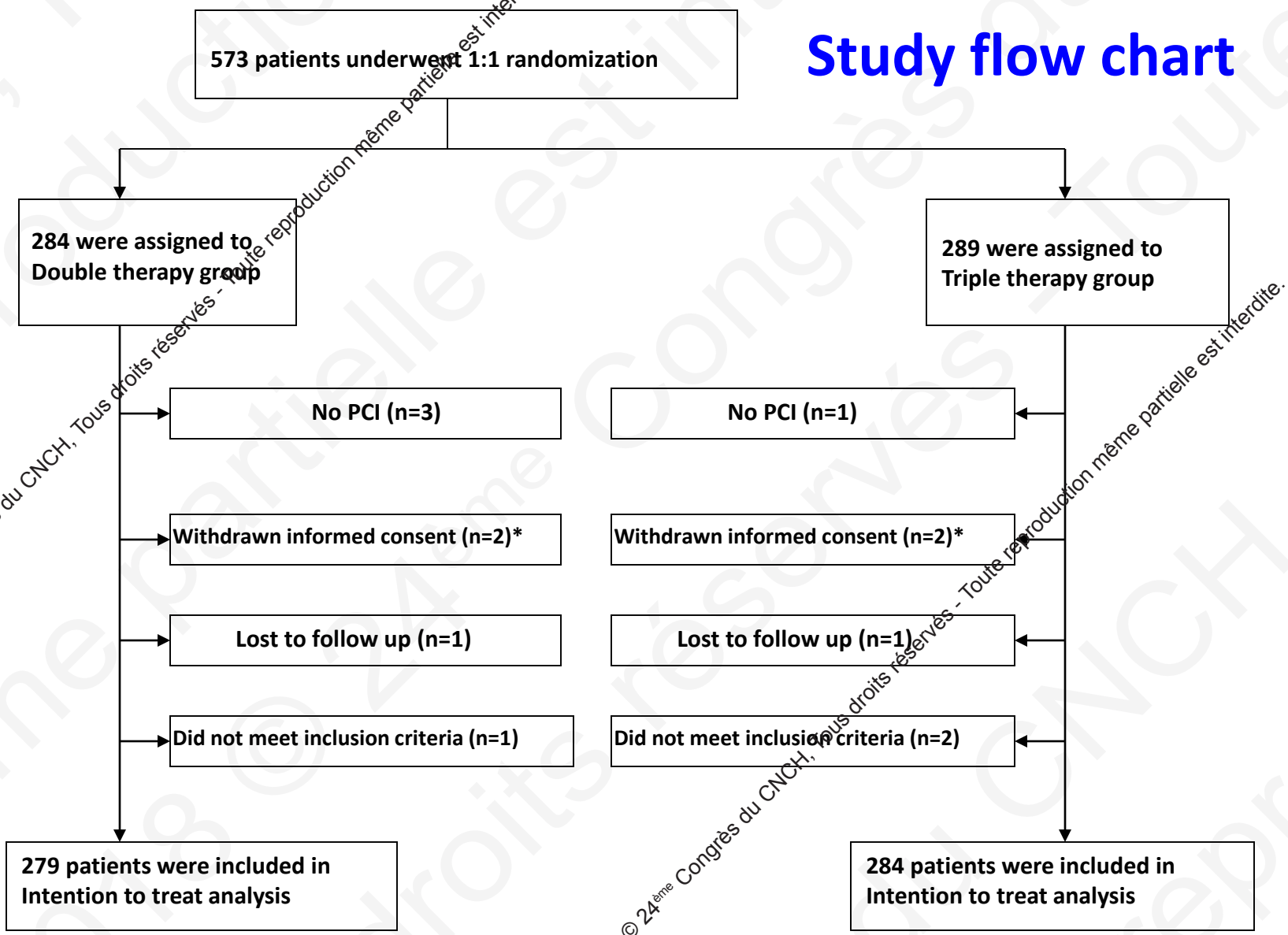
- Quel ACO et quel AA?
- Quelles l'association a utilisée?
- Quelles est la durée de cette association?

  - En fonction du tableau clinique.
  - En fonction du risque hémorragique.
  - En fonction du type de Stent

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

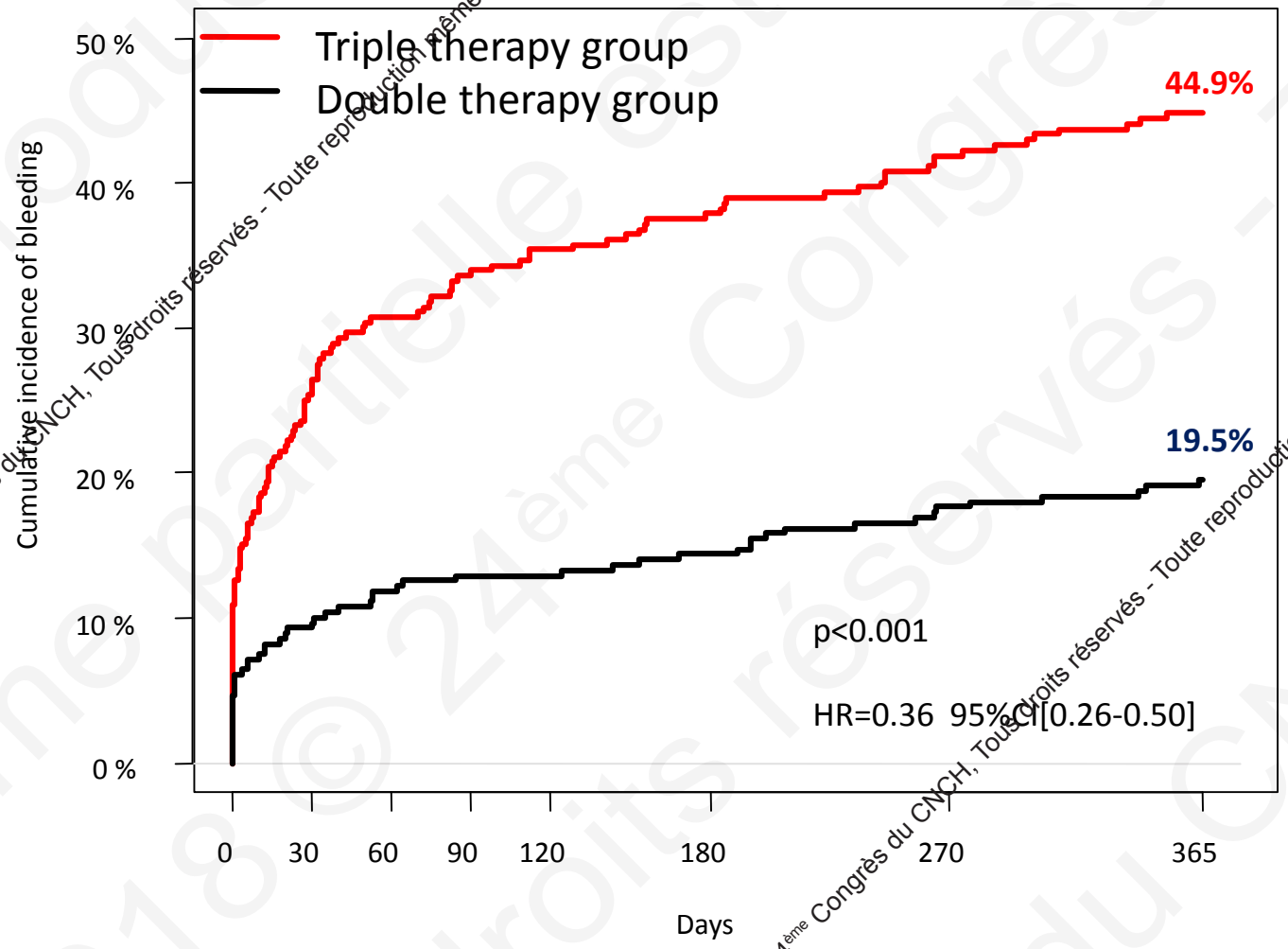
WOEST

Study flow chart



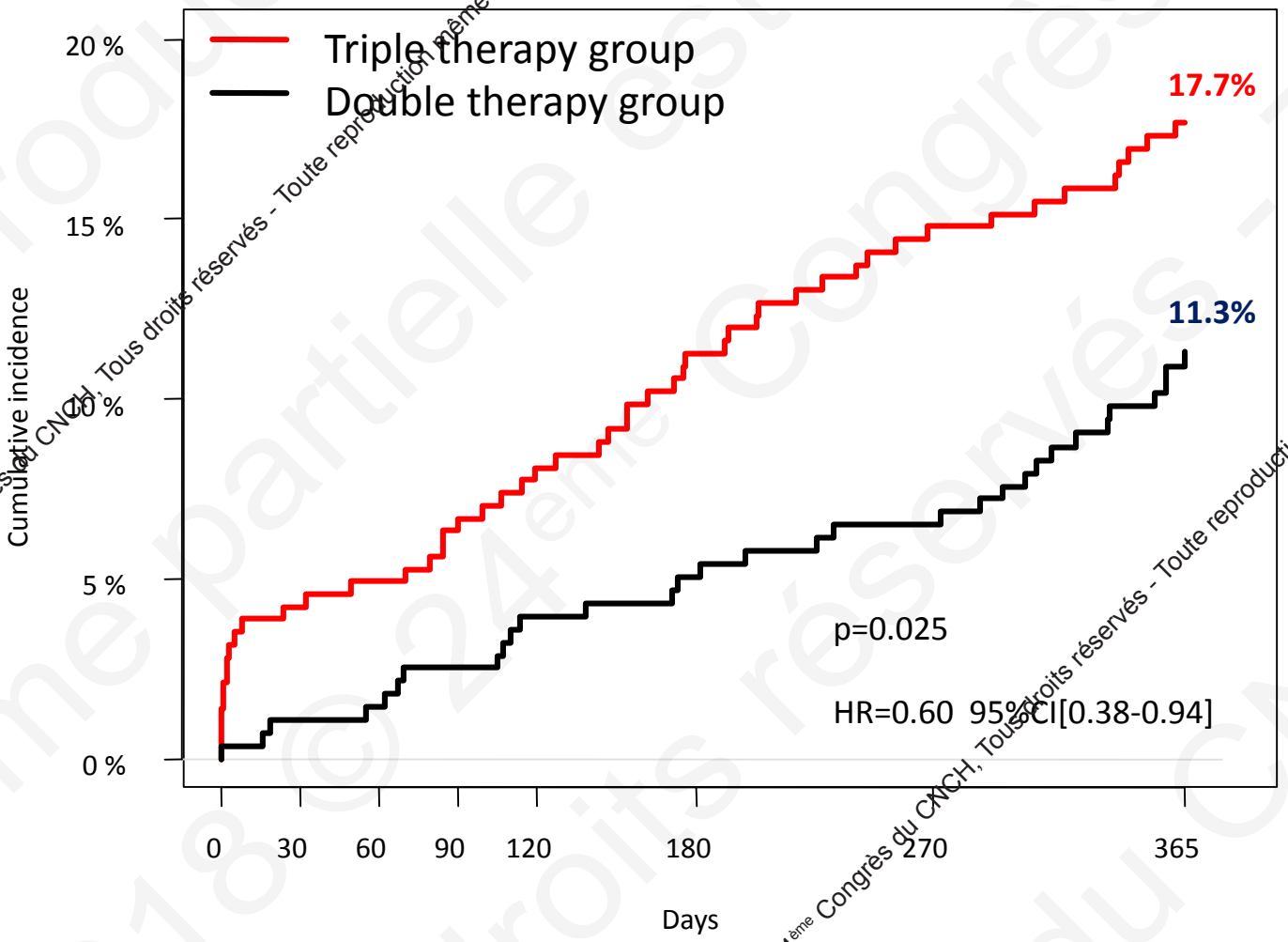
* withdrawn informed consent; in double group 2 patients and triple group 1 patient were included in intention to treat analysis until the day of withdrawal

Primary Endpoint: Total number of TIMI bleeding events



WOEST

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



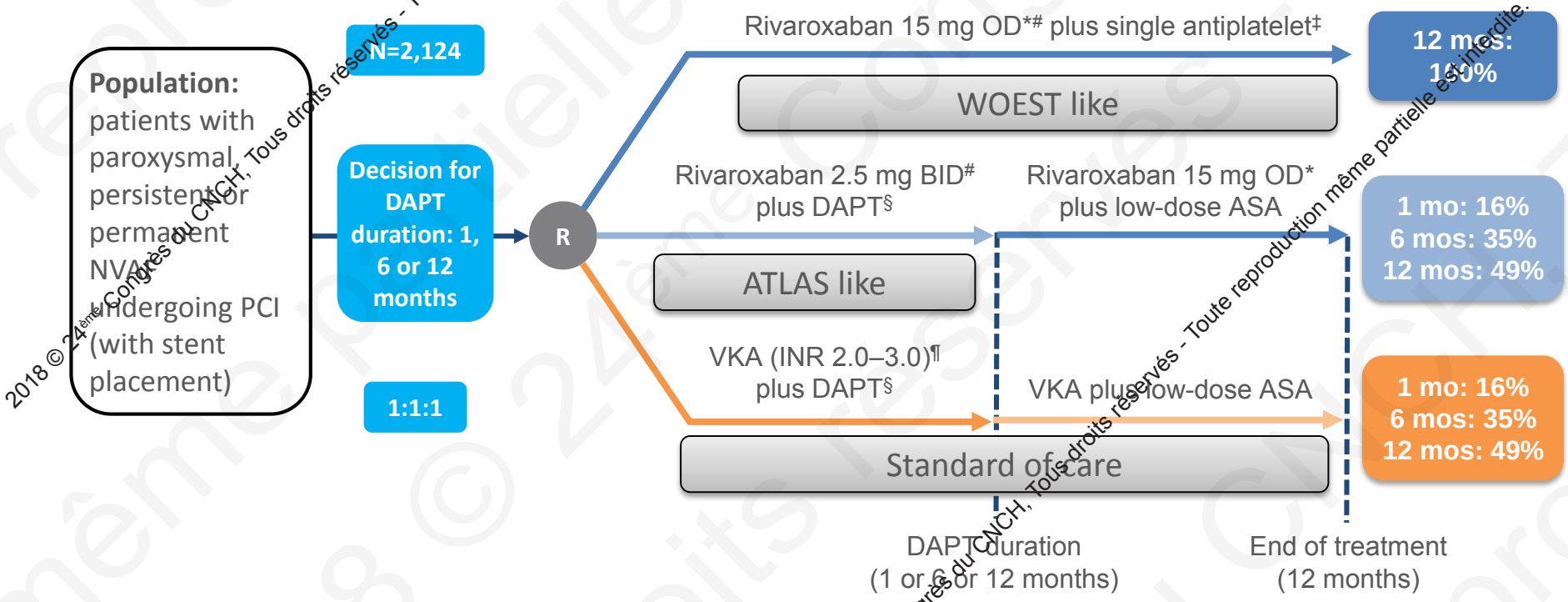
Implications

We propose that a strategy of oral anticoagulants plus clopidogrel, but without aspirin could be applied in this group of high-risk patients on OAC when undergoing PCI

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Rivaroxaban is the First & Currently Only NOAC to Provide Data From a Dedicated RCT in AF-PCI

Design: An open-label, randomized, controlled phase IIIb safety study

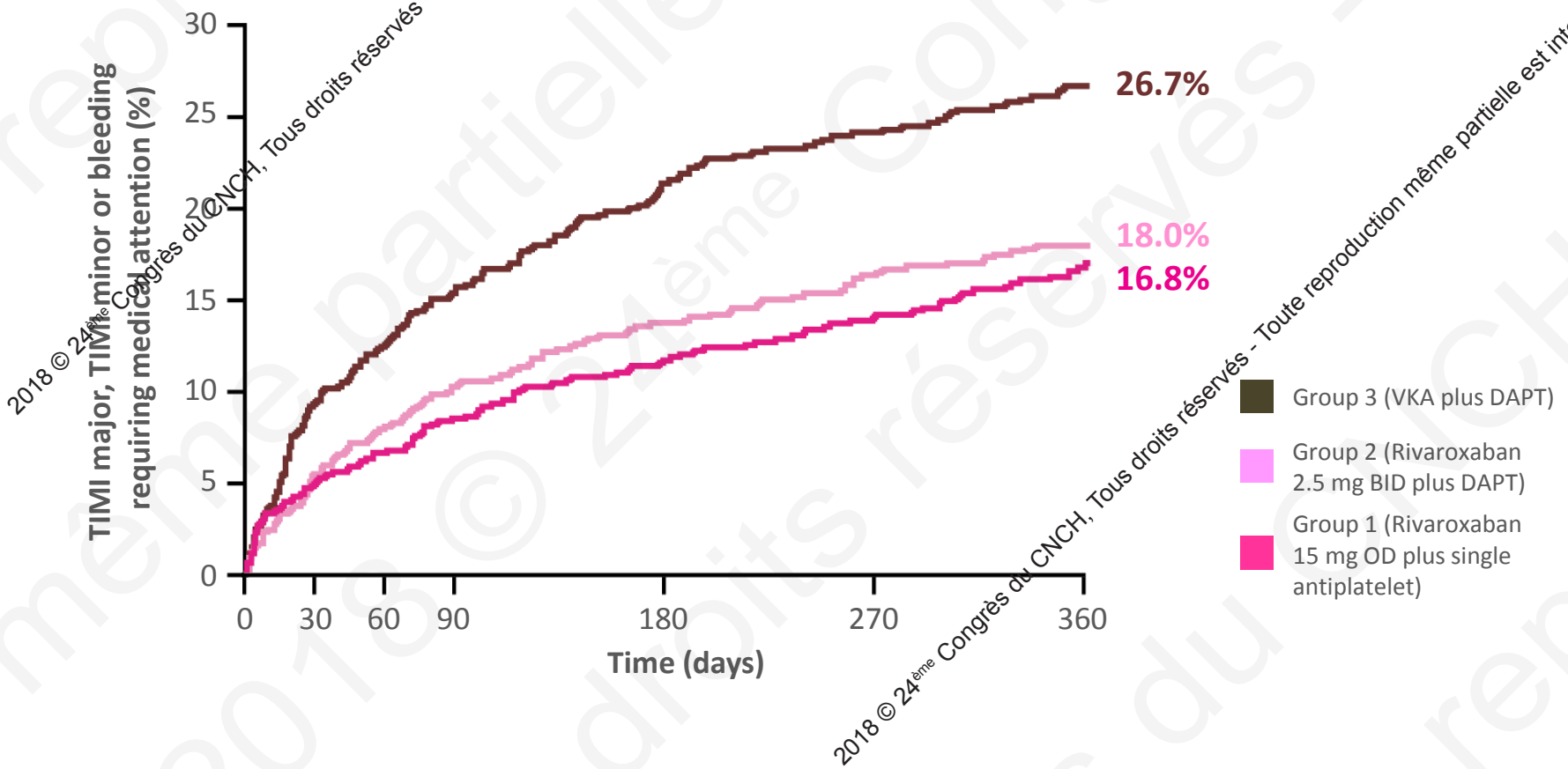


*CrCl 30–49 ml/min: 10 mg OD; #first dose 72–96 hours after sheath removal; ‡clopidogrel (75 mg daily) (alternative use of prasugrel or ticagrelor allowed, but capped at 15%); §ASA (75–100 mg daily) plus clopidogrel (75 mg daily) (alternative use of prasugrel or ticagrelor allowed, but capped at 15%); ¶first dose 12–72 hours after sheath removal

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

Both Rivaroxaban Strategies was Associated With Significantly Improved Safety

- **Rivaroxaban 15 mg OD plus single antiplatelet vs VKA plus DAPT: HR=0.59; (95% CI 0.47–0.76); *p*<0.001**
- **Rivaroxaban 2.5 mg BID plus DAPT vs VKA plus DAPT: HR=0.63 (95% CI 0.50–0.80); *p*<0.001**



2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

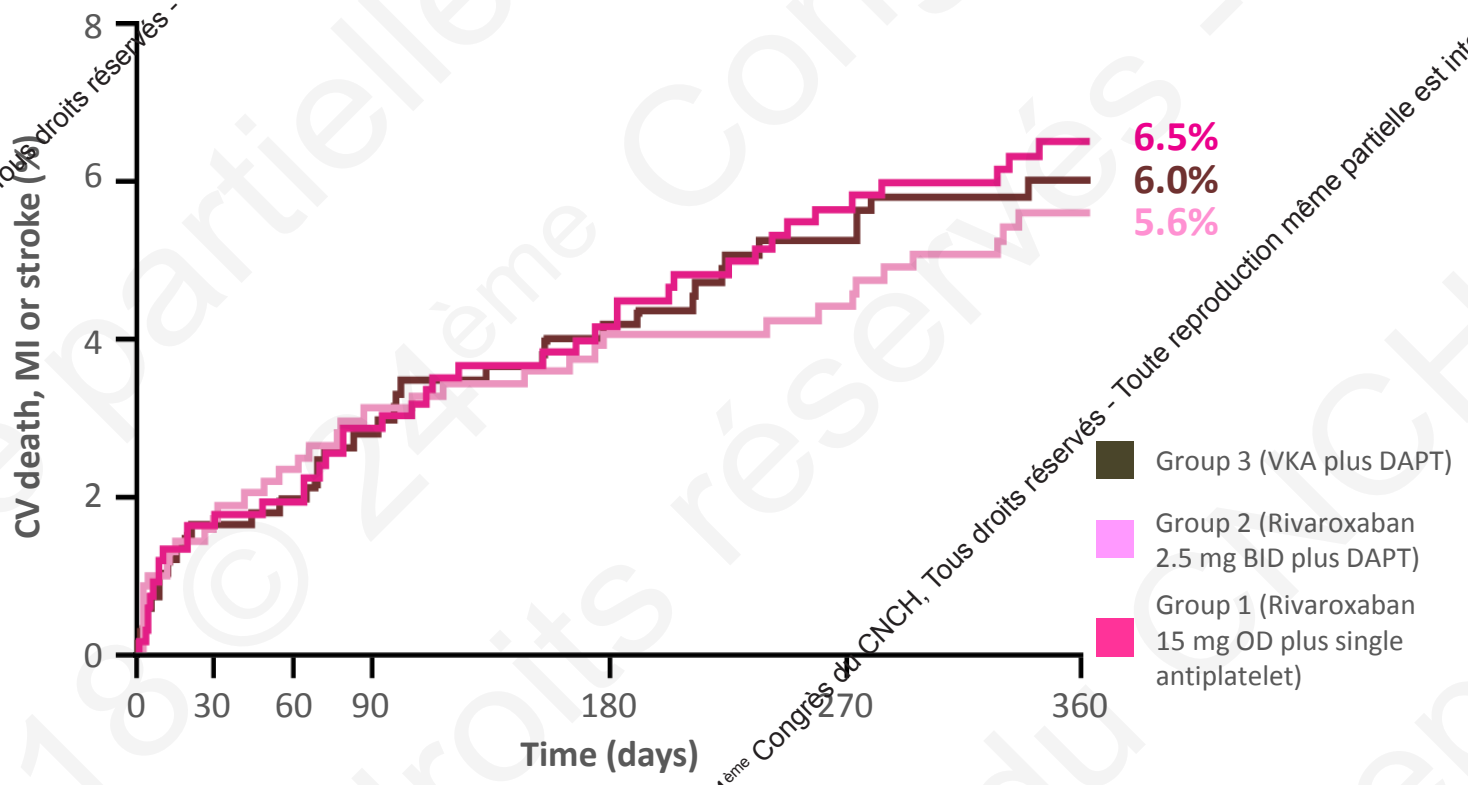
Gibson CM et al, *New Engl J Med* 2016; doi: 10.1056/NEJMoa1611594]

PIONEER AF-PCI

Efficacy was Comparable Between All Three Treatment Strategies*

Rivaroxaban 15 mg OD plus single antiplatelet vs VKA plus DAPT: HR=1.08; (95% CI 0.69–1.68); p=0.750

Rivaroxaban 2.5 mg BID plus DAPT vs VKA plus DAPT: HR=0.93 (95% CI 0.59–1.48); *p*=0.765

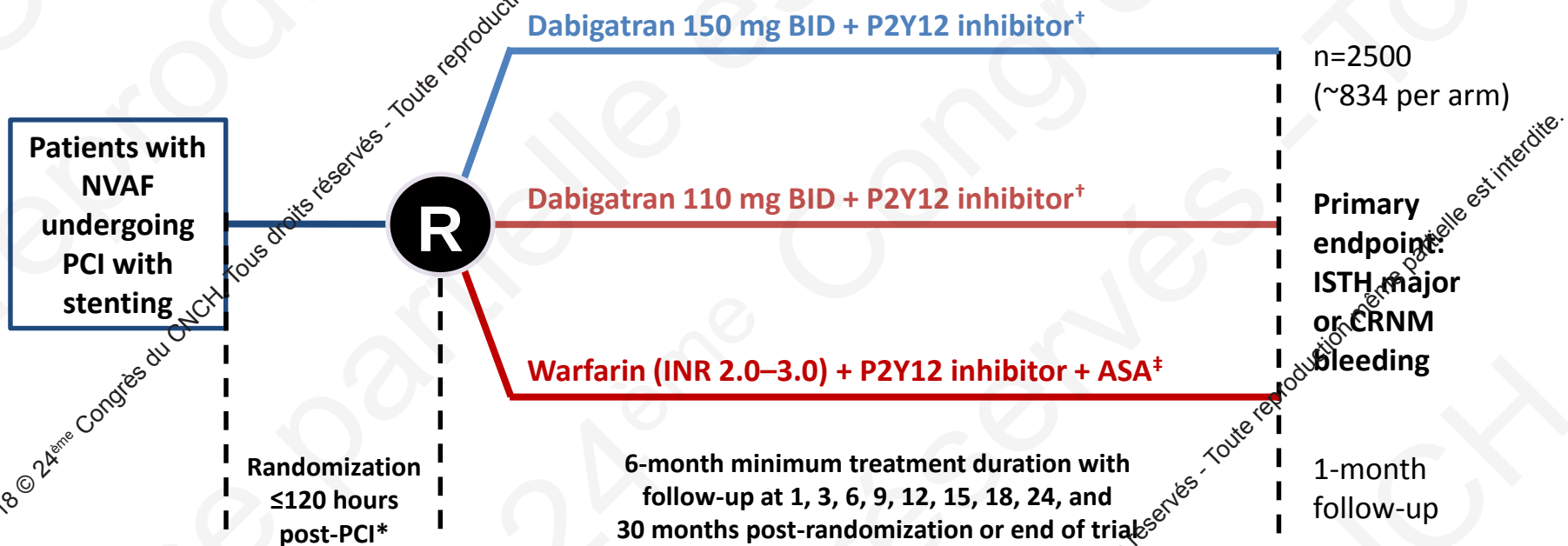


*Trial not powered to definitively demonstrate either superiority or non-inferiority for efficacy endpoints

Gibson CM et al, *New Engl J Med* 2016; doi: 10.1056/NEJMoa1611594

PIONEER AF-PCI

RE-DUAL PCI™ tests the hypothesis of non-inferiority in safety of dual antithrombotic therapy with dabigatran vs triple therapy with VKA



Estimated completion March 2017

***Study drug should be administered 6 hours after sheath removal and no later than ≤120 hrs post-PCI (≤72 hrs is preferable). †Dabigatran arms: ASA discontinued at randomization. ‡Warfarin arm: ASA discontinued 1 month after bare metal stent or 3 months after drug-eluting stent.**

ASA, acetylsalicylic acid; CRNM, clinically-relevant non-major; ISTH, International Society on Thrombosis and Haemostasis; PCI, percutaneous coronary intervention; R, randomization. Boehringer Ingelheim Clinical Trial Protocol, Trial No. 1160.186; ClinicalTrials.gov: NCT02164864; BI, data on file

RE-DUAL PCI™
Study in NVAF patients undergoing PCI

RE-DUAL PCI
Study in NVAF patients undergoing PCI

Study objective and design

RE-DUAL PCI tests the safety and efficacy of two regimens of dual therapy with dabigatran without aspirin vs triple therapy with warfarin

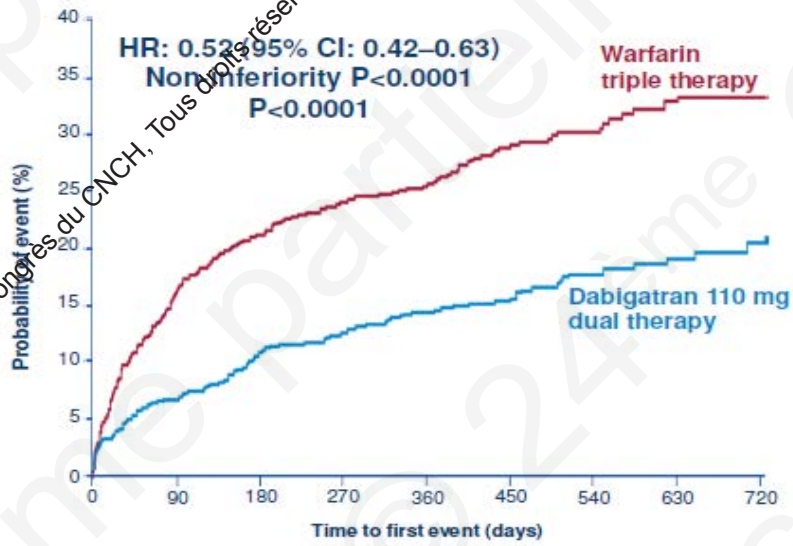
- The primary endpoint was time to first ISTH major or clinically relevant non-major bleeding
- Formally tested and powered endpoints included:
  - Non-inferiority of 110 mg and 150 mg dual therapy groups on time to first ISTH major or clinically relevant non-major bleeding event.
  - Non-inferiority of both dual therapy groups combined on time to first event of death, thromboembolic event (MI, stroke, systemic embolism) or unplanned revascularization
  - Superiority testing of the bleeding endpoints
- 100% of outcome events were independently adjudicated by blinded external committee

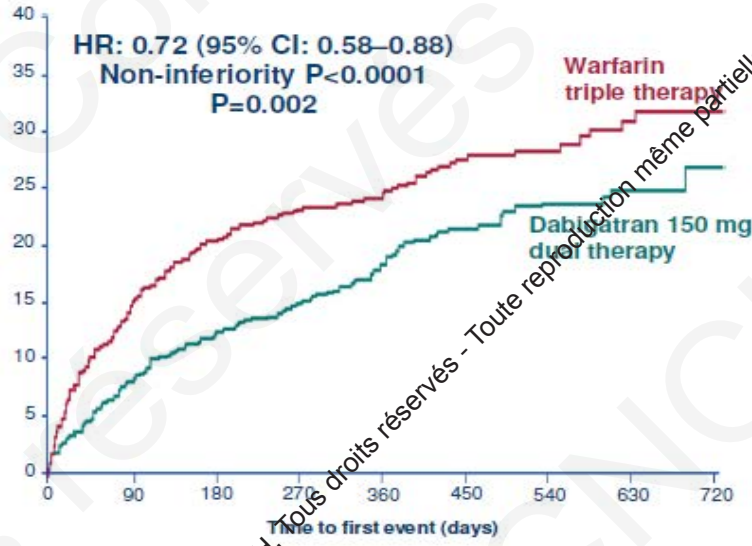
ISTH, International Society of Thrombosis and Haemostasis; MI, myocardial infarction Non-inferiority testing (margin 1.38)

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

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

RE-DUAL PCI
Study in NVAF patients undergoing PCI



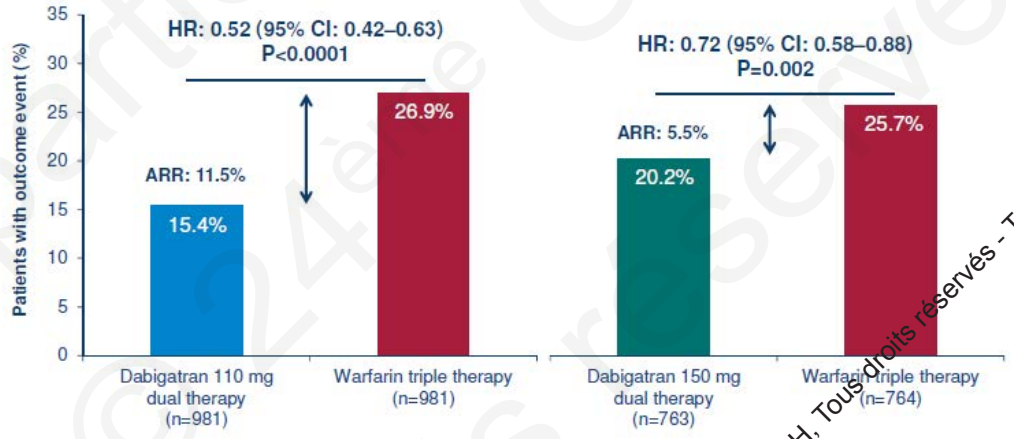


Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 mg vs warfarin comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≥70 in Japan and <80 or ≥80 years old elsewhere). For the dabigatran 150 mg vs warfarin comparison, an unstratified 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)

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.
2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Primary endpoint: ISTH major or clinically relevant non-major bleeding event

RE-DUAL PCI
Study in NVAF patients undergoing PCI

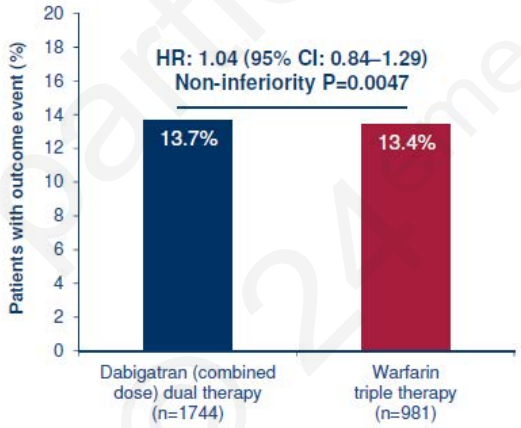


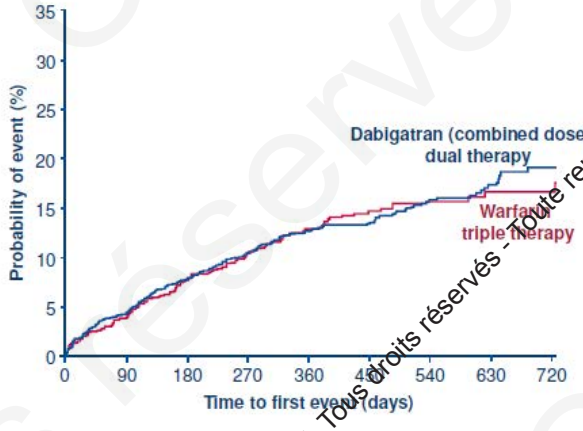
Wald two-sided P value from (stratified) Cox proportional-hazard model (alpha=0.05). ARR, absolute risk reduction

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Time to death or thromboembolic event, or unplanned revascularization

RE-DUAL PCI
Study in NVAF patients undergoing PCI





Non-inferiority P value is one sided (alpha=0.025). Results presented are Step 3 of hierarchical testing procedure, testing non-inferiority of dabigatran dual therapy (combined doses) to warfarin triple therapy in death or thromboembolic event and unplanned revascularization

2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

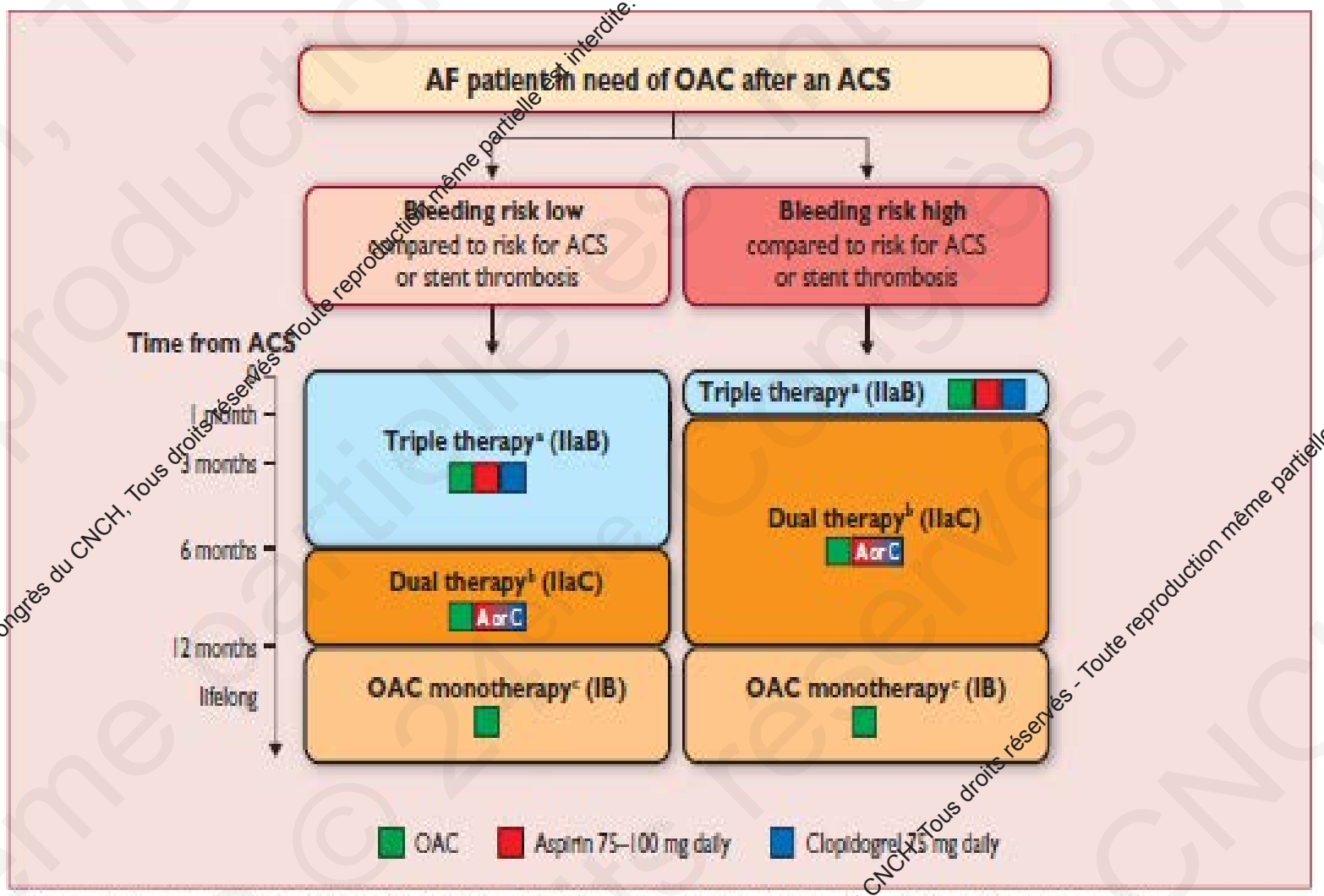
Conclusions

RE-DUAL PCI
Study in NVAF patients undergoing PCI

In patients with AF who have undergone PCI:

- Dual therapy with dabigatran and a P2Y12 antagonist **significantly reduced the risk of bleeding versus warfarin triple therapy**, with non-inferiority for overall thromboembolic events
- Absolute risk reductions with dabigatran dual therapy were **11.5% and 5.5%** in ISTH major or clinically relevant non-major bleeding at the 110 mg and 150 mg doses, respectively, compared with warfarin triple therapy
- These dabigatran dual therapy regimens, using doses approved worldwide for stroke prevention, offer clinicians two additional options for managing Afib patients post-PCI

2018 © 24ème Congrès du CNCH, tous droits réservés - Toute reproduction même partielle est interdite.
2018 © 24ème Congrès du CNCH, tous droits réservés - Toute reproduction même partielle est interdite.

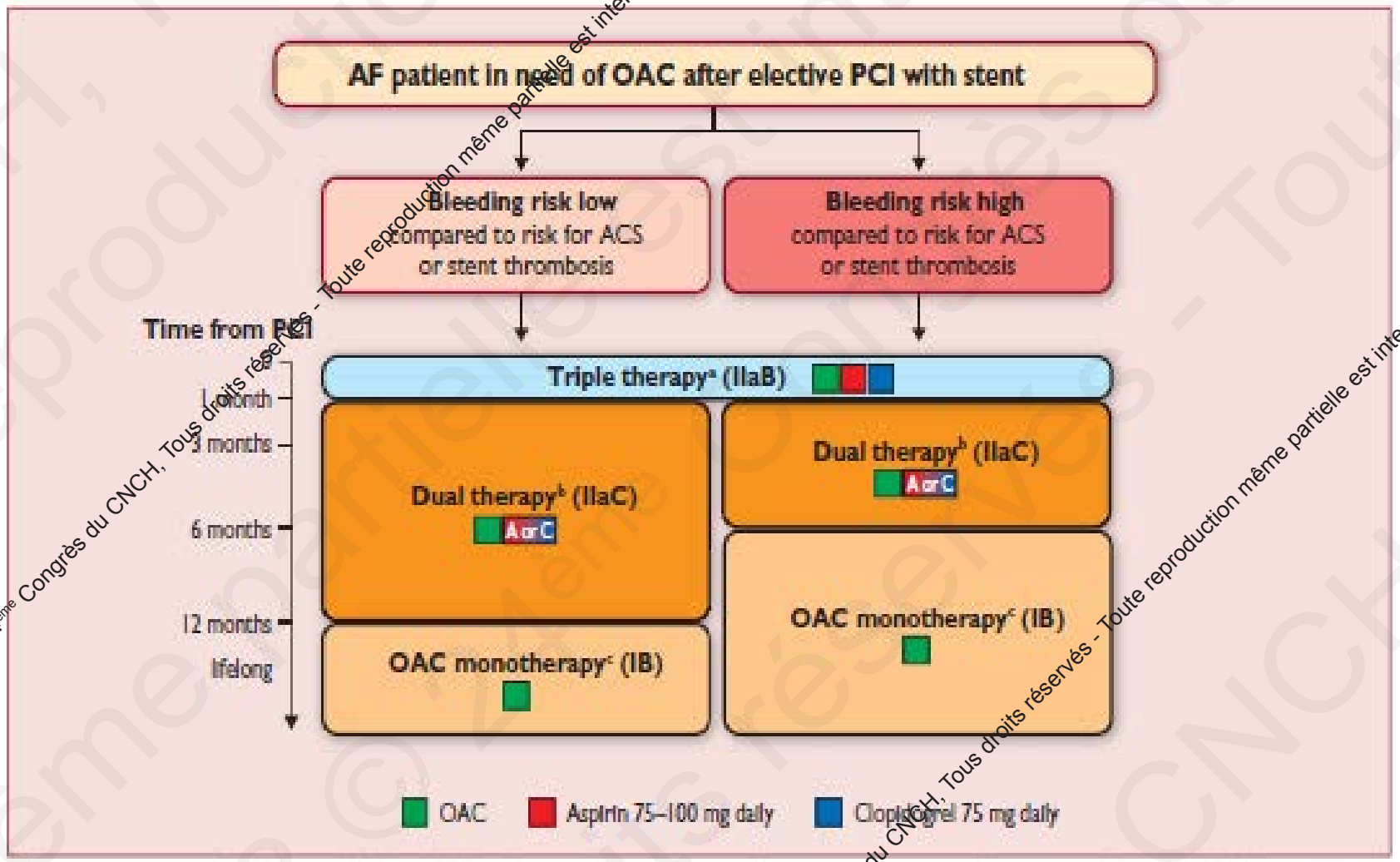


ACS = acute coronary syndrome; AF = atrial fibrillation; OAC = oral anticoagulation (using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants); PCI = percutaneous coronary intervention.

[a]Dual therapy with OAC and aspirin or clopidogrel may be considered in selected patients, especially those not receiving a stent or patients at a longer time from the index event.

[b]OAC plus single antiplatelet.

[c]Dual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.



ACS = acute coronary syndrome; AF = atrial fibrillation; OAC = oral anticoagulation (using vitamin K antagonists or non-vitamin K antagonist oral anticoagulants); PCI = percutaneous coronary intervention.

[a]Dual therapy with OAC and aspirin or clopidogrel may be considered in selected patients.

[b]OAC plus single antiplatelet.

[c]Dual therapy with OAC and an antiplatelet agent (aspirin or clopidogrel) may be considered in patients at high risk of coronary events.

Demographics

Device Patients

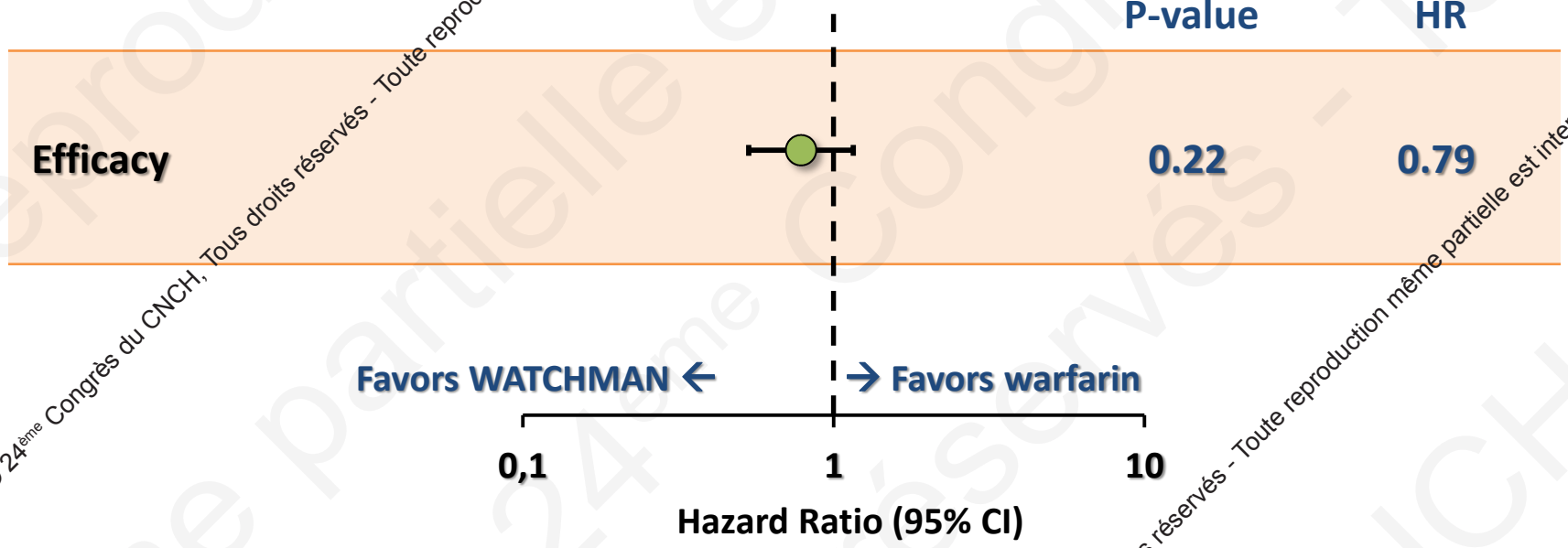
Characteristic	PROTECT AF N=463	PREVAIL N=269	P value
Age, years	71.7 ± 8.8 (463) (46.0, 95.0)	74.0 ± 7.4 (269) (50.0, 94.0)	<0.001
Gender (Male)	326/463 (70.4%)	182/269 (67.7%)	0.252
$CHADS_2$ Score (Continuous)	2.2 ± 1.2 (1.0, 6.0)	2.6 ± 1.0 (1.0, 6.0)	<0.001
$CHADS_2$ Risk Factors			
CHF	124/463 (26.8%)	63/269 (23.4%)	
Hypertension	415/463 (89.6%)	238/269 (88.5%)	
Age ≥ 75	190/463 (41.0%)	140/269 (52.0%)	
Diabetes	113/463 (24.4%)	91/269 (33.8%)	
Stroke/TIA	82/463 (17.7%)	74/269 (27.5%)	

Most notable differences:
Age, Diabetes, and Prior Stroke/TIA

PROTECT AF and CAP: Reddy, VY et al. Circulation. 2011;123:417-424.
PREVAIL: Holmes, DR et al. *JACC* 2014; *In Press*

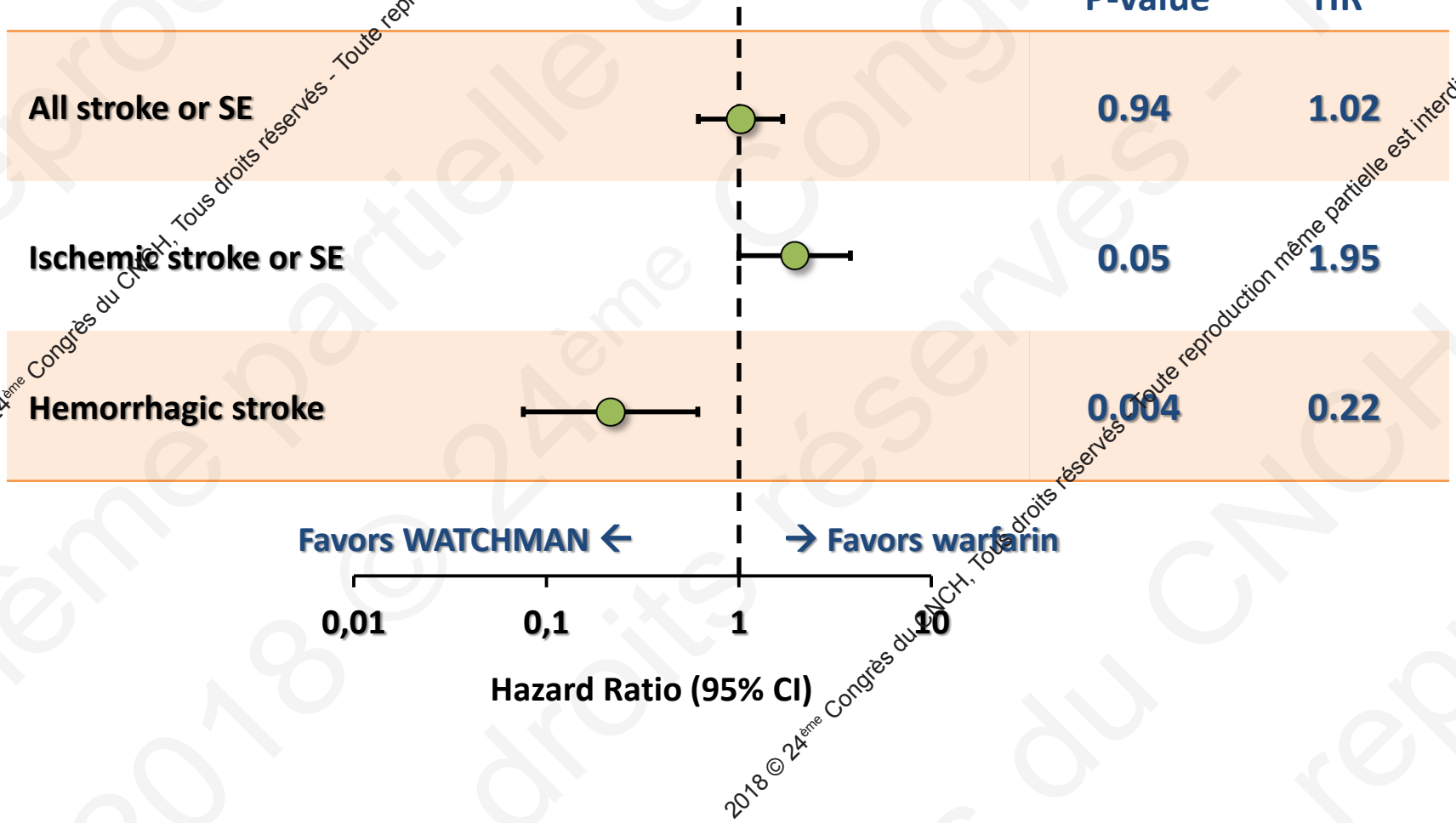
Patient-Level Meta-Analysis

Efficacy



Patient-Level Meta-Analysis

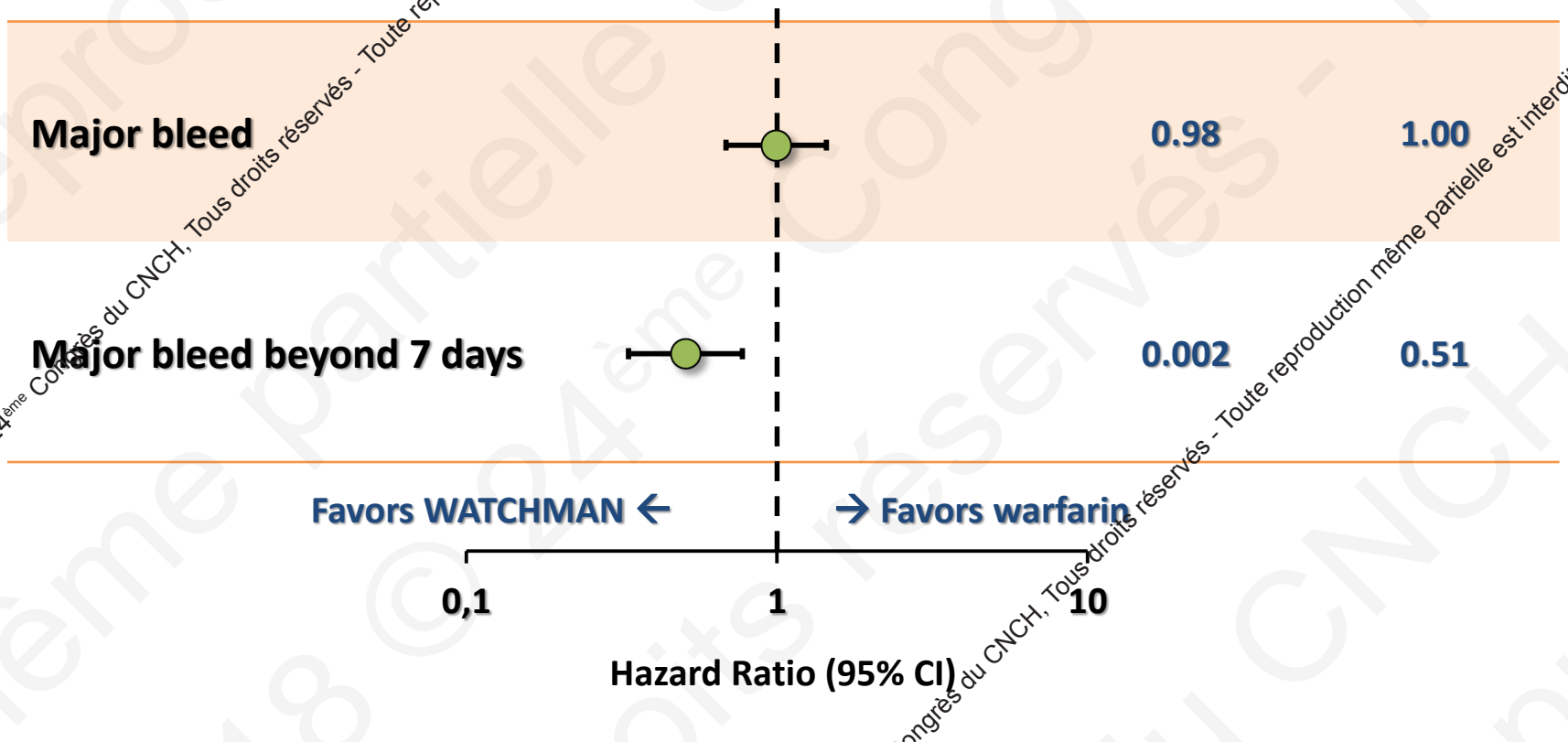
Stroke



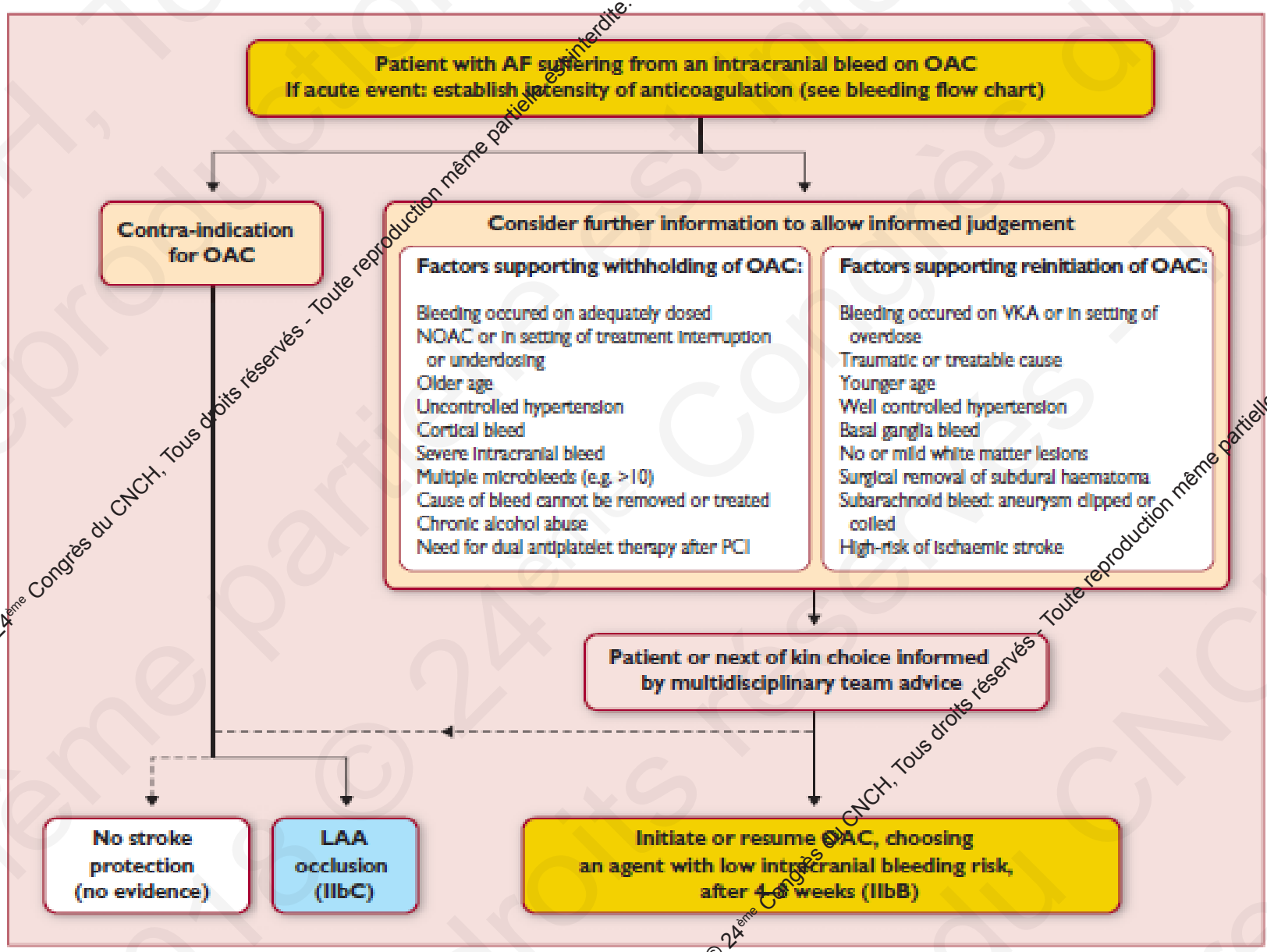
2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.
2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.

Patient-Level Meta-Analysis

Major Bleeding



2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.
2018 © 24ème Congrès du CNCH, Tous droits réservés - Toute reproduction même partielle est interdite.



AF = atrial fibrillation; LAA = left atrial appendage; NOAC = non-vitamin K antagonist oral anticoagulant; OAC = oral anticoagulation; PCI = percutaneous coronary intervention; VKA = vitamin K antagonist.

Conclusion

- L’association FA et coronaropathie est fréquente.
- Le recours à l’angioplastie doit nous faire réfléchir sur l’association thérapeutique a mettre en place.
- L’alternative au traitement médicamenteux est la fermeture de l’auricule