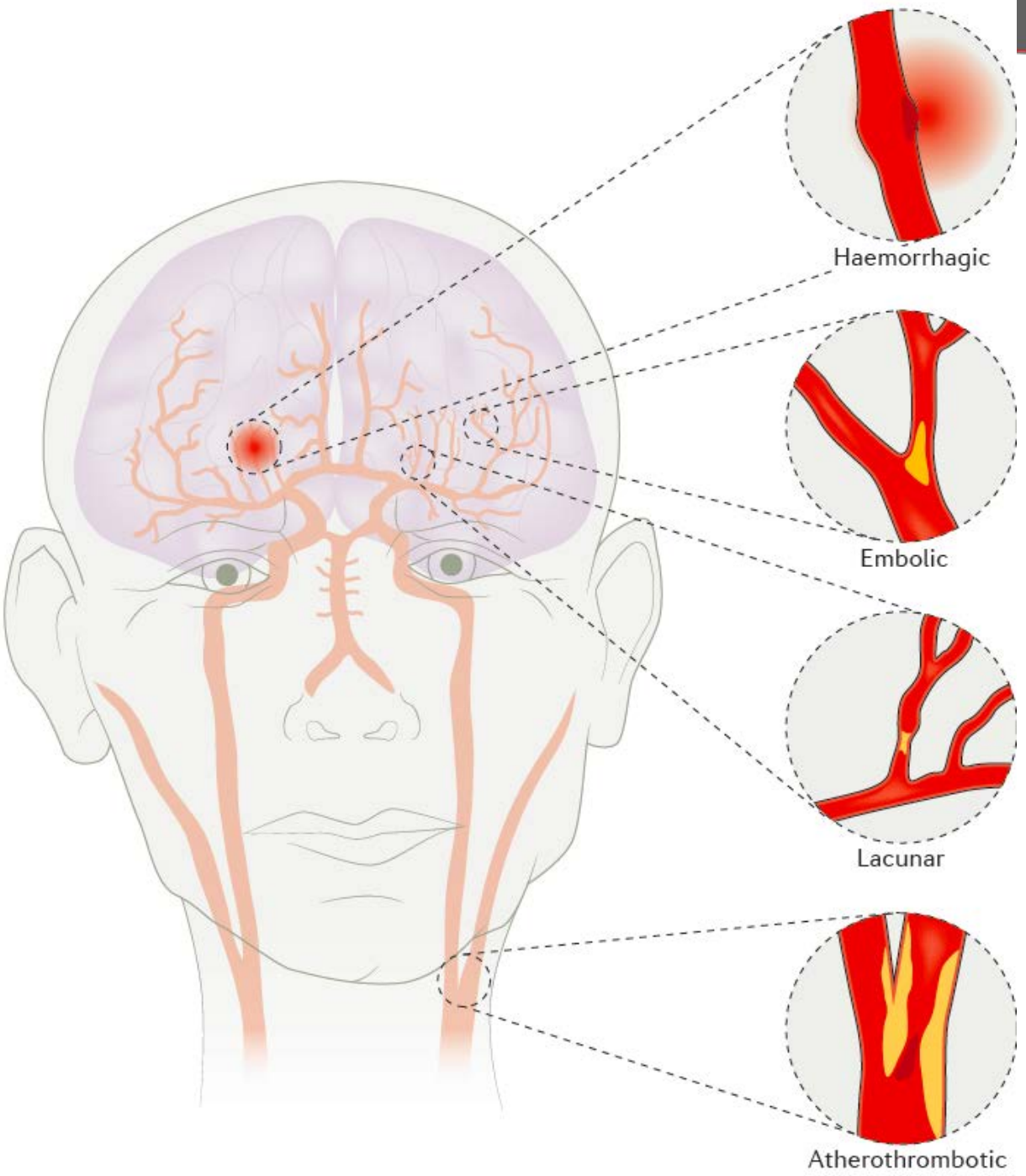
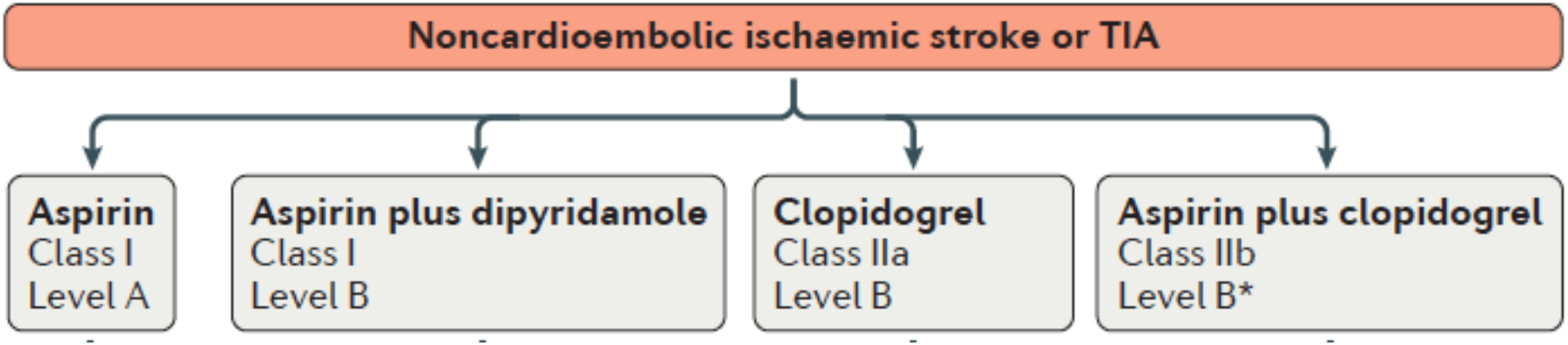
Quels anti-thrombotiques dans la prise en charge des AVC ischémiques ? Intérêt des nouveaux ou double anti-agrégants ?

Pr MA Sevestre CHU Amiens

- Liens d’intérêt

- Leo Pharma, Bayer SA, Pfizer BMS, Aspen et Daichii


Haemorrhagic
Embolic
Lacunar
Atherothrombotic

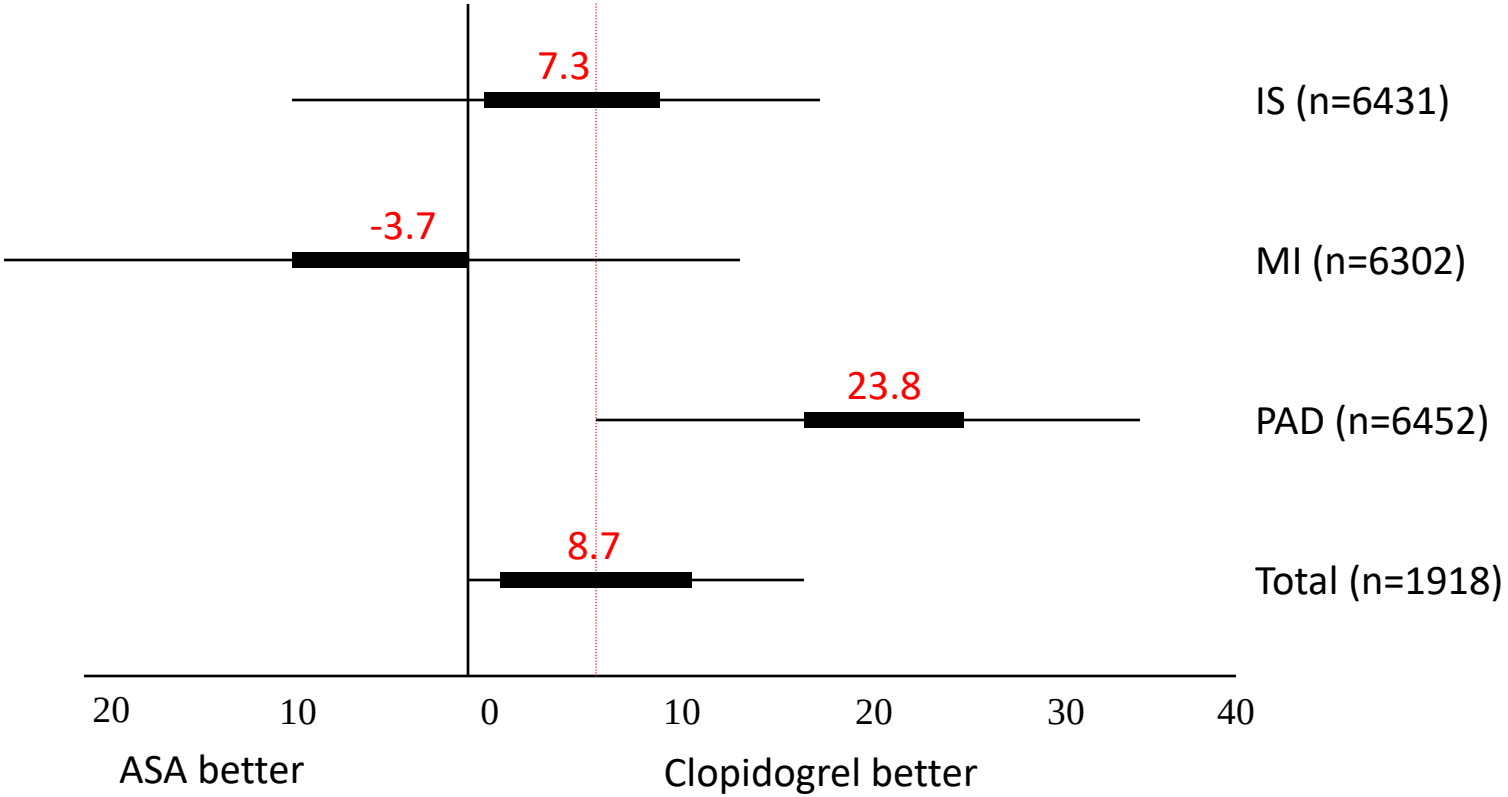


APTC ESPS-1,2 ESPRIT PROFESS CAPRIE MATCH, FASTER, CHANCE

L'ajout de l'aspirine au clopidogrel réduit les évènements ischémiques cérébraux de façon diverse

Inclusion d'AVC ischémiques lacunaires ?
L'association aspirine clopidogrel est efficace pour les patients à risque athérothrombotique

Relative Risk Reduction* by qualifying entry criteria

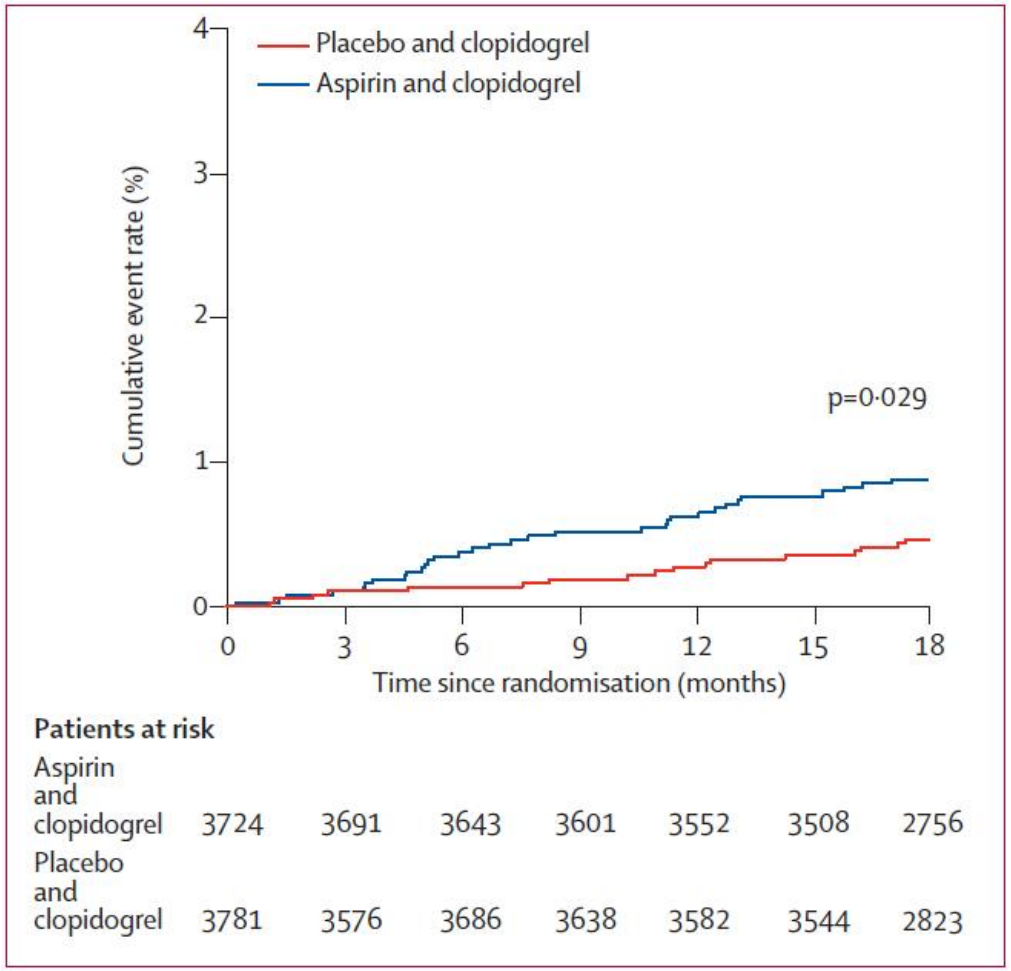


*Cluster of IS, MI, or vascular death.

CAPRIE

Lancet 1996;348:1329-1339.

MATCH – Clopidogrel + ASA vs Clopidogrel
Intracranial hemorrhage



Patients at risk

Aspirin and clopidogrel	3724	3691	3643	3601	3552	3508	2756
Placebo and clopidogrel	3781	3576	3686	3638	3582	3544	2823

Diener HC, et al. *Lancet*. 2004; 364:331-337.

The NEW ENGLAND JOURNAL of MEDICINE

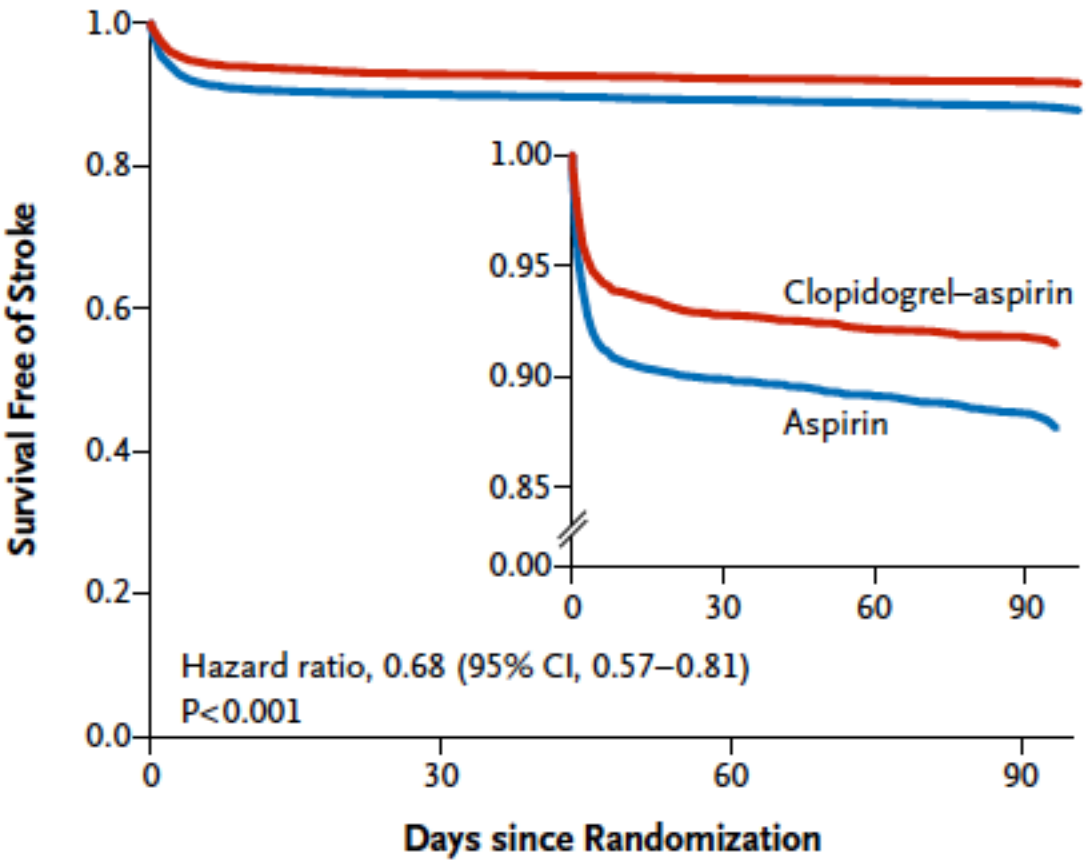
ORIGINAL ARTICLE

Clopidogrel with Aspirin in Acute Minor Stroke or Transient Ischemic Attack

Yongjun Wang, M.D., Yilong Wang, M.D., Ph.D., Xingquan Zhao, M.D., Ph.D., Liping Liu, M.D., Ph.D., David Wang, D.O., F.A.H.A., F.A.A.N., Chunxue Wang, M.D., Ph.D., Chen Wang, M.D., Hao Li, Ph.D., Xia Meng, M.D., Ph.D., Liying Cui, M.D., Ph.D., Jianping Jia, M.D., Ph.D., Qiang Dong, M.D., Ph.D., Anding Xu, M.D., Ph.D., Jinsheng Zeng, M.D., Ph.D., Yansheng Li, M.D., Ph.D., Zhimin Wang, M.D., Haiqin Xia, M.D., and S. Claiborne Johnston, M.D., Ph.D., for the CHANCE Investigators*

N Engl J Med 2013;369:11-19.

Outcome	Aspirin (N=2586)		Clopidogrel and Aspirin (N=2584)		Hazard Ratio (95% CI)	P Value
	Patients with Event *no.*	Event Rate %	Patients with Event *no.*	Event Rate %		
Primary outcome						
Stroke	303	11.7	212	8.2	0.68 (0.57–0.81)	<0.001
Secondary outcomes						
Stroke, myocardial infarction, or death from cardiovascular causes	307	11.9	216	8.4	0.69 (0.58–0.82)	<0.001
Ischemic stroke	295	11.4	204	7.9	0.67 (0.56–0.81)	<0.001
Hemorrhagic stroke	8	0.3	8	0.3	1.01 (0.38–2.70)	0.98
Myocardial infarction	2	0.1	3	0.1	1.44 (0.24–8.63)	0.69
Death from cardiovascular causes	5	0.2	6	0.2	1.16 (0.35–3.79)	0.81
Death from any cause	10	0.4	10	0.4	0.97 (0.40–2.33)	0.94
Transient ischemic attack	47	1.8	39	1.5	0.82 (0.53–1.26)	0.36



No. at Risk

Aspirin	2586	2307	2287	1906
Clopidogrel–aspirin	2584	2376	2361	1989

Conclusion

- L'Essai CHANCE montre une réduction de récidive des AVC ischémiques en cas d'AIT ou d'AVC mineur (NIH < 3) dans le groupe traité par Clopidogrel 300mg (J1) puis 75 mg et aspirine 75 mg pendant 21 jours et clopidogrel 75 mg J90 vs aspirine 75mg jusqu'à J90
- Population sélectionnée
- Patients asiatiques/ superposables aux européens ?

AOD en prévention secondaire de l'athérothrombose : patients coronariens

Drug	FDA recommendations		European recommendations	
	Indication	Particular recommendations for patients with prior CVD	Indication	Particular recommendations for patients with prior CVD
Rivaroxaban	Not approved	Not approved	Prevention of atherothrombotic events in adults with ACS who have elevated levels of cardiac biomarkers	Contraindicated in patients with concomitant treatment of ACS with antiplatelet therapy and prior stroke or TIA

ATLAS ACS 2

Rivaroxaban 2,5mg en plus des 2 AAP

Apixaban: étude APPRAISAL négative

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ATLAS ACS 2

Rivaroxaban 2,5mg en plus des 2 AAP

Apixaban: étude APPRAISAL négative

Rivaroxaban Versus Aspirin in Secondary Prevention of Stroke and Prevention of Systemic Embolism in Patients With Recent Embolic Stroke of Undetermined Source (ESUS) (NAVIGATE ESUS)

Dabigatran Etexilate for Secondary Stroke Prevention in Patients With Embolic Stroke of Undetermined Source (RE-SPECT ESUS)

Rivaroxaban for the Prevention of Major Cardiovascular Events in Coronary or Peripheral Artery Disease

Efficacy and Safety of Rivaroxaban in Reducing the Risk of Major Thrombotic Vascular Events in Subjects With Symptomatic Peripheral Artery Disease Undergoing Peripheral Revascularization Procedures of the Lower Extremities (VOYAGER PAD)

Rivaroxaban Versus Aspirin in Secondary Prevention of Stroke and Prevention of Systemic Embolism in Patients With Recent Embolic Stroke of Undetermined Source (ESUS

En cours

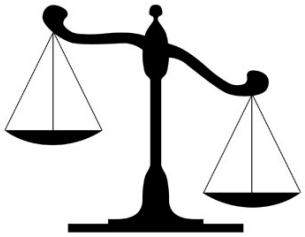
[Rivaroxaban for the Prevention of Major Cardiovascular Events in Coronary or Peripheral Artery Disease]

Efficacy and Safety of Rivaroxaban in Reducing the Risk of Major Thrombotic Vascular Events in Subjects With Symptomatic Peripheral Artery Disease Undergoing Peripheral Revascularization Procedures of the Lower Extremities (VOYAGER PAD)

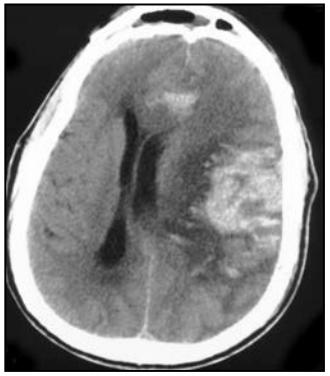
Que faire en cas d'Infarctus cérébral/AIT chez un patient en FA (non anticoagulé) ?

Quel traitement donner et quand?

Récidive précoce d'infarctus cérébral



Transformation hémorragique symptomatique



- Meta-analyse[1], 7 essais, 4624 patients, AVC cardio-embolique < 48h
- Anticoagulants vs. Aspirine ou Placebo

Récidive d'infarctus cérébral
3% vs 4.9% , OR 0.68 (0.44 – 1.06)
p = 0.09, NNT 53

Hémorragie intracrânienne symptomatique
2.5% vs 0.7%, OR 2.89 (1.19 – 7.01)
p=0.02, NNH 55

1. Paciaroni et al, Stroke 2007

ACCP guidelines 2012
Chest 2012

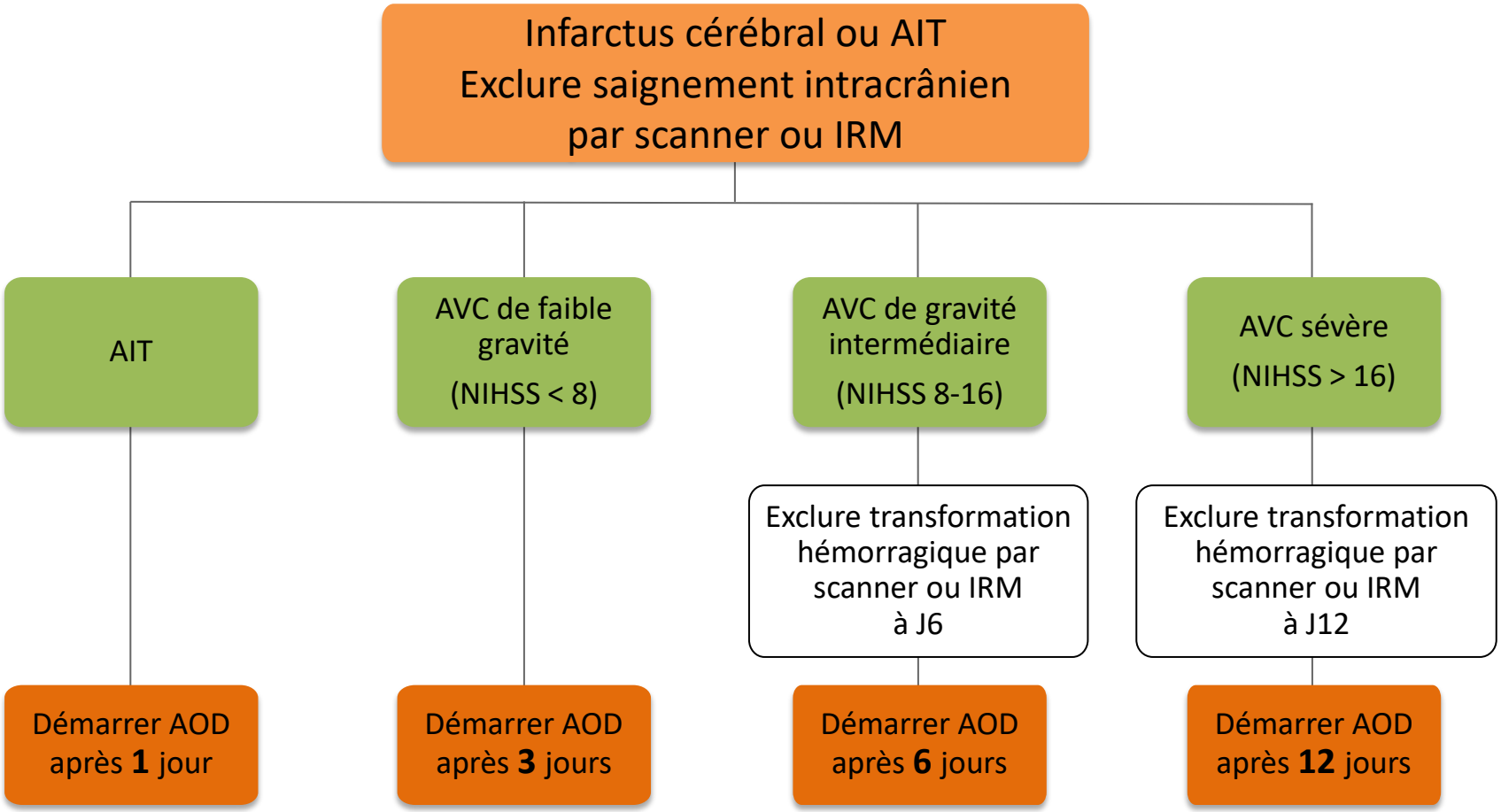
- Oral anticoagulation should generally be initiated within 1 to 2 weeks after stroke onset.
- Earlier anticoagulation can be considered for patients at low risk of bleeding complications (eg, those with a small infarct burden and no evidence of hemorrhage on brain imaging).
- Delaying anticoagulation should be considered for patients at high risk of hemorrhagic complications (eg, those with extensive infarct burden or evidence of significant hemorrhagic transformation on brain imaging).

AHA ASA guidelines 2014
Stroke 2014

- For most patients with a stroke or TIA in the setting of AF, it is reasonable to initiate oral anticoagulation within 14 days after the onset of neurological symptoms (Class IIa; Level of Evidence B). (New recommendation)
- In the presence of high risk for hemorrhagic conversion (ie, large infarct, hemorrhagic transformation on initial imaging, uncontrolled hypertension, or hemorrhage tendency), it is reasonable to delay initiation of oral anticoagulation beyond 14 days (Class IIa; Level of Evidence B). (New recommendation)

Infarctus cérébral/AIT chez un patient en FA

Quand débuter un traitement par AOD?



Heidbuchel et al. European Heart Rhythm Association, Europace 2015

Infarctus cérébral sous AOD: Revascularisation

DERNIERE PRISE	OCCLUSION PROXIMALE	PAS D'OCCLUSION PROXIMALE
> 48h	rtPA + Thrombectomie	rtPA
< 48h ou ? ou ClCr < 50 ml/mn	Thrombectomie	rtPA (si AOD < 50 ng/ml)
	rtPA (si AOD < 50 ng /ml) + Thrombectomie	
	Antidote + rtPA + Thrombectomie	Antidote + rtPA

Take Home message

- **Pas d'indication pour les AOD en prévention secondaire pour le moment après AVC sans FA**
- **Double antiagrégation plaquettaire possible à la phase initiale après AIT ou mini stroke pendant 90j (aspirine clopidogrel)**
- **AAP unique par la suite**
- **La cause de l'AVC guidera le choix par la suite (lacunes ? Thrombose? Embolies?)**