What's up in 2010 ?

Que s'est-t-il passé en 2010?

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Guidelines for the management of atrial fibrillation

EUROPEAN SOCIETY OF CARDIOLOGY®

The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC)

The European Society of Cardiology 2010

Nouveautés dans la prise en charge de la Fibrillation Atriale

Score EHRA
Symptômes associés à la FA

Table 6 EHRA score of AF-related symptoms

Classification of AF-related symptoms (EHRA score)	
EHRA class	**Explanation**
EHRA I	'No symptoms'
EHRA II	'Mild symptoms'; normal daily activity not affected
EHRA III	'Severe symptoms'; normal daily activity affected
EHRA IV	'Disabling symptoms'; normal daily activity discontinued

AF = atrial fibrillation; EHRA = European Heart Rhythm Association.

Classification de la Fibrillation Atriale

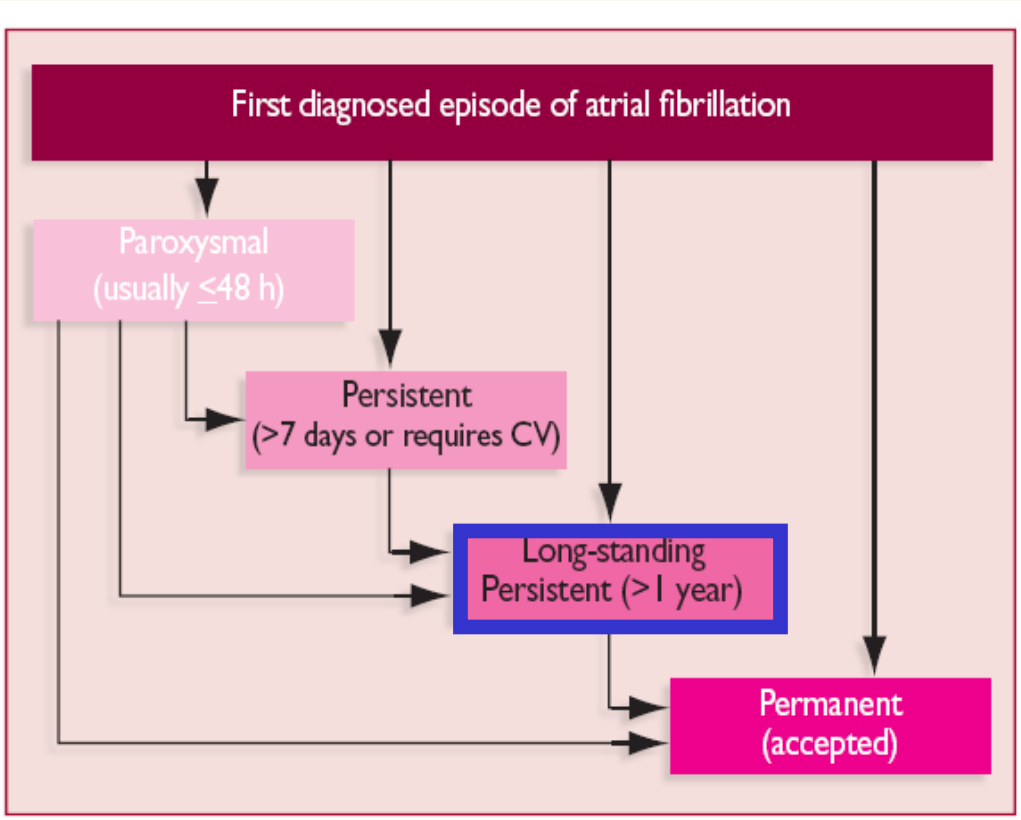


Figure 2 Different types of AF. AF = atrial fibrillation; CV = cardioversion. The arrhythmia tends to progress from paroxysmal (self-terminating, usually <48 h) to persistent [non-self-terminating or requiring cardioversion (CV)], long-standing persistent (lasting longer than 1 year) and eventually to permanent (accepted) AF. First-onset AF may be the first of recurrent attacks or already be deemed permanent.

Long-standing persistent
FA >1 année dont la décision a été de contôlée la FC

Nouveau type de FA

$CHADS_2$: évaluation du risque d'AVC chez des patients avec FA non valvulaire

Recommandations ESC 2006

$CHADS_2$ score	Patients (n = 1733)	Adjusted stroke rate (%/year)[a] (95% confidence interval)
0	120	1.9 (1.2–3.0)
1	463	2.8 (2.0–3.8)
2	523	4.0 (3.1–5.1)
3	337	5.9 (4.6–7.3)
4	220	8.5 (6.3–11.1)
5	65	12.5 (8.2–17.5)
6	5	18.2 (10.5–27.4)

Score $CHADS_2$

Congestive HF
Hypertension
Age > 75 ans
Diabète
Stroke

Fuster V, et al. ACC/AHA/ESC 2006 guidelines for the management of patients with atrial fibrillation. 2006 Sep;8(9):651-745.

FA valvulaire = FA + prothèse Valvulaire ou RM

>>> AVK

(a) Prior myocardial infarction, peripheral artery disease, aortic plaque

(a) Risk factors for stroke and thrombo-embolism in non-valvular AF

'Major' risk factors	'Clinically relevant non-major' risk factors
Previous stroke, TIA, or systemic embolism Age ≥75 years	Heart failure or moderate to severe LV systolic dysfunction (e.g. LV EF ≤40%) Hypertension - Diabetes mellitus Female sex - Age 65–74 years Vascular disease[a]

(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA_2DS_2-VASc

(Note: maximum score is 9 since age may contribute 0, 1, or 2 points)

Nouveau score de risque thrombo-embolique

C H A_2 D S_2 V A Sc

Risk factor	Score
Congestive heart failure/LV dysfunction **< 40 %**	1
Hypertension	1
Age ≥75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease[a]	1
Age 65–74	1
Sex category (i.e. female sex)	1
Maximum score	**9**

Table 9 Approach to thromboprophylaxis in patients with AF

Risk category	CHA_2DS_2-VASc score	Recommended antithrombotic therapy
One 'major' risk factor or ≥2 'clinically relevant non-major' risk factors	≥ 2	OAC[a]
One 'clinically relevant non-major' risk factor	1	Either OAC[a] or aspirin 75–325 mg daily. Preferred: OAC rather than aspirin.
No risk factors	0	Either aspirin 75–325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin.

AF = atrial fibrillation; CHA_2DS_2-VASc = cardiac failure, hypertension, age ≥75 (doubled), diabetes, stroke (doubled)-vascular disease, age 65–74 and sex category (female); INR = international normalized ratio; OAC = oral anticoagulation, such as a vitamin K antagonist (VKA) adjusted to an intensity range of INR 2.0–3.0 (target 2.5).

Patient =0 (CHA2DS2-VASc) Pas de traitement

« Patients aged < 60 years, with 'lone AF', i.e. no clinical history or echocardiographic evidence of cardiovascular disease, carry a very low cumulative stroke risk, estimated to be **1.3% over 15 years**. »

FA et antithrombotiques

d'une recommandation à l'autre…

Patiente =70 ans avec FAX sur coeur sain
En 2006, score $CHADS_2 = 0$ …. **Aspirine ou RIEN**
En 2010, score $CHA_2DS_2\text{-}VASc = 2$ …..**TT AVK**

Patiente 75 ans FAP, préopératoire PTH
En 2006, score $CHADS_2 = 1$ …. Stop 7 jours avant
En 2010, score $CHA_2DS_2\text{-}VASc = 3$ …..**Stop 48 heures avant**

Nouveauté en 2010: FA et AVC= scanner (éliminer Hgie)
Si scanner hémorragique = rien
Si scanner normal (AVK) immédiat (Contôle HTA)
Si scanner (large AVC), AVK dans 15 jours
Si récidive AVC sur FA+AV …. INR=3,5 (+AAP non indiqué)

FA et Coronaropathie

Angioplastie coronaire per-cutanée / SCA

Calcul du score de risque hémorragique

HAS-BLED

Connaître la nature du stent (Acier, Actif)

Prescription

-Bithérapie

-Trithérapie durée ???

Table 10 Clinical characteristics comprising the HAS-BLED bleeding risk score

Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

Nouveau score de risque Hémorragique

Score *HASBLED* ≥ 3

=

Patients à haut risque

Initiation du trt, suivi régulier

'Hypertension' is defined as systolic blood pressure >160 mmHg.

'Abnormal kidney function' is defined as the presence of chronic dialysis or renal transplantation or serum creatinine ≥200 mmol/L.

'Abnormal liver function' is defined as chronic hepatic disease (e.g. cirrhosis) or biochemical evidence of significant hepatic derangement

'Bleeding' refers to previous bleeding history and/or predisposition to bleeding, e.g. bleeding diathesis, anaemia, etc.

'Labile INRs' refers to unstable/high INRs or poor time in therapeutic range (e.g.< 60%).

'Drugs/alcohol use' refers to concomitant use of drugs, such as APA, NSAI drugs, or alcohol abuse

Table 11 Antithrombotic strategies following coronary artery stenting in patients with AF at moderate to high thrombo-embolic risk (in whom oral anticoagulation therapy is required) Classe IIa Niveau de preuve C !

Haemorrhagic risk	Clinical setting	Stent implanted	Anticoagulation regimen
Low or intermediate (e.g. HAS-BLED score 0–2)	Elective	Bare-metal	1 month: triple therapy of VKA (INR 2.0–2.5) + aspirin ≤100 mg/day + clopidogrel 75 mg/day Lifelong: VKA (INR 2.0–3.0) alone
	Elective	Drug-eluting	3 (-olimus[a] group) to 6 (paclitaxel) months: triple therapy of VKA (INR 2.0–2.5) + aspirin ≤100 mg/day + clopidogrel 75 mg/day Up to 12th month: combination of VKA (INR 2.0–2.5) + clopidogrel 75 mg/day[b] (or aspirin 100 mg/day) Lifelong: VKA (INR 2.0–3.0) alone
	ACS	Bare-metal/ drug-eluting	6 months: triple therapy of VKA (INR 2.0–2.5) + aspirin ≤100 mg/day + clopidogrel 75 mg/day Up to 12th month: combination of VKA (INR 2.0–2.5) + clopidogrel 75 mg/day[b] (or aspirin 100 mg/day) Lifelong: VKA (INR 2.0–3.0) alone
High (e.g. HAS-BLED score ≥3) **= stent nu recommandé**	Elective	Bare-metal[c]	2–4 weeks: triple therapy of VKA (INR 2.0–2.5) + aspirin ≤100 mg/day + clopidogrel 75 mg/day Lifelong: VKA (INR 2.0–3.0) alone
	ACS	Bare-metal[c]	4 weeks: triple therapy of VKA (INR 2.0–2.5) + aspirin ≤100 mg/day + clopidogrel 75 mg/day Up to 12th month: combination of VKA (INR 2.0–2.5) + clopidogrel 75 mg/day[b] (or aspirin 100 mg/day) Lifelong: VKA (INR 2.0–3.0) alone

Stent actif ou SCA = jusqu'à 6 mois de triple association AVK + Aspirine 75 mg/j + Clopidogrel puis jusqu'à 1 an de double association AVK + clopidogrel puis AVK en monothérapie au long cours

RESUME

- Si HAS-BLED <3
  - ACTP programmée stent acier :
    - Triple TT (INR<2,5) puis AVK seul (INR 2 à 3)
  - ACTP stent actif ou SCA:
    - Triple TT (INR<2,5) 6 mois puis 2 TT (INR<2,5) 6 mois puis AVK seul

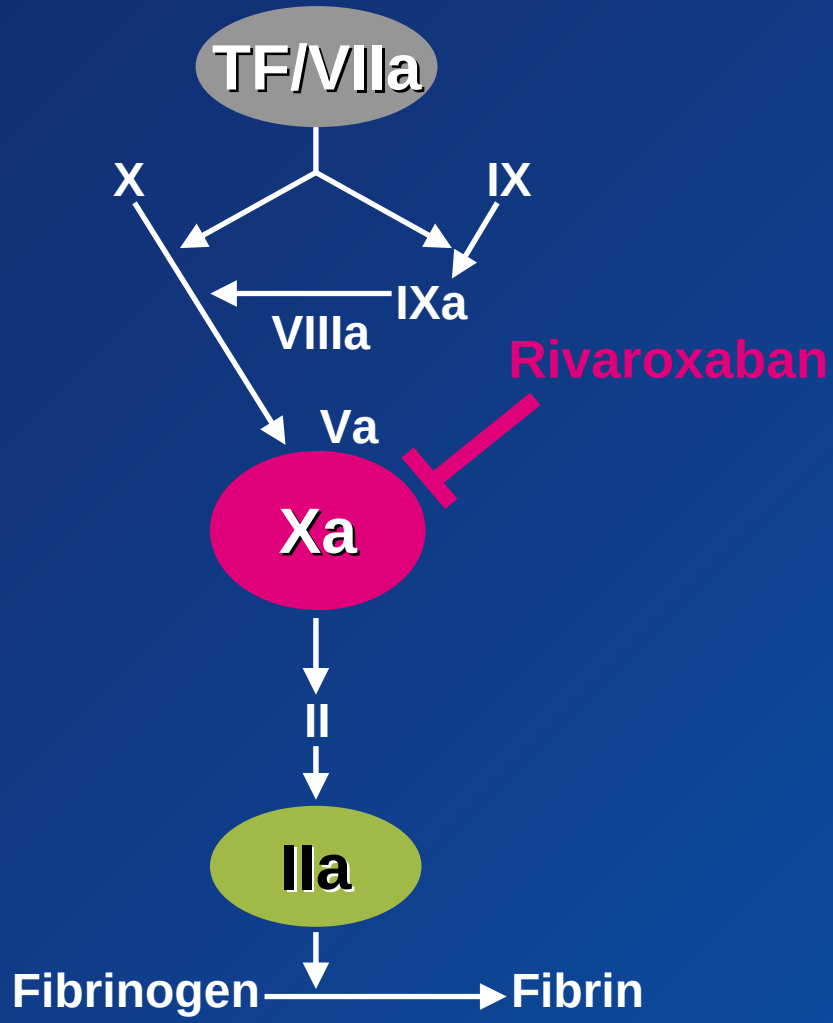
- Si HAS-BLED > 3 = stent acier recommandé
  - ACTP programmée: Triple TT (INR<2,5) 1 mois puis AVK seul (INR 2 à 3)
  - SCA: Triple TT (INR<2,5) 1mois puis 2 TT (INR<2,5) 1 an puis AVK seul

What’s up en 2010

Traitement anti-thrombotique de FA

Background
Rivaroxaban

- Direct, specific, competitive factor Xa inhibitor
- Half-life 5-13 hours
- Clearance :
  - 1/3 direct renal excretion
  - 2/3 metabolism via CYP 450 enzymes
- Oral, once daily dosing without need for coagulation monitoring
- Studied in >25,000 patients in post-op, DVT, PE and ACS patients



Adapted from Weitz *et al*, 2005; 2008

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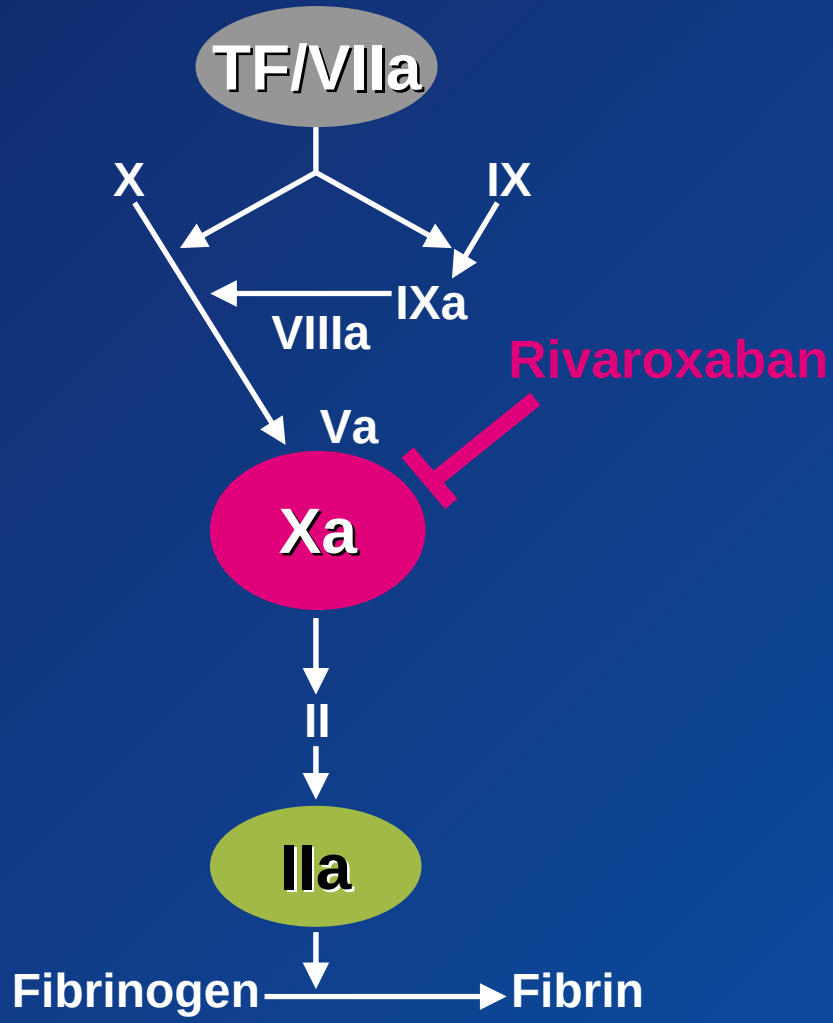


Adapted from Weitz *et al*, 2005; 2008

Study Design

Risk Factors
- CHF
- Hypertension
- Age ≥ 75
- Diabetes

At least 2 or 3 required*

OR
- Stroke, TIA or Systemic embolus

Atrial Fibrillation

Rivaroxaban

20 mg daily
15 mg for Cr Cl 30-49 ml/min

Randomize
Double Blind / Double Dummy
(n ~ 14,000)

Warfarin

INR target - 2.5
(2.0-3.0 inclusive)

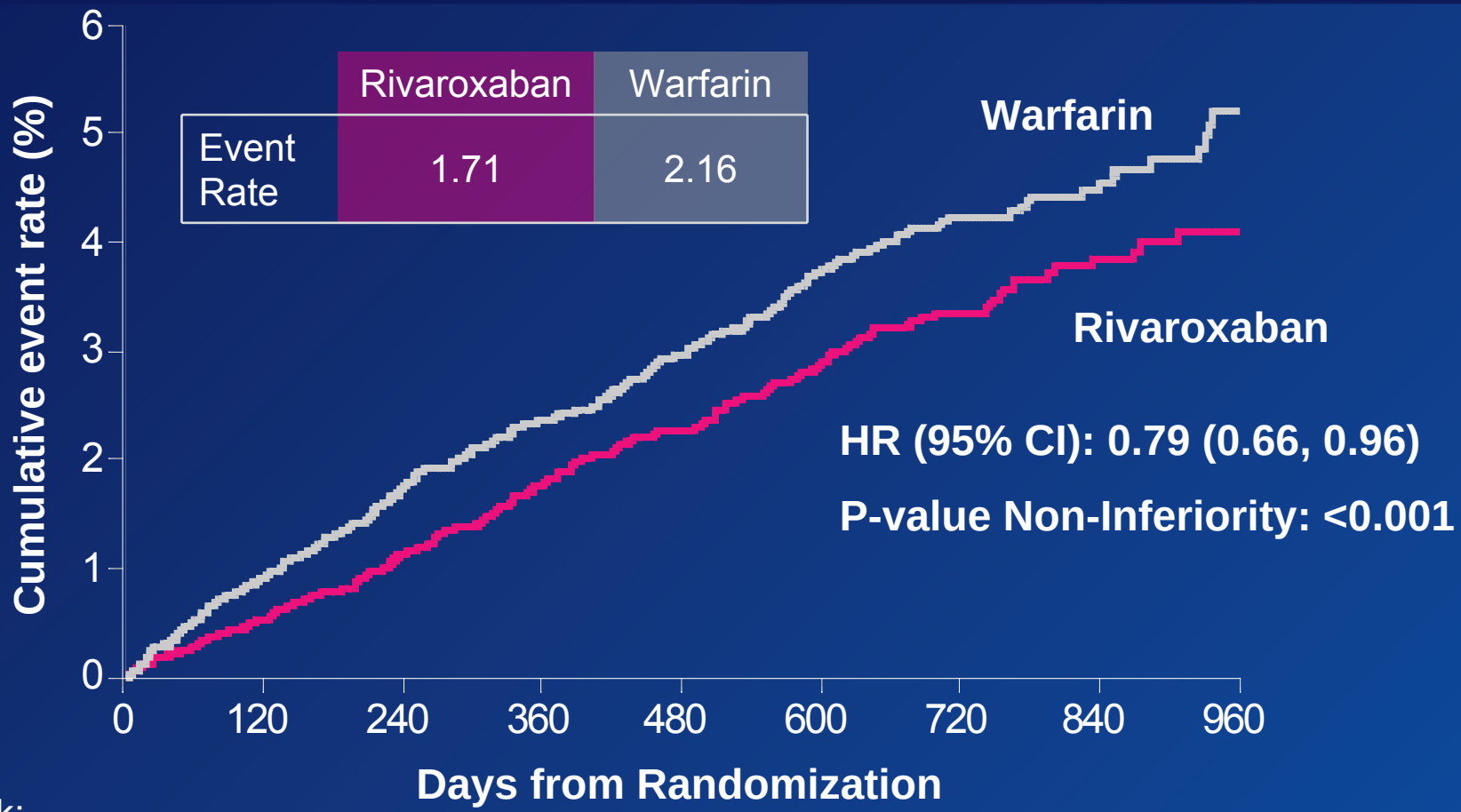
Monthly Monitoring
Adherence to standard of care guidelines

Primary Endpoint: Stroke or non-CNS Systemic Embolism

* Enrollment of patients without prior Stroke, TIA or systemic embolism and only 2 factors capped at 10%

ROCKET AF

Primary Efficacy Outcome
Stroke and non-CNS Embolism



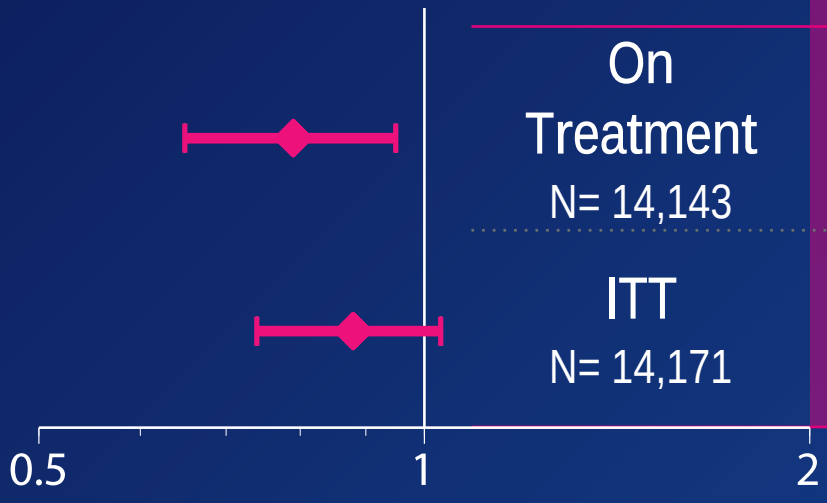
No. at risk:

Rivaroxaban	6958	6211	5786	5468	4406	3407	2472	1496	634
Warfarin	7004	6327	5911	5542	4461	3478	2539	1538	655

Event Rates are per 100 patient-years
Based on Protocol Compliant on Treatment Population

ROCKET AF

Primary Efficacy Outcome
Stroke and non-CNS Embolism



	Rivaroxaban Event Rate	Warfarin Event Rate	HR (95% CI)	P-value
On Treatment N= 14,143	1.70	2.15	0.79 (0.65,0.95)	0.015
ITT N= 14,171	2.12	2.42	0.88 (0.74,1.03)	0.117

Event Rates are per 100 patient-years
Based on Safety on Treatment or Intention-to-Treat thru Site Notification populations

ROCKET AF

Primary Safety Outcomes

	Rivaroxaban	Warfarin		
	Event Rate or N (Rate)	Event Rate or N (Rate)	HR (95% CI)	P-value
Major	3.60	3.45	1.04 (0.90, 1.20)	0.576
≥2 g/dL Hgb drop	2.77	2.26	1.22 (1.03, 1.44)	0.019
Transfusion (> 2 units)	1.65	1.32	1.25 (1.01, 1.55)	0.044
Critical organ bleeding	0.82	1.18	0.69 (0.53, 0.91)	0.007
Bleeding causing death	0.24	0.48	0.50 (0.31, 0.79)	0.003
Intracranial Hemorrhage	55 (0.49)	84 (0.74)	0.67 (0.47, 0.94)	0.019
Intraparenchymal	37 (0.33)	56 (0.49)	0.67 (0.44, 1.02)	0.060
Intraventricular	2 (0.02)	4 (0.04)		
Subdural	14 (0.13)	27 (0.27)	0.53 (0.28, 1.00)	0.051
Subarachnoid	4 (0.04)	1 (0.01)		

Event Rates are per 100 patient-years
Based on Safety on Treatment Population

ROCKET AF

Guidelines for the management of atrial fibrillation

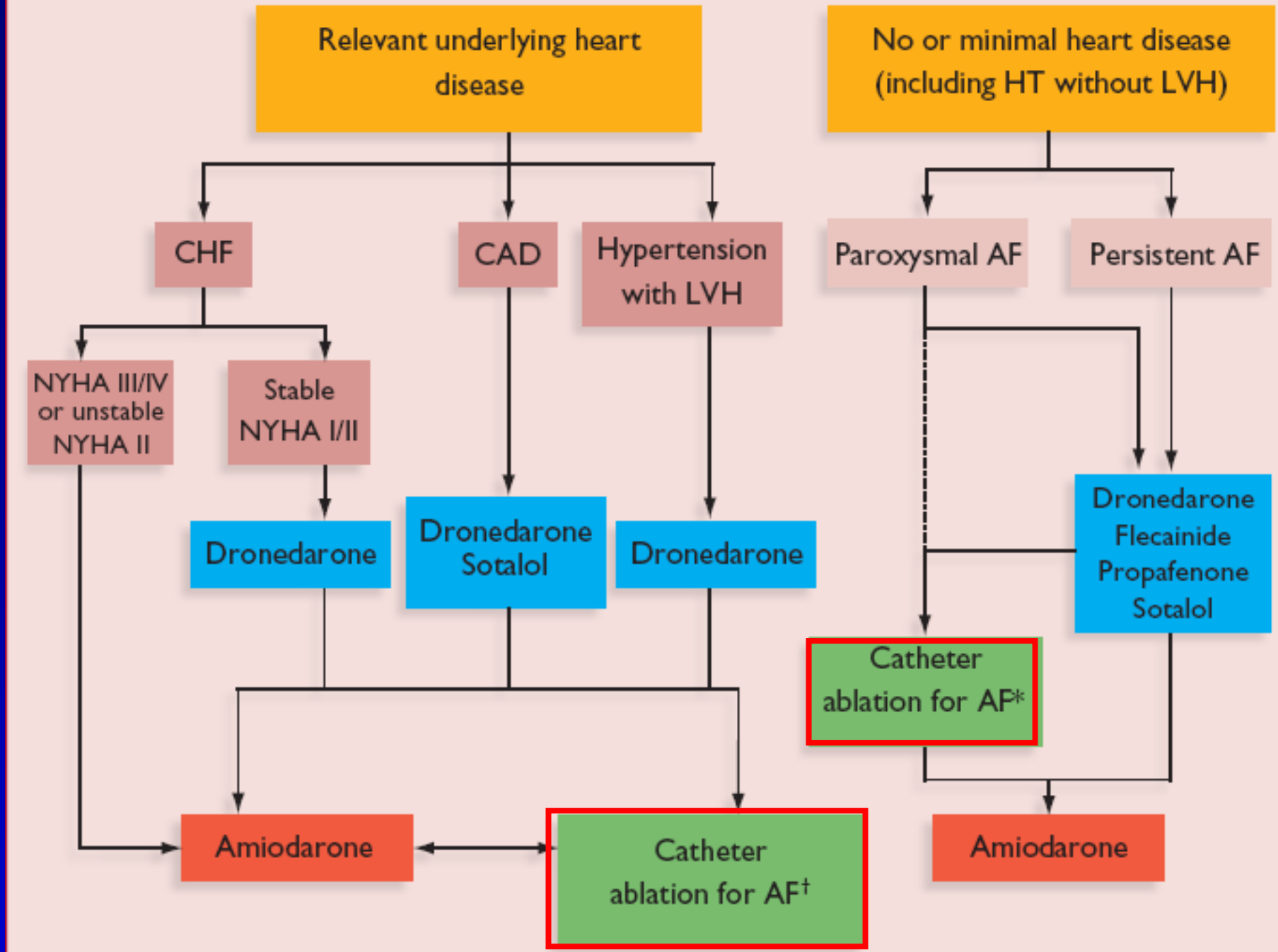
EUROPEAN SOCIETY OF CARDIOLOGY®

The Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC)

The European Society of Cardiology 2010

Le Traitement non-Antiarythmique de la Fibrillation Atriale

CRYO-ABLATION…


Relevant underlying heart disease
No or minimal heart disease (including HT without LVH)
CHF
CAD
Hypertension with LVH
Paroxysmal AF
Persistent AF
NYHA III/IV or unstable NYHA II
Stable NYHA I/II
Dronedarone
Dronedarone Sotalol
Dronedarone
Dronedarone Flecainide Propafenone Sotalol
Catheter ablation for AF*
Amiodarone
Catheter ablation for AF†
Amiodarone

La place de l'ablation de la FA

Ablation of common atrial flutter is recommended as part of an AF ablation procedure if documented prior to the ablation procedure or occurring during the AF ablation.	I	B
Catheter ablation for paroxysmal AF should be considered in symptomatic patients who have previously failed a trial of antiarrhythmic medication.	IIa	A
Ablation of persistent symptomatic AF that is refractory to antiarrhythmic therapy should be considered a treatment option.	IIa	B
In patients post-ablation, LMWH or i.v. UFH should be considered as 'bridging therapy' prior to resumption of systemic OAC, which should be continued for a minimum of 3 months. Thereafter, the individual stroke risk factors of the patient should be considered when determining if OAC therapy should be continued.	IIa	C

Précision en fonction du type de FA

Niveaux de preuves A et B

La place de l'ablation de la FA

Continuation of OAC therapy post-ablation is recommended in patients with I 'major' ('definitive') or ≥2 'clinically relevant non-major' risk factors (i.e. CHA_2DS_2-VASc score ≥2).	IIa	B
Catheter ablation of AF in patients with heart failure may be considered when antiarrhythmic medication, including amiodarone, fails to control symptoms.	IIb	B
Catheter ablation of AF may be considered prior to antiarrhythmic drug therapy in symptomatic patients despite adequate rate control with paroxysmal symptomatic AF and no significant underlying heart disease.	IIb	B
Catheter ablation of AF may be considered in patients with symptomatic long-standing persistent AF refractory to antiarrhythmic drugs.	IIb	C

Nouveauté: Ablation de FA après échec d'un trt bradycardisant
Classe IIb

Nouveauté: Ablation de FA > 1 an
Classe IIb

What’up dans IC

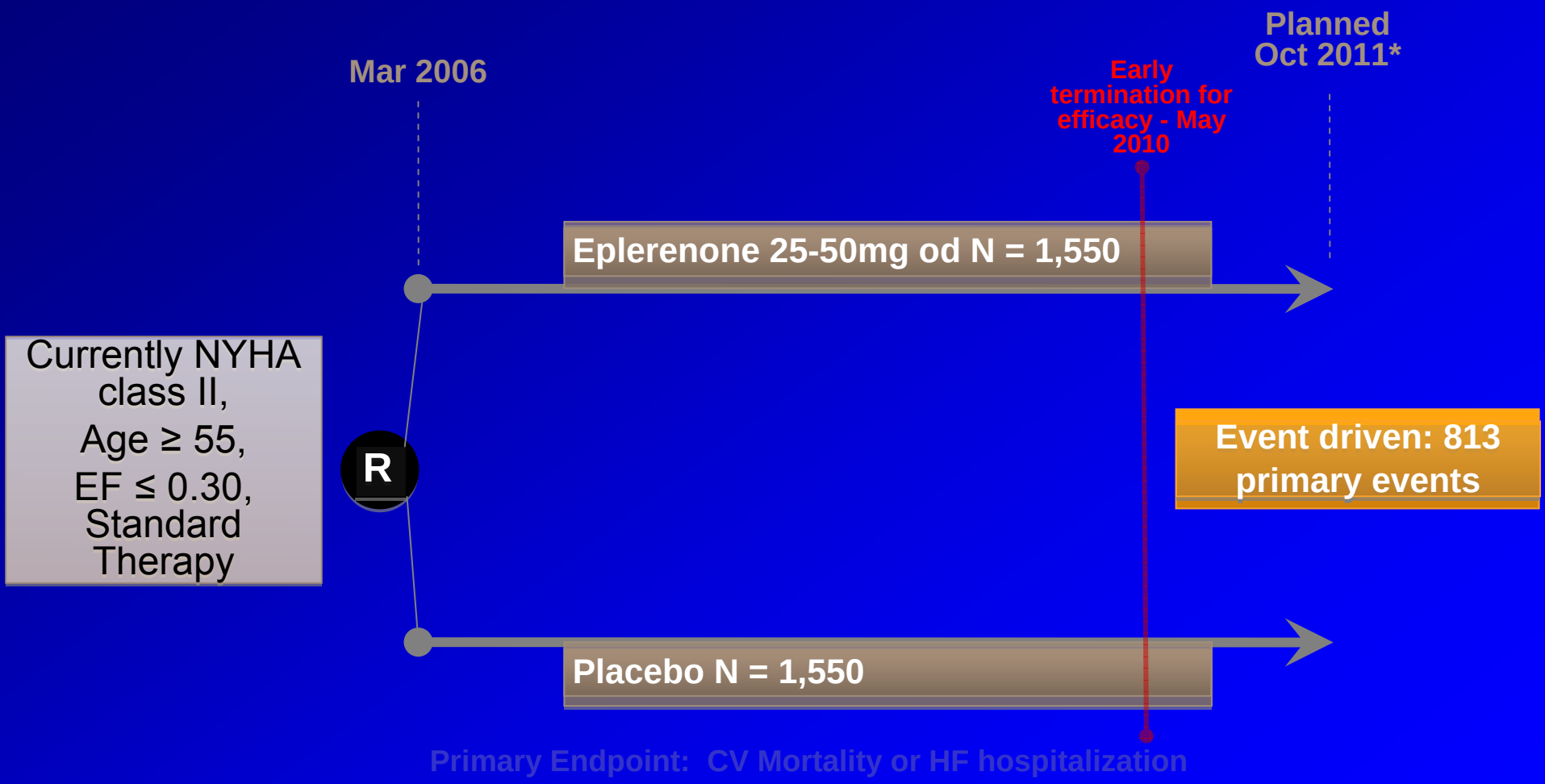
- Etude EMPHASIS-HF

- Etude SCHIFT

What’up dans IC

- Etude EMPHASIS-HF

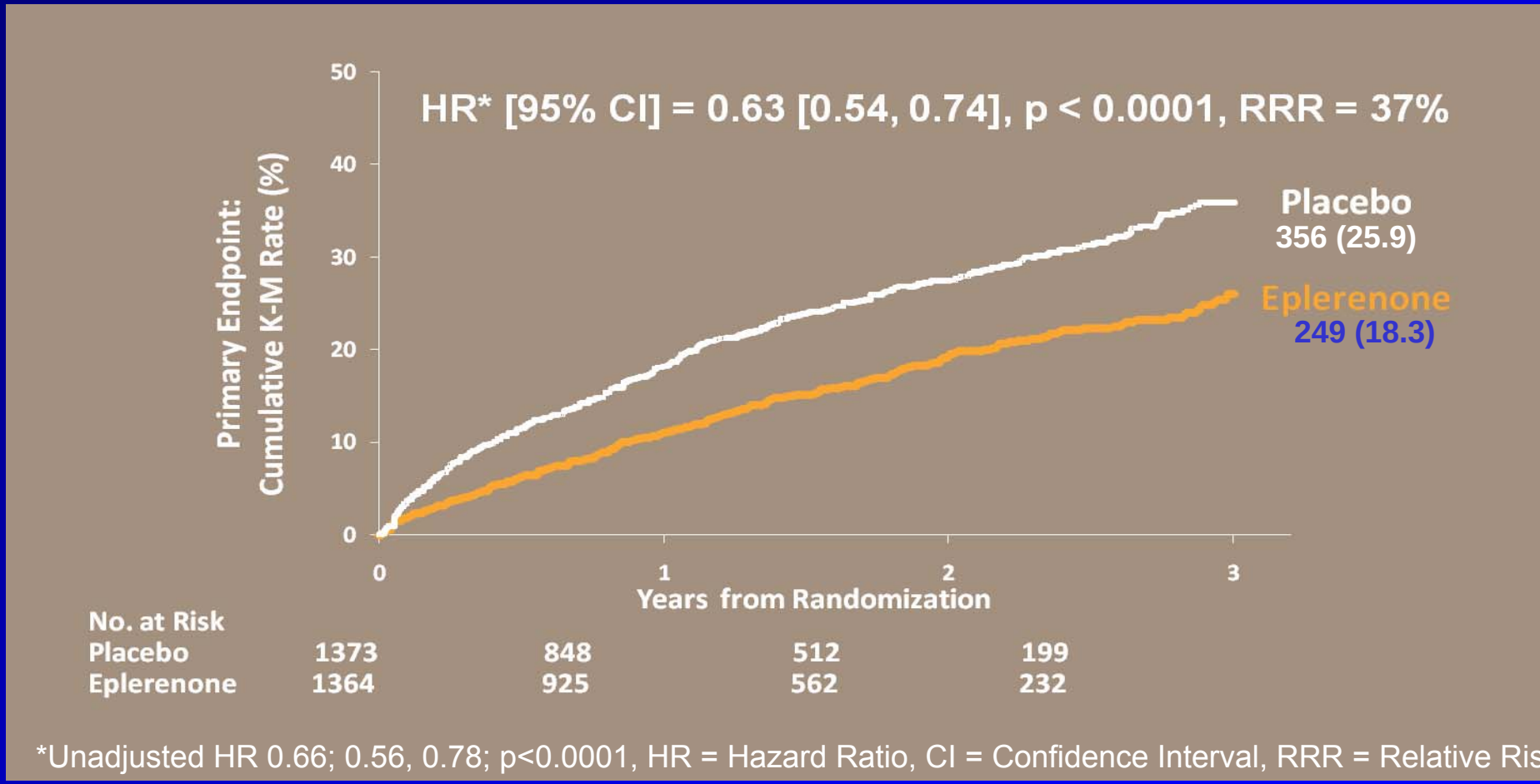
EMPHASIS-HF Study
DESIGN



* See Current Status slide

Zannad F et al. Eur J Heart Fail 2010;12:617-622.

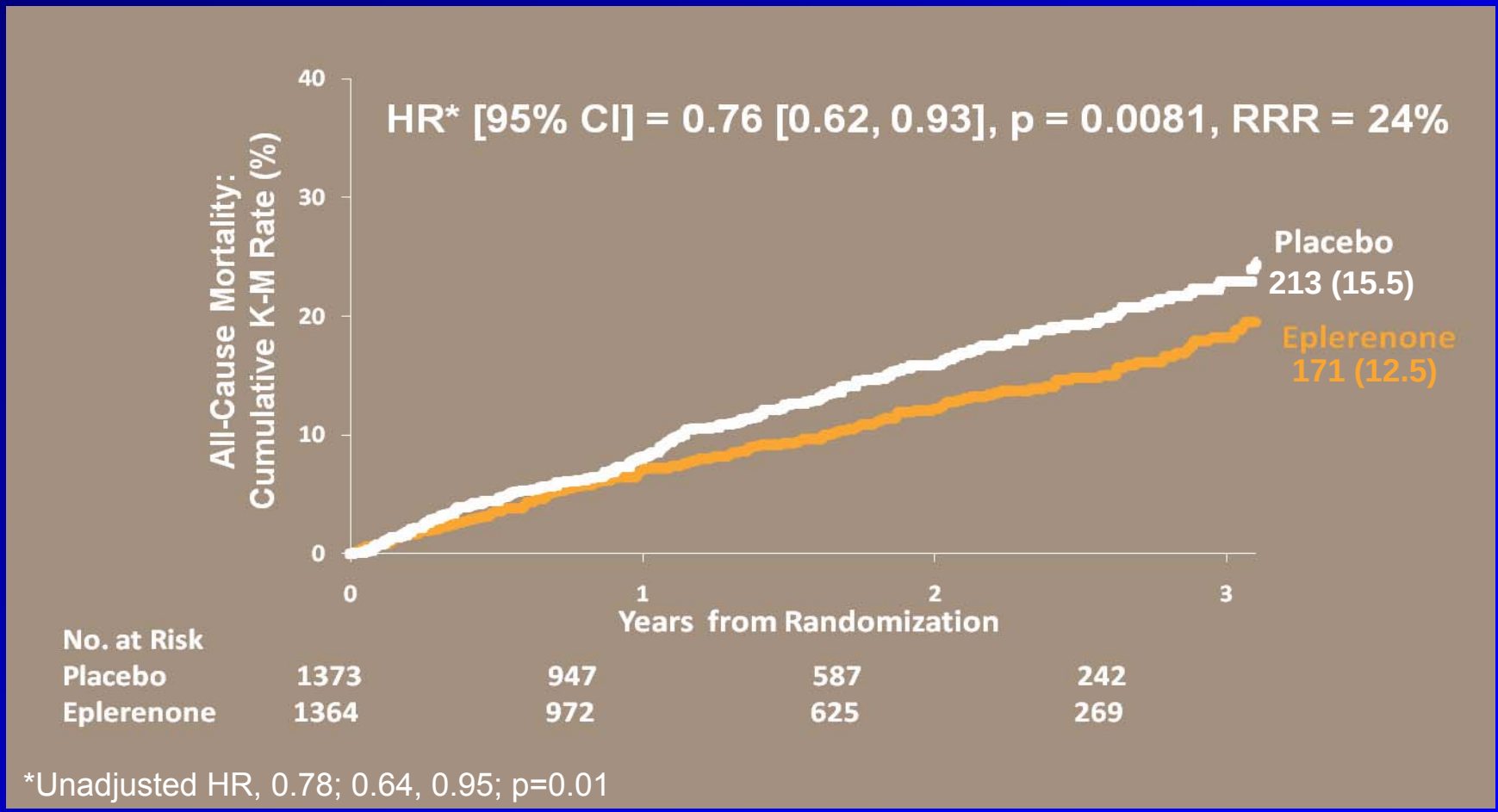
EMPHASIS-HF Study
PRIMARY ENDPOINT RESULTS
CV DEATH OR HOSPITALIZATION FOR HF



*Unadjusted HR 0.66; 0.56, 0.78; p<0.0001, HR = Hazard Ratio, CI = Confidence Interval, RRR = Relative Risk

Zannad F et al. N Engl J Med. 2010 Nov 14. [Epub ahead of print]

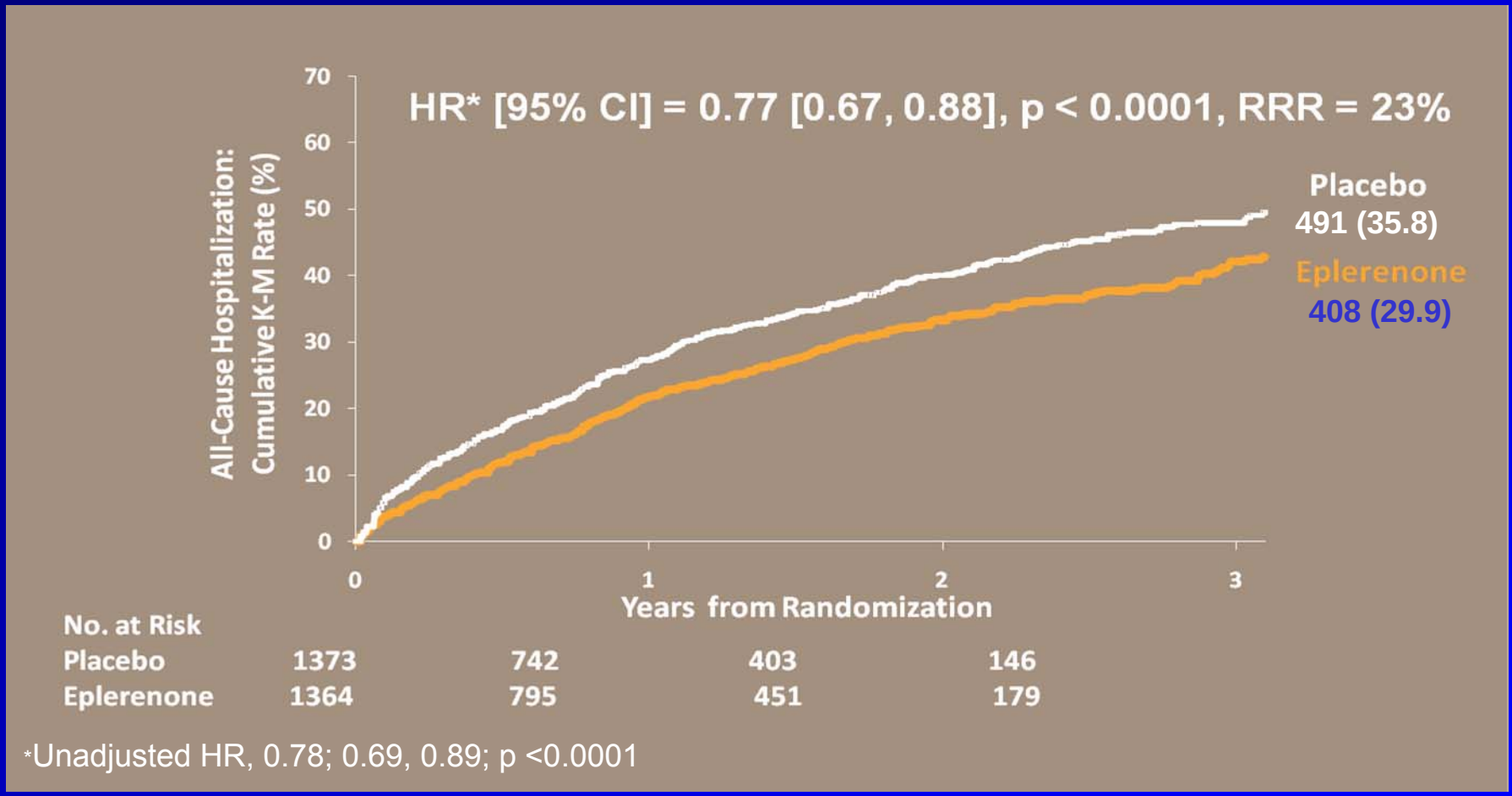
EMPHASIS-HF Study
SECONDARY ENDPOINT RESULTS
MORTALITY FROM ANY CAUSE



*Unadjusted HR, 0.78; 0.64, 0.95; p=0.01

Zannad F et al. N Engl J Med. 2010 Nov 14. [Epub ahead of print]

EMPHASIS-HF Study
SECONDARY ENDPOINT RESULTS
HOSPITALIZATION FOR ANY CAUSE

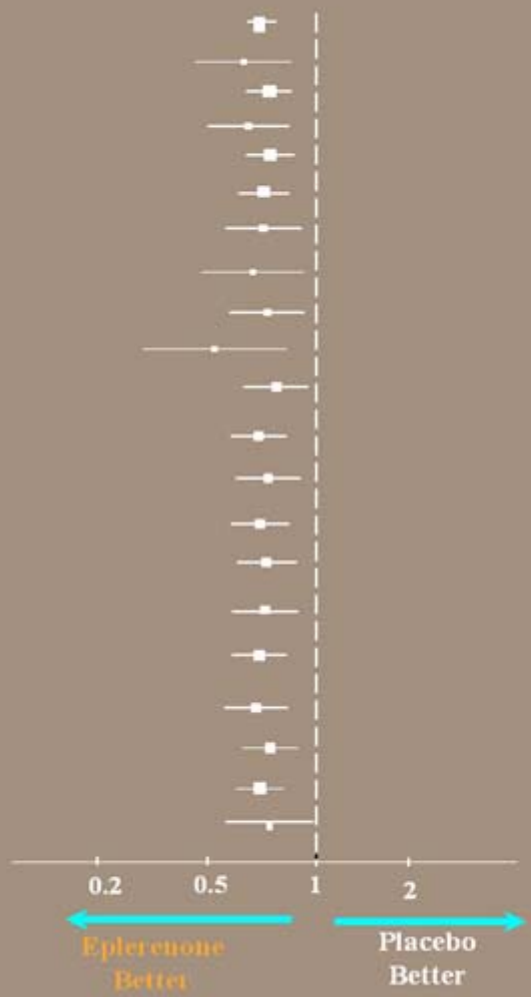


*Unadjusted HR, 0.78; 0.69, 0.89; p <0.0001

Zannad F et al. N Engl J Med. 2010 Nov 14. [Epub ahead of print]

EMPHASIS-HF Study
PRIMARY ENDPOINT RESULTS
SUBGROUP ANALYSIS (NNT= 19)

Baseline Variable	Subgroup	No. of Patients	P-value for Interaction
Overall		2,737	
Gender	Female	610	0.36
	Male	2,127	
Age	< 65 yr	883	0.37
	>= 65 yr	1,854	
Age	< 75 yr	2,080	1.00
	>= 75 yr	657	
Region	Asia/Middle East/ Africa	380	0.46
	East Europe	911	
	South/North America	346	
	West Europe / Australia	1,100	
Systolic BP	< Median	1,352	0.65
	>= Median	1,384	
Pulse Pressure	< Median	1,272	0.75
	>= Median	1,464	
Heart Rate	< Median	1,340	0.79
	>= Median	1,383	
eGFR	< 60 ml/min/1.73m2	912	0.50
	>= 60 ml/min/1.73m2	1,821	
Primary Diagnosis	Ischaemic Heart Failure	1,886	0.73
	Non-Ischaemic Heart Failure	846	



Zannad F et al. N Engl J Med. 2010 Nov 14. [Epub ahead of print]

EMPHASIS-HF Study
SAFETY
ADVERSE EVENTS

Patients with an adverse event (AE)*

Outcome	Eplerenone (N=1360)	Placebo (N=1373)	P Value
All	979 (72)	1007 (73.6)	0.37
Hyperkalemia – n (%)	109 (8)	50 (3.7)	<0.001
Hypokalemia – n (%)	16 (1.2)	30 (2.2)	0.05
Renal failure – n (%)	38 (2.8)	41 (3.0)	0.82
Hypotension – n (%)	46 (3.4)	37 (2.7)	0.32
Gynecomastia and other breast disorders – n (%)	10 (0.7)	14 (1.0)	0.54

*Investigator reported adverse events

Zannad F et al. N Engl J Med. 2010 Nov 14. [Epub ahead of print]

What’up dans IC

- Etude SCHIFT

Progrès dans l'amélioration du pronostic des insuffisants cardiaques

Taux de décès pour insuffisance cardiaque (%)

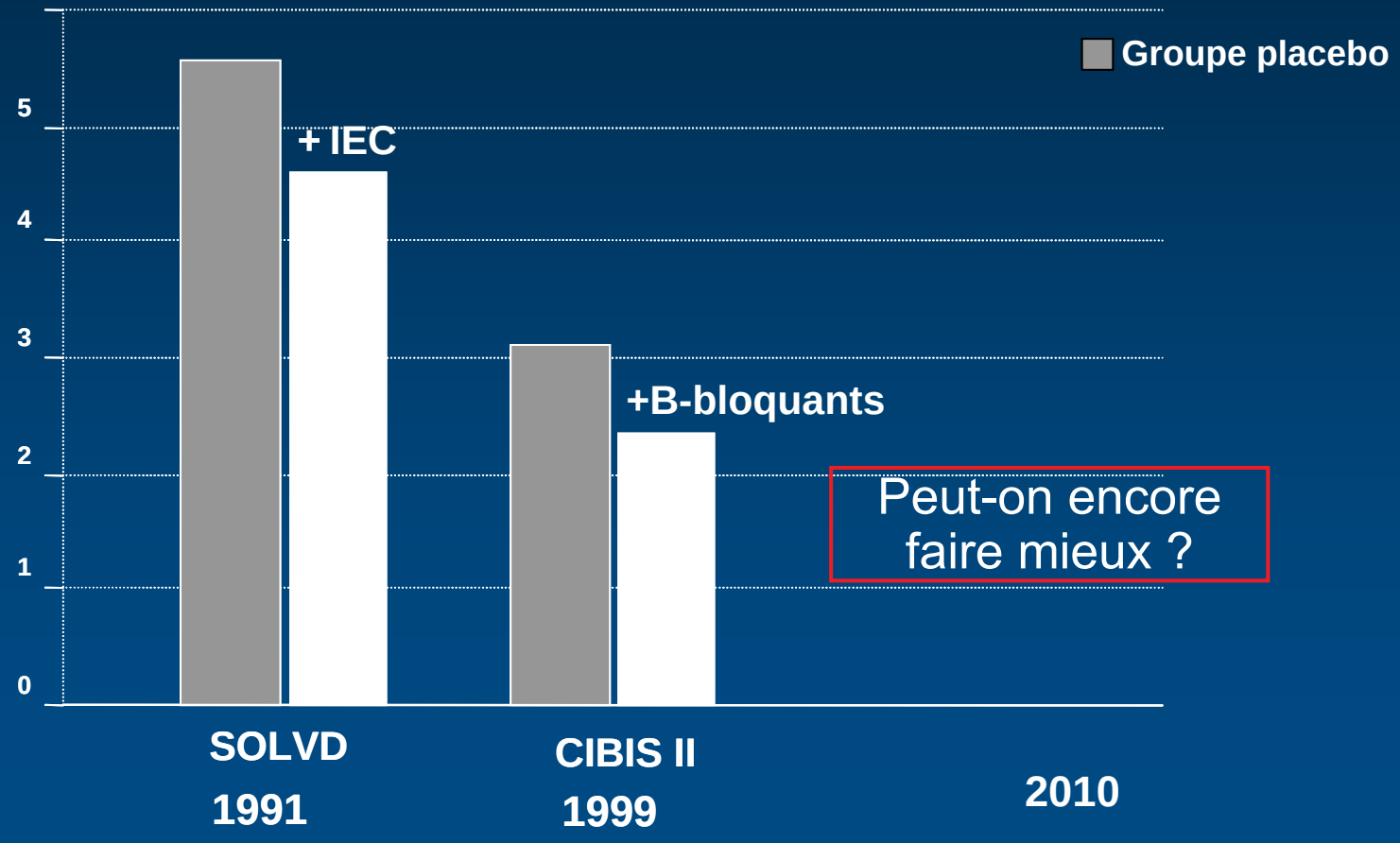
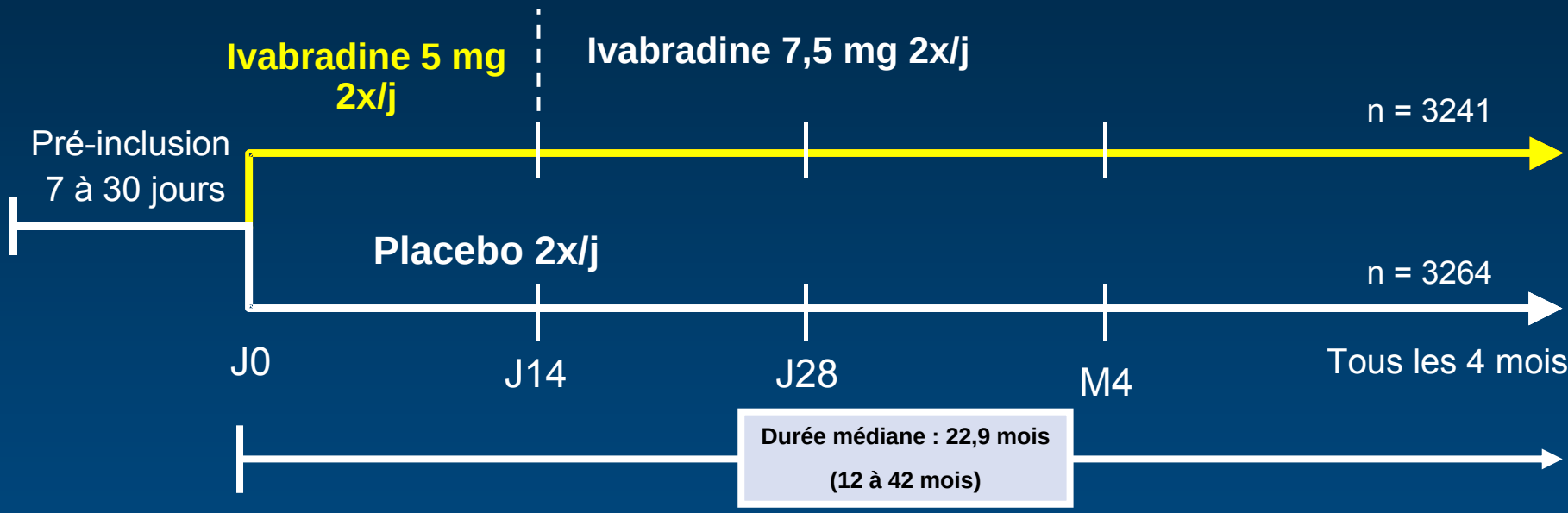


Schéma de l'étude



Traitement par Procoralan

- Dose d'initiation de 5 mg x 2/j
- Après 14 jours : passage à 7,5 mg x 2/j sauf si la FC de repos est ≤ 60 bpm
- Si FC ≤ 50 bpm ou symptômes de bradycardie → 2,5 mg x 2/j (puis arrêt si persistance)

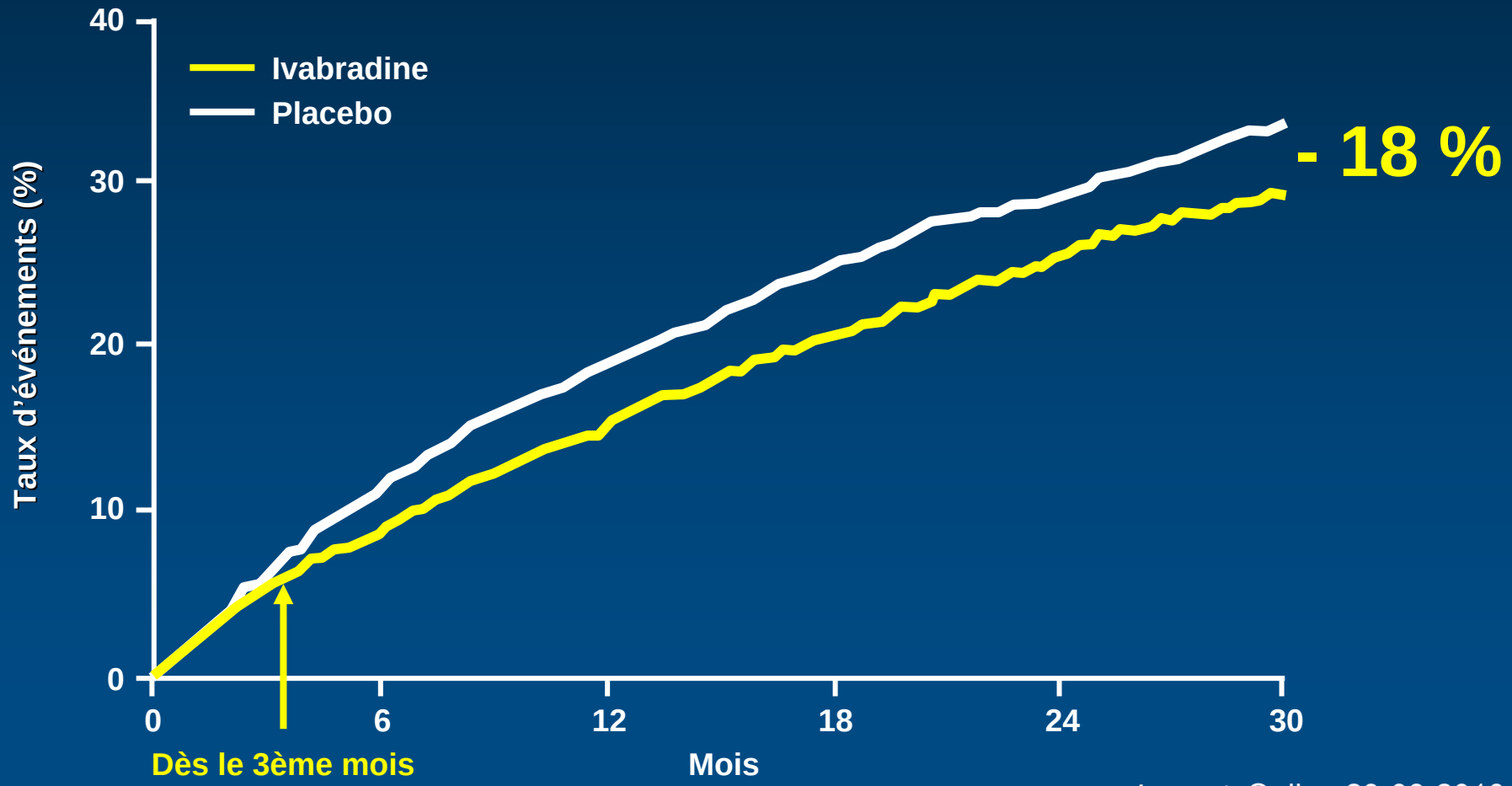
(les adaptations posologiques sont autorisées à n'importe quel temps de l'étude)

Swedberg K, et al. *Eur J Heart Fail.* 2010;12:75-81.

Critère primaire

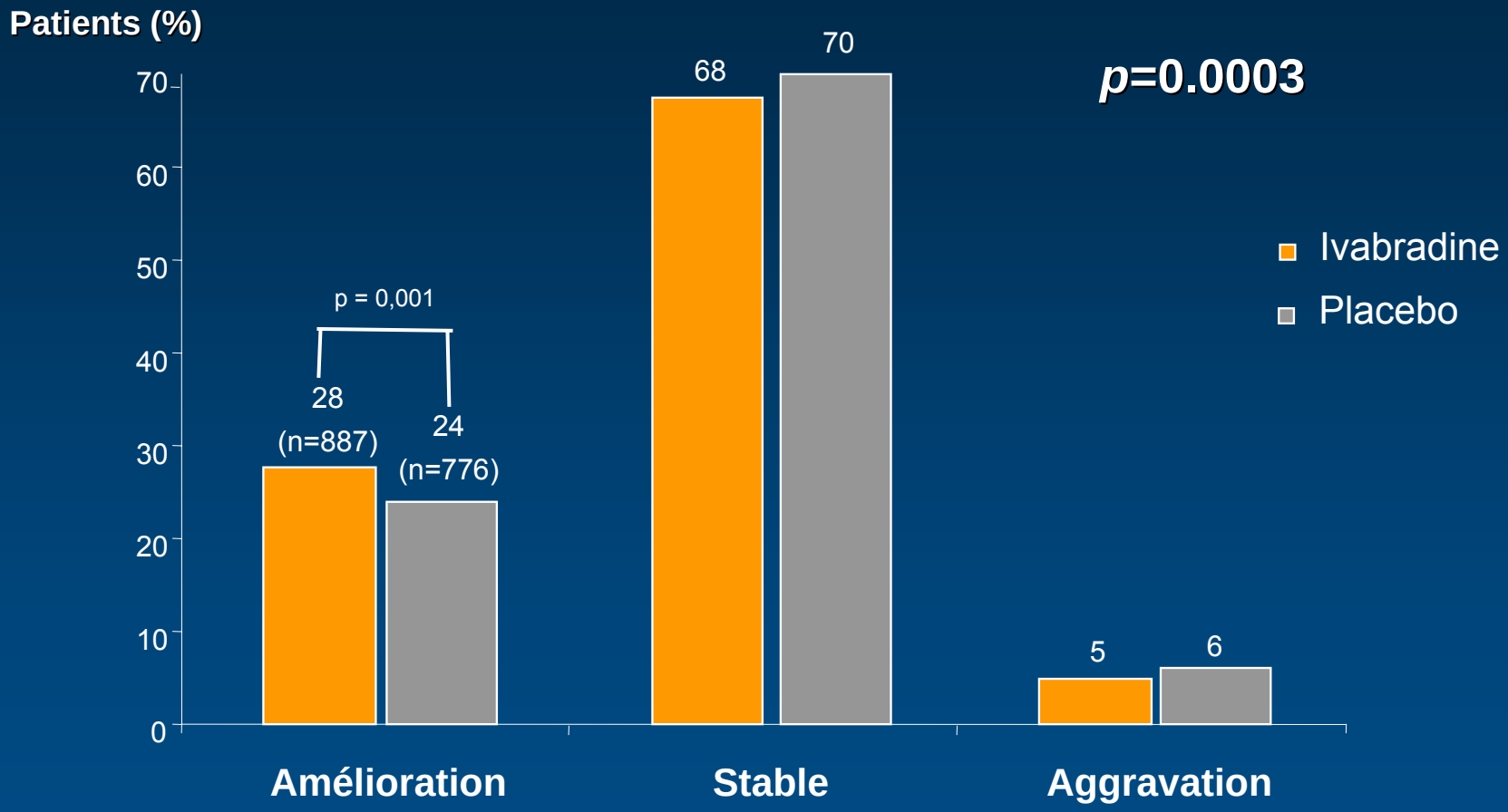
Ivabradine n=793 (14,5% /an) Placebo n=937 (17,7% /an)

HR = 0,82 p<0,0001



Lancet. Online 29-08-2010

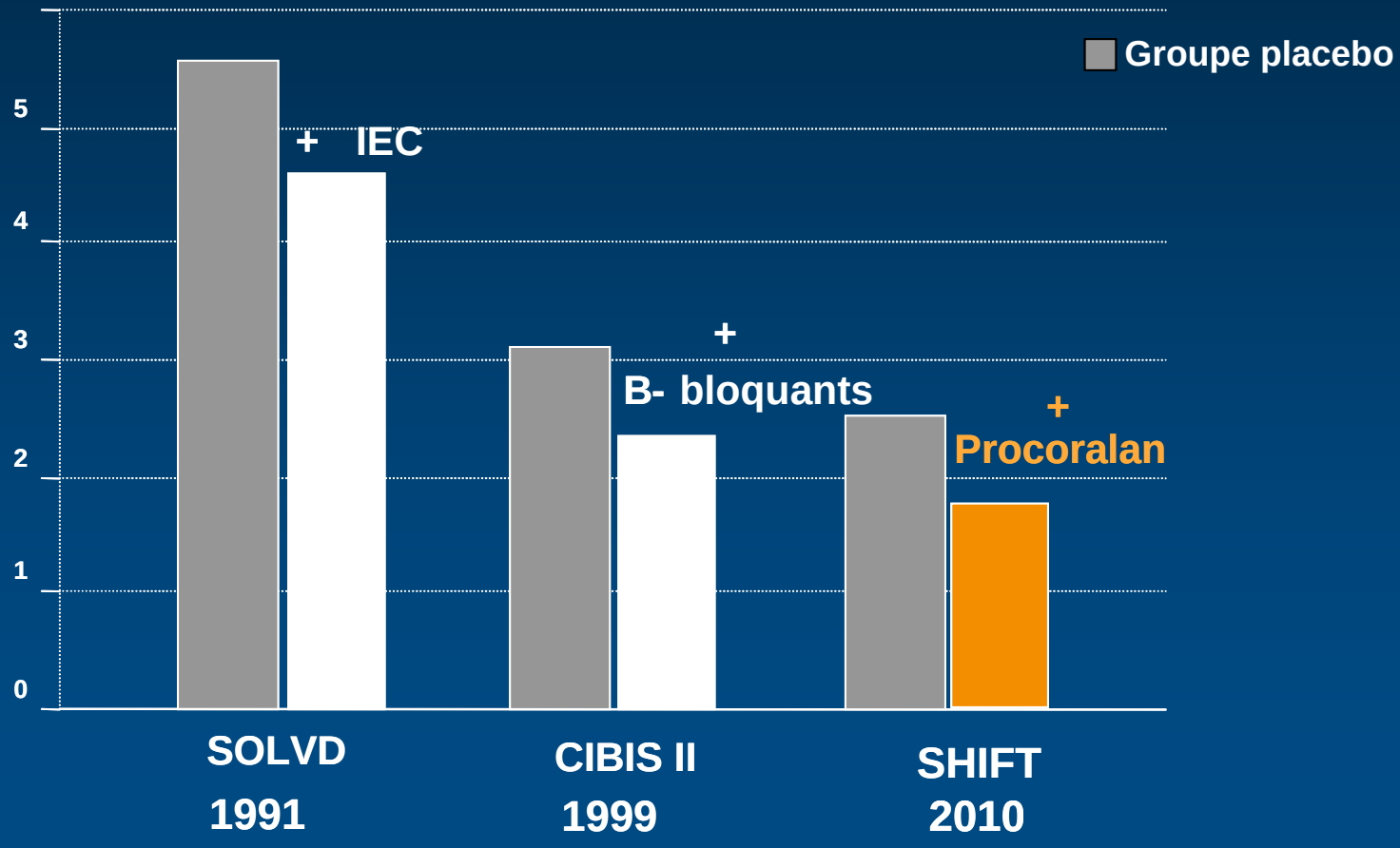
Changement de classes NYHA



Lancet. Online 29-08-2010

Progrès dans l'amélioration du pronostic des insuffisants cardiaques

Taux de décès pour insuffisance cardiaque, %



What’up en coronaropathie

- Aspirine
- Clopidogrel
- Prasugrel
- Ticagrelor

Study Design

UA / NSTEMI (moderate-high risk) **STEMI** (if primary PCI)
All receiving ASA; clopidogrel-treated or -naïve;
randomised within 24 h of index event

(N=18,657)

Clopidogrel
If pretreated, no additional loading dose;
if naïve, standard 300 mg loading dose,
then 75 mg od maintenance;
(additional 300 mg allowed pre PCI)

AZD6140
180 mg loading dose, then
90 mg bd maintenance;
(additional 90 mg pre-PCI)

12-month maximum exposure

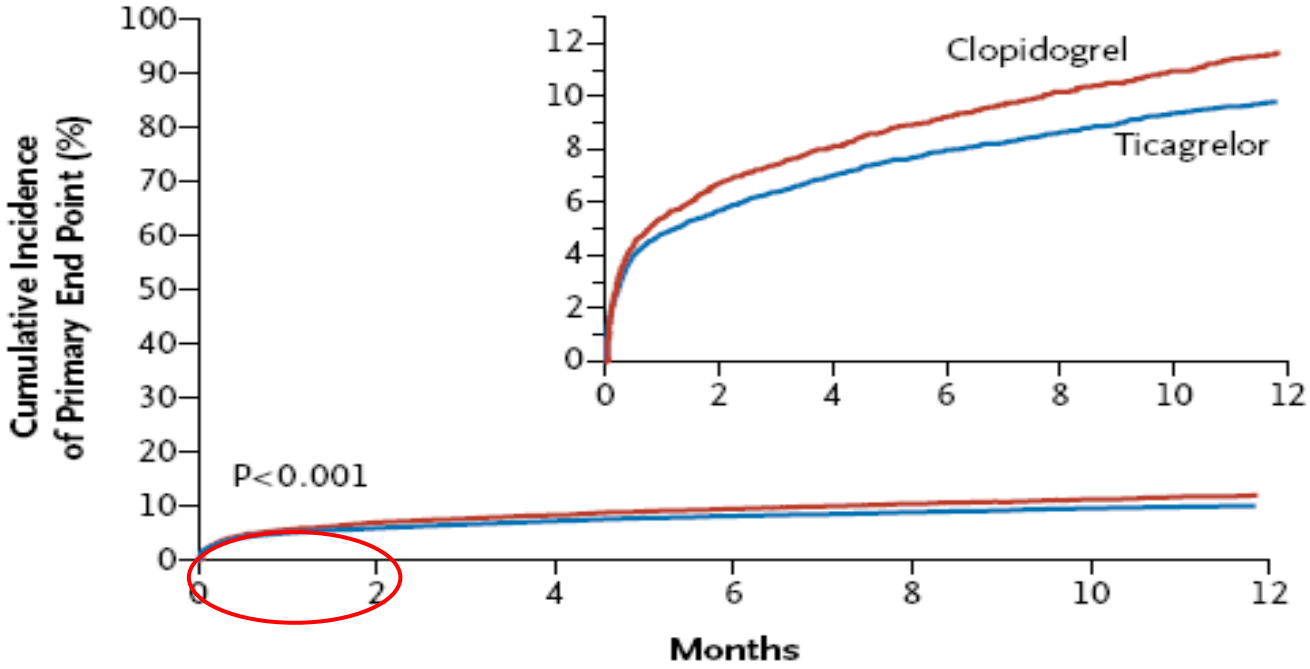
Primary end point:
- CVD / MI / stroke

Secondary end point:
- CVD / MI / stroke in patients with intent for invasive management
- CVD / MI / stroke / recurrent ischaemia / TIA / other arterial thrombotic events

bd = twice daily; CVD = cardiovascular death; od = once daily; TIA = transient ischaemic attack.

Ticagrelor : Etude PLATO

Evénements ischémiques

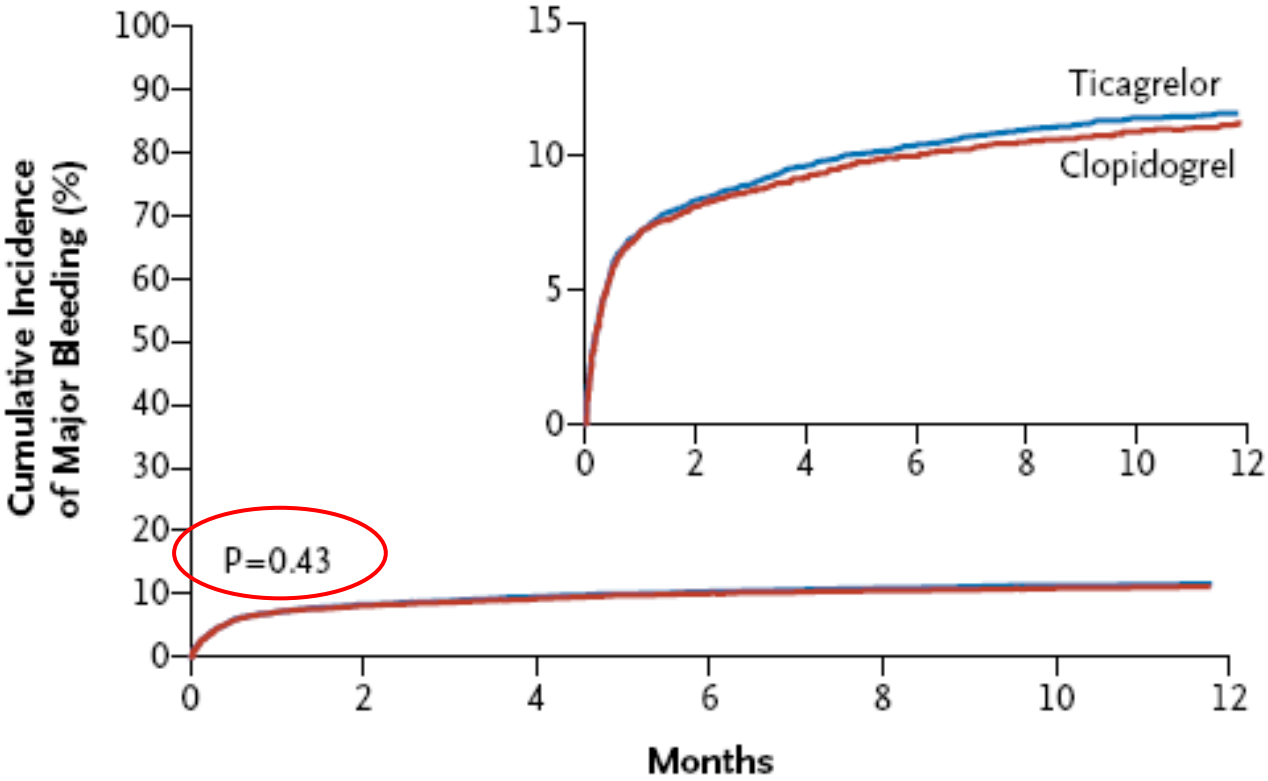


Wallentin L et al; NEJM 2009

AstraZeneca

Ticagrelor : Etude PLATO

Evénements hémorragiques



Wallentin L et al; NEJM 2009

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PLATO : bénéfice sur la mortalité

End Point	Ticagrelor Group	Clopidogrel Group	Hazard Ratio for Ticagrelor Group (95% CI)	P Value†
Primary end point: death from vascular causes, MI, or stroke — no./total no. (%)	864/9333 (9.8)	1014/9291 (11.7)	0.84 (0.77–0.92)	<0.001‡
Secondary end points — no./total no. (%)				
Death from any cause, MI, or stroke	901/9333 (10.2)	1065/9291 (12.3)	0.84 (0.77–0.92)	<0.001‡
Death from vascular causes, MI, stroke, severe recurrent ischemia, recurrent ischemia, TIA, or other arterial thrombotic event	1290/9333 (14.6)	1456/9291 (16.7)	0.88 (0.81–0.95)	<0.001‡
MI	504/9333 (5.8)	593/9291 (6.9)	0.84 (0.75–0.95)	0.005‡
Death from vascular causes	353/9333 (4.0)	442/9291 (5.1)	0.79 (0.69–0.91)	0.001‡
Stroke	125/9333 (1.5)	106/9291 (1.3)	1.17 (0.91–1.52)	0.22
Ischemic	96/9333 (1.1)	91/9291 (1.1)		0.74
Hemorrhagic	23/9333 (0.2)	13/9291 (0.1)		0.10
Unknown	10/9333 (0.1)	2/9291 (0.02)		0.04
Other events — no./total no. (%)				
Death from any cause	399/9333 (4.5)	506/9291 (5.9)	0.78 (0.69–0.89)	<0.001
Death from causes other than vascular causes	46/9333 (0.5)	64/9291 (0.8)	0.71 (0.49–1.04)	0.08
Severe recurrent ischemia	302/9333 (3.5)	345/9291 (4.0)	0.87 (0.74–1.01)	0.08
Recurrent ischemia	500/9333 (5.8)	536/9291 (6.2)	0.93 (0.82–1.05)	0.22
TIA	18/9333 (0.2)	23/9291 (0.3)	0.78 (0.42–1.44)	0.42
Other arterial thrombotic event	19/9333 (0.2)	31/9291 (0.4)	0.61 (0.34–1.08)	0.09
Death from vascular causes, MI, stroke — no./total no. (%)				
Invasive treatment planned§	569/6732 (8.9)	668/6676 (10.6)	0.84 (0.75–0.94)	0.003‡
Event rate, days 1–30	443/9333 (4.8)	502/9291 (5.4)	0.88 (0.77–1.00)	0.045
Event rate, days 31–360¶	413/8763 (5.3)	510/8688 (6.6)	0.80 (0.70–0.91)	<0.001
Stent thrombosis — no. of patients who received a stent/total no. (%)				
Definite	71/5640 (1.3)	106/5649 (1.9)	0.67 (0.50–0.91)	0.009
Probable or definite	118/5640 (2.2)	158/5649 (2.9)	0.75 (0.59–0.95)	0.02
Possible, probable, or definite	155/5640 (2.9)	202/5649 (3.8)	0.77 (0.62–0.95)	0.01

Wallentin L, et al; NEJM 2009

What'up en 2010

- Dans la FA
  - Anti-Xa= rivaroxaban
  - AVK + AAP
  - HAS-BLED
  - Ablation (cryo-ablation)
  - FA et AVC
- Dans la coronaropathie
  - ticagrelor
- Dans insuffisance cardiaque
  - Eplerenone
  - ivrabradine