

Optimisation du traitement de l'IC

Quelles avancées?

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Liens d'intérêt

- **Consultant / Member of Advisory Boards and Committees:**
Bristol Myers Squibb, Novartis, Servier, Torrent,
MSD, Novo Nordisk, Sanofi, Amgen.

- **Speaker:**
AstraZeneca, BMS, MSD, Sanofi-Aventis, Servier,
Novartis.

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)

Developed with the special contribution of the Heart Failure Association (HFA) of the ESC

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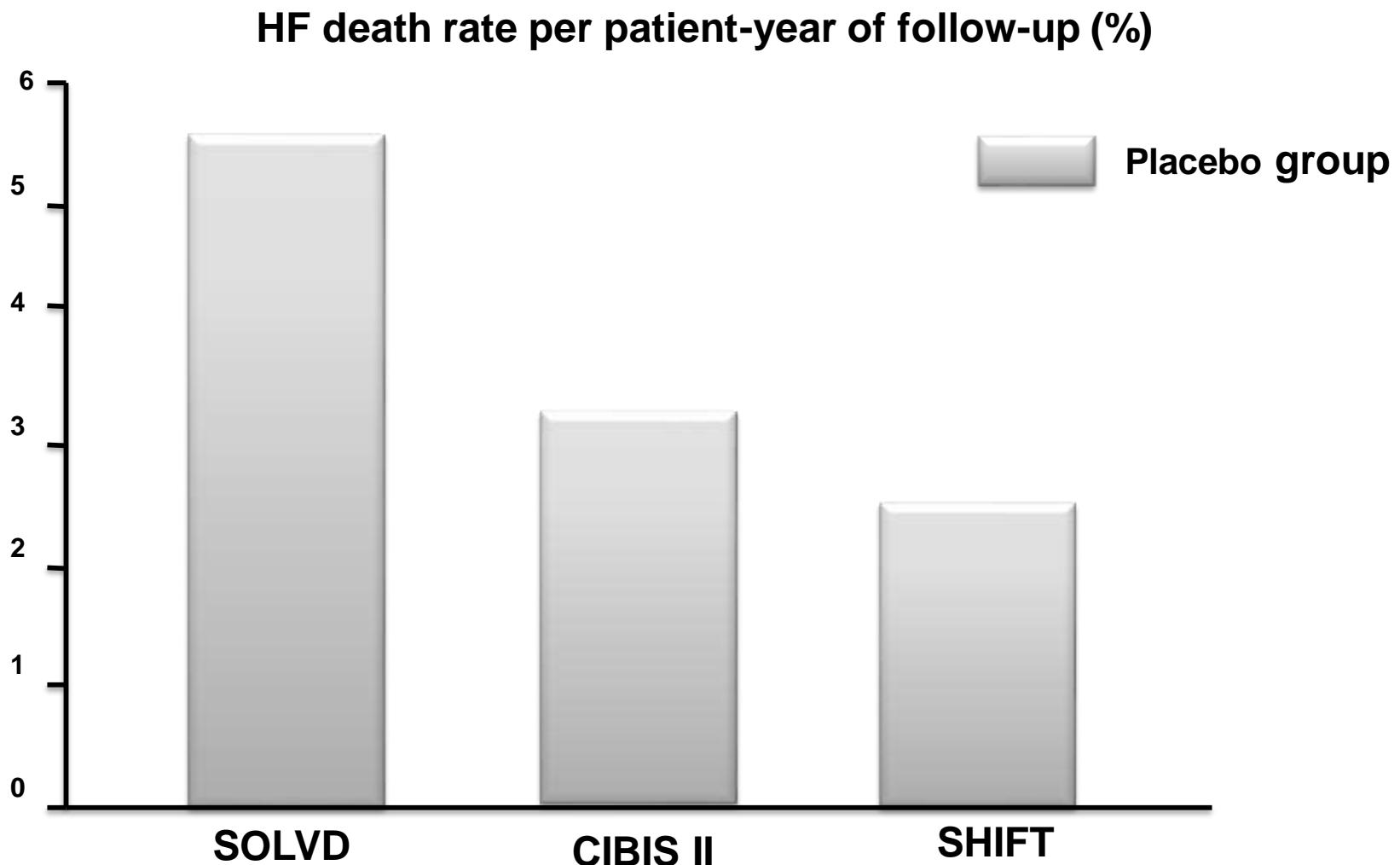
Prévention de l'insuffisance cardiaque

- * **Traiter les facteurs de risque**(hypertension, diabète, obésité, tabac).
- * **Statines** chez les patients à haut risque **de maladie coronaire**
- * **IEC** chez les patients avec **dysfonction VG asymptomatique/maladie coronaire stable** .
- * - **Beta-bloquants** chez les patients avec **dysfonction VG asymptomatique et IDM**

Objectifs du traitement de l'IC à FE altérée

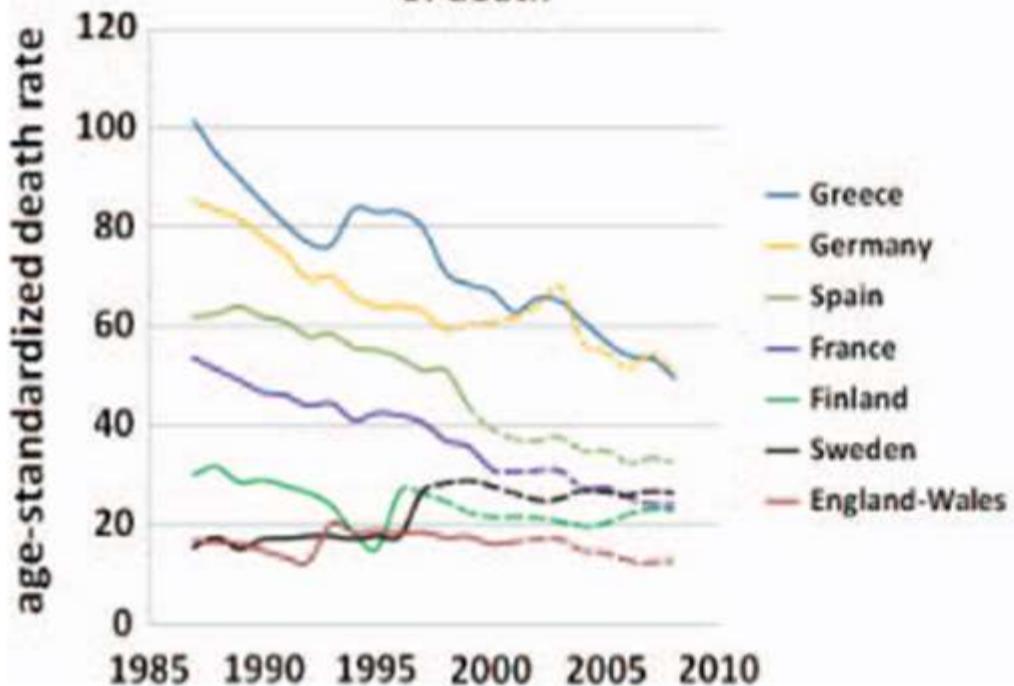
- **Réduire la mortalité**
- **Améliorer**
 - Etat clinique
 - Capacité fonctionnelle
 - Qualité de vie
- **Prévenir les (ré) hospitalisations**

Mortalité par IC essais cliniques

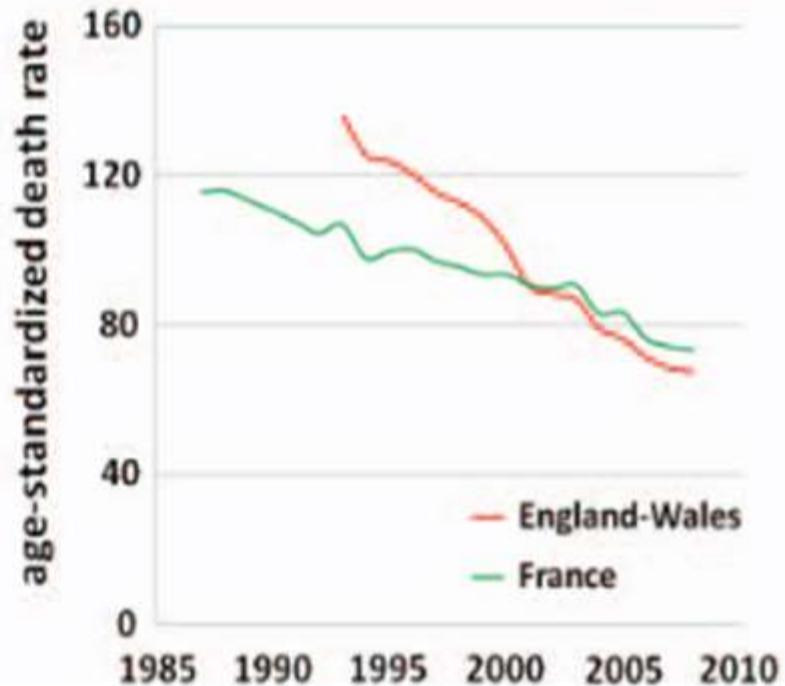


Mortalité par IC en Europe

A Heart Failure as underlying cause of death

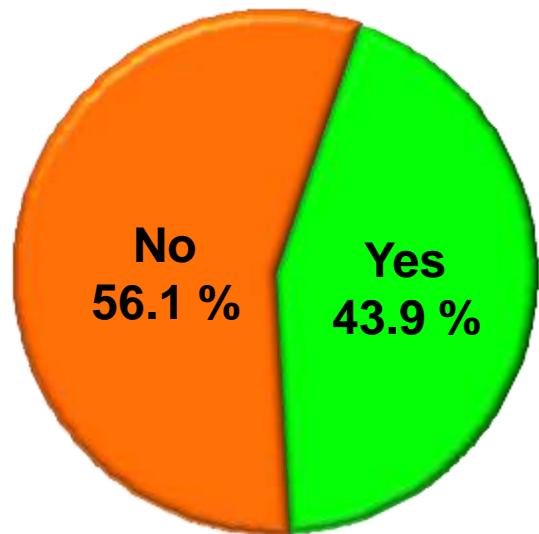


B Heart Failure as multiple cause of death

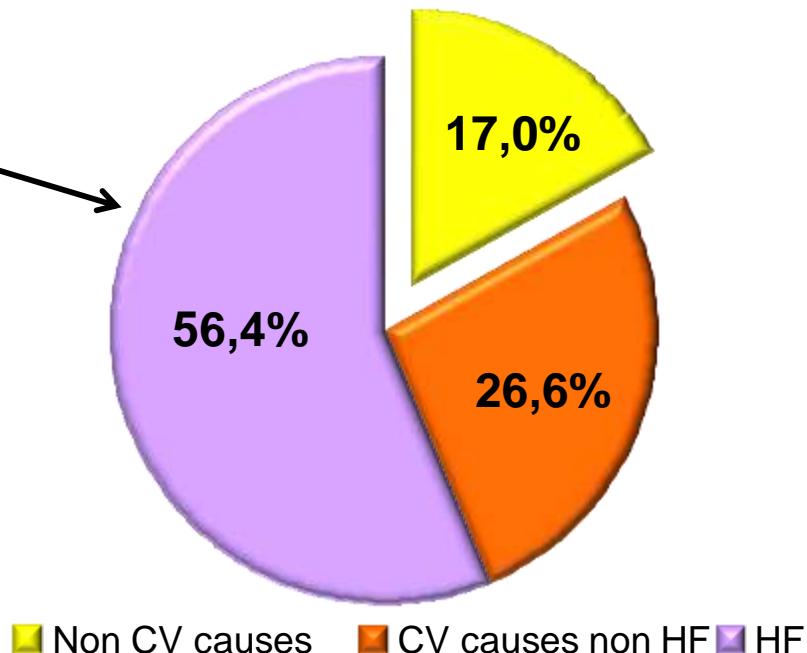


Registre ESC IC décompensée

Re-hospitalizations during the follow-up*

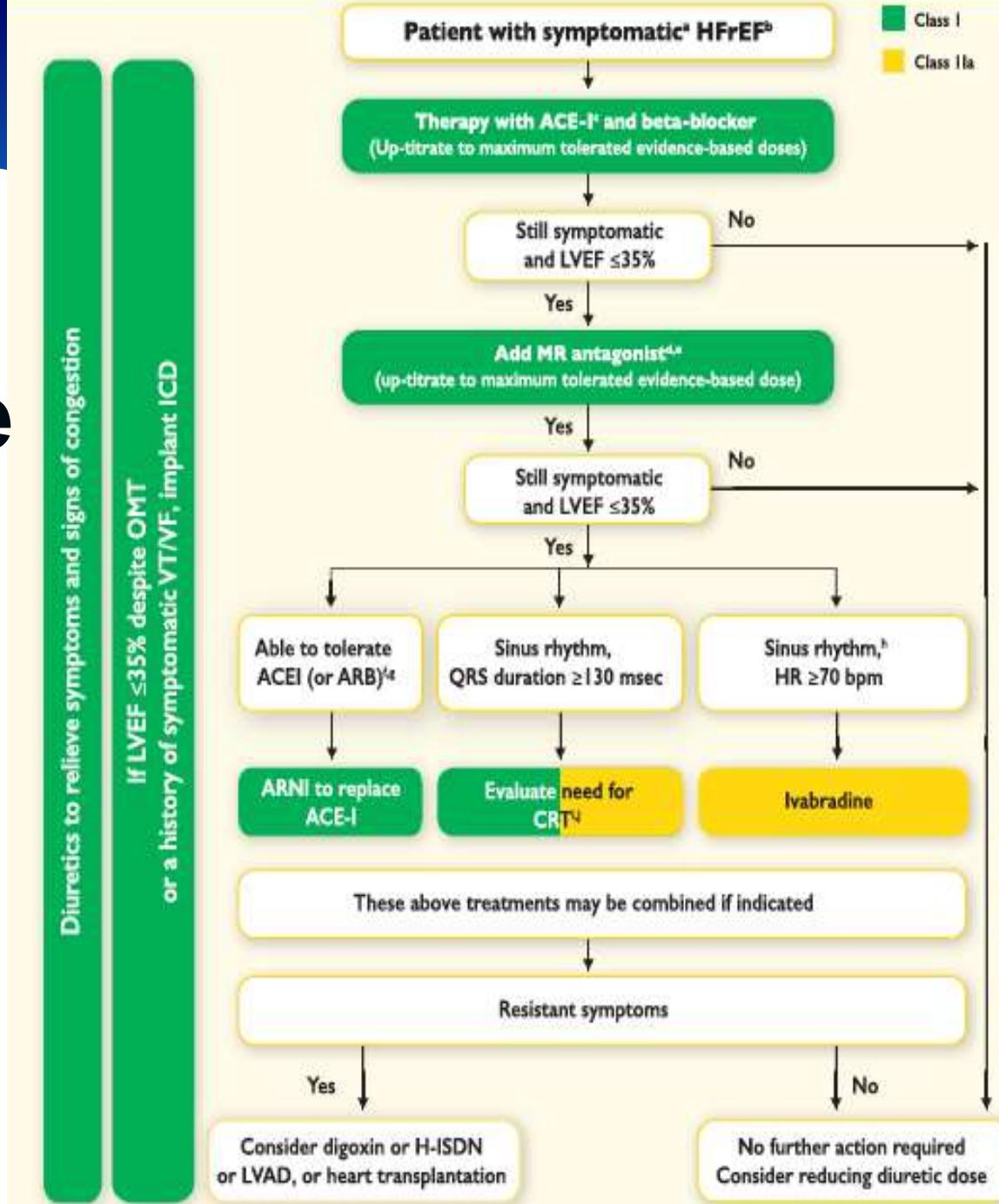


Causes of hospitalization



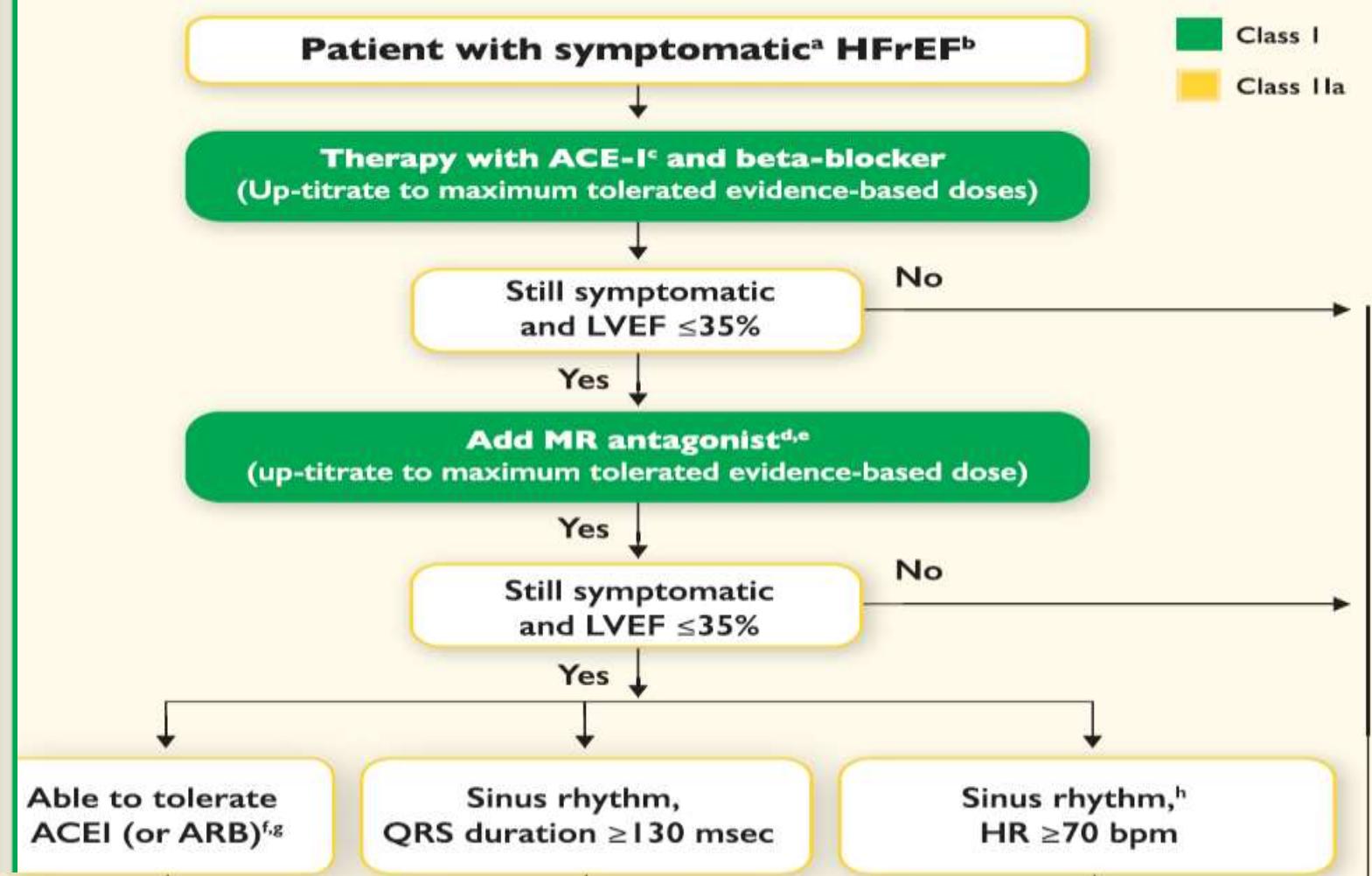
*median follow-up 349 days [252-365]

Algorithme de traitement IC à FE altérée



Initial management of symptomatic HF with reduced ejection fraction

Diuretics to relieve symptoms and signs of congestion



Therapeutic algorithm for a patient with persistent symptomatic HF with reduced ejection fraction

Diuretics to relieve symptoms and signs of congestion

Able to tolerate ACEI (or ARB)^{f,g}

ARNI to replace ACE-I

CRT^{i,j}

Sinus rhythm,^h
HR ≥70 bpm

Ivabradine

These above treatments may be combined if indicated

Resistant symptoms

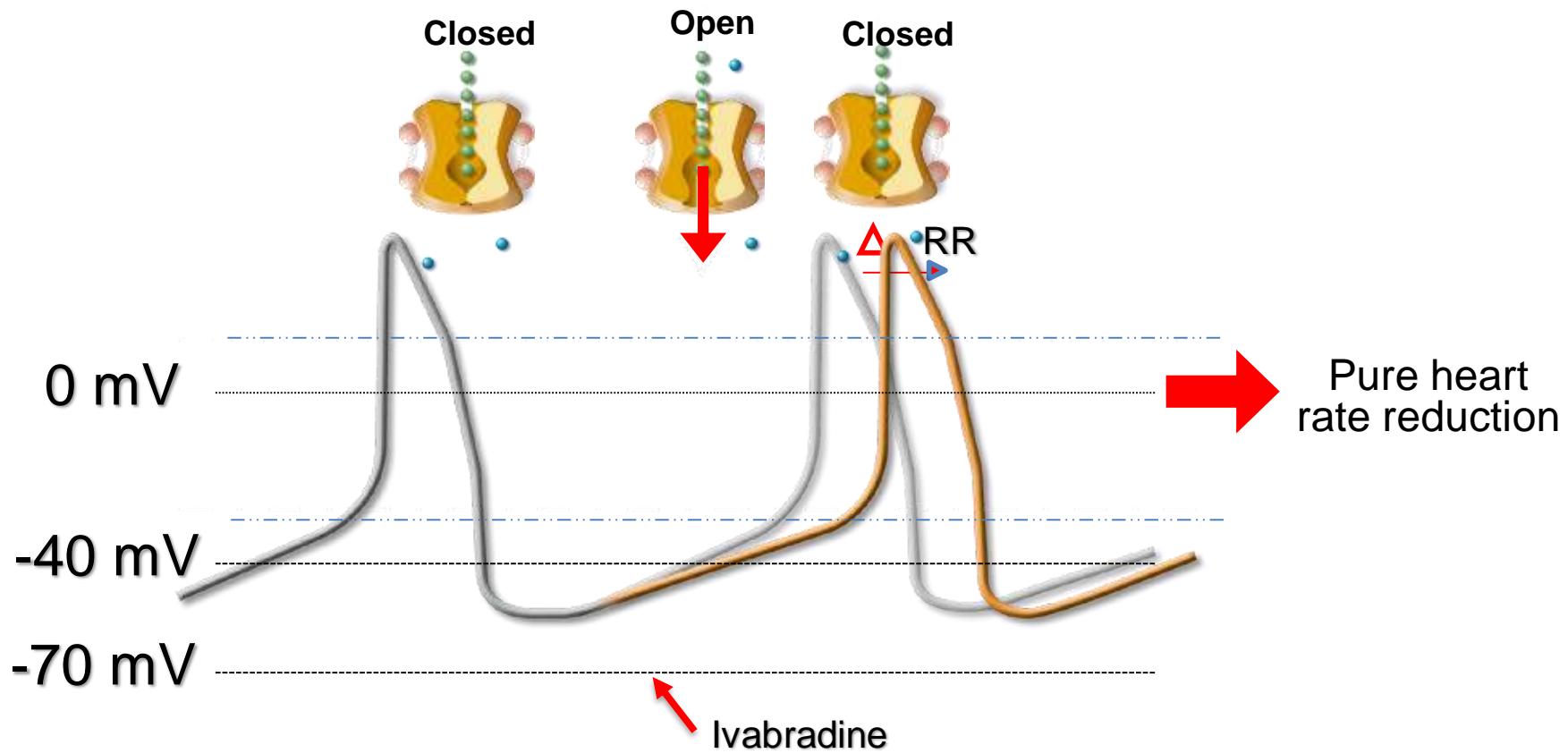
Yes

Consider digoxin or H-ISDN
or LVAD, or heart transplantation

No

No further action required
Consider reducing diuretic dose

Mécanisme d'action de l'Ivabradine

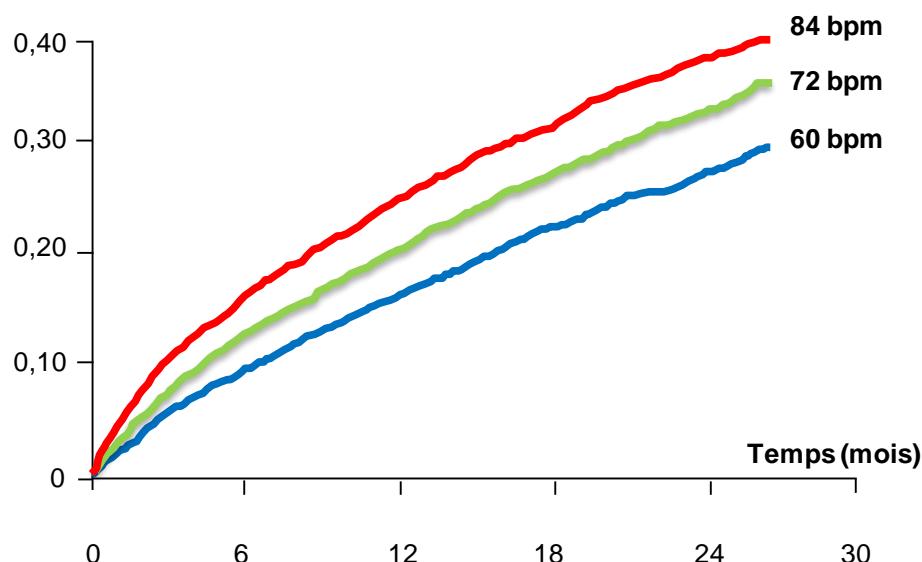


I_f inhibition reduces the diastolic depolarization slope, and thereby lowers heart rate

FC: un marqueur de risque

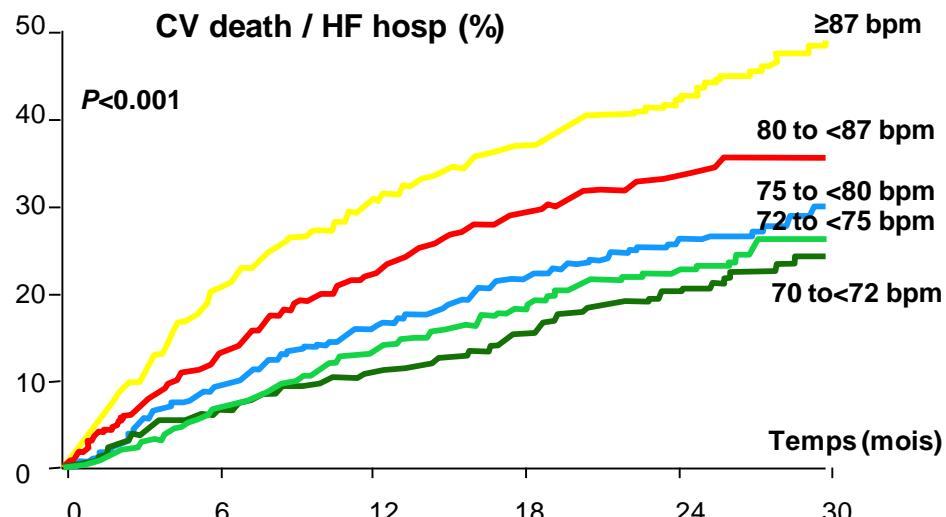
CHARM

CV death/hospitalization



SHIFT

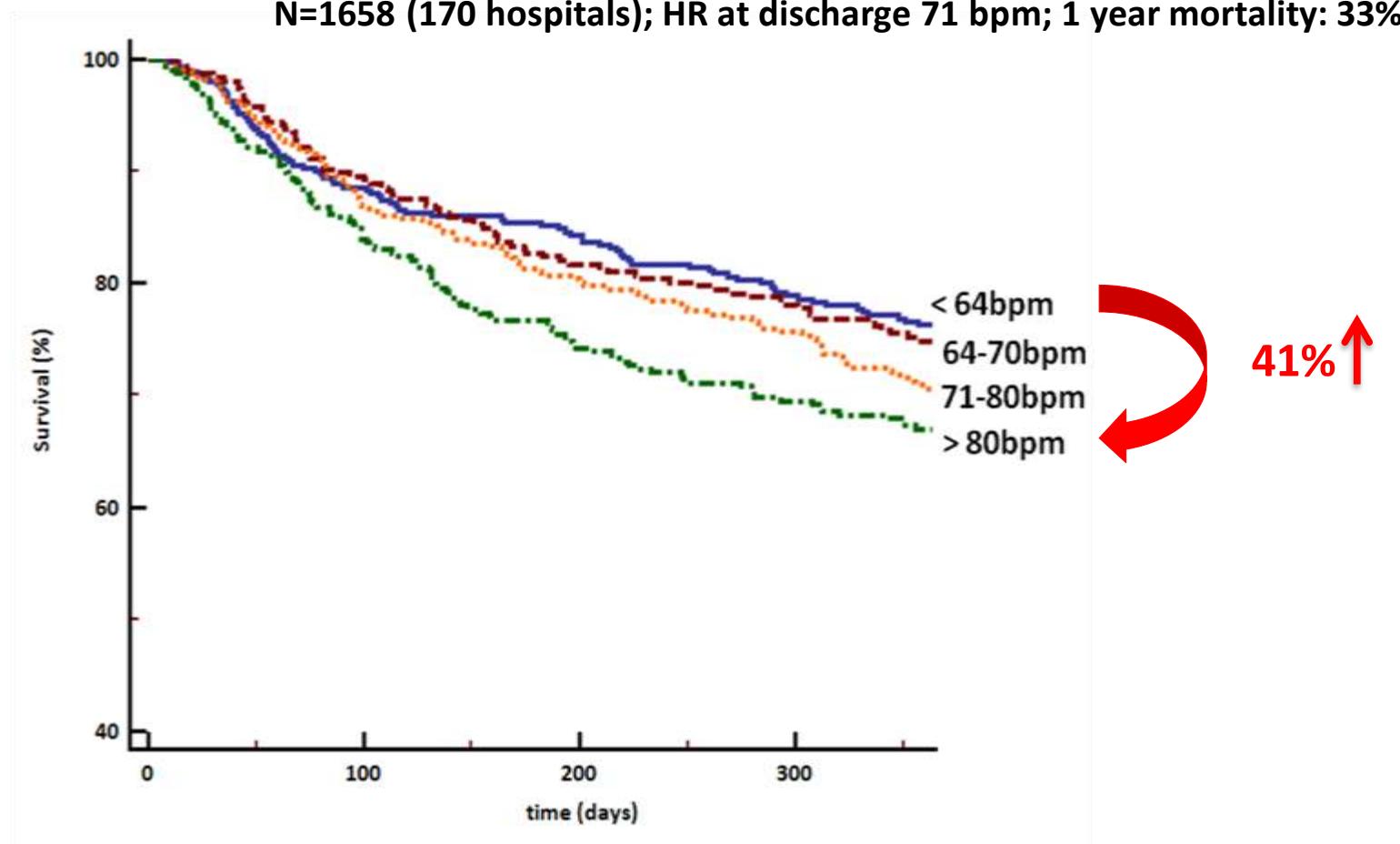
CV death / HF hosp (%)



Castagno et al. J Am Coll Cardiol 2012;59:1785–95

Böhm M, et al. Lancet. 2010;376:886-894.

FC à la sortie et risque de mortalité à un an (OFICA)



Données de registres

IMPACT RECO III

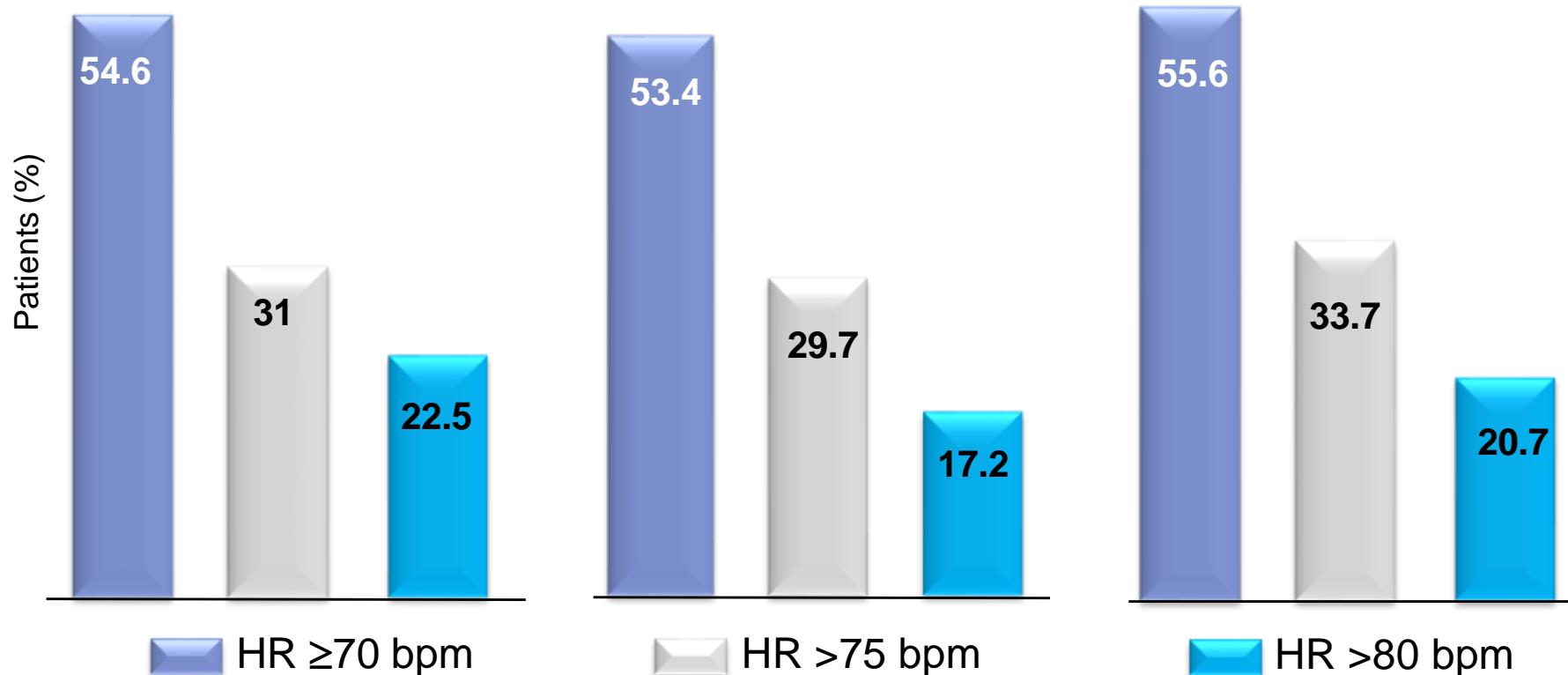
1407 patients

HF OUTCOME*

3480 patients

ESC PILOT HF**

2450 patients



*Courtesy of Prof Tavazzi

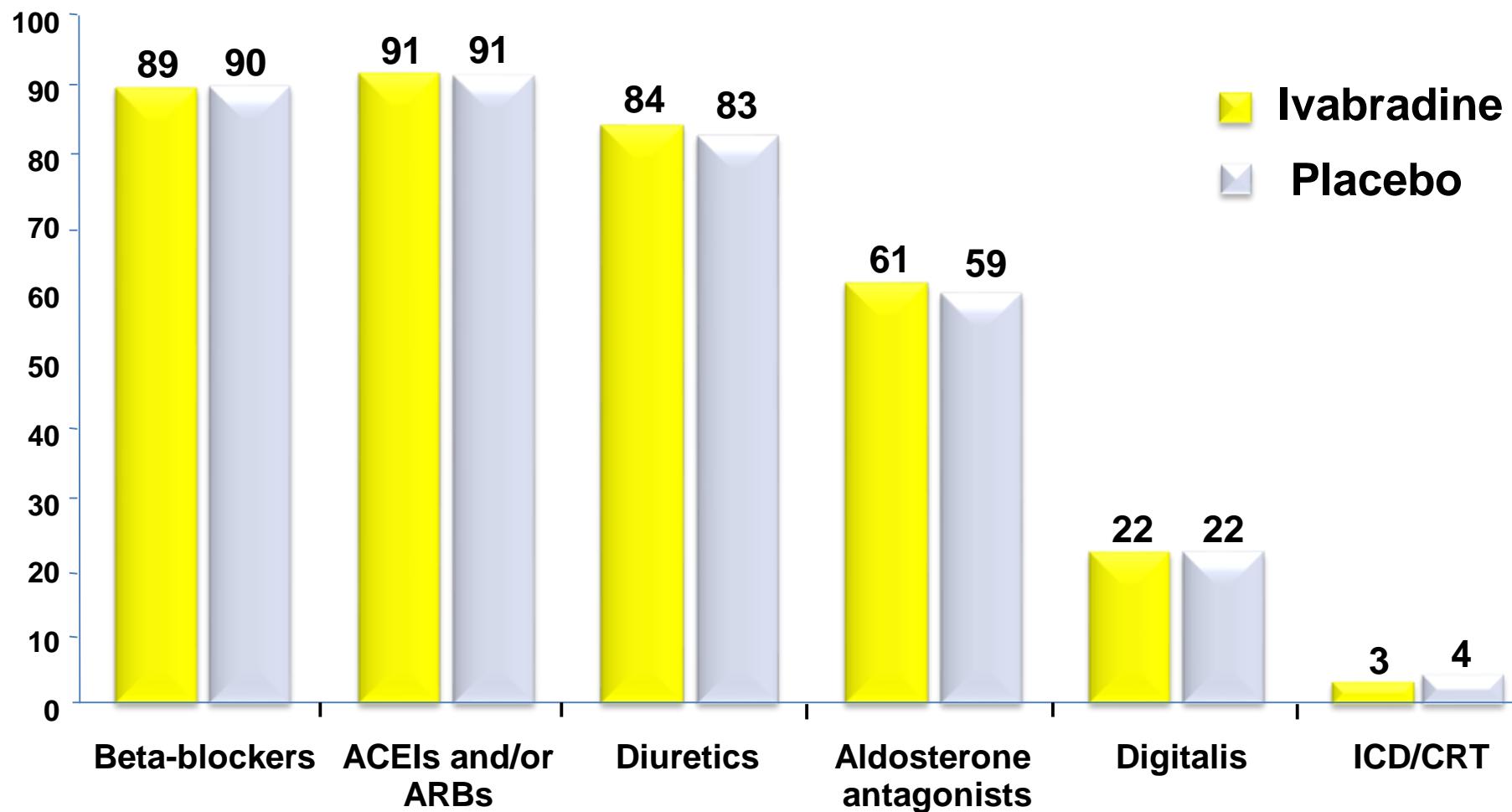
**Courtesy of Prof Maggioni

SHIFT

- IC à fraction d'éjection altérée modérée à moyenne Fe<35%
- Traitement optimal incluant beta bloquants (90%)
- Rythme sinusal
- FC>70 bpm

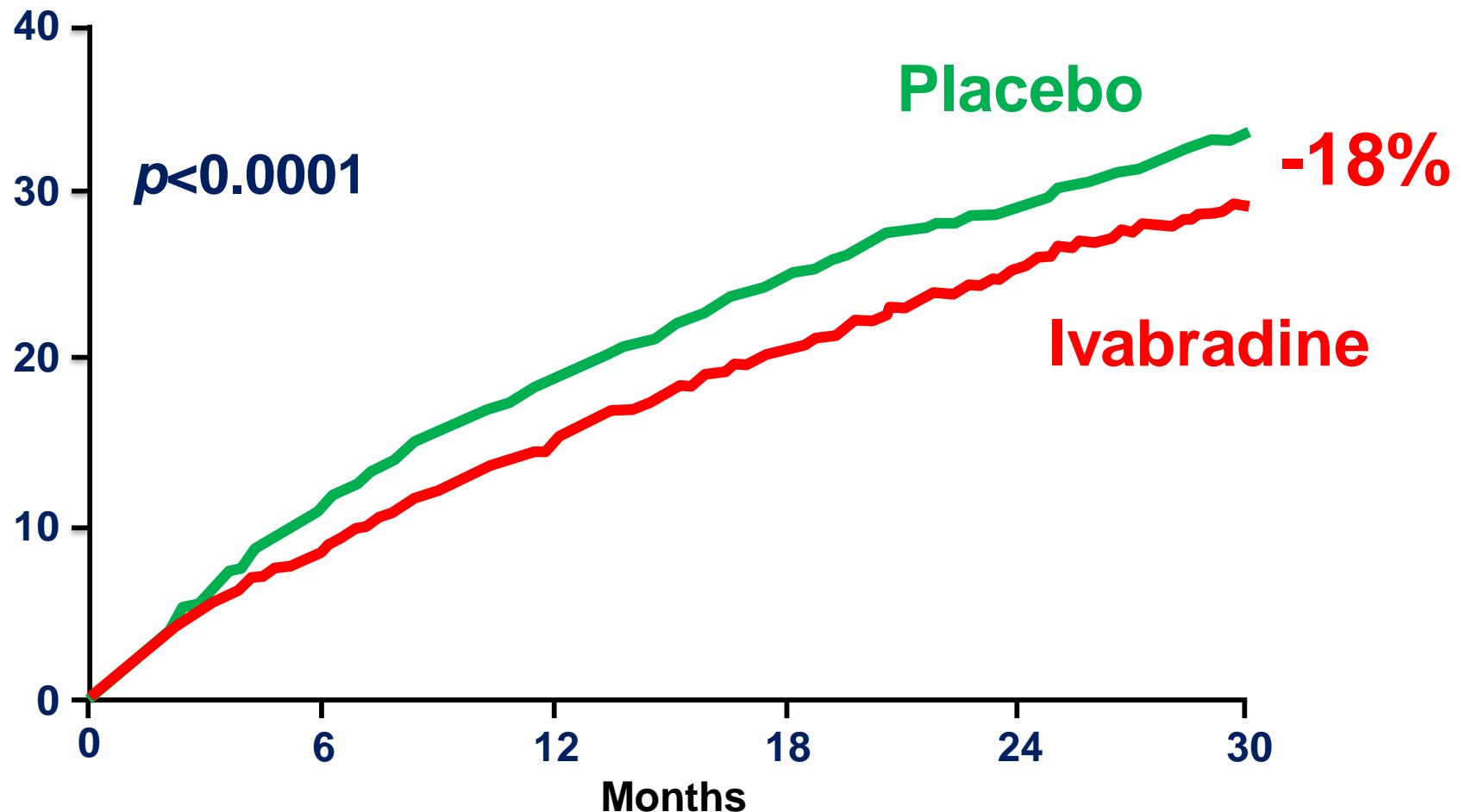
Traitement de fond

Patients (%)

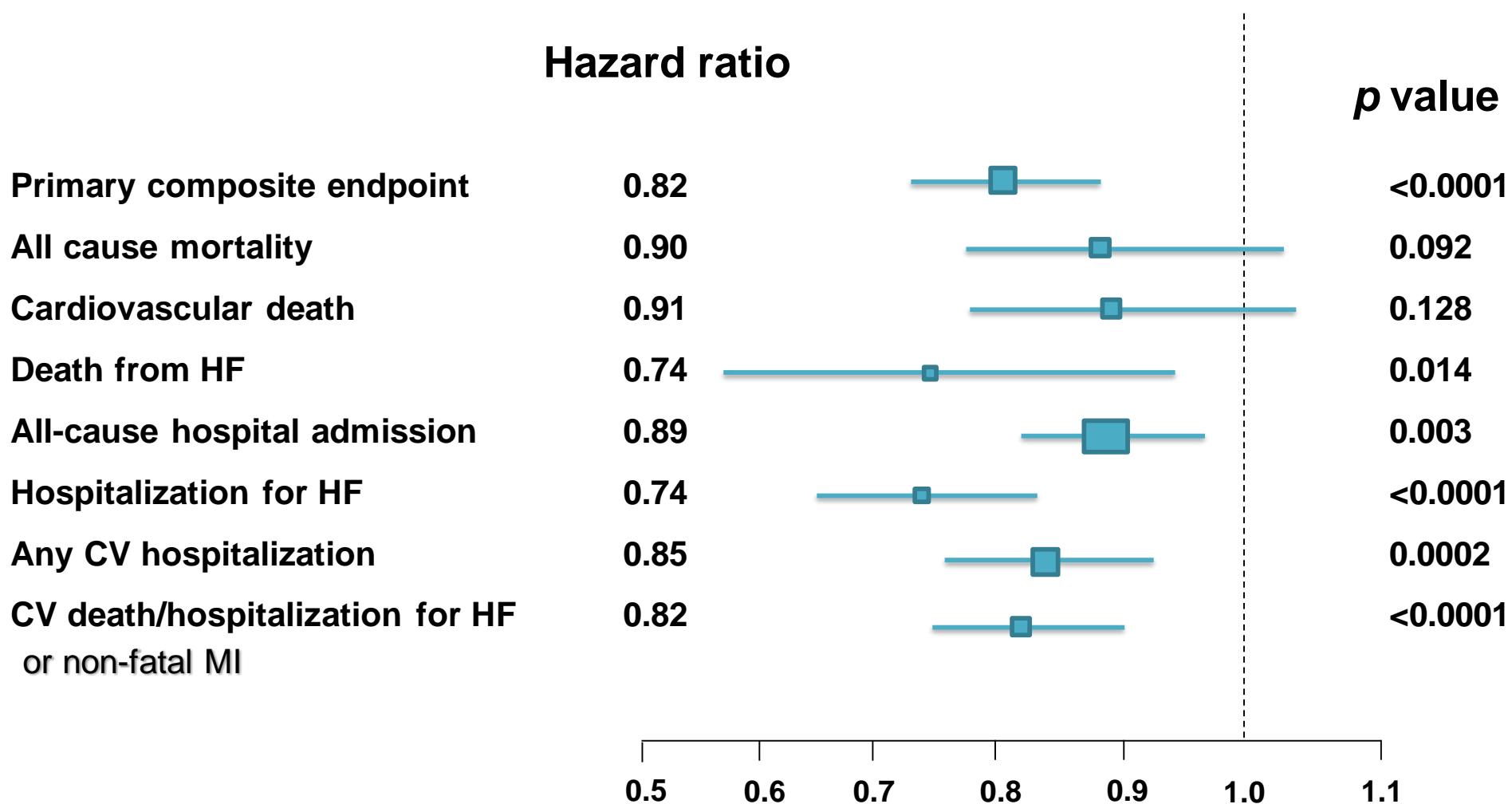


SHIFT

Décès CV / hospitalisation pour IC

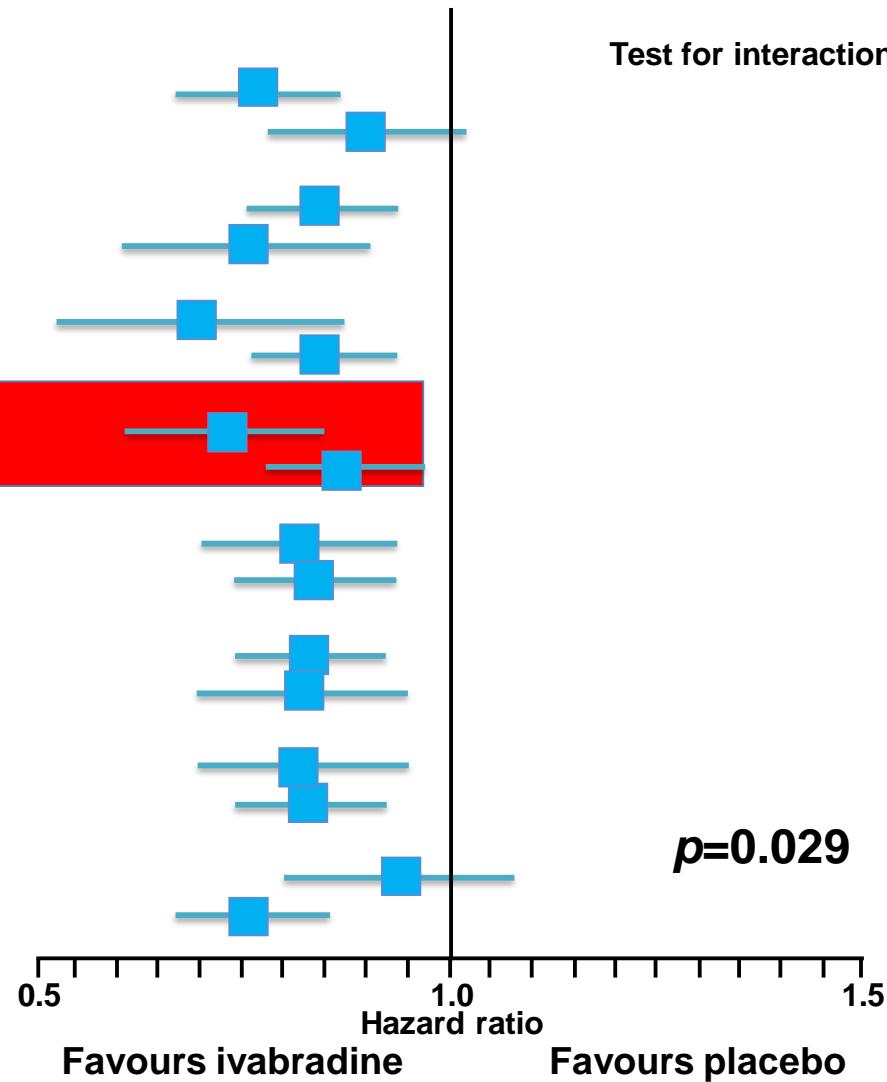


Effet de l'ivabradine sur les critères cliniques



Effect of ivabradine in prespecified subgroups

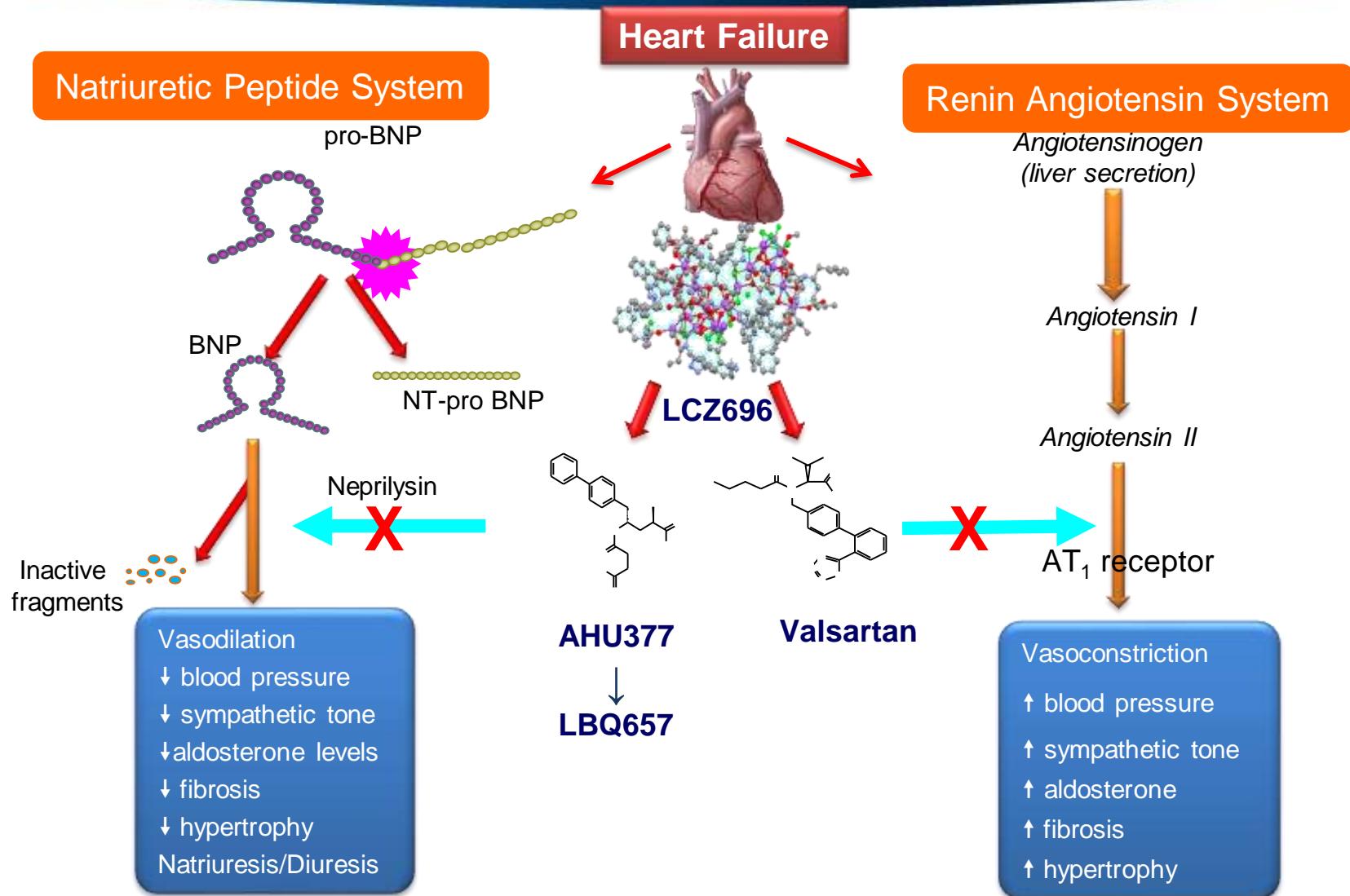
- ◆ **Age**
 - <65 years
 - ≥65 years
- ◆ **Sex**
 - Male
 - Female
- ◆ **Beta-blockers**
 - No
 - Yes
- Aetiology of heart failure**
 - Non-ischaemic
 - Ischaemic
- ◆ **NYHA class**
 - NYHA class II
 - NYHA class III or IV
- ◆ **Diabetes**
 - No
 - Yes
- ◆ **Hypertension**
 - No
 - Yes
- ◆ **Baseline heart rate**
 - <77 bpm
 - ≥77 bpm



Effets secondaires ivabradine

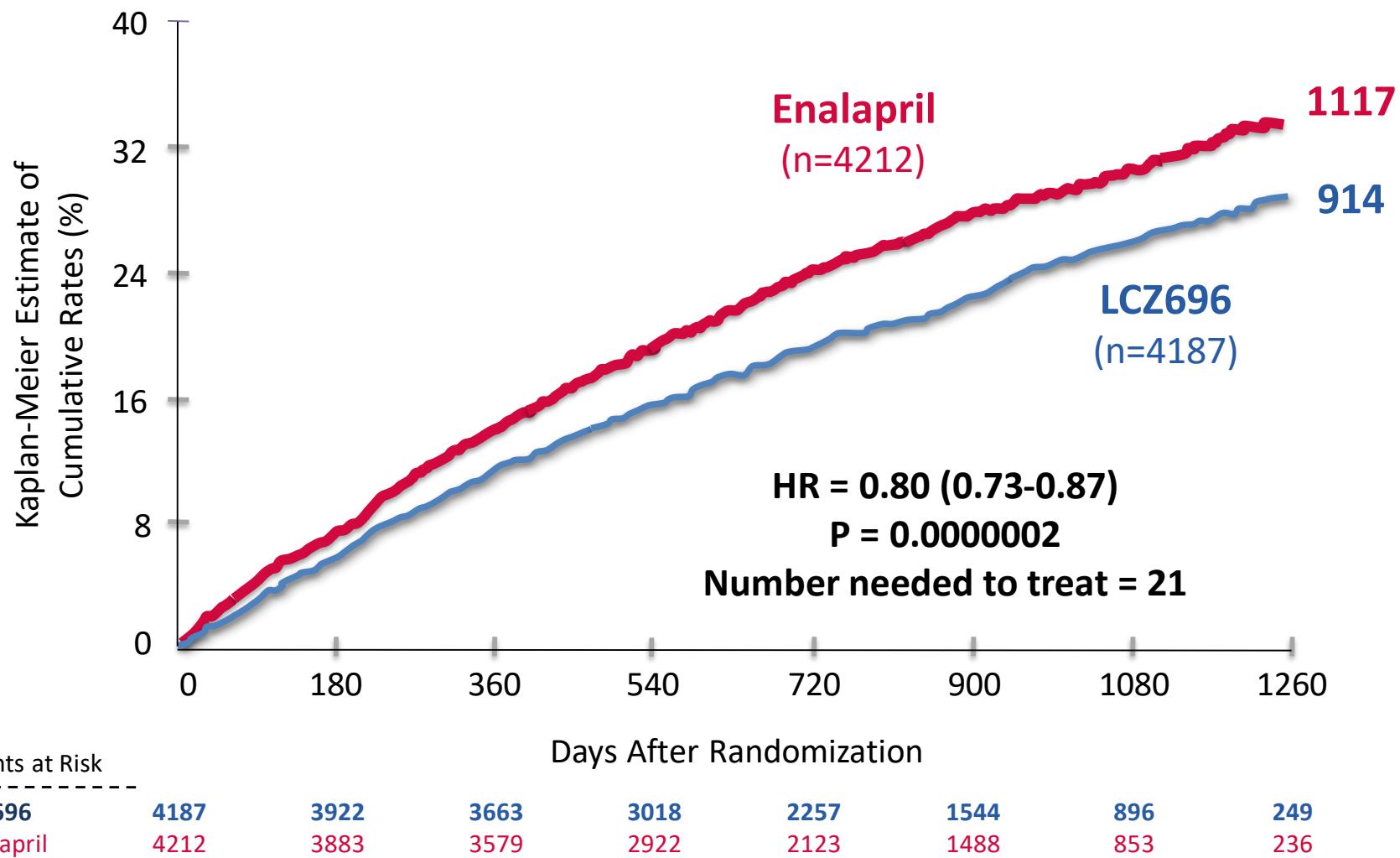
- Bradycardie**
- Troubles visuels transitoires**
- Pas d'effet sur la pression artérielle.**
- Pas d'effet chez les patients en FA permanente**

LCZ 696: Angiotensin Receptor Neprilysin Inhibitor



PARADIGM HF

Décès CV/Hosp pour IC



Effets secondaires LCZ 696

- **Angio-oedème: pas d'utilisation concomittante avec les IEC+++**
- **Hypotension artérielle**
- **CI si PAs<100 mm Hg**
- **Kaliémie >5.4 mMoles / l**

Ivabradine en pratique clinique

Quelle sécurité d'emploi de l'ivabradine associée aux beta bloquants?

Analyse holter à 8 mois

	Ivabradine (n=254)	Placebo (n=247)
≥ 1 episode HR <30 bpm	0	0
≥ 1 episode HR <40 bpm	54	21
RR > 2.5 seconds	3	4
RR> 3 seconds	0	1
Atrial fibrillation/Flutter	6	5
AV block II or high-degree block	4	9
AV block III	0	0
Non-sustained VT	71	81
Sustained VT	0	0

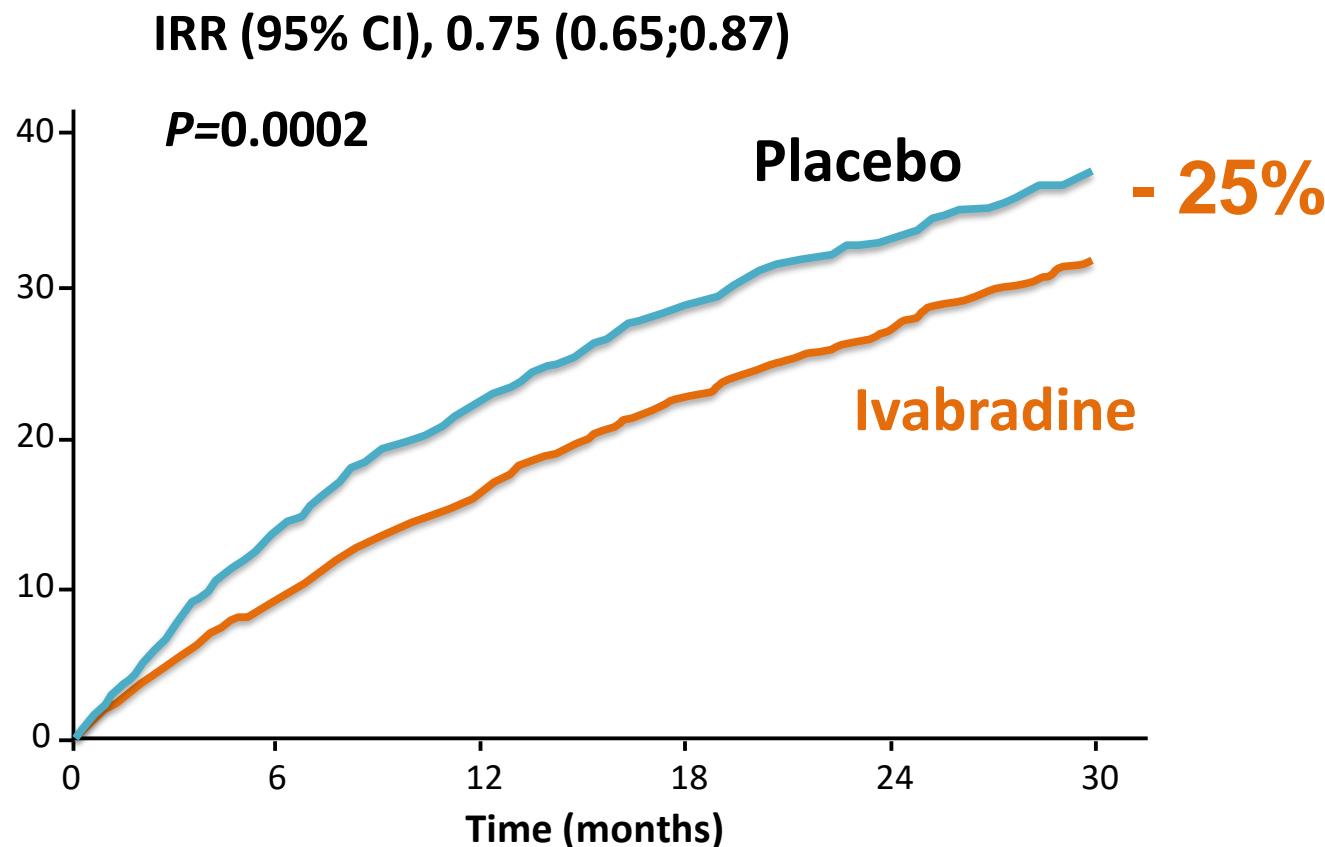


Systolic Heart failure treatment with the I_f inhibitor ivabradine Trial

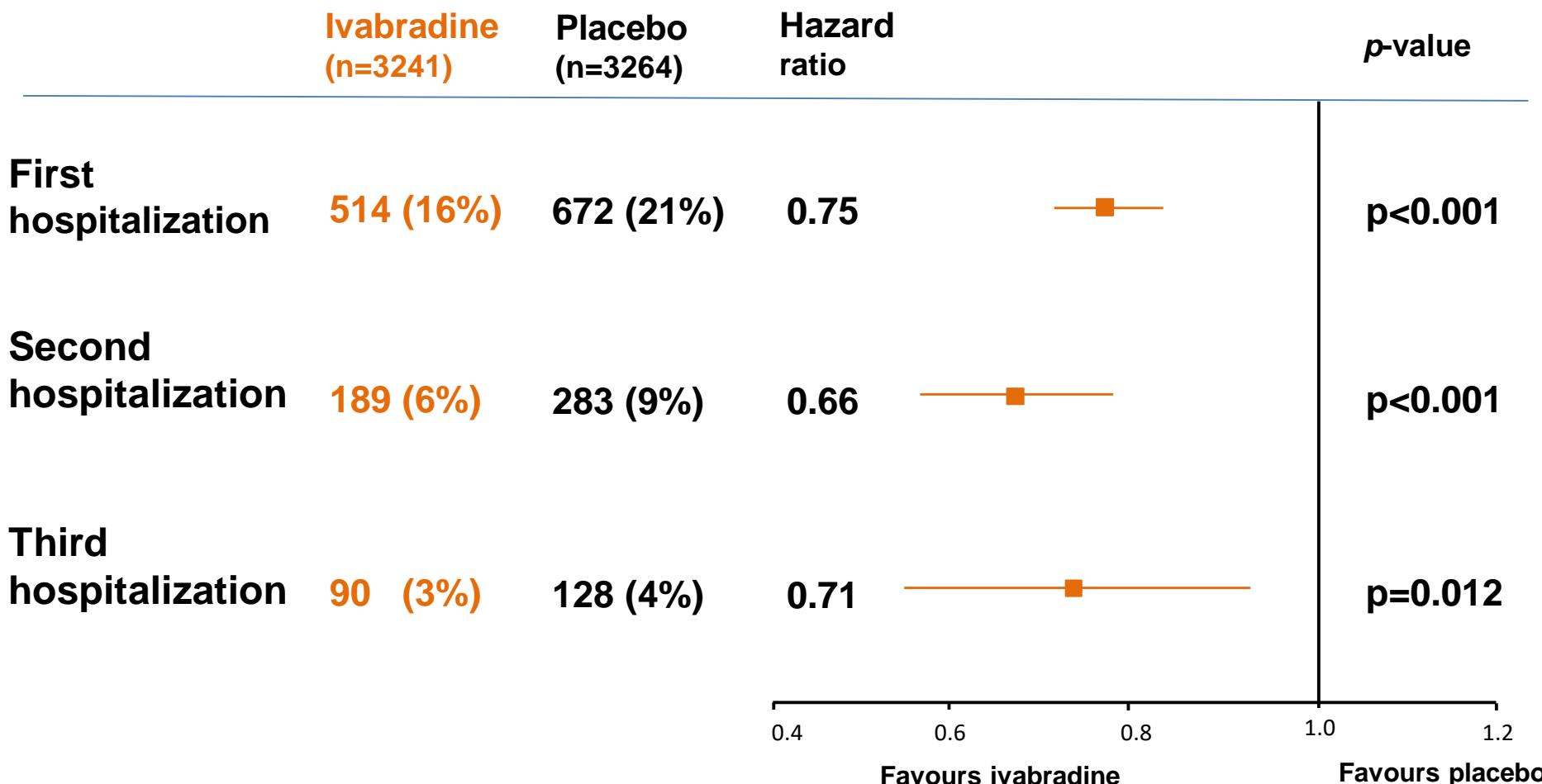
Quel est l'effet sur les réhospitalisations pour IC?

Effet de l'ivabradine sur le nombre total d'hospitalisations

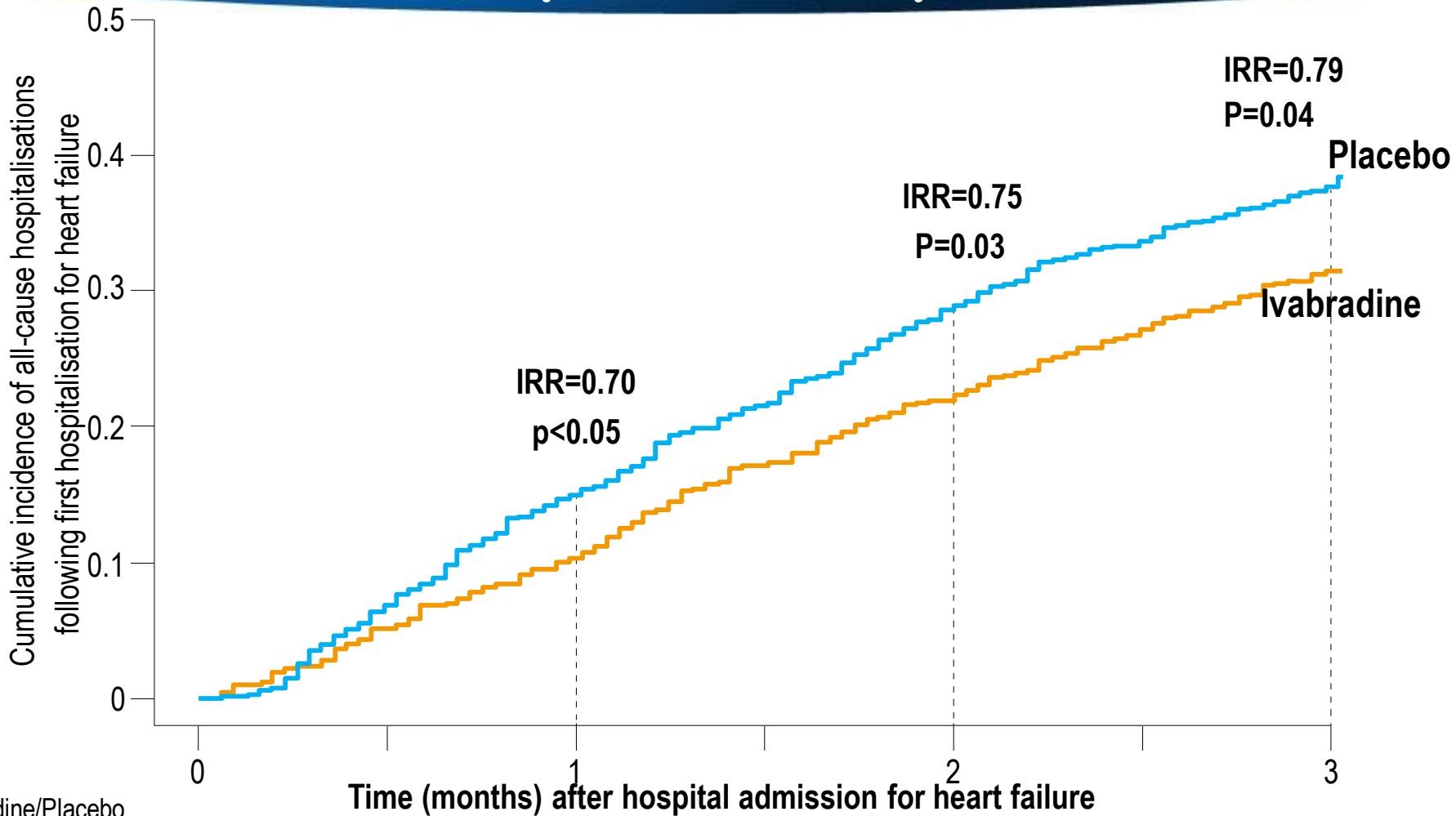
Cumulative incidence of HF hospitalizations (first and repeated)



Hospitalisations récurrentes pour IC



Effect de l' ivabradine sur les réhospitalisations précoces



Effet de l'ivabradine sur les réhospitalisations CV et pour IC à trois mois

	Cumulative number of events		Incidence rate ratio (95% CI) (adjusted for prognostic factors)
	Ivabradine (N=514)	Placebo (N=672)	
Cardiovascular hospitalisations			
1 month	38	76	0.66 (0.44–1.01)
2 months	90	155	0.77 (0.57–1.02)
3 months	131	221	0.79 (0.62–1.01)
Heart failure hospitalisations			
1 month	21	42	0.67 (0.40–1.13)
2 months	56	97	0.77 (0.55–1.09)
3 months	86	148	0.78 (0.59–1.02)



Systolic Heart failure treatment with the I_f inhibitor ivabradine Trial

L'ivabradine améliore-t-elle la qualité de vie ?

Kansas City Cardiomyopathy Questionnaire (KCCQ)

Self reported instrument ranging from 0 to 100
(higher score better HQoL)

- **CSS (clinical summary score)**
- **Physical Limitation**

- **Total Symptom**

Symptom frequency

Symptom burden

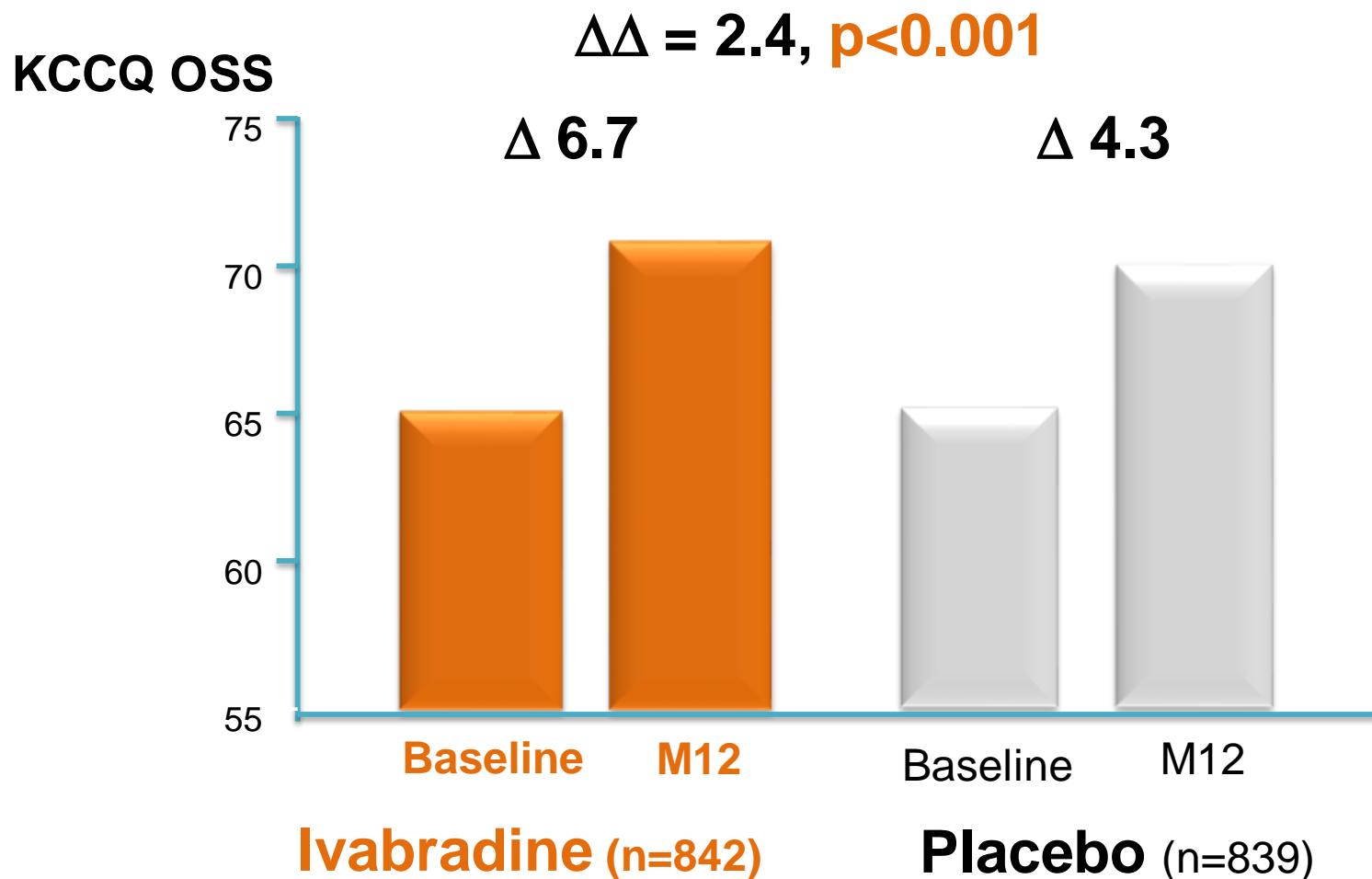
- **OSS (overall summary score)**

Quality of Life

Social limitation

KCCQ-OSS

Change from baseline to 12 months

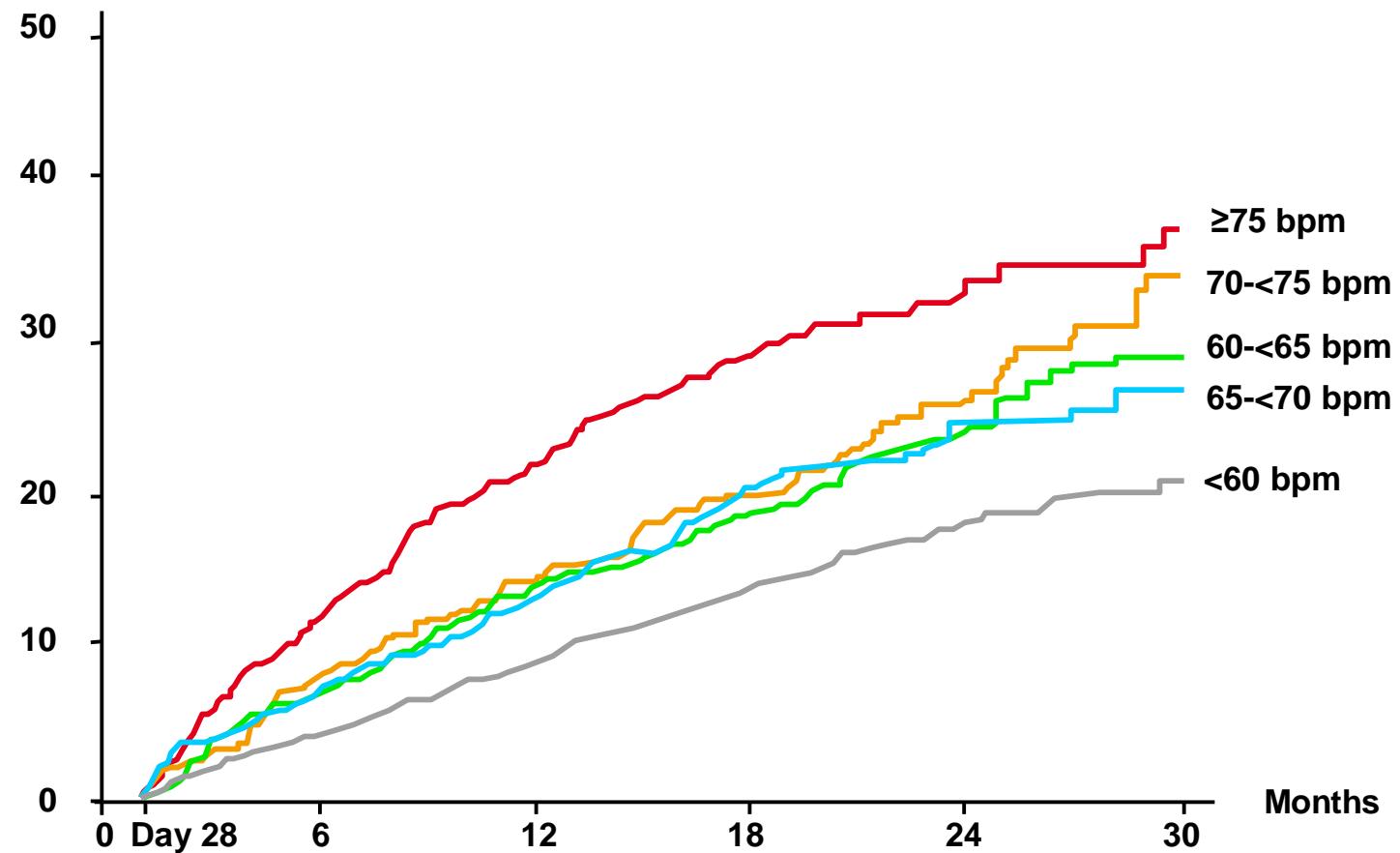




Systolic Heart failure treatment with the I_f inhibitor ivabradine Trial

Quelle est la fréquence cardiaque optimale dans l'IC à FE altérée ?

Patients with **primary composite endpoint (%)**

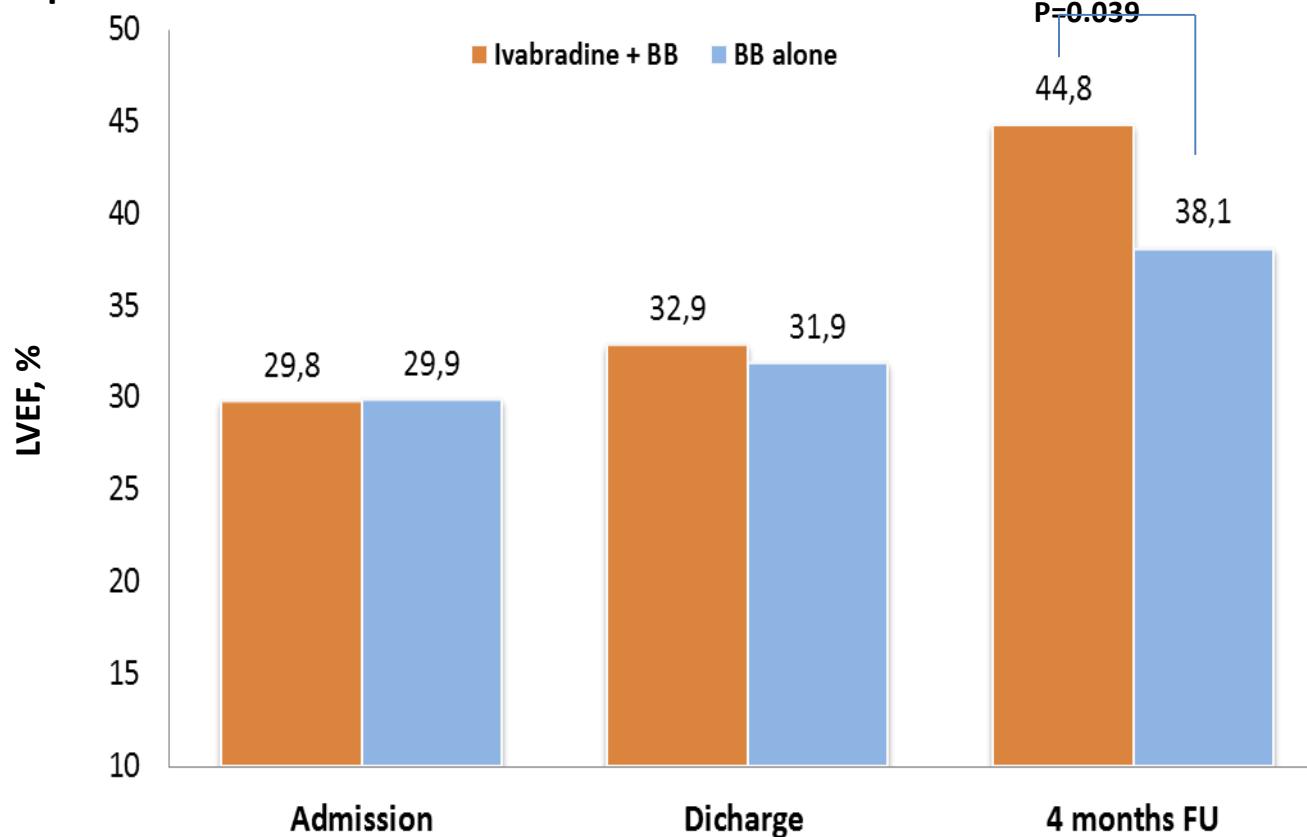


La co-administration précoce avec les beta bloquants est elle bénéfique?

Effect of early treatment of Procoralan with BBs vs BB alone in patients hospitalized for WHF: ETHIC study

Greater improvement in LVEF

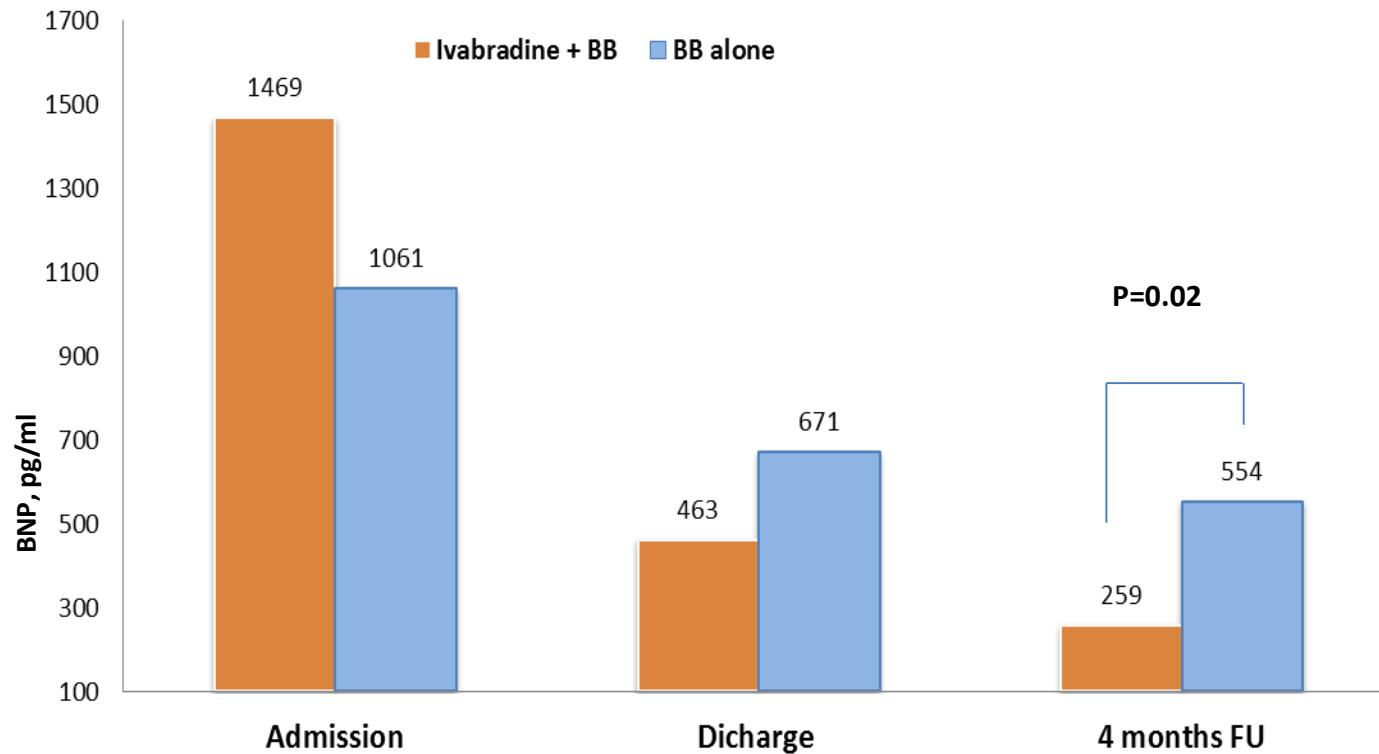
n=71 patients hospitalized for WHF

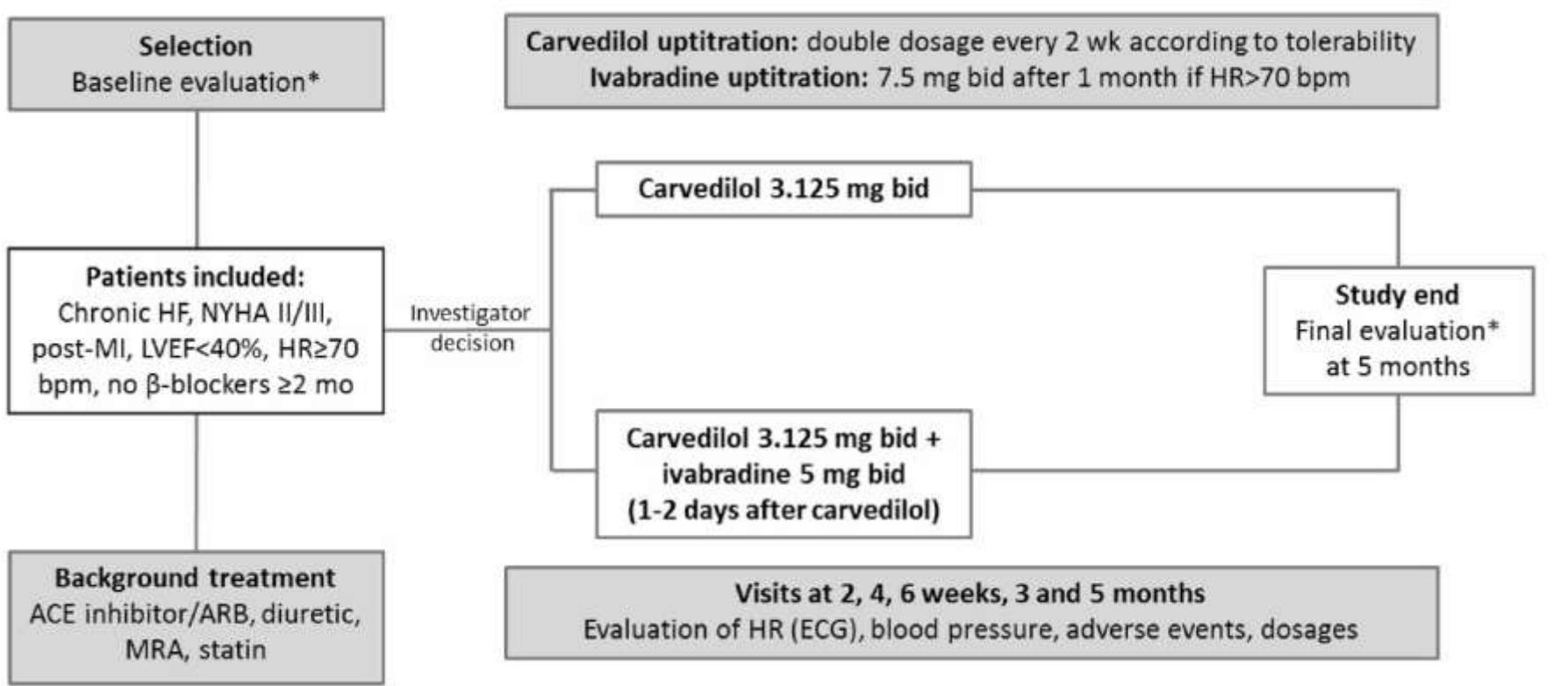


Effect of early treatment of Procoralan with BBs vs BB alone in patients hospitalized for WHF: ETHIC study

Better reduction in BNP

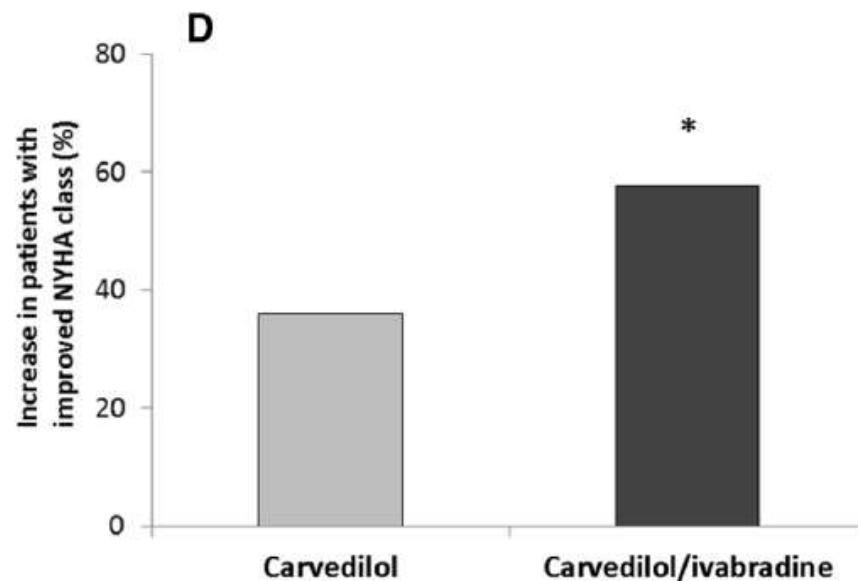
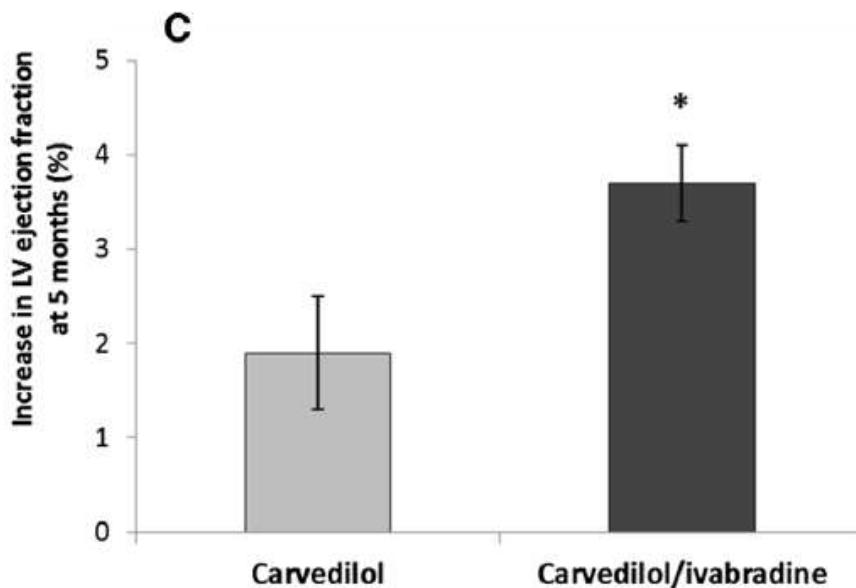
n=71 patients hospitalized for WHF





Clinical solution: Facilitating β -Blocker Uptitration

Ivabradine in combination improves LVEF in CHF

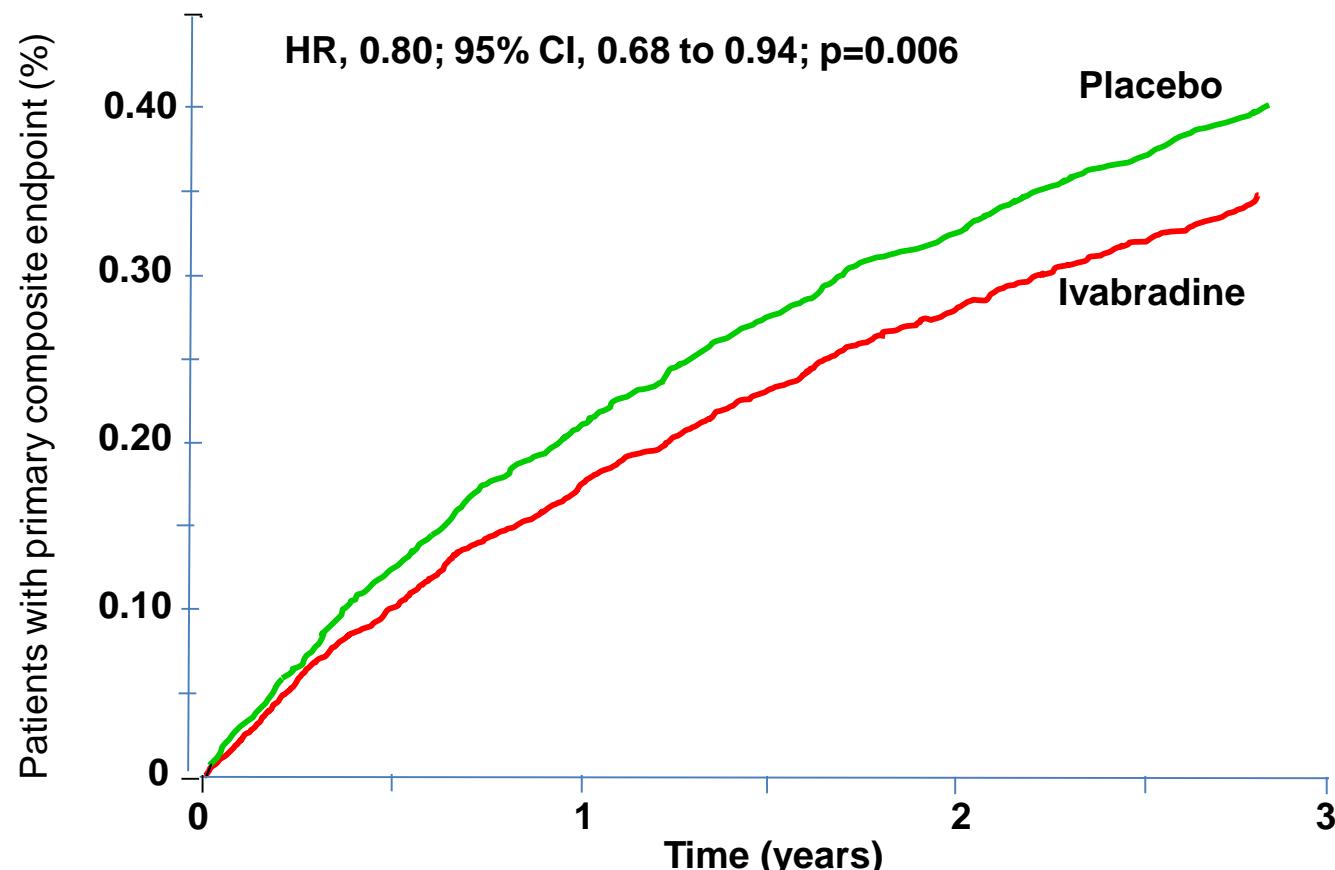




Systolic Heart failure treatment with the I_f inhibitor ivabradine Trial

L'effet est-il identique chez l'IC diabétique?

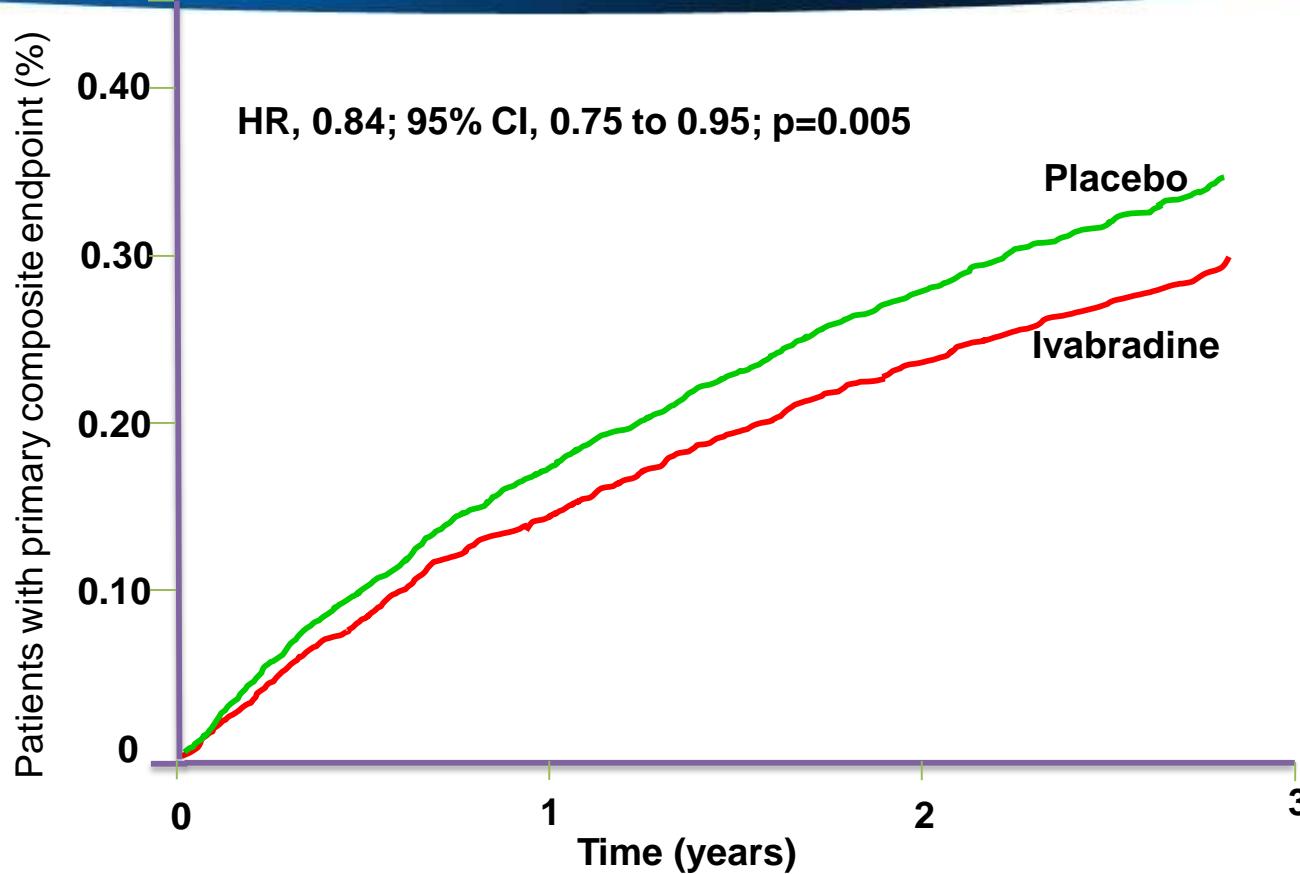
Critère principal .Diabétiques



Patients at risk :

Ivabradine	973	876	769	641	340	131	9
Placebo	1006	877	750	619	315	119	4

Critère principal. Non diabétiques



Patients at risk :

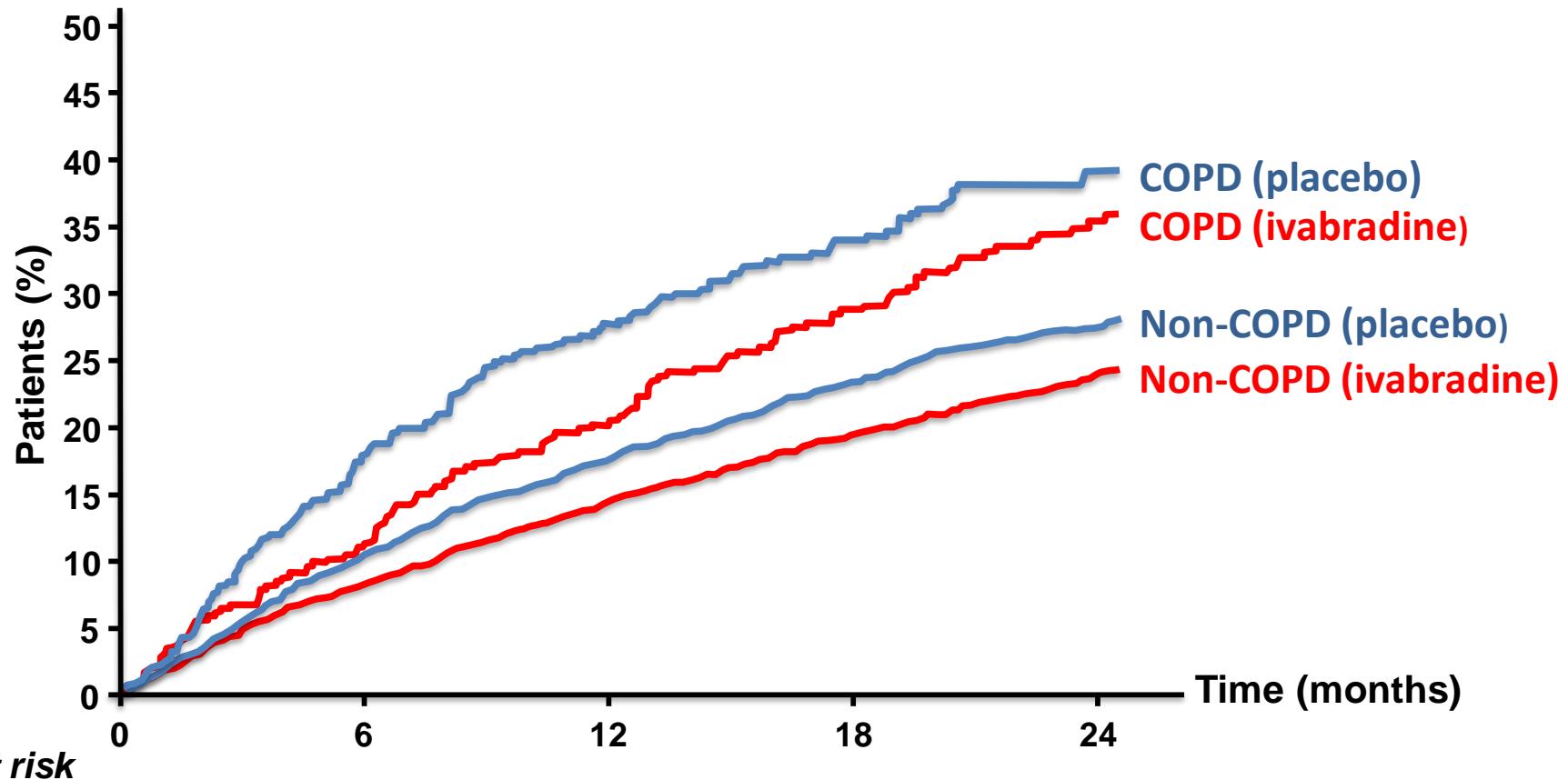
Ivabradine	2268	2052	1831	1532	851	316	7
Placebo	2258	1991	1739	1442	774	320	13



Systolic Heart failure treatment with the I_f inhibitor ivabradine Trial

Quel est l'effet de l'ivabradine chez les patients avec BPCO?

Effet de l'ivabradine sur décès CV / hospitalisations pour IC



N at risk

	0	6	12	18	24
COPD (pl)	372	298	250	209	110
COPD (iva)	358	312	266	216	124
NCOPD (pl)	2892	2570	2239	1852	979
NCOPD (iva)	2883	2616	2334	1957	1067

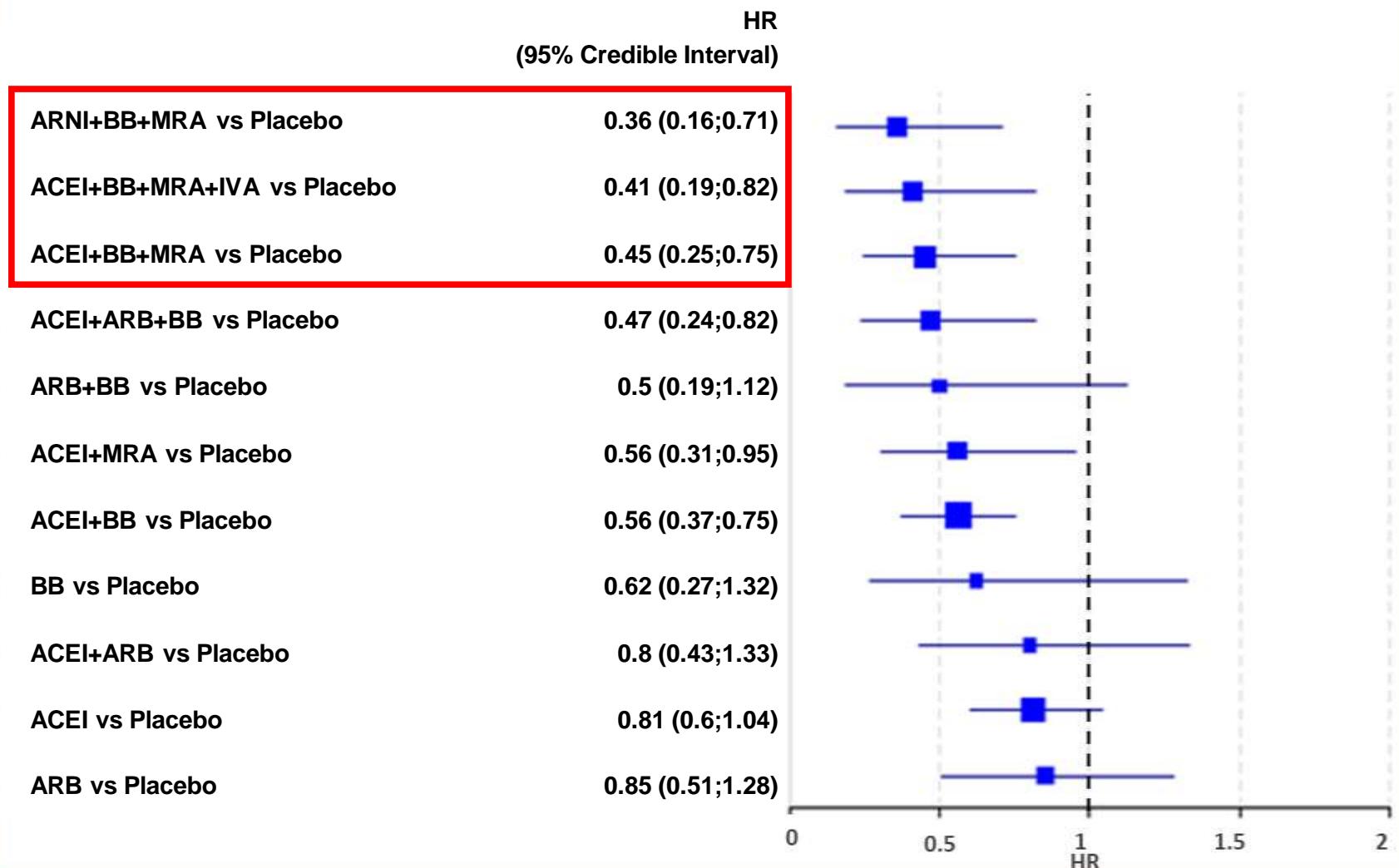
**L'application des
recommandations est elle
bénéfique ?**

Incremental benefit of drug therapies for chronic heart failure with reduced ejection fraction: a network meta-analysis

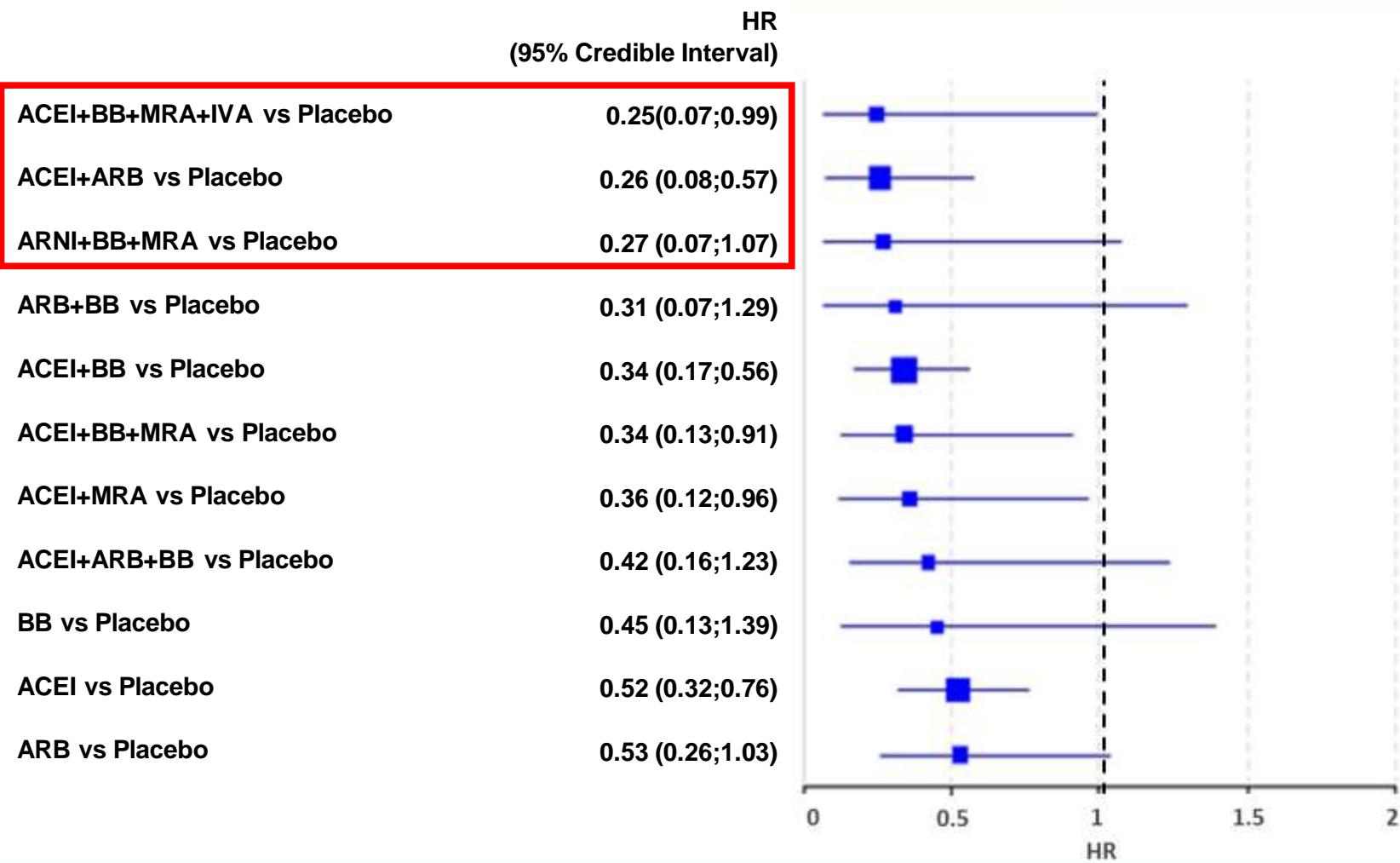
Michel Komajda (hopital Saint Joseph Paris France)

on behalf of
M Böhm, JS Borer, I Ford, L Tavazzi, M Pannaux, and K Swedberg

Hazard ratios Mortalité CV



Hazard ratios hospitalisations pour IC





547 centres dans 36 pays

N=7127 patients

North America
Canada

Europe

Ireland
Portugal
Spain
France

Germany
Denmark
Greece

Hungary
Belarus
Lithuania
Austria

Romania
Poland
Slovakia
Russia
Ukraine

South America
Ecuador

Middle East
Bahrain
Kuwait
Oman
Qatar
UAE

Jordan
Kazakhstan
Turkey
Lebanon
Egypt

Caucasus
Armenia
Georgia
Azerbaijan

Africa
Morocco

Asia
Brunei
China
Korea
Malaysia
Thailand

Australia

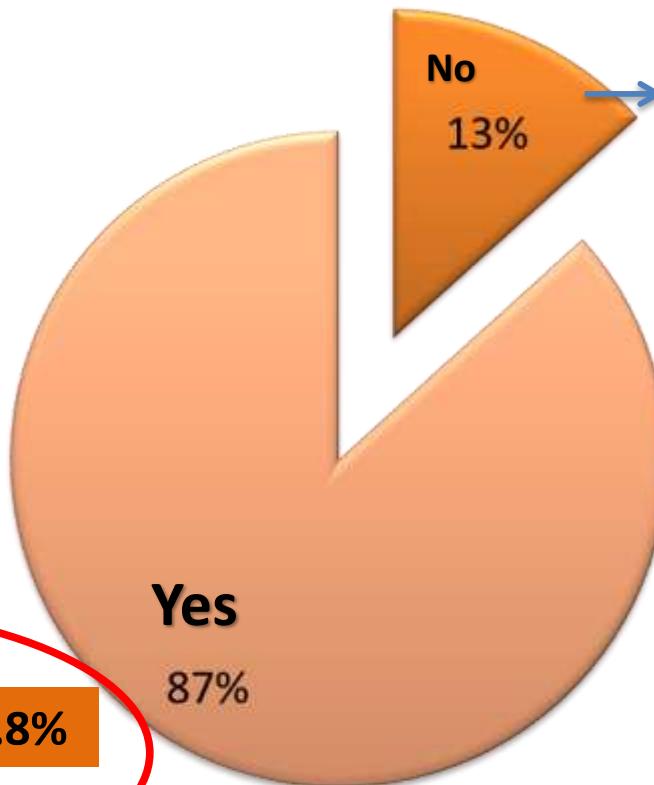


Taux de prescription

- Beta bloquants 87%
- MRAs: 69%
- ACE I: 66%
- Ivabradine :33%
- ARBs:21%

Beta bloquants

Patients treated with beta-blockers= 86.7%



Not indicated	35.3%
Contraindicated	22.4%
Not tolerated	36.3%

Reasons

Asthma/COPD worse	28.3%
Hypotension	21.9%
Fatigue	20.6%
Bradycardia	19.7%
Dizziness	6.4%

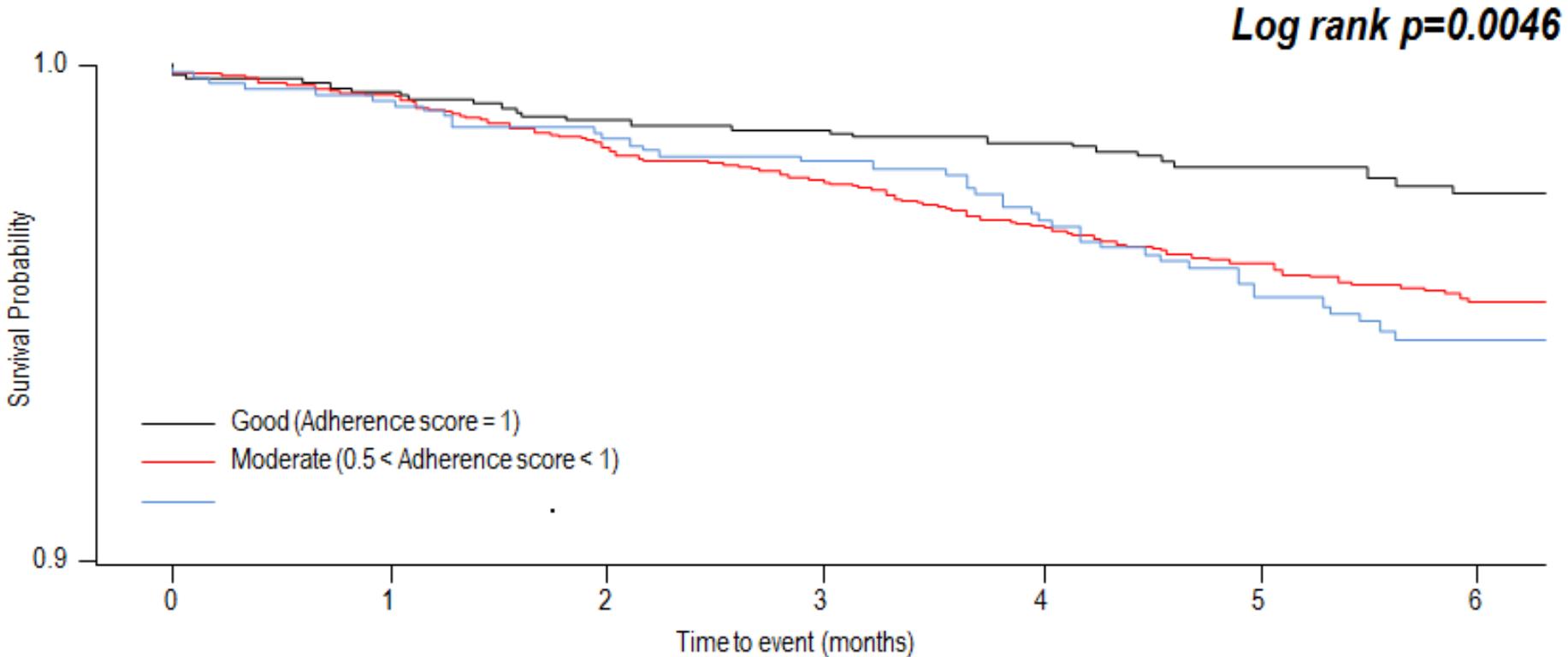
Other reasons

Patients at TD* 14.8%

Patients at $\geq 50\%$ TD 51.8%

*Target dosages suggested by the current guidelines

Mortalité CV à six mois Fonction du score

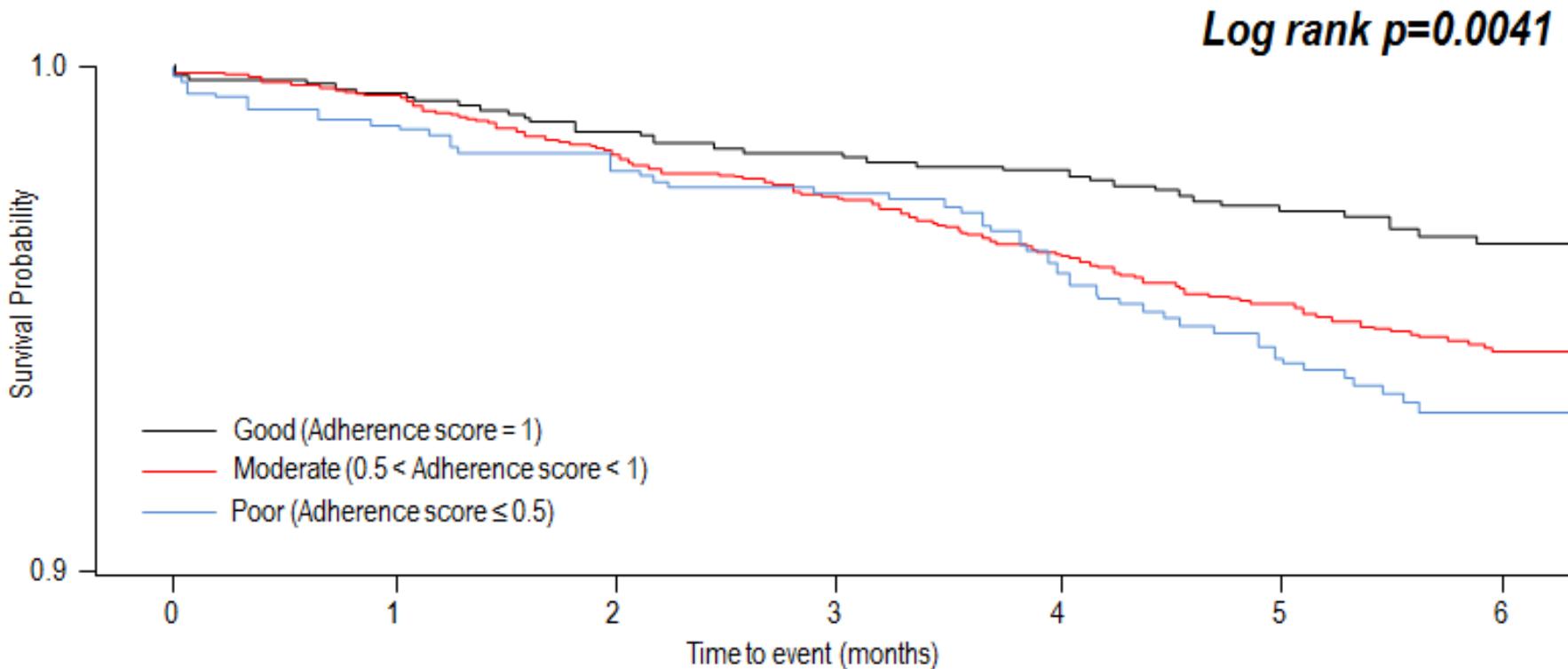


Number at risk

	0	1	2	3	4	5	6
Good	1543	1187	1157	1112	1050	909	474
Moderate	3627	2619	2515	2382	2231	1962	1054
Poor	1493	906	862	809	726	638	323

Hospitalisations pour IC à six mois

Fonction du score d'adhésion



Number at risk

	0	1	2	3	4	5	6
Good	1543	1187	1157	1112	1050	909	474
Moderate	3627	2618	2514	2381	2230	1961	1053
Poor	1493	906	862	809	726	638	323

Conclusion 1

Recommandations ESC 2016:

- **Pas de changement dans le traitement initial de l'IC à FE altérée**
- **Deux options pharmacologiques en traitement de troisième ligne:**
 - **Ivabradine disponible en Tunisie**
 - **Sacubitril/valsartan non disponible**

Conclusion 2

L'adhérence aux recommandations améliore le pronostic et les réhospitalisations.

L'ivabradine a un effet bénéfique en particulier sur les hospitalisations pour IC.

L'ivabradine a peu d'effets secondaires et peut être utilisée chez les patients en IC avec comorbidités

A large, colorful word cloud centered around the words "thank you" in various languages. The word "thank" is in red, "you" is in yellow, and "you" is in green. The background is white with a subtle grid pattern.