Traitement pharmacologique de l'insuffisance cardiaque chronique en 2014

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M Z. F. 61 ans

Consultation: dyspnée NYHA II-III, fatigue, toux grasse, o DRS

- ATCD: RVM 2009 + Maze pour FA (SM)
  FEVG normale pré-op, post-op 50 %
  Bronchite août 2010
- Traitement: Dilzem, 90 mg x2/j Beloc 150 mg/j (arrêtés)
- Status: EGC, TA 110/80 mmHg pouls irrég à 132/min, râles ddc,
- ECG FA avec réponse ventriculaire env. 120/min ,
- Rx thorax : signes d'IC (œdème interstitiel)
- Labo: proBNP **5'214** ng/l, créatinine 85 µmol/l K+ 3.8 mmol/l

Que faites vous ?

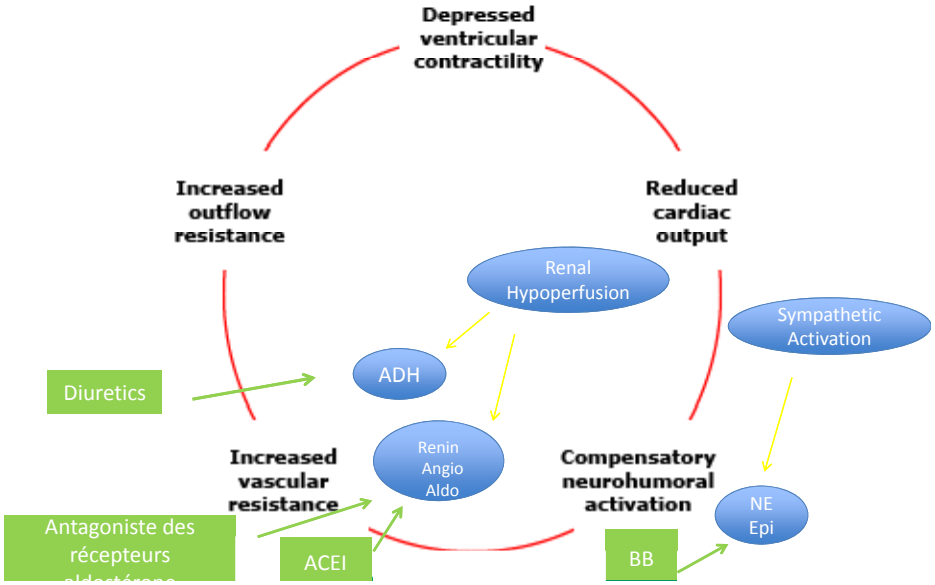
- Hospitaliser le patient ?
- Remettre Dilzem ?
- Digoxine?
- Introduire un IEC ?
- Introduire un BB ?
- Autre traitement et lequel?

Plan de présentation

- Traitements pharmacologiques « first line »
- Autres traitements
- Traitements non recommandés

Soulagent les signes et les symptômes
Prévenir les hospitalisations
Améliorer la survie
IEC/(sartan) BB Spironolactone

Neurohumoral activation in HF

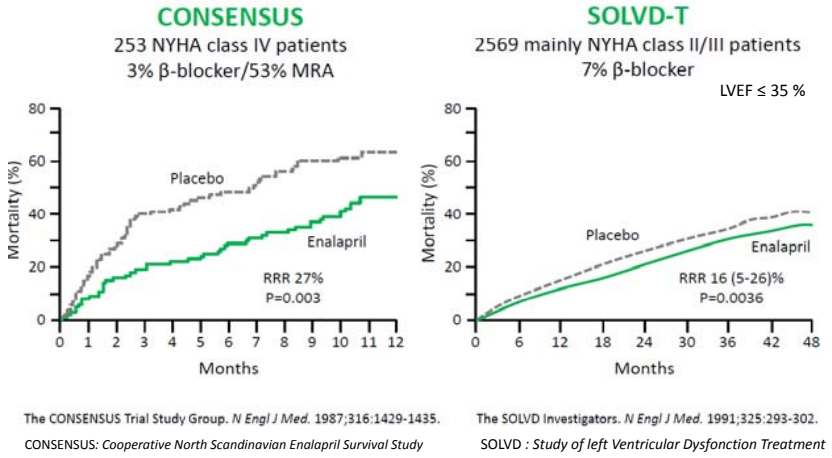


IEC DANS L'INSUFFISANCE CARDIAQUE
Enalapril vs placebo

Stade NYHA	Médicaments	Essai (pts tts)
NYHA I , 67% NYHA II, 33%	Enalapril Diurétiques 27% Digoxine 18%	**SOLVD Prevention** (2111) FEVG ≤ 35 %
NYHA I , 11% NYHA II, 57% NYHA III, 30%	Enalapril Diurétiques 86% Digoxine 66%	**SOLVD Treatment** (1285) FEVG ≤ 35 %
NYHA IV, 100%	Enalapril Furosémide 77% Digoxine 72%	**CONSENSUS**

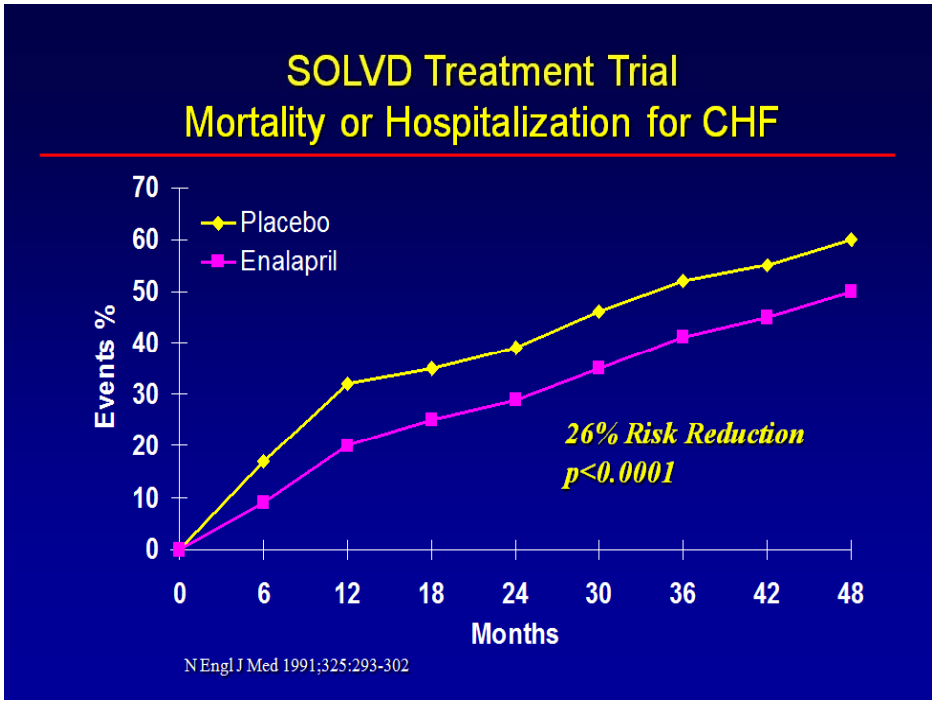
Endpoint 1er:
- Diminution de la mortalité
- Retarder l'apparition de l'IC
- Améliorer les signes et les symptômes

Inhibiteurs de l'enzyme de conversion (IEC) vs placébo



The CONSENSUS Trial Study Group. *N Engl J Med.* 1987;316:1429-1435.
CONSENSUS: *Cooperative North Scandinavian Enalapril Survival Study*

The SOLVD Investigators. *N Engl J Med.* 1991;325:293-302.
SOLVD : *Study of left Ventricular Dysfonction Treatment*



Inhibiteurs de l'enzyme de conversion (IEC)

- Attention: Créatinine > 221 µmol/L ou GFR < 30 mL/min,
- hyperK⁺ > 5 mmol/L
- TA < 90 mmHg

Comment utiliser?

- Commencer à faible dose, ↑ 2 semaines après +labo

Acceptable:

- ↑ < 50 % de la fonction rénale (créat < 266 µmol/L)
- hyperK⁺ <5.5 mmol/L

- Expliquer les bénéfices et les délais, effets secondaires

« Un peu d'IEC, mieux que pas d'IEC »

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Bêta-bloquants

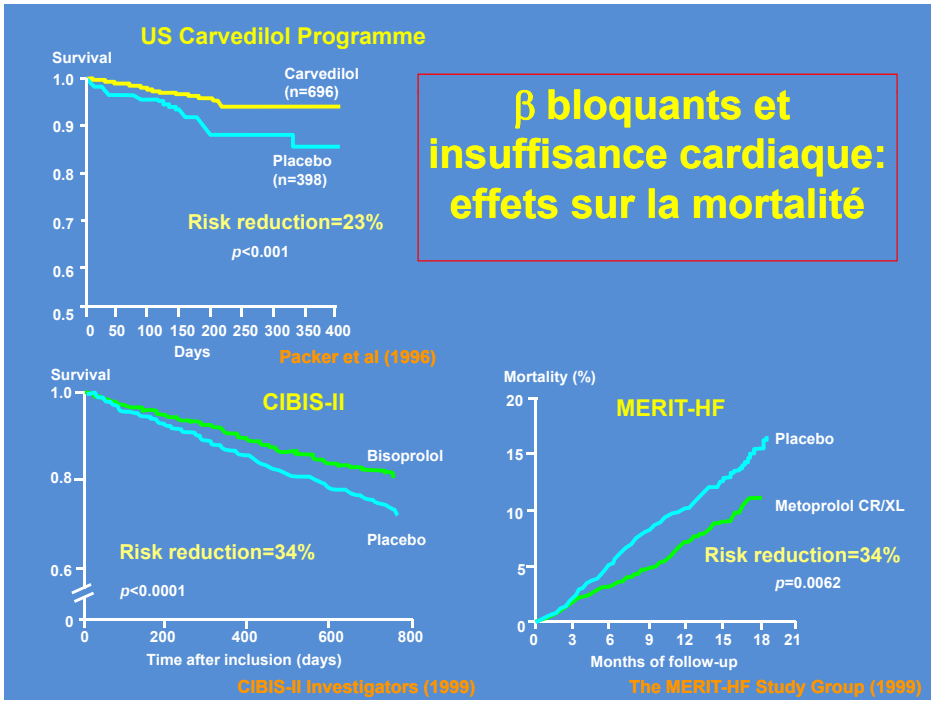
Rationnel du ttt par des bêtabloquants:

Inotrope négatif

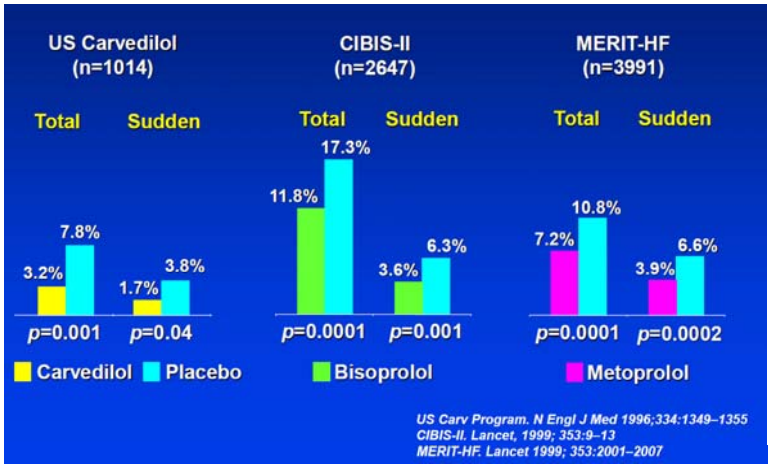
Chronotrope négatif

Contrecarrent l'effet du système sympathique:

- catécholamines
- ↓ taux des vasoconstricteurs (NE, rénine, endothelines)



Bêta-bloquants



Bêta-bloquants

CIND: asthme, BAV II /III ° non appareillé

Prudence:

- NYHA IV décompensé < 4 semaines
- FC < 60/min
- Signe de congestion ou TA < 90 mmHg
- « start low , go slow »
- Doubler dose 2 semaines après

Bisoprolol
Carvedilol
Métoprolol
Nebivolol

- Expliquer pt : amélioration progressive , délais et fatigue transitoire
- Si péjoration IC, fatigue ou FC < 50/min, ↓ dose à 1/2

« un peu de BB, mieux que pas de BB »

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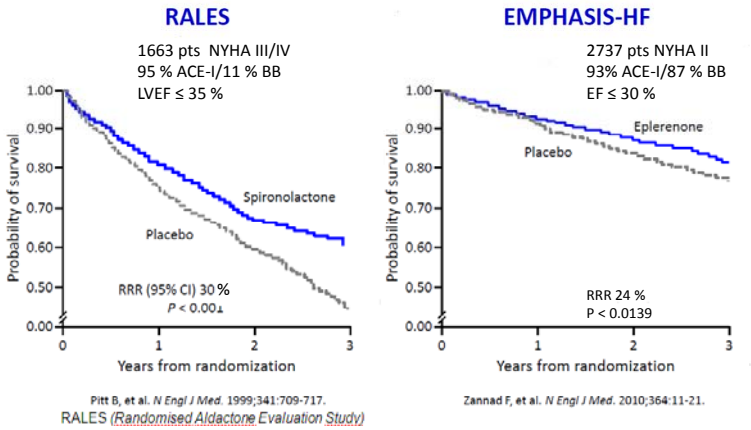
Antagonistes des récepteurs de l'aldostérone

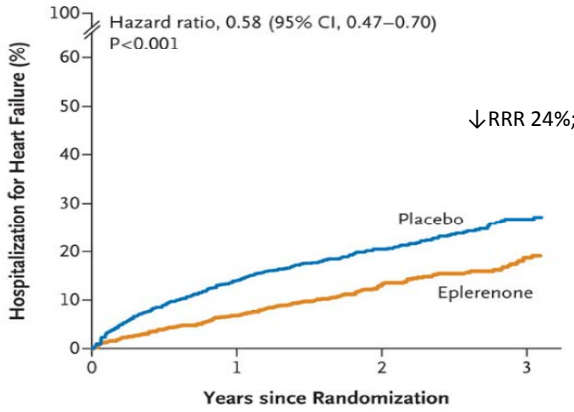


Pitt B, et al. *N Engl J Med.* 1999;341:709-717.
RALES *(Randomised Aldactone Evaluation Study)*

Zannad F, et al. *N Engl J Med.* 2010;364:11-21.

EMPHASIS-HF

Eplerenone in Patients with Systolic Heart Failure and Mild Symptoms



↓RRR 24%; P<0.001),

Antagonistes des récepteurs de l'aldostérone

- Attention
- HyperK+ > 5mmol/l
- Créat. > 220 umol/l (GFR<30ml/min)
- Sel de substitution
- ACEI / sartans /
- AINS
- Bactrim (aldosterone like)
- Eplerenone: inhibiteur CYP 3A4

Autres traitements

Antagonistes des récepteurs de l'angiotensine II

Candesartan in Heart Failure-Assessment of Reduction in Mortality and Morbidity *CHARM* PROGRAME

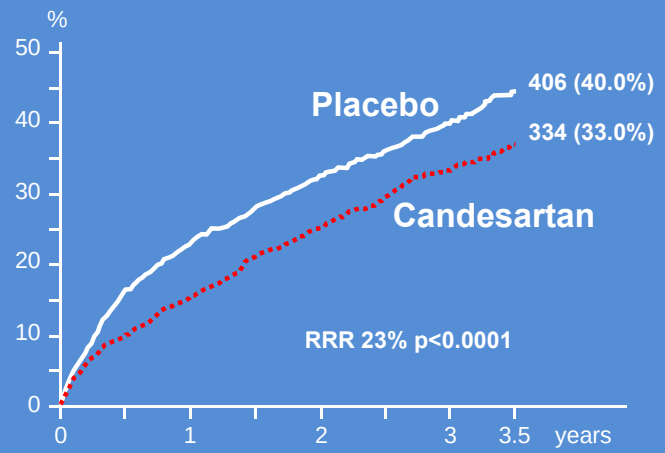
3 groupes **candesartan** vs placebo
chez pts avec IC symptômatique

CHARM Alternative	CHARM Added	CHARM Preserved
n=2028	n=2548	n=3025
LVEF ≤40% ACE inhibitor intolerant	LVEF ≤40% ACE inhibitor treated	LVEF >40% ACE inhibitor treated/not treated

Outcome primaire: décès cv ou hospitalisation pour IC

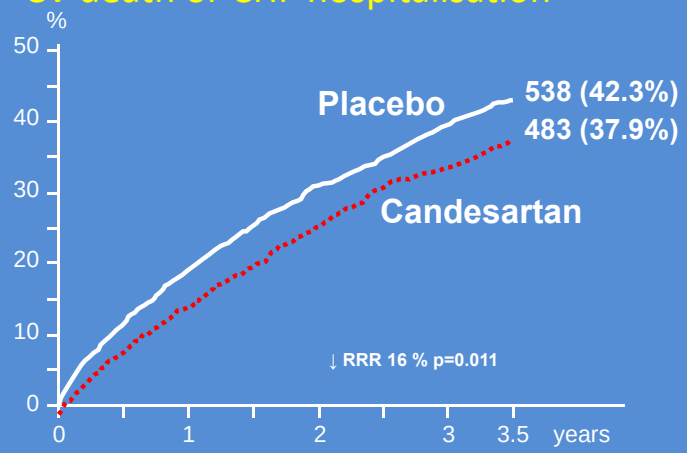
Outcome primaire pour tout le programme: mortalité toute cause

CHARM-Alternative: Primary outcome
CV death or CHF hospitalisation



Circulation. 2004;110:2180-2183

CHARM-Added: Primary outcome
CV death or CHF hospitalisation

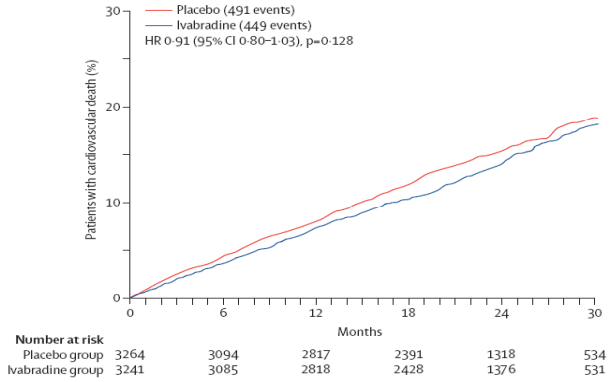


Circulation. 2004;110:2180-2183

Ivabradine (Procorolan) (inhibe canaux I_f NS)

SHIFT (*The Systolic Heart failure treatment with the I_f inhibitor ivabradine Trial*)

3268 pts Ivabradine vs 3290 placébo NYHA II-IV, FE ≤ 35 %
1 endpoint: décès CV ou réhospitalisation IC
FC > 70/min sous dose max BB ou CIND aux BB



Mortalité pour cause cardio-vasculaire

Swedberg K et al. Lancet 2010; 376: 875–85

SHIFT

	Ivabradine group (n=3241)	Placebo group (n=3264)	HR (95% CI)	p value
Primary endpoint				
Cardiovascular death or hospital admission for worsening heart failure	793 (24%)	937 (29%)	0·82 (0·75–0·90)	<0·0001
Mortality endpoints				
All-cause mortality	503 (16%)	552 (17%)	0·90 (0·80–1·02)	0·092
Cardiovascular mortality	449 (14%)	491 (15%)	0·91 (0·80–1·03)	0·128
Death from heart failure	113 (3%)	151 (5%)	0·74 (0·58–0·94)	0·014
Other endpoints				
All-cause hospital admission	1231 (38%)	1356 (42%)	0·89 (0·82–0·96)	0·003
Hospital admission for worsening heart failure	514 (16%)	672 (21%)	0·74 (0·66–0·83)	<0·0001
Any cardiovascular hospital admission	977 (30%)	1122 (34%)	0·85 (0·78–0·92)	0·0002
Cardiovascular death, or hospital admission for worsening heart failure, or hospital admission for non-fatal myocardial infarction	825 (25%)	979 (30%)	0·82 (0·74–0·89)	<0·0001

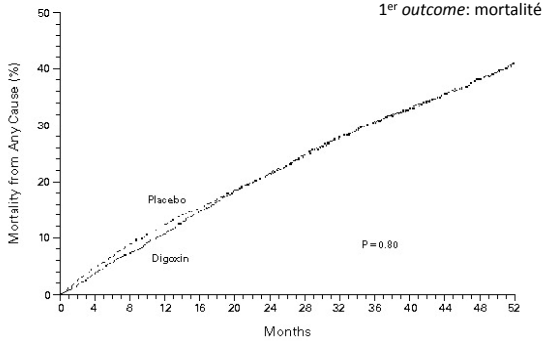
Data are number of first events (%), hazard ratio (HR; 95% CI), and p values.

Table 3: Effects on primary and major secondary endpoints

Digoxine dans l'insuffisance cardiaque

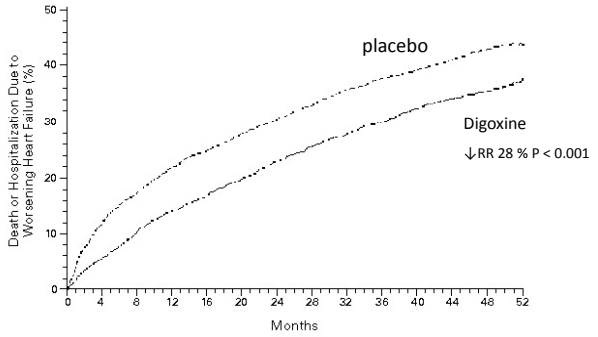
DIG (*The Digitalis Investigation Group*)

3397pts digoxine vs 3403 placebo
FEVG ≤ 45 % NYHA II-IV (diurétiques, IEC 94%)
1er *outcome*: mortalité



The Effect of Digoxin on Mortality and Morbidity in Patients with Heart Failure.
The Digitalis Investigation Group. N Engl J Med 1997; 336:525-533

Digoxine (DIG)



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The Digitalis Investigation Group. N Engl J Med 1997; 336:525-533

European Heart Journal (2012) 33, 1787–1847
doi:10.1093/eurheartj/ehs104

ESC GUIDELINES

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012

The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC

Pharmacological treatments indicated in potentially all patients with symptomatic (NYHA functional class II–IV) systolic heart failure

Recommendations	Class[a]	Level[b]	Ref[c]
An ACE inhibitor is recommended, in addition to a beta-blocker, for all patients with an EF ≤40% to reduce the risk of HF hospitalization and the risk of premature death.	I	A	87–91
A beta-blocker is recommended, in addition to an ACE inhibitor (or ARB if ACE inhibitor not tolerated), for all patients with an EF ≤40% to reduce the risk of HF hospitalization and the risk of premature death.	I	A	92–98
An MRA is recommended for all patients with persisting symptoms (NYHA class II–IV) and an EF ≤35%, despite treatment with an ACE inhibitor (or an ARB if an ACE inhibitor is not tolerated) and a beta-blocker, to reduce the risk of HF hospitalization and the risk of premature death.	I	A	99, 100

Other treatments with less-certain benefits in patients with symptomatic (NYHA class II–IV) systolic heart failure

Recommendations	Class[a]	Level[b]	
ARB			
Recommended to reduce the risk of HF hospitalization and the risk of premature death in patients with an EF ≤40% and unable to tolerate an ACE inhibitor because of cough (patients should also receive a beta-blocker and an MRA).	I	A	
Recommended to reduce the risk of HF hospitalization in patients with an EF ≤40% and persisting symptoms (NYHA class II–IV) despite treatment with an ACE inhibitor and a beta-blocker who are unable to tolerate an MRA.[d]	I	A	
Ivabradine			
Should be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35%, a heart rate remaining ≥70 b.p.m., and persisting symptoms (NYHA class II–IV) despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE inhibitor (or ARB), and an MRA (or ARB).[e]	IIa	B	
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤35% and a heart rate ≥70 b.p.m. who are unable to tolerate a beta-blocker. Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).[e]	IIb	C	
Digoxin			
May be considered to reduce the risk of HF hospitalization in patients in sinus rhythm with an EF ≤45% who are unable to tolerate a beta-blocker (ivabradine is an alternative in patients with a heart rate ≥70 b.p.m.). Patients should also receive an ACE inhibitor (or ARB) and an MRA (or ARB).	IIb	B	
May be considered to reduce the risk of HF hospitalization in patients with an EF ≤45% and persisting symptoms (NYHA class II–IV) despite treatment with a beta-blocker, ACE inhibitor (or ARB), and an MRA (or ARB).	IIb	B	

Traitements non recommandés (pts NYHA II-IV)

- Anticalciques (sauf amlodipine et felodipine) (inotropes négatifs)
- AINS et inhibiteurs Cox-2 (rétention saline et hydrique -> péjoration IR et IC)
- Addition d'un sartan à une association IEC + antagoniste de minéralocorticoides
- Glytazones (Actos, Avandia)

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Les médicaments ne travaillent pas seul

- Education thérapeutique des patients
- Perte pondérale
- Restriction sodique < 3 g/j
- Exercices (réhabilitation cardiaque)
- Approche multidisciplinaire avec des programmes de prise en charge de l'IC