Recommandations dans l'insuffisance cardiaque de la théorie à la pratique

PRISE EN CHARGE DE L'INSUFFISANCE CARDIAQUE EN 2023 : **LES RECOMMANDATIONS VERSUS LES DONNEES DE VRAIE VIE**

FAUVEL Charles
Cardiologue – CHU de Rouen

DÉCLARATION DE LIENS D'INTÉRÊT POTENTIELS

Intervenant : Charles FAUVEL, Rouen

☑ Je déclare les liens d'intérêt potentiels suivants :

Nom de la Société	Type d'affiliation	Période
JANSSEN	Consulting fees	2021-…
PFIZER, NOVARTIS, Servier	Grant	2021-2022
AstraZeneca, Boerhinger Ingelheim, Zoll	Honoraria for lectures	2023
Pfizer	Travel fees	2023

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ESC GUIDELINES 2021

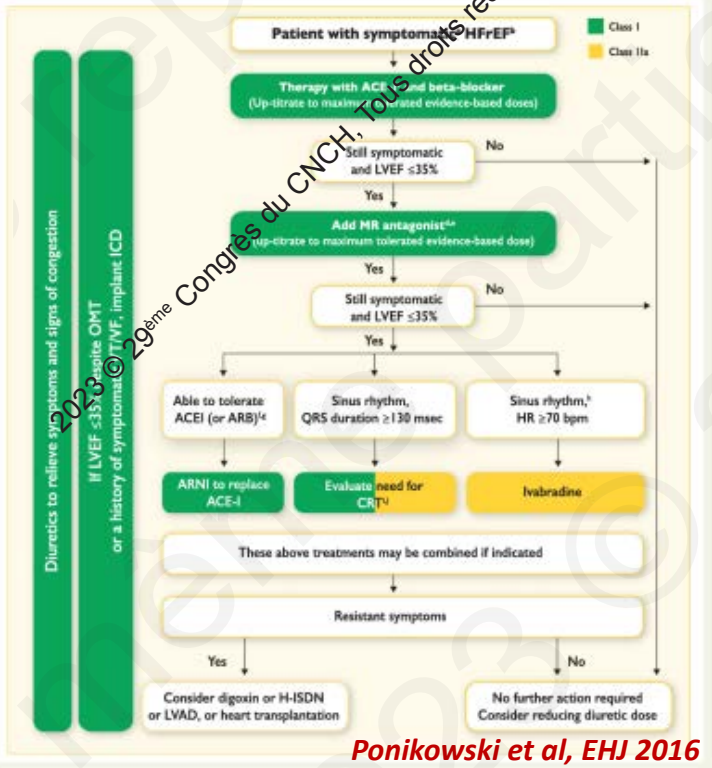
HFrEF management

European Heart Journal (2016) 37, 2129–2200
doi:10.1093/eurheartj/ehw128

ESC GUIDELINES

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)



Ponikowski et al, EHJ 2016

Stratégie séquentielle, verticale, « add-on »

ESC European Society of Cardiology
European Heart Journal (2021)

ESC GUIDELINES

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

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

To reduce mortality - for all patients

ACE-I/ARNI | BB | MRA | SGLT2i

McDonagh et al, EHJ 2021

Pharmacological treatments indicated in patients with (NYHA class II–IV) heart failure with reduced ejection fraction (LVEF ≤40%)

Recommendations	Class[a]	Level[b]
An ACE-I is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[110–113]	I	A
A beta-blocker is recommended for patients with stable HFrEF to reduce the risk of HF hospitalization and death.[114–120]	I	A
An MRA is recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[121,122]	I	A
Dapagliflozin or empagliflozin are recommended for patients with HFrEF to reduce the risk of HF hospitalization and death.[108,109]	I	A
Sacubitril/valsartan is recommended as a replacement for an ACE-I in patients with HFrEF to reduce the risk of HF hospitalization and death.[105]	I	B

© ESC 2021

Stratégie horizontalisée, quadrithérapie pour tous

→ ARNi to replace ACEi/ARB

ESC GUIDELINES 2021

Circulation

AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

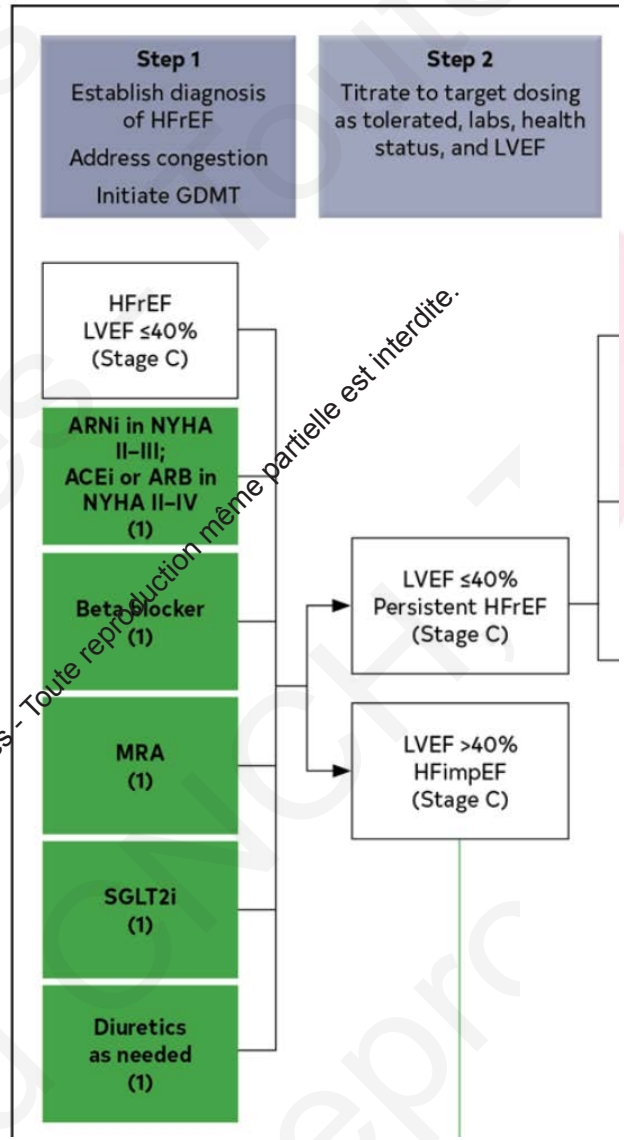
2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Executive Summary: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

TAKE-HOME MESSAGE NO. 1

Guideline-directed medical therapy (GDMT) for HF with reduced ejection fraction (HFrEF) now includes 4 medication classes that include SGLT2i. The 4 groups are: 1) renin-angiotensin system inhibition with angiotensin receptor-neprilysin inhibitors (ARNi), angiotensin-converting enzyme inhibitors (ACEi), or angiotensin (II) receptor blockers (ARB) alone; 2) beta blockers; 3) mineralocorticoid receptor antagonists (MRAs); and 4) the new group, SGLT2i (Figure 1).

→ ARNi for NYHA II-III, ACEi/ARB for NYHA IV

HFrEF management



ESC GUIDELINES 2021

HFrEF management

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

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

Not only the fantastic four!

To reduce HF hospitalization/mortality - for selected patients

Volume overload
- Diuretics

SR with LBBB ≥ 150 ms	*SR with LBBB 130–149 ms or non LBBB≥ 150 ms*
CRT-P/D	CRT-P/D

Ischaemic aetiology	*Non-ischaemic aetiology*
ICD	ICD

Atrial fibrillation	*Atrial fibrillation*	*Coronary artery disease*	*Iron deficiency*
Anticoagulation	Digoxin, PVI	CABG	Ferric carboxymaltose

Aortic stenosis	*Mitral regurgitation*	*Heart rate SR>70 bpm*	*Black Race*	*ACE-I/ARNI intolerance*
SAVR/TAVI	TEE MV Repair	Ivabradine	Hydralazine/ISDN	ARB

For selected advanced HF patients

Heart transplantation	MCS as BTT/BTC	Long-term MCS as DT

To reduce HF hospitalization and improve QOL - for all patients

- Exercise rehabilitation
- Multi-professional disease management

McDonagh et al, EHJ 2021

ESC GUIDELINES update 2023

HFpEF management

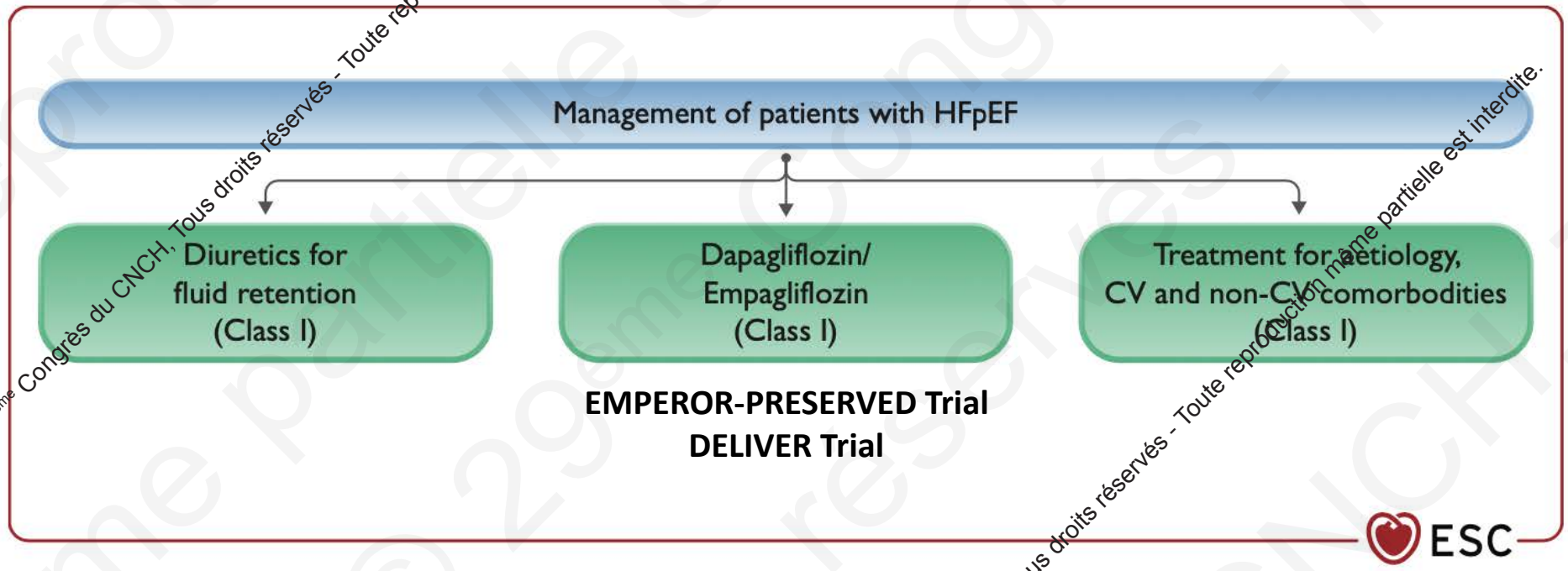


Figure 2 Management of patients with heart failure with preserved ejection fraction. CV, cardiovascular; HFpEF, heart failure with preserved ejection fraction.

McDonagh et al, EHJ 2023

ESC GUIDELINES en pratique

QU'EN EST IL EN **PRATIQUE COURANTE** ?

PATIENTS (ULTRA) SELECTIONNES des RCT

VS

REGISTRES DE « VRAI VIE »

(« Real world data and evidence »)

ESC GUIDELINES en pratique

Penser vous **qu'en phase de titration, ajouter une nouvelle classe thérapeutique** soit plus importante que **d'obtenir la dose maximale des traitements déjà présent** ?

- OUI
- NON

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ESC GUIDELINES en pratique

Adoptez-vous un **schéma de titration différentiel** entre les patients insuffisants cardiaques vu en ambulatoire, en post-hospitalisation pour IC, en post-choc cardiogénique ?

- OUI
- NON

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ESC GUIDELINES en pratique

Selon vous, dans **combien de % des cas** arrivez-vous à obtenir **une titration maximale (dose maximale tolérée)** chez vos patients IC à FEVG altérée ?

- < 25% des cas
- 25-50% des cas
- 50-75% des cas
- > 75% des cas

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ESC GUIDELINES en pratique

Selon vous, **en combien de temps arrivez-vous** à obtenir l'**introduction** des **4 classes thérapeutiques** pour IC à FEVG altérée **en hospitalisation** ?

- < 6 jours
- 1-2 semaines
- 2 à 4 semaines
- > 4 semaines

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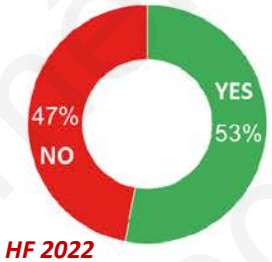
ESC GUIDELINES en pratique

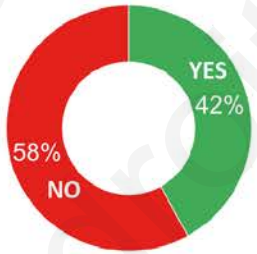
INTERNATIONAL ACADEMIC SURVEY REGARDING THE LATEST ESC HEART FAILURE GUIDELINES

- 55 different countries
- 615 Cardiologists
- 58% from University Hospital
- 26% of Heart Failure specialists
- 61% LVEF ≤ 40%: best threshold to define HFrEF

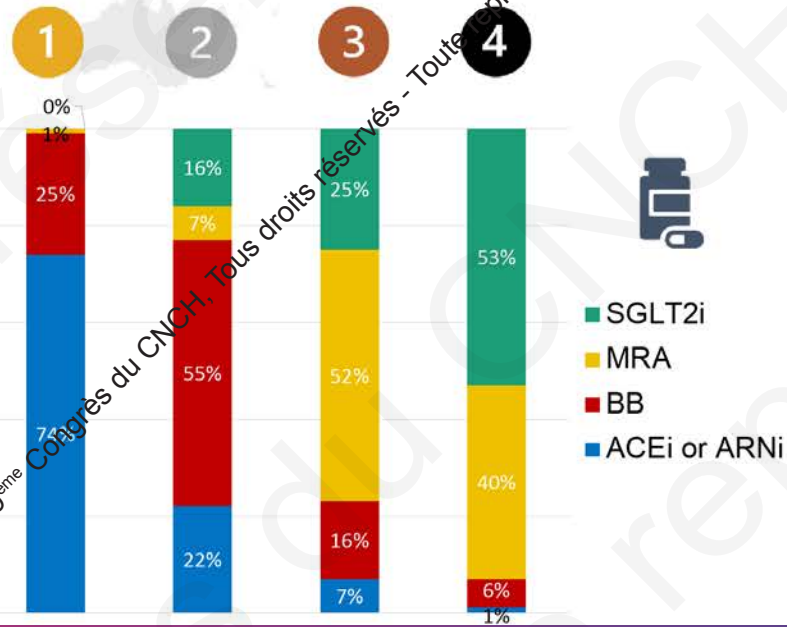
ARNI FIRST INSTEAD OF ACEI?



UP-TITRATING MORE IMPORTANT THAT ADDING?



PREFERED HFrEF DRUG SEQUENCING INTRODUCTION



Differences between heart failure specialists and non-specialists regarding heart failure drug implementation and up-titration

Interestingly, 44% of non-specialists thought that titration is more important than adding another HF drug, whereas a majority (64%) of HF specialists thought otherwise, and this difference tended to be significant ($p = 0.063$).

Fauvel et al, EHJ HF 2022
Fauvel et al, EHJ HF 2023

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ESC GUIDELINES update 2023

Pre– and early post-discharge FU after AHF

Recommendation Table 3 — Recommendation for pre-discharge and early post-discharge follow-up of patients hospitalized for acute heart failure

Recommendation	Class[a]	Level[b]
An intensive strategy of initiation and rapid up-titration of evidence-based treatment before discharge and during frequent and careful follow-up visits in the first 6 weeks following a HF hospitalization is recommended to reduce the risk of HF rehospitalization or death.[c,d,e] [16]	I	B

6 WEEKS FOR UP-TITRATION

McDonagh et al, EHJ 2023

STRONG-HF

CONTEMPORARY POST-DISCHARGE MANAGEMENT IN HEART-FAILURE

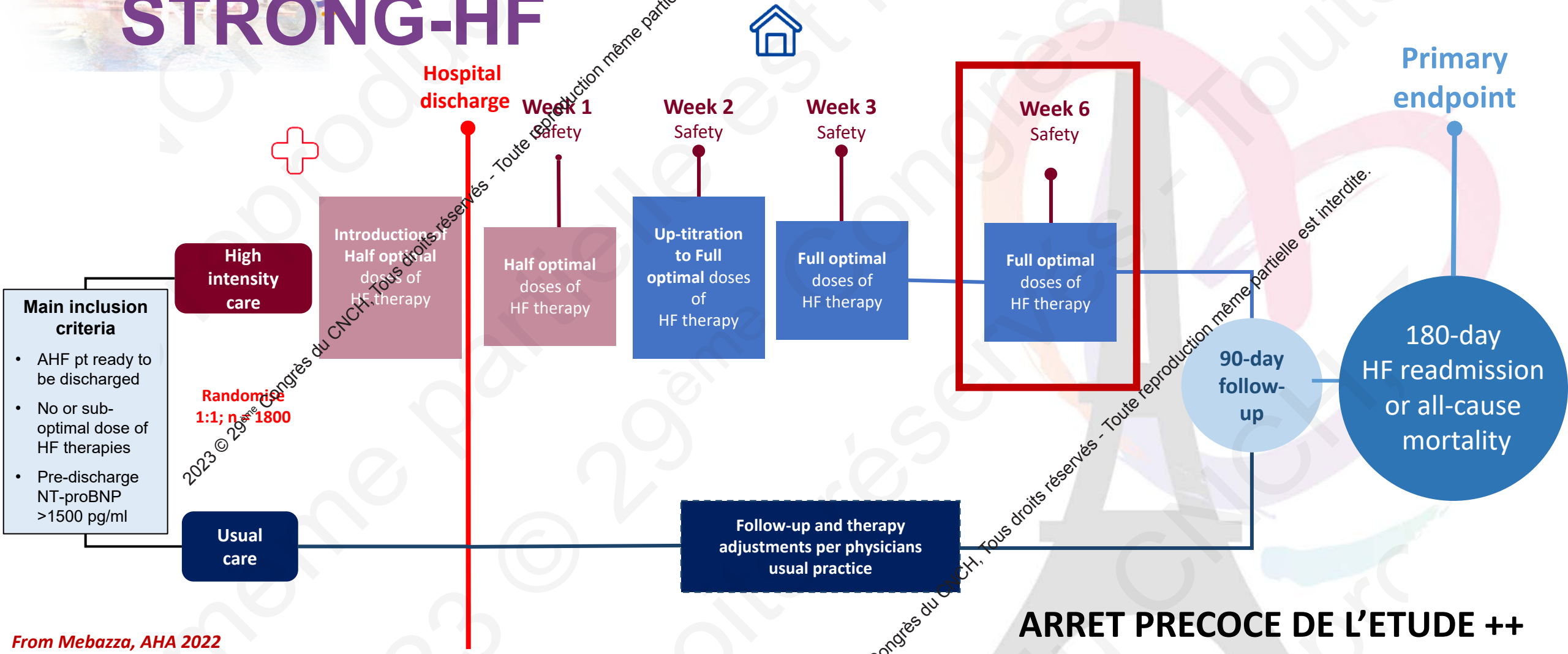
Safety, tolerability and efficacy of up-titration of guideline-directed medical therapy for acute heart failure (STRONG-HF): a multinational, open-label, randomised, trial

Alexandre Mebazaa, Beth Davison, Ovidiu Chioncel, Alain Cohen-Solal, Rafael Diaz, Gerasimos Filippatos, Marco Metra, Piotr Ponikowski, Karen Sliwa, Adriaan A Voors, Christopher Edwards, Maria Novosadova, Koji Takagi, Albertino Damasceno, Hadiza Saidu, Etienne Gayat, Peter S Pang, Jelena Celutkiene, Gad Cotter

Mebazaa et al, Lancet 2022

STRONG-HF

STRONG-HF
CONTEMPORARY POST-DISCHARGE MANAGEMENT IN HEART-FAILURE



From Mebazza, AHA 2022
Mebazaa et al, Lancet 2022

ARRET PRECOCE DE L'ETUDE ++

HF therapy: combining ACEi/ARB/ARNi & BB & MRA

Collège National des Cardiologues des Hôpitaux

STRONG-HF

Comparable à la randomisation, le taux de prescription (au moins 50% dose cible) est largement supérieur dans le groupe titration haute intensité qq que soit la molécule considérée

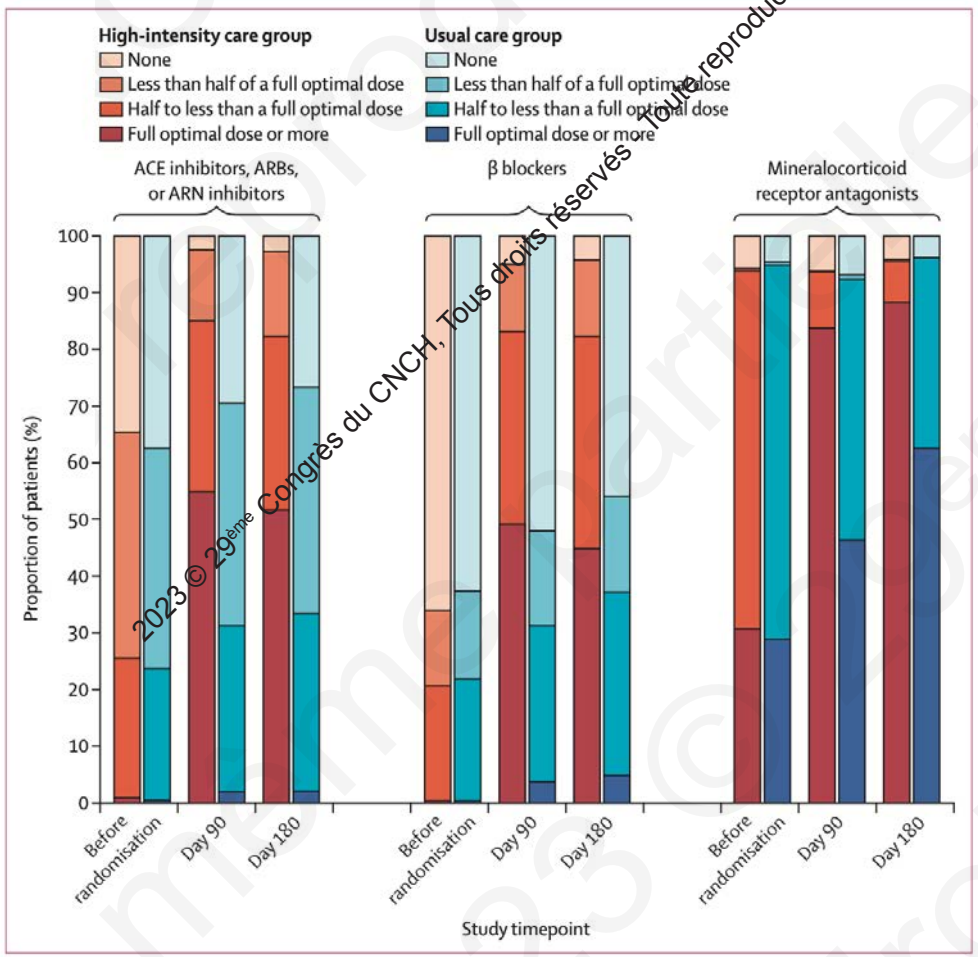
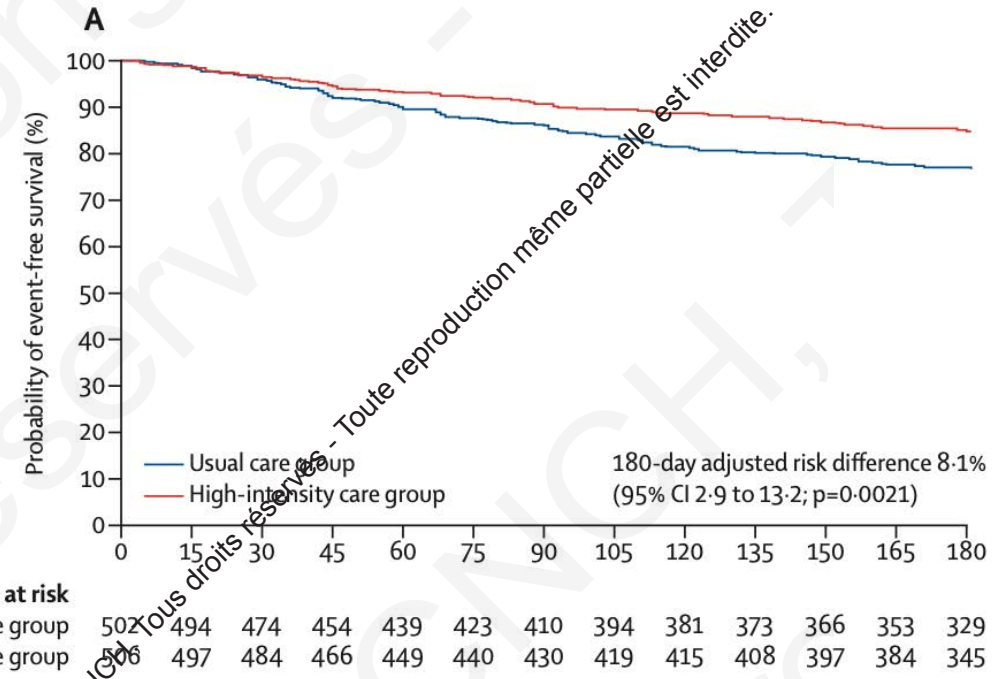


Figure 2: **Oral guideline-directed medical therapies for heart failure prescribed, in high-intensity care and usual care groups by visit**
Full optimal doses for each treatment are given in the appendix (p 5). ACE=angiotensin converting enzyme. ARB=angiotensin receptor blocker. ARN=angiotensin receptor-neprilysin.

STRONG-HF
CONTEMPORARY POST-DISCHARGE MANAGEMENT IN HEART-FAILURE

All-cause death of HF readmission



Mebazaa et al, Lancet 2022

Collège National des Cardiologues des Hôpitaux

WE HAVE TO BE STRONG… THEN, OPTIMAL SEQUENCE ?

- EXPERT

Circulation

PERSPECTIVE

How Should We Sequence the Treatments for Heart Failure and a Reduced Ejection Fraction?

A Redefinition of Evidence-Based Medicine

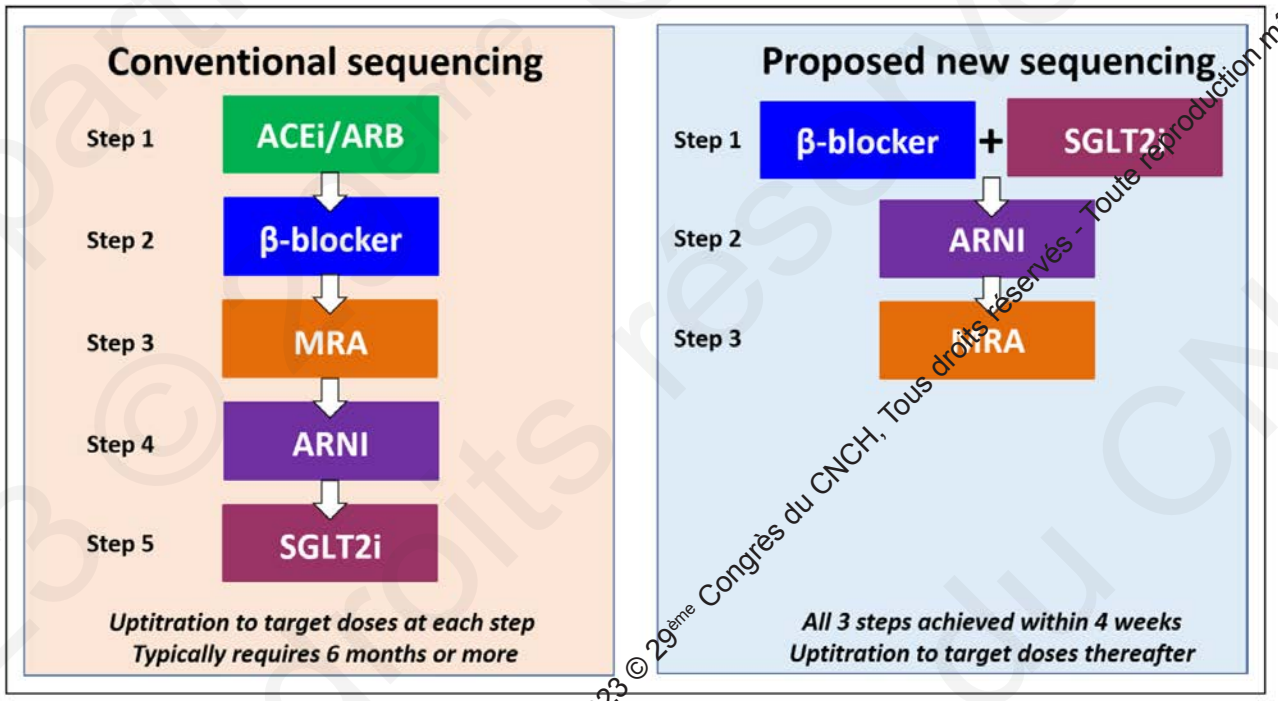
ESC European Society of Cardiology

European Journal of Heart Failure (2021) 23, 882–894
doi:10.1002/ejhf.2149

REVIEW

Rapid evidence-based sequencing of foundational drugs for heart failure and a reduced ejection fraction

Milton Packer[1,2]* and John J.V. McMurray[3]



McMurray, Packer, Circ 2021

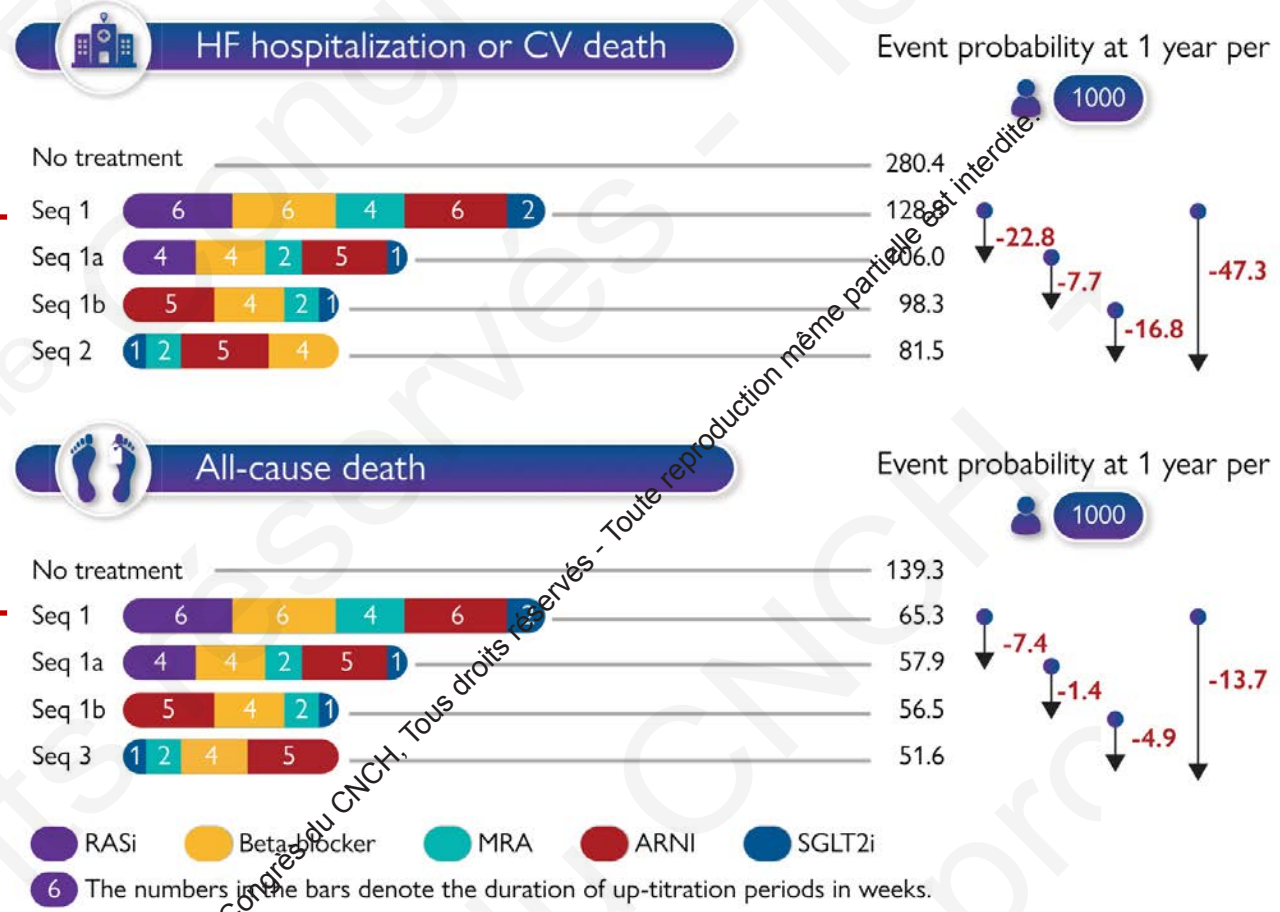
WE HAVE TO BE STRONG… THEN, OPTIMAL SEQUENCING?

ESC European Society of Cardiology
European Heart Journal (2022) 00, 1–15
https://doi.org/10.1093/eurheartj/ehac210
CLINICAL RESEARCH
Heart failure and cardiomyopathies

Accelerated and personalized therapy for heart failure with reduced ejection fraction

Li Shen[1,2], Pardeep Singh Jhund[2], Kieran Francis Docherty[2], Muthiah Vaduganathan[3], Mark Colquhoun Petrie[2], Akshay Suvas Desai[3], Lars Køber[4], Morten Schou[5], Milton Packer[6,7], Scott David Solomon[3], Xingwei Zhang[1], and John Joseph Valentine McMurray[2]*

Séquence « historique » ←



Séquence « historique » ←

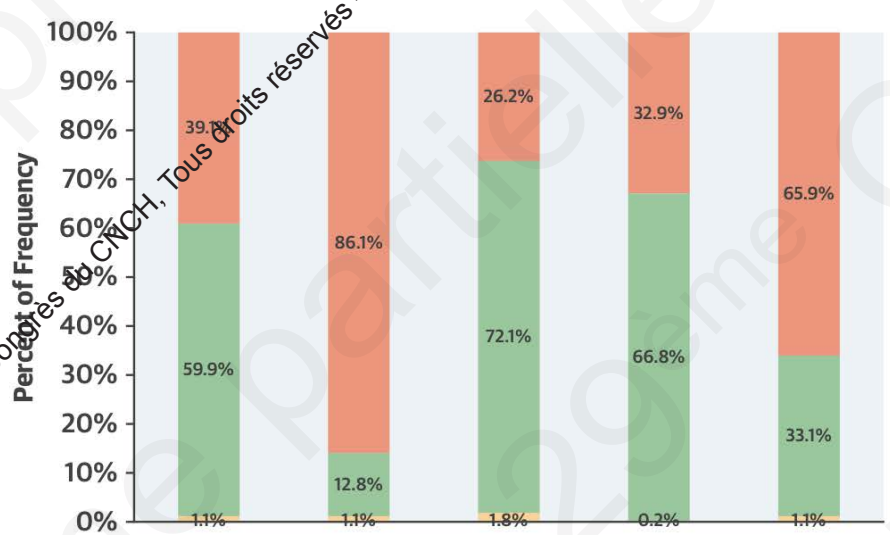
Conventional approach may not be the best and alternative is needed…

WHAT REGISTRIES SAY?

CHAMP-Registry

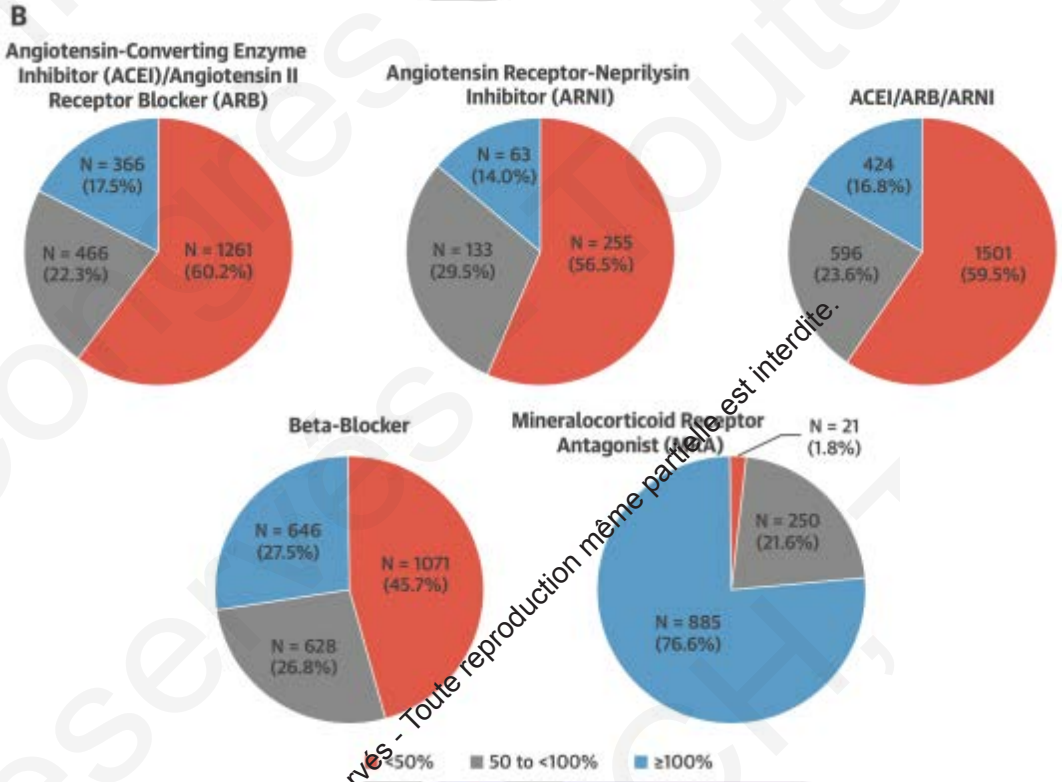
- 3,518 US outpatients with HFrEF with at least 1-treatment
- Baseline analysis

A



	ACEI/ARB	ARNI	ACEI/ARB/ ARNI	Beta-Blocker	MRA
Without Contraindication and Not Treated	1374	3029	920	1159	2317
Treated	2107	452	2536	2351	1163
With Contraindication	37	37	62	8	38

B



GDMT UNDER PRESCRIPTION

→ Among eligible: 27%, 33%, 67% not prescribed ACEI/ARB/ARNI, BB, MRA

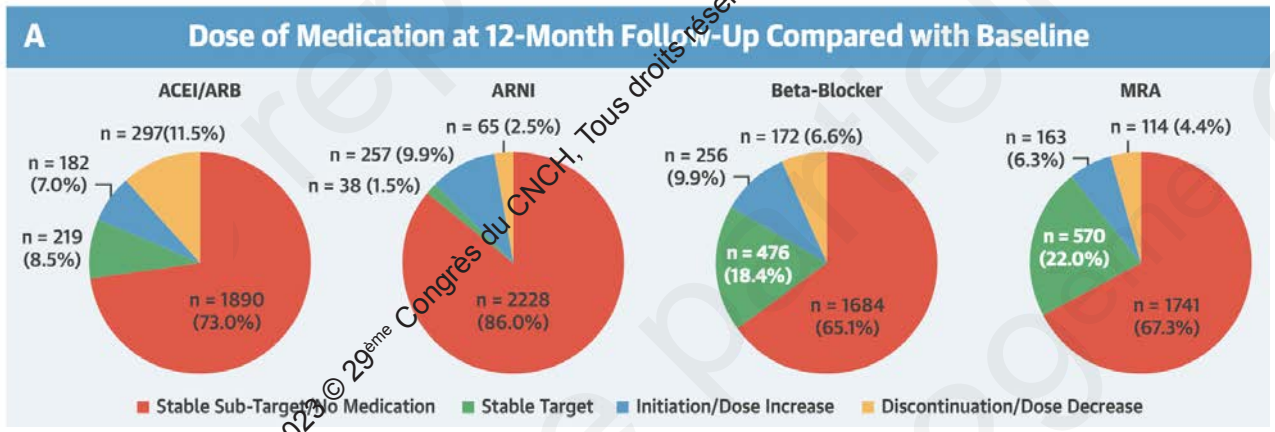
→ When prescribed few patients receiving BB, ACEI/ARB/ARNI target doses

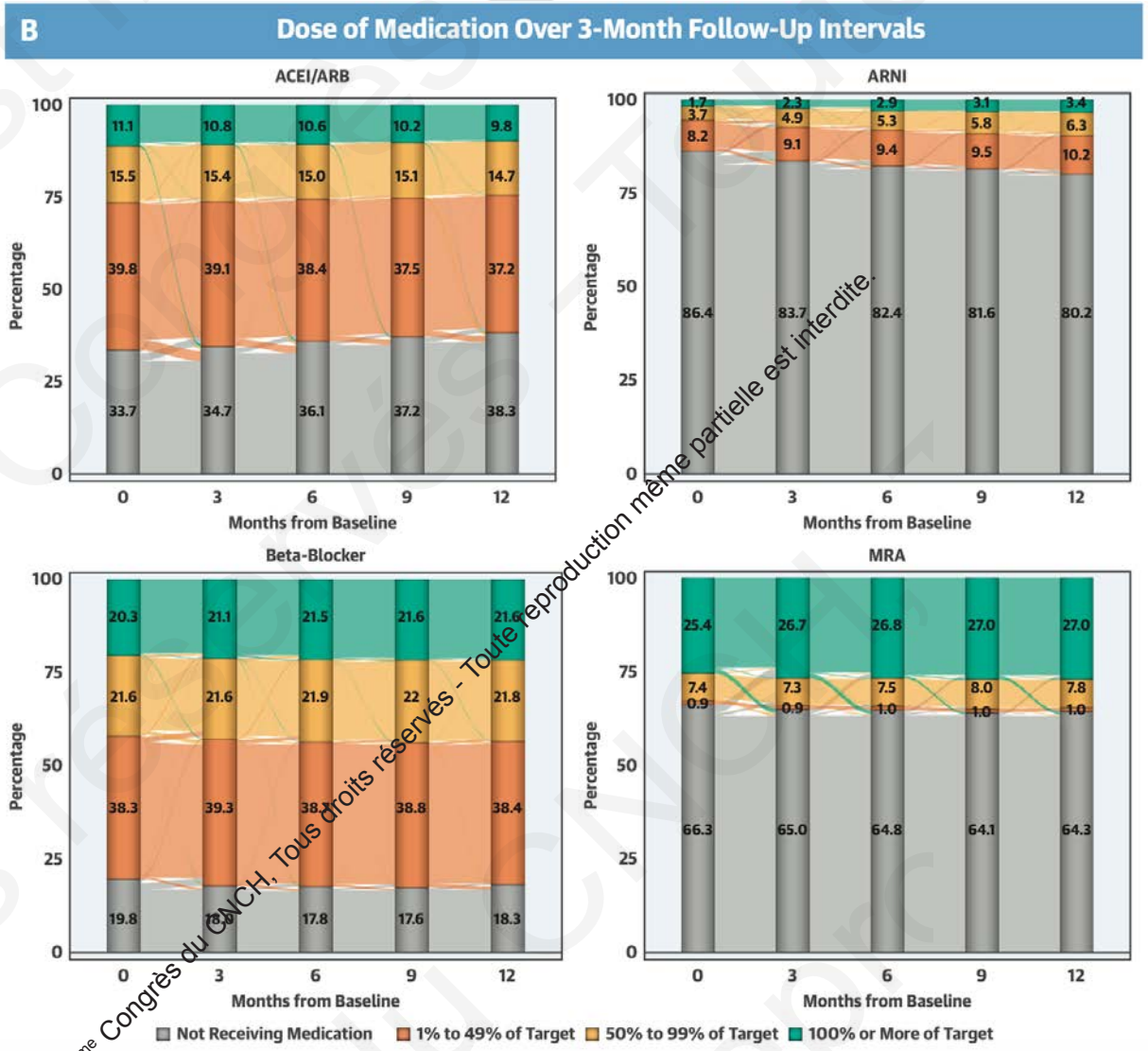
S.J.Greene, JACC 2018

WHAT REGISTRIES SAY?

CHAMP-Registry

- 2,588 US outpatients with HFrEF
- 2015-2017
- FU analysis





GDMT EVOLUTION OVER TIME IS SUBOPTIMAL

→ Most eligible HFrEF patients dit not receive target doses therapy

→ When initiated, the dose do not increase

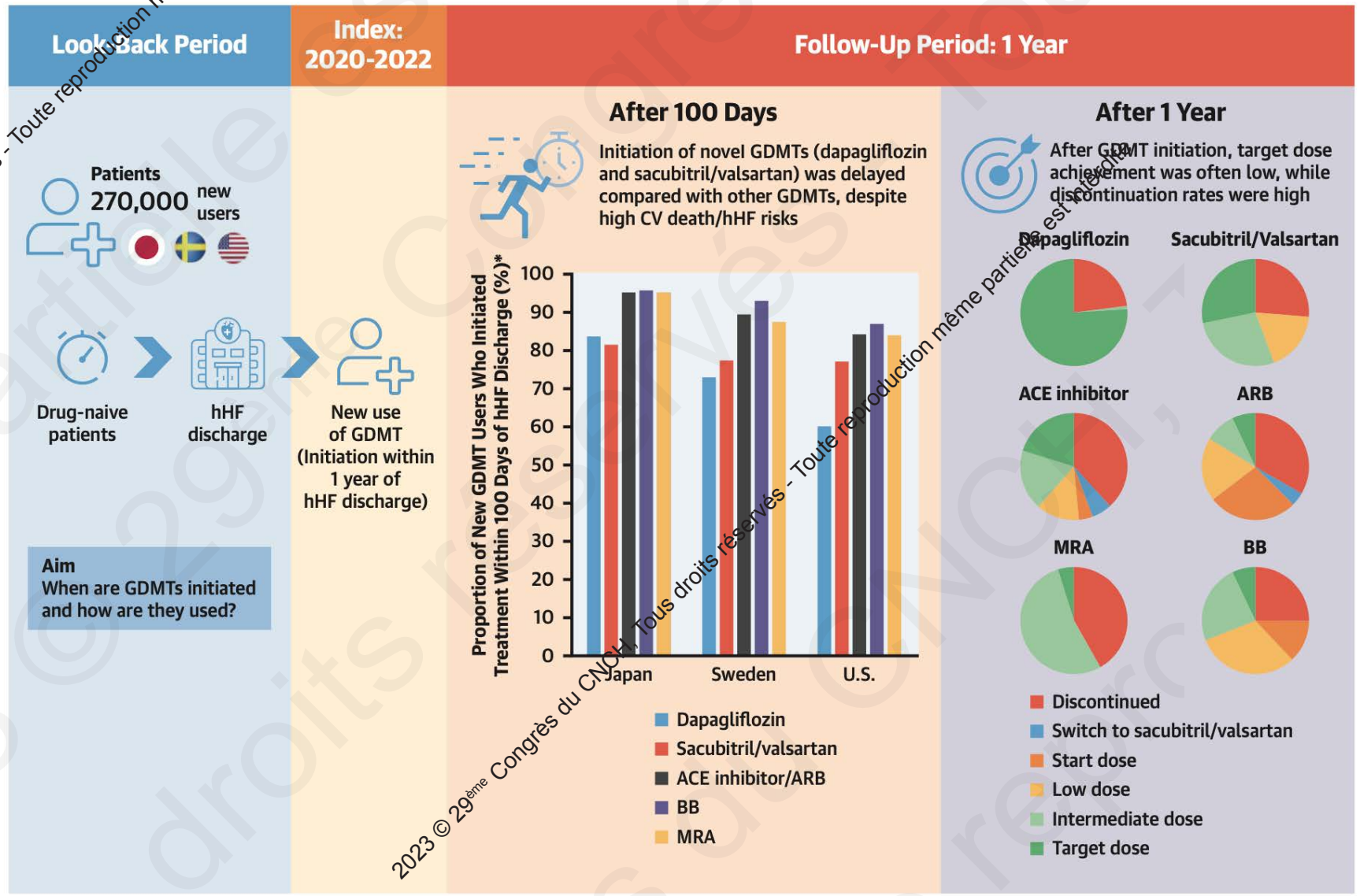
S.J.Greene, JACC 2019

WHAT REGISTRIES SAY?

EVOLUTION-HF registry

- Japan, Sweden and US
- Patients initiating GDMT < 12 months after AHF hospitalization
- n=266,589 patients

CENTRAL ILLUSTRATION Initiation, Titration to Target Dose, and Discontinuation of GDMTs Among New Users of GDMTs After hHF, in Japan, Sweden, and the United States



WHAT REGISTRIES SAY?

ESC European Society of Cardiology
European Journal of Heart Failure (2021) 23, 1499–1511
doi:10.1002/ejhf.2271
RESEARCH ARTICLE

Heart failure drug titration, discontinuation, mortality and heart failure hospitalization risk: a multinational observational study (US, UK and Sweden)

Look-back period | **Index:** 2016–2019 | **Analysis period:** 1-year results

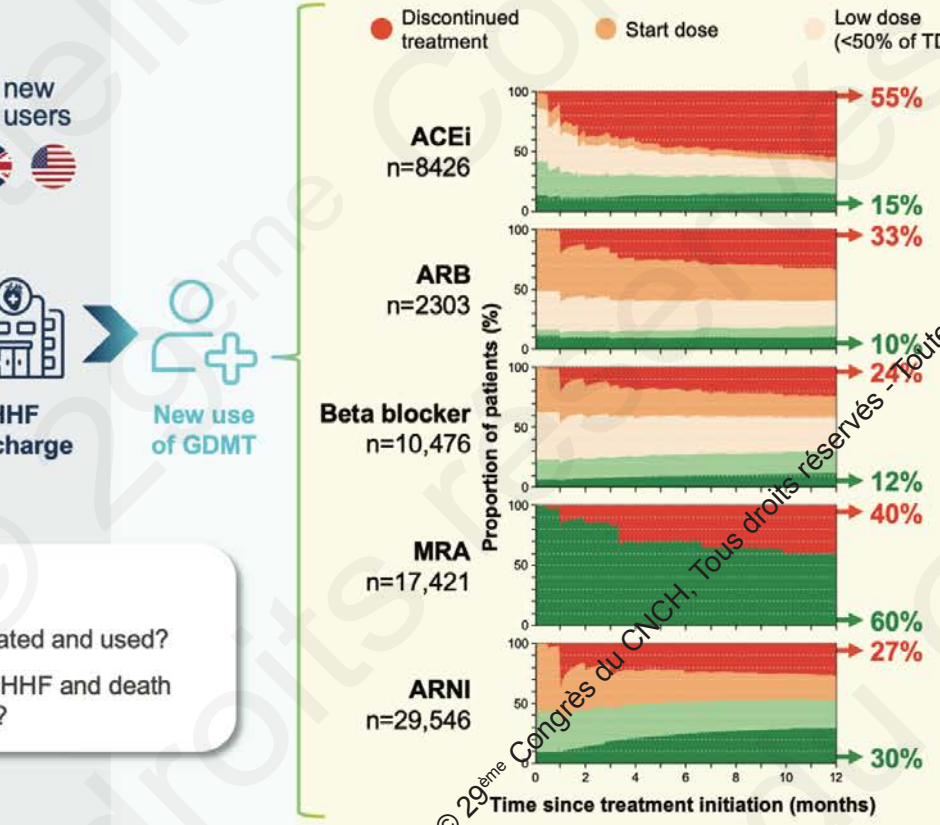
Patients
68,172 new users

Drug-naïve patients → HHF discharge → New use of GDMT

Aim

How are GDMTs initiated and used?

What are the risks of HHF and death after GDMT initiation?



Risks of HHF or death (events/100 patient-years)

	HHF or ACD*	HHF	ACD*
ACEi	40.0	18.9	24.0
ARB	43.3	24.4	21.1
Beta blocker	45.9	22.4	28.8
MRA	53.6	27.9	31.0
ARNI	86.9	46.8	21.3

Treatment initiation immediately after HHF. *Sweden and UK only.

The high risks do not relate to the effectiveness of the drugs, but the point in the HF disease journey at which the drug has been initiated.

Conclusion

New initiation of GDMT was followed by consistent patterns of low up-titration and early discontinuation in the three countries involved.

During GDMT utilisation, patients are at high risk, demonstrating the urgent need to move away from a prolonged, sequential approach.

ACD, all-cause death; ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; GDMT, guideline-directed medical therapy; HF, heart failure; HHF, hospitalisation for heart failure; MRA, mineralocorticoid receptor antagonist; TD, target dose.

G.Savarese, EHJ HF 2021

WHAT REGISTRIES SAY?

EPIC-HF Trial post-hoc analysis

Study Cohort

292 patients completed cardiology clinic visit

- 107 patients (36.7%) with treatment intensification
- 185 patients (63.4%) with no treatment intensification

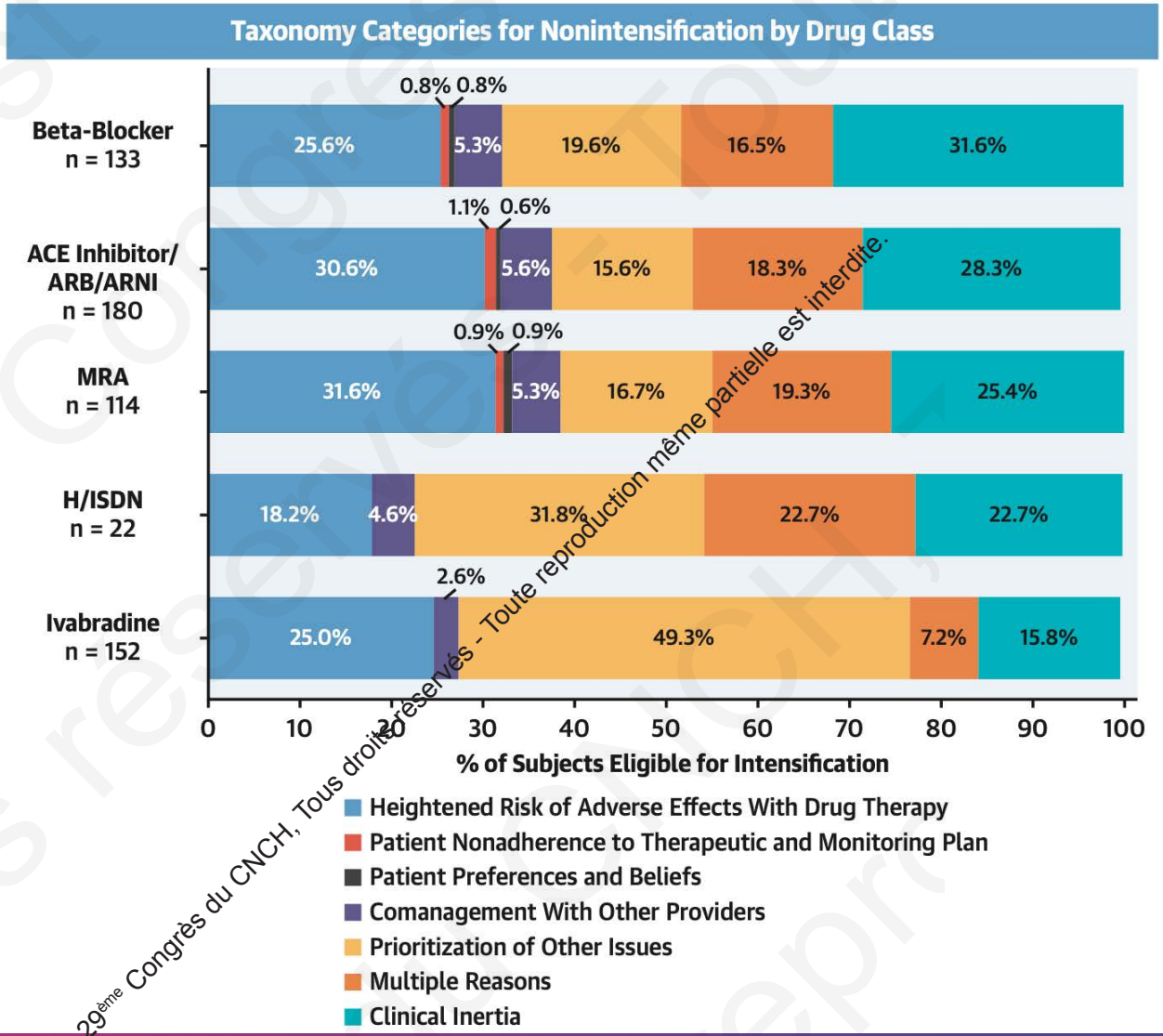
Clinical Inertia

Defined as either:

1) Clinician provided recognition of nonintensification that was not medically justified (eg, "Patient stable, will not change medications") without additional reasoning
2) No documentation regarding nonintensification

90/185 patients (48.6%) had clinical inertia for reason of nonintensification for at least one drug class

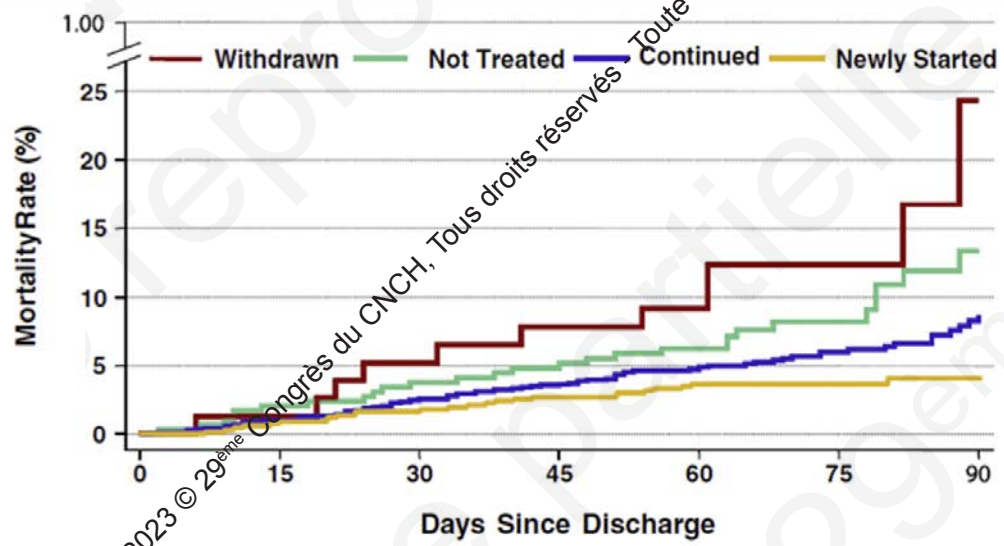
Clinical inertia as only reason for nonintensification varied from **15.8% to 31.6%** by drug class



WHAT REGISTRIES SAY?

Effect of treatment withdrawal

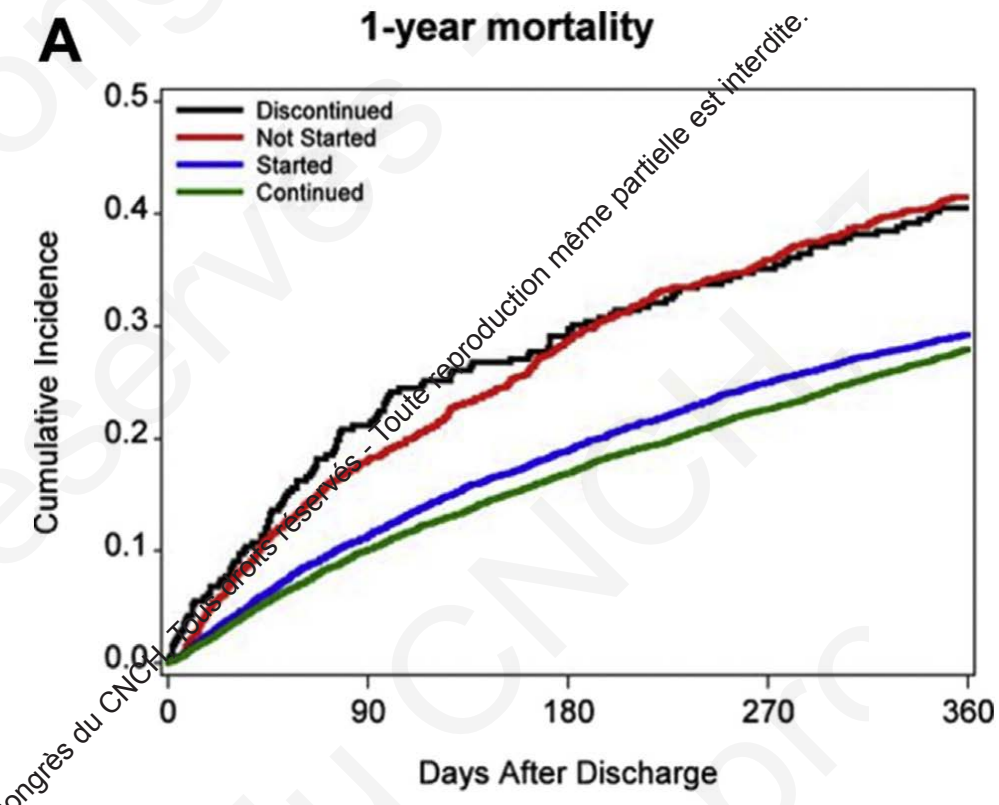
FIGURE 2 Post-Discharge Survival by Beta-Blocker Treatment Groups



Patients at risk:							
Withdrawn	79	77	73	68	66	26	10
Not Treated	303	275	269	262	242	114	51
Continued	1350	1303	1268	1236	1123	536	224
NewlyStarted	632	609	591	575	531	274	110

Kaplan-Meier survival curve of patients newly started, continued, withdrawn, and not treated with beta-blocker therapy. Reproduced with permission from Fonarow et al. (7).

FIGURE 3 Post-Discharge Outcomes by ACEI Treatment Groups

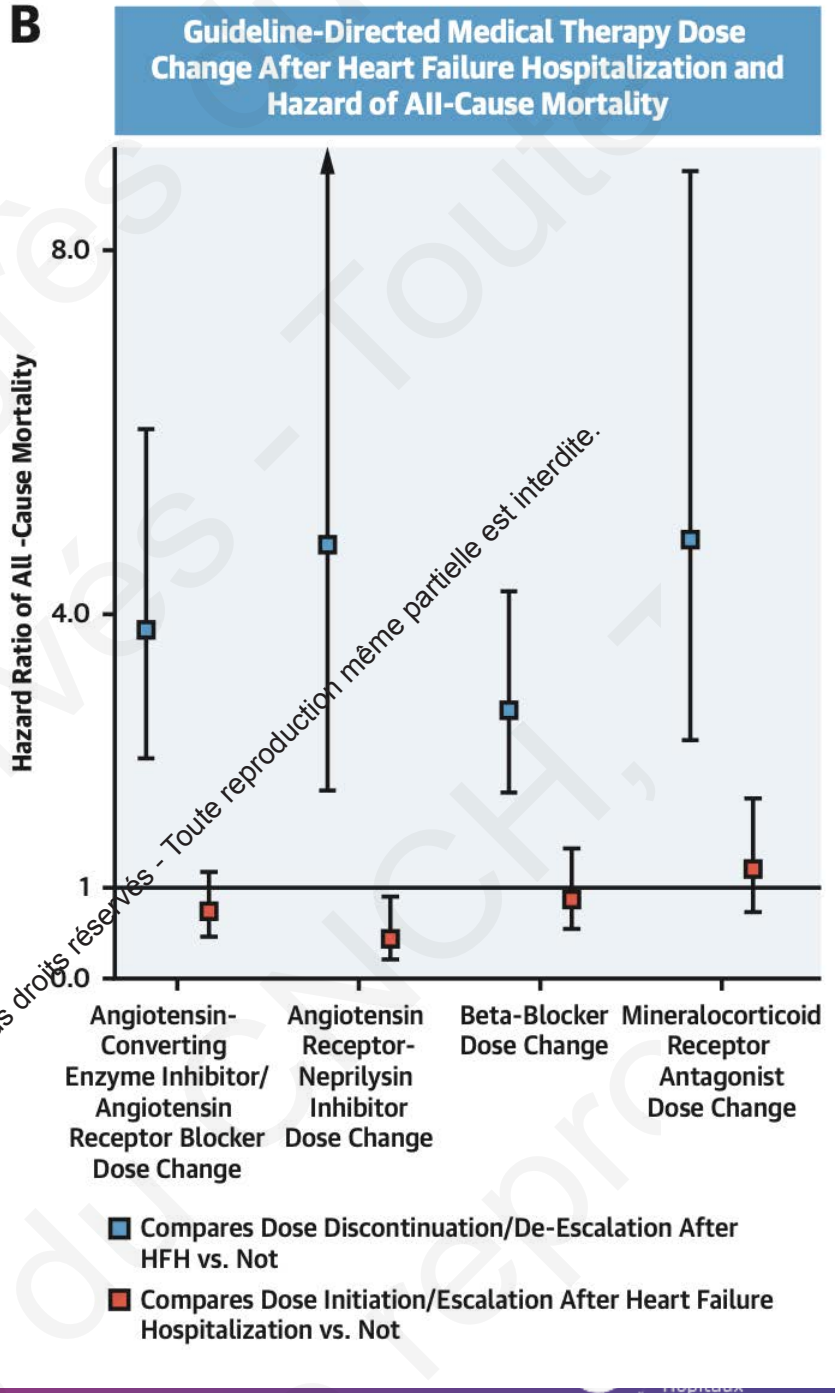


WHAT REGISTRIES SAY?

Effect of treatment discontinuation/de-escalation

- From CHAMP-Registry

RESULTS HFH (compared with no HFH) was positively associated with initiation of angiotensin-converting enzyme (ACE) inhibitor/angiotensin receptor blocker (ARB), angiotensin receptor-neprilysin inhibitor, beta-blocker, and mineralocorticoid receptor antagonist (MRA). HFH positively associated with dose escalation of ACE inhibitor/ARB (probability ratio: 1.71, 95% confidence interval [CI]: 1.36 to 2.16) and MRA (probability ratio: 8.71, 95% CI: 4.19 to 18.10). In those on prior therapy, HFH was associated with discontinuation and de-escalation of all classes of GDMT. ACE inhibitor/ARB, angiotensin receptor-neprilysin inhibitor, beta-blocker, and MRA de-escalation/discontinuation after HFH was associated with increased risk of all-cause mortality with hazard ratios of 3.82 (95% CI: 2.42 to 6.03), 4.76 (95% CI: 2.06 to 11.03), 2.94 (95% CI: 2.04 to 4.25), and 4.81 (95% CI: 2.61 to 8.87), respectively.



WHAT REGISTRIES SAY?

Is it possible in elderly/frailty patient?

ESC European Society of Cardiology
European Journal of Heart Failure (2023) 25, 1145–1155
doi:10.1002/ejhf.2920
RESEARCH ARTICLE

Safety, tolerability and efficacy of up-titration of guideline-directed medical therapies for acute heart failure in elderly patients: A sub-analysis of the STRONG-HF randomized clinical trial

Mattia Arrigo[1*], Jan Biegus[2], Ayu Asakage[3], Alexandre Mebazaa[3,4], Beth Davison[3,5], Christopher Edwards[6], Marianna Adamo[7], Marianela Barros[6], Jelena Celutkiene[8], Kamilė Čerlinskaitė-Bajorė[8], Ovidiu Chioncel[9], Albertino Damasceno[10], Rafael Diaz[11], Gerasimos Filippatos[12], Etienne Gayat[3,4], Antoine Kimmoun[13,14], Carolyn S.P. Lam[15], Marco Metra[7], Maria Novosadova[6], Matteo Pagnesi[7], Peter S. Pang[16], Piotr Ponikowski[2], Hadiza Saidu[3], Karen Sliwa[18], Koji Takagi[6], Jozine M. Ter Maaten[19], Daniela Tomasoni[7], Adriaan A. Voors[19], Gad Cotter[3,5], and Alain Cohen-Solal[3,20]

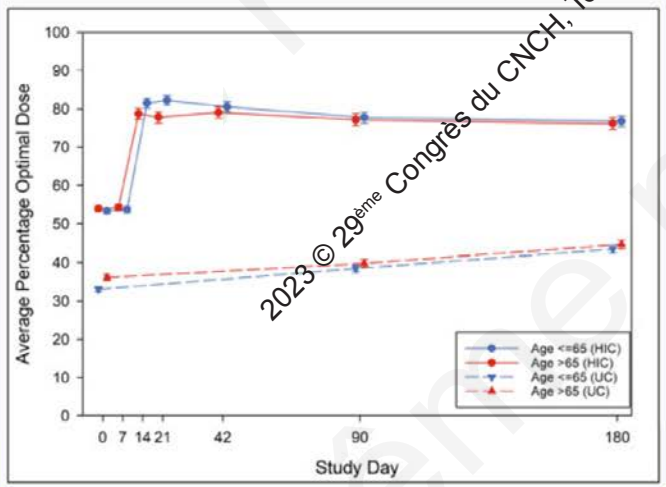
Aim

To assess the role of age on efficacy and safety of high-intensity care strategy (HIC; rapid up-titration of guideline-directed medical therapy (GDMT) and close follow-up) after acute heart failure (AHF) admission.

Population

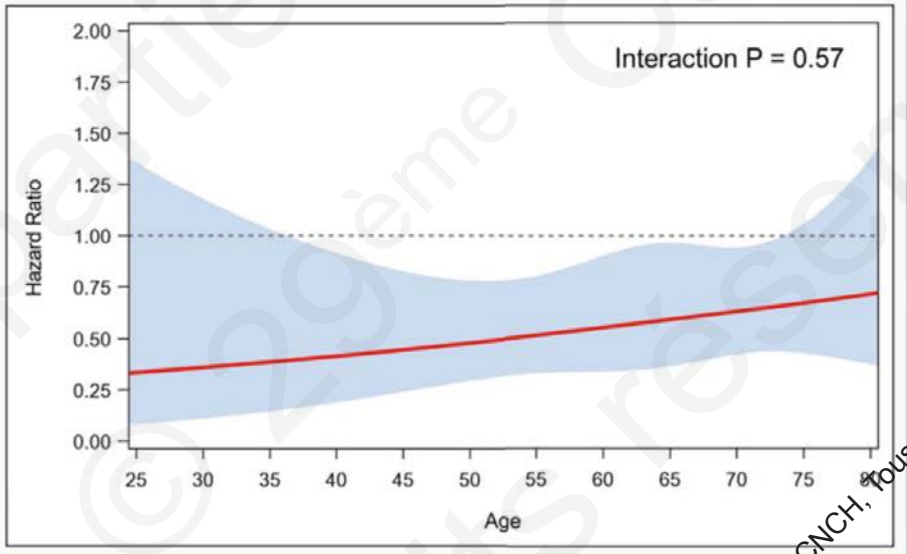
1078 patients from 14 countries.
"older" (> 65 years), mean age 74±5 years.
"younger" (≤ 65 years), mean age aged 53±11.

Uptitration of GDMT



Results

Treatment effect of high-intensity care vs. usual care on all-cause death or HF readmission according to age (excluding COVID-19 deaths)



Conclusion

High-intensity care strategy after AHF was safe and resulted in a significant reduction of all-cause death or HF readmission at 180 days across the study age spectrum.

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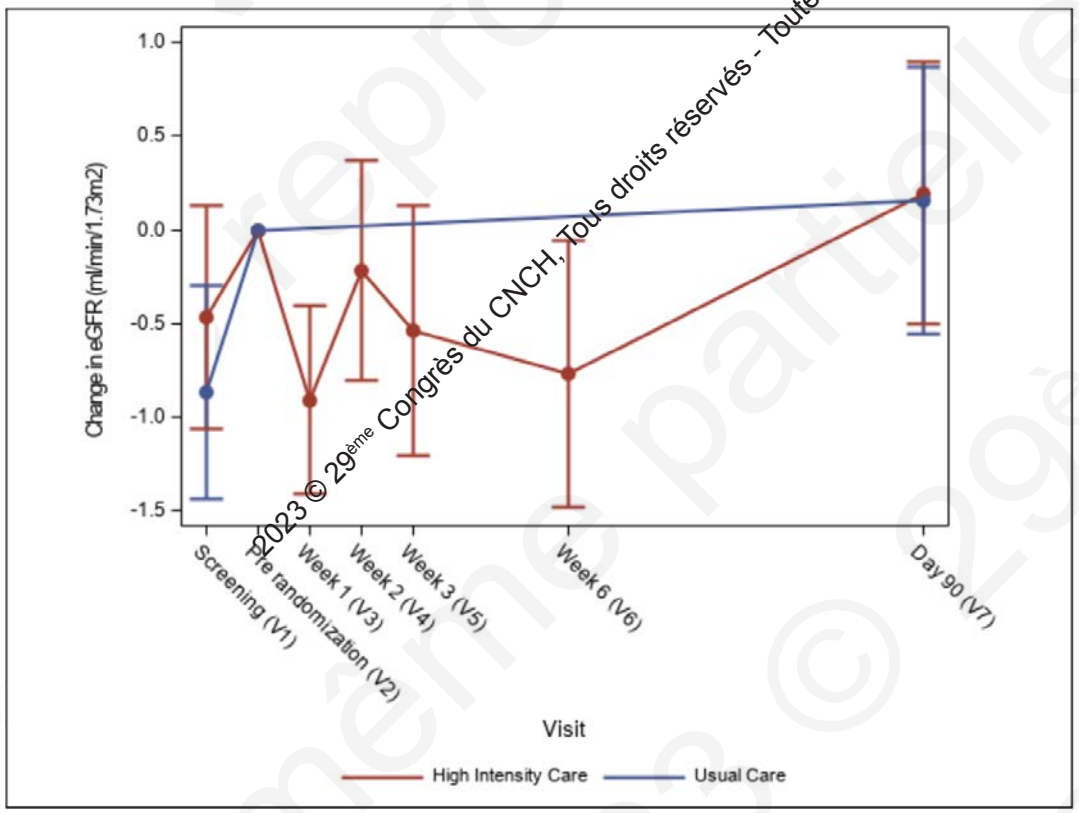
WHAT REGISTRIES SAY?

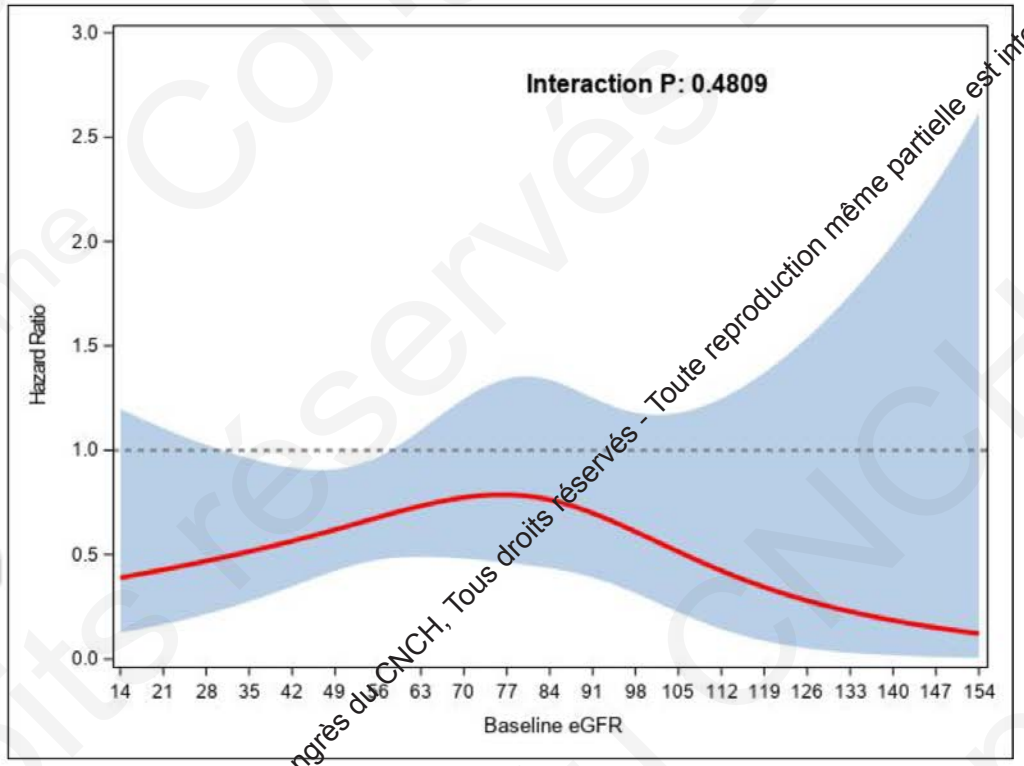
Baseline eGFR influence?

Figure 1. Change from baseline in eGFR by visit



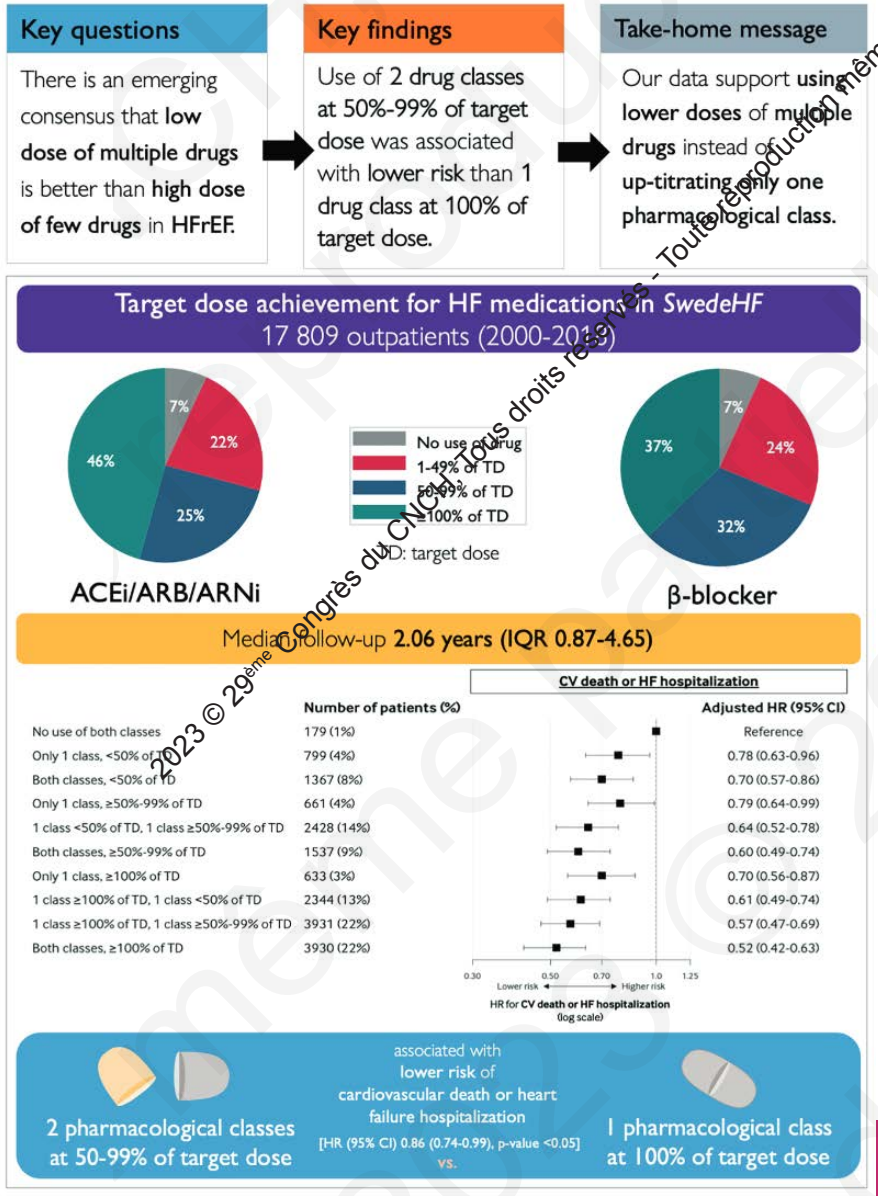
Early changes in renal function during rapid uptitration of guideline directed medical therapy following an admission for acute heart failure

Figure 2. Treatment effect of high-intensity care versus usual care on the endpoint death or HF readmission at 180 days according to baseline eGFR



WHAT REGISTRIES SAY?

Mono vs bi vs tri vs quadri ?



D'Amario et al, EHJ HF 2022

Recently, the American College of Cardiology Expert Consensus Pathway for HF Therapies addressed some of the issues of dosing of various medications (*Figure 4*):[66]

(i) In all patients, it is best to achieve maximum doses of all four biologic targets including angiotensin II modulation, beta-blockade, aldosterone antagonism, and neprilysin inhibition.

(ii) If this is not possible, then the second best option is to use lower doses of all drugs rather than higher doses of one and omitting another.

(iii) If the patient is able to tolerate higher doses of one but lower doses of the other therapy due to blood pressure, then preferences should to be given to beta-blockers over angiotensin II modulation based on better dose response data with adrenergic blockade.[1,2,23]

Marti et al, EHJ HF 2019

WHAT REGISTRIES SAY?

Mono vs bi vs tri vs quadri ?

Estimating lifetime benefits of comprehensive disease-modifying pharmacological therapies in patients with heart failure with reduced ejection fraction: a comparative analysis of three randomised controlled trials

Muthiah Vaduganathan, Brian L Claggett, Pardeep S Jhund, Jonathan W Cunningham, João Pedro Ferreira, Faiez Zannad, Milton Packer, Gregg C Fonarow, John J V McMurray, Scott D Solomon

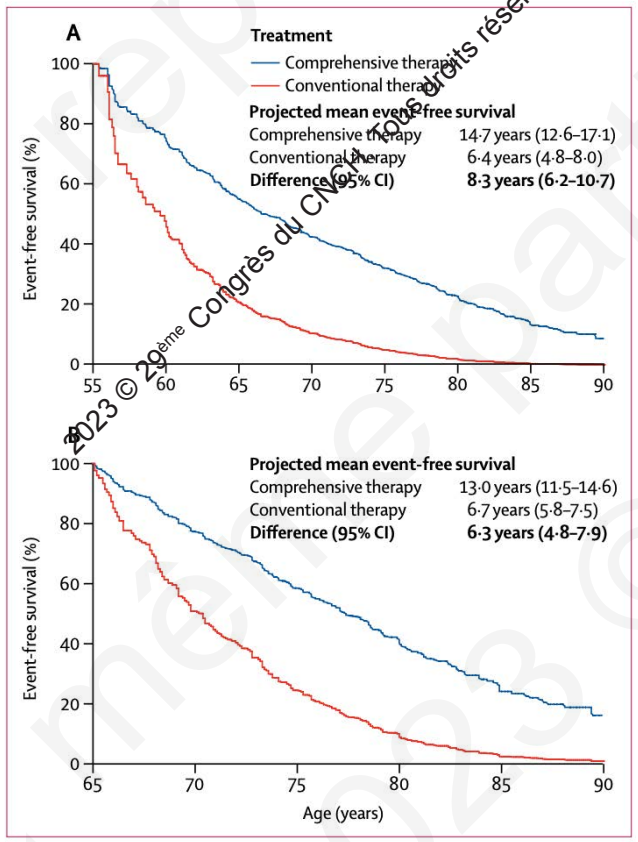


Figure 2: **Event-free survival with comprehensive disease-modifying therapy *vs* conventional therapy**

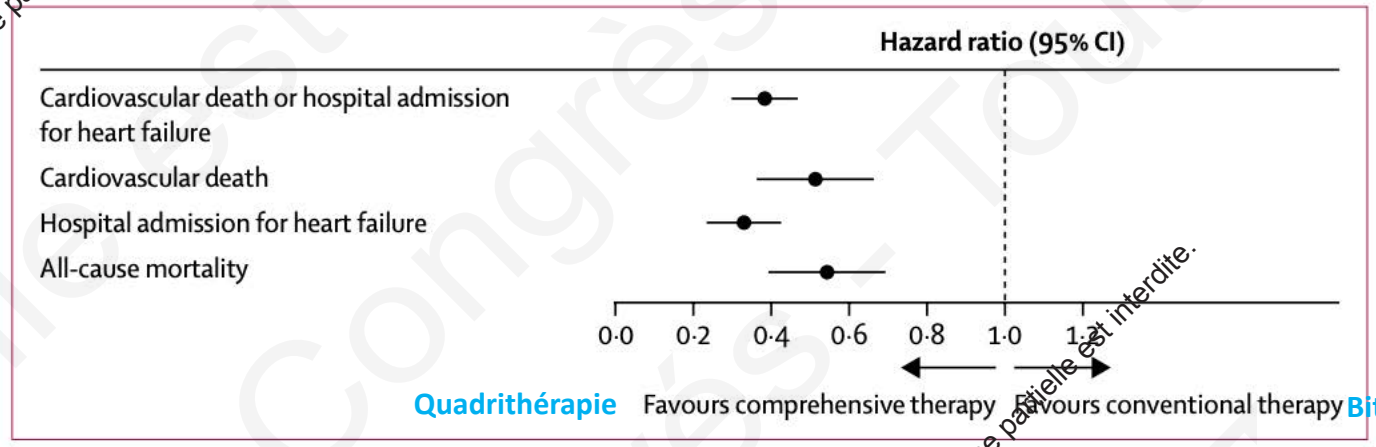


***Figure 1:* Estimation of relative treatment effects of comprehensive disease-modifying pharmacological therapy on key cardiovascular events**

Comprehensive therapy consisted of an ARNI, β blocker, MRA, and SGLT2 inhibitor; conventional therapy consisted of an ACE inhibitor or ARB and β blocker. ACE inhibitor=angiotensin-converting enzyme inhibitor. ARB=angiotensin receptor blocker. ARNI=angiotensin receptor–neprilysin inhibitor. MRA=mineralocorticoid receptor antagonist. SGLT2 inhibitor=sodium/glucose cotransporter 2 inhibitor.

Patients from

- 2011 - EMPHASIS-HF (n=2737) – Eplerenone (CV death or AHF H)
- 2014 - PARADIGM-HF (n=8399) – Sacubitril/Valsartan (CV death or AHF H)
- DAPA-HF (n=4744) – Dapagliflozin (Worsening HF or CV death)

Primary endpoint: composite of CV death or first hospital admission for AHF

Vaduganathan et al. Lancet 2020

WHAT REGISTRIES SAY?

ESC European Society of Cardiology
European Journal of Heart Failure (2020) 22, 1472–1482
doi:10.1002/ejhf.1869

RESEARCH ARTICLE

Effects of combined renin–angiotensin–aldosterone system inhibitor and beta-blocker treatment on outcomes in heart failure with reduced ejection fraction: insights from BIOSTAT-CHF and ASIAN-HF registries

Wouter Ouwerkerk[1,2†], Tiew-Hwa K. Teng[1,3,4†], Jasper Tromp[1,4], Wan Ting Tay[1], John G. Cleland[6], Dirk J. van Veldhuisen[5], Kenneth Dickstein[7,8], Leong L. Ng[9], Chim C. Lang[10], Stefan D. Anker[11], Faiez Zannad[12], Chung-Leh Hung[13,14], Jitendra P.S. Sawhney[15], Ajay Naik[16], Wataru Shimizu[17], Nobuhisa Hagiwara[18], Gurpreet Singh Wander[19], Inder Anand[20‡], A. Mark Richards[21,22], Adriaan A. Voors[5], and Carolyn S.P. Lam[1,4,5*]

- N=6787 HFrEF patients
- Mean age 62.6+/-13.7 yo
- 77% men
- LVEF 27.7+/-7.2%

Table 2 Hazard ratio (95% confidence interval) of patients achieving specific target dose for mortality or heart failure hospitalization, mortality, and heart failure hospitalization

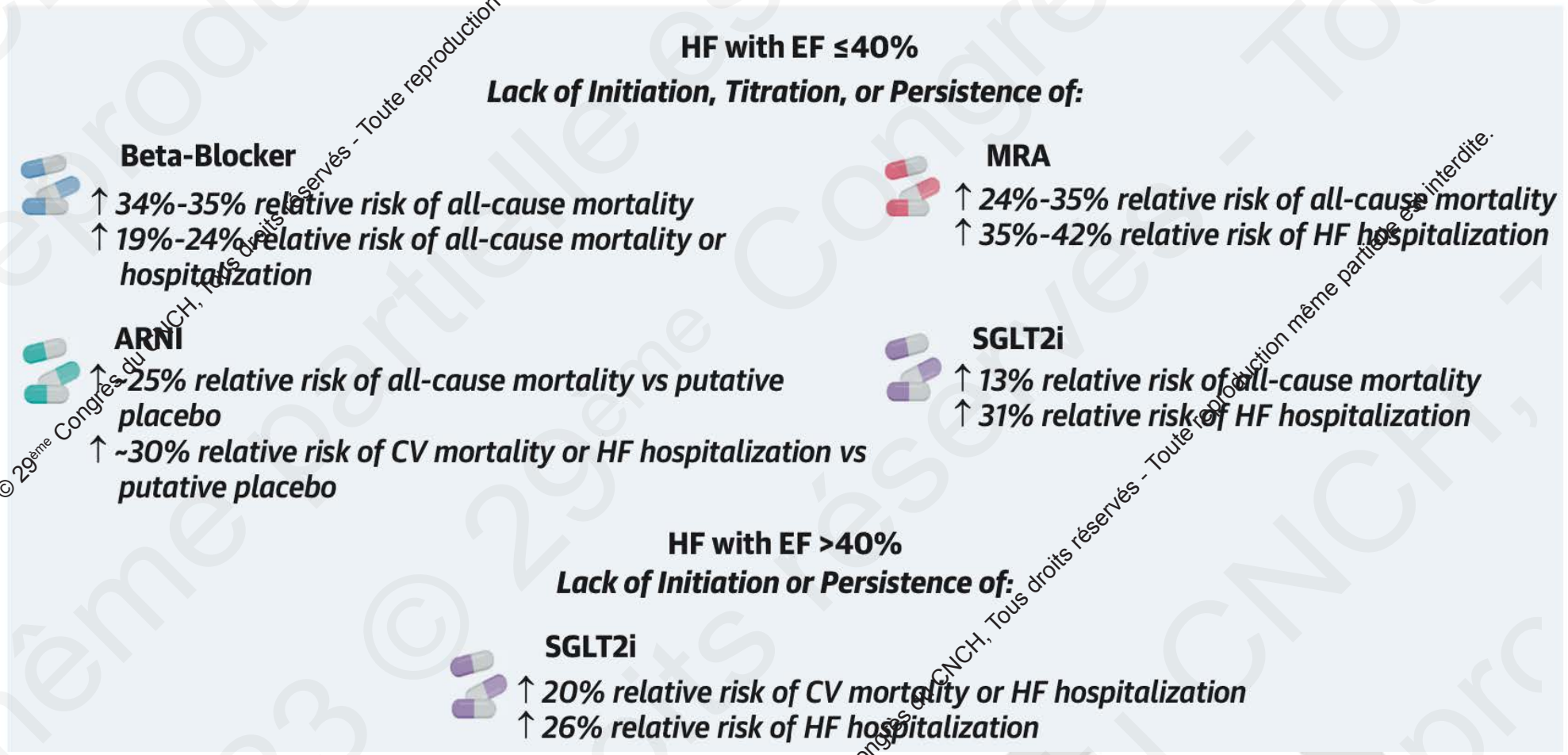
	0% BB	1–49% BB	50–99% BB	100% BB
Mortality or HF hospitalization				
0% ACEi/ARB	1.00 (reference)	0.98 (0.83–1.17) 0.85	0.90 (0.71–1.15) 0.41	0.68 (0.49–0.93) 0.02
1–49% ACEi/ARB	0.90 (0.73–1.10) 0.30	0.71 (0.61–0.84) <0.001	0.61 (0.49–0.75) <0.001	0.80 (0.62–1.04) 0.10
50–99% ACEi/ARB	0.67 (0.52–0.87) 0.002	0.50 (0.42–0.61) <0.001	0.64 (0.54–0.75) <0.001	0.57 (0.48–0.68) <0.001
100% ACEi/ARB	0.71 (0.52–0.96) 0.03	0.52 (0.42–0.64) <0.001	0.66 (0.56–0.77) <0.001	0.32 (0.26–0.39) <0.001
Mortality				
0% ACEi/ARB	1.00 (reference)	0.75 (0.60–0.92) 0.006	0.65 (0.48–0.87) 0.004	0.40 (0.25–0.63) <0.001
1–49% ACEi/ARB	0.74 (0.57–0.95) 0.02	0.57 (0.47–0.69) <0.001	0.39 (0.29–0.51) <0.001	0.58 (0.42–0.81) 0.001
50–99% ACEi/ARB	0.57 (0.42–0.78) <0.001	0.33 (0.26–0.42) <0.001	0.42 (0.34–0.51) <0.001	0.27 (0.21–0.34) <0.001
100% ACEi/ARB	0.75 (0.53–1.07) 0.11	0.40 (0.30–0.52) <0.001	0.38 (0.31–0.46) <0.001	0.19 (0.14–0.24) <0.001
HF hospitalization				
0% ACEi/ARB	1.00 (reference)	1.42 (1.14–1.77) 0.002	1.48 (1.12–1.95) 0.006	1.10 (0.76–1.59) 0.62
1–49% ACEi/ARB	1.26 (0.97–1.63) 0.08	1.08 (0.88–1.33) 0.43	0.94 (0.72–1.21) 0.64	1.14 (0.83–1.57) 0.41
50–99% ACEi/ARB	0.80 (0.57–1.11) 0.18	0.75 (0.59–0.95) 0.02	0.93 (0.76–1.14) 0.50	1.14 (0.92–1.41) 0.22
100% ACEi/ARB	0.71 (0.46–1.09) 0.12	0.81 (0.62–1.05) 0.12	1.14 (0.93–1.40) 0.20	0.85 (0.68–1.06) 0.17

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, β-blocker; HF, heart failure.

Conclusion This study shows that best outcomes were observed in patients attaining GRTD for both ACEi/ARB and β-blockers, unfortunately this was rarely achieved. Achieving >50% GRTD of both drug classes was associated with better outcome than target dose of monotherapy. Up-titrating β-blockers to target dose was associated with greater mortality reduction than up-titrating ACEi/ARB.

WHAT ARE THE CONSEQUENCES?

FIGURE 1 Risks of Delaying or Omitting Guideline-Directed Heart Failure Medications



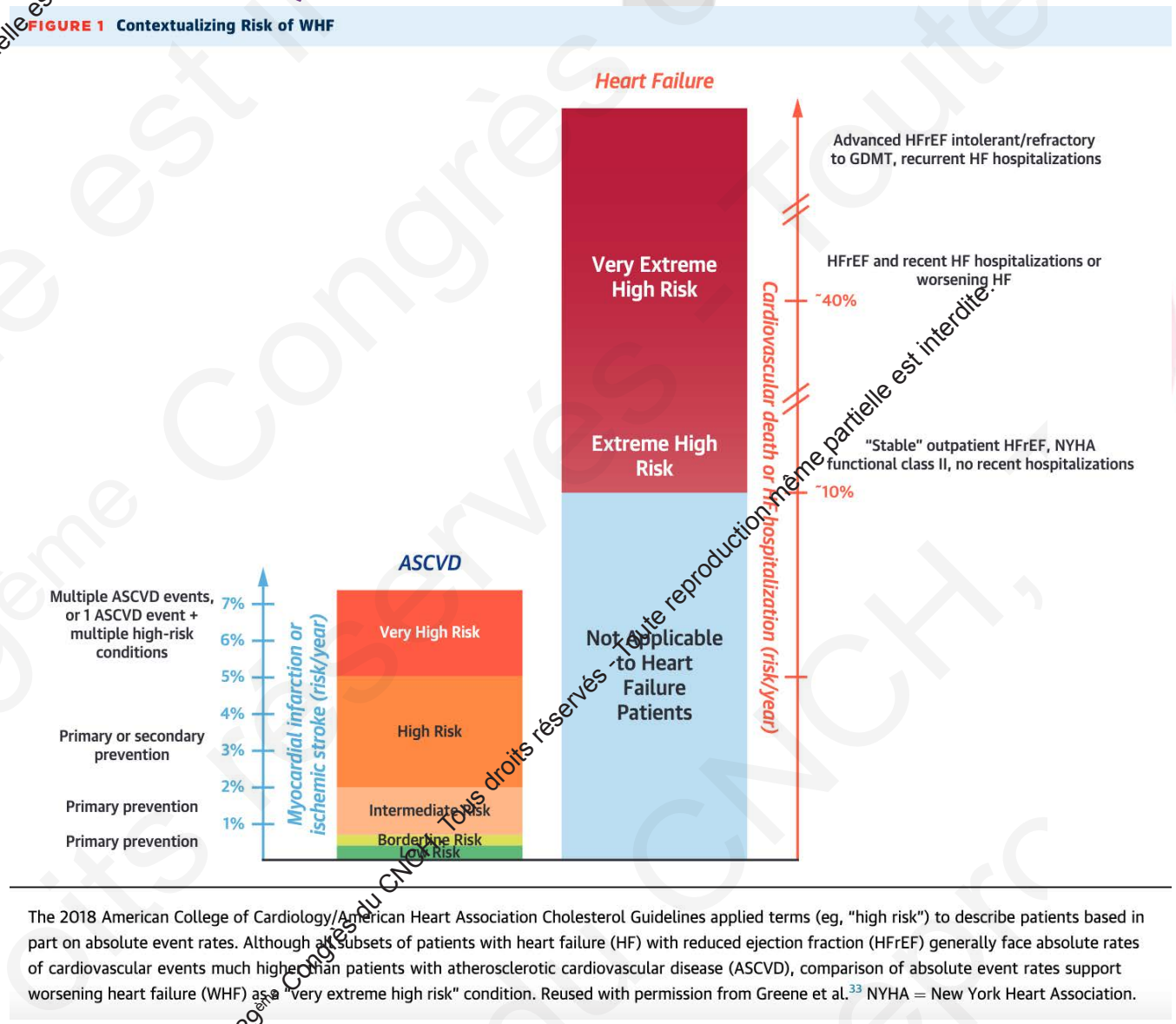
G.Fonarow, S.J.Greene, JACC 2023

WHAT ARE THE CONSEQUENCES?

Misperception of the real risk!

« Stable » outpatient HF ≠ « low risk »

Inability of physician to detect asymptomatique but clinically meaningfull worsening



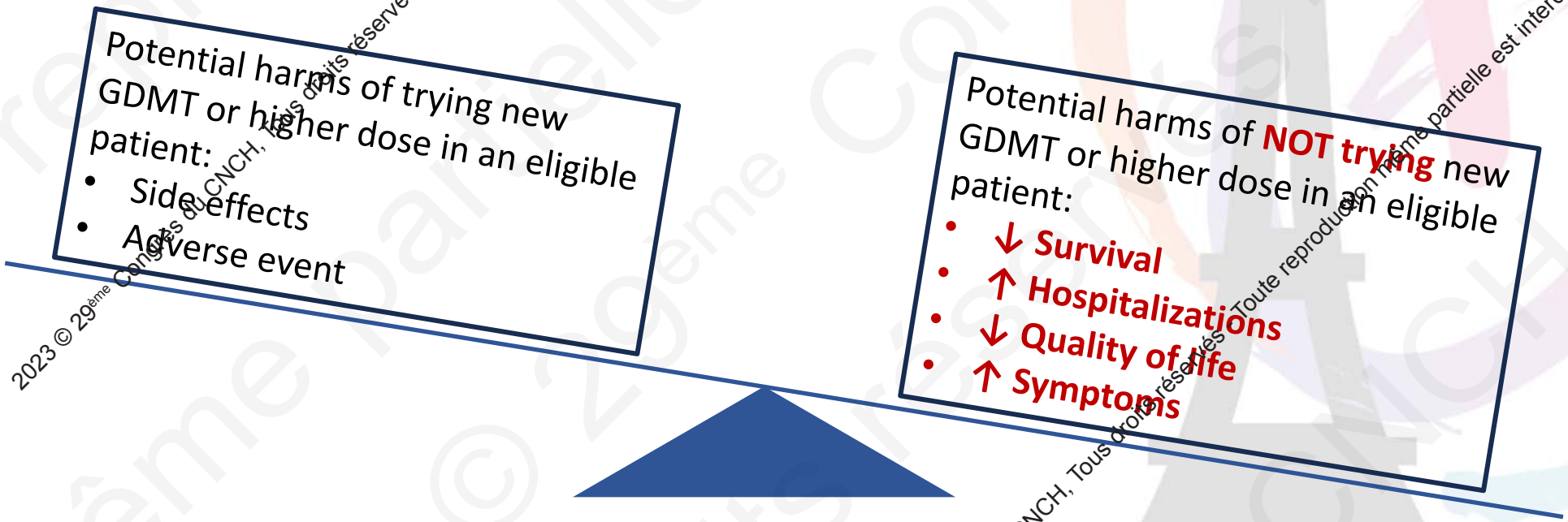
The 2018 American College of Cardiology/American Heart Association Cholesterol Guidelines applied terms (eg, "high risk") to describe patients based in part on absolute event rates. Although all subsets of patients with heart failure (HF) with reduced ejection fraction (HFrEF) generally face absolute rates of cardiovascular events much higher than patients with atherosclerotic cardiovascular disease (ASCVD), comparison of absolute event rates support worsening heart failure (WHF) as a "very extreme high risk" condition. Reused with permission from Greene et al.[33] NYHA = New York Heart Association.

S.J.Greene, JACC 2023

WHAT ARE THE CONSEQUENCES?

Delaying or Omitting GDMT in Eligible Patients With Heart Failure Associated With:

- Patient never being initiated on GDMT, or substantial delay
- Worse quality of life and health status
- Excess risk of disease progression
- Preventable deaths and hospitalizations



COST EFFECTIVENESS

JACC: Heart Failure
Volume 11, Issue 5, May 2023, Pages 541-551

Clinical Research

Cost-Effectiveness of Comprehensive Quadruple Therapy for Heart Failure With Reduced Ejection Fraction

Neal M. Dixit MD, MBA [a], Neil U. Parikh BS [b], Roback Ziaeian MD, PhD [c d], Nicholas Jackson PhD, MPH [e], Gregg C. Fonarow MD [c]

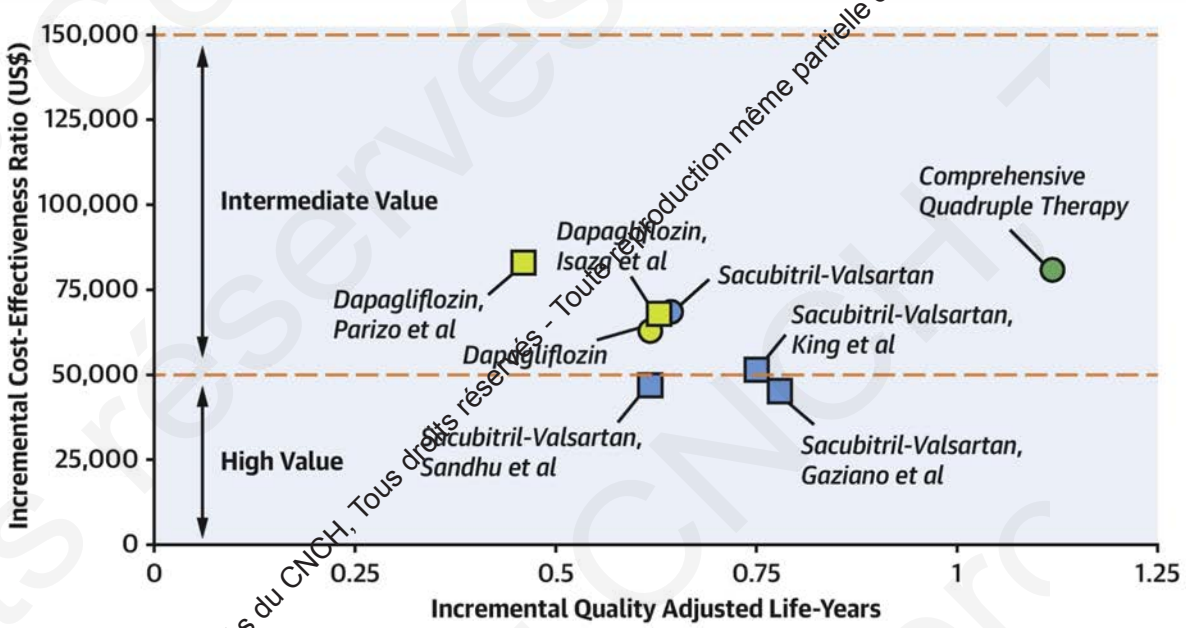
Results

Treatment with quadruple therapy resulted in an increase of 1.73 and 2.87 life-years compared with triple therapy and double therapy, respectively, and an increase in quality-adjusted life-years of 1.12 and 1.85 years, respectively. The incremental cost-effectiveness ratios of quadruple therapy vs triple therapy and double therapy were $81,000 and $51,081, respectively. In 91.7% and 99.9% of probabilistic simulations quadruple therapy had an incremental cost-effectiveness ratio of<$150,000 compared with triple therapy and double therapy, respectively.

Conclusions

At current pricing, the use of quadruple therapy in patients with HFrEF was cost effective compared with triple therapy and double therapy. These findings highlight the need for improved access and optimal implementation of comprehensive quadruple therapy in eligible patients with HFrEF.

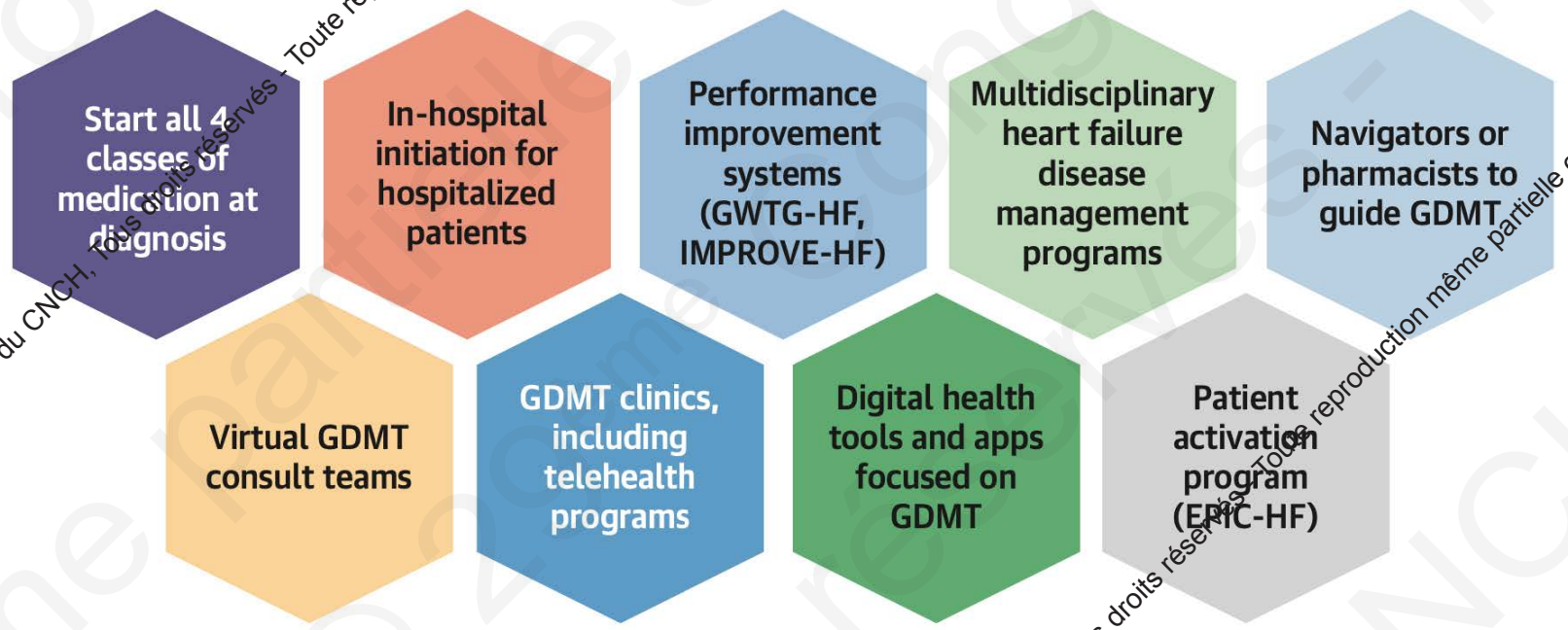
CENTRAL ILLUSTRATION: Comparative Cost-Effectiveness of Novel HFrEF Medical Therapy



Dixit NM, et al. J Am Coll Cardiol HF. 2023;11(5):541-551.

HOW TO DEAL WITH THESE ISSUES?

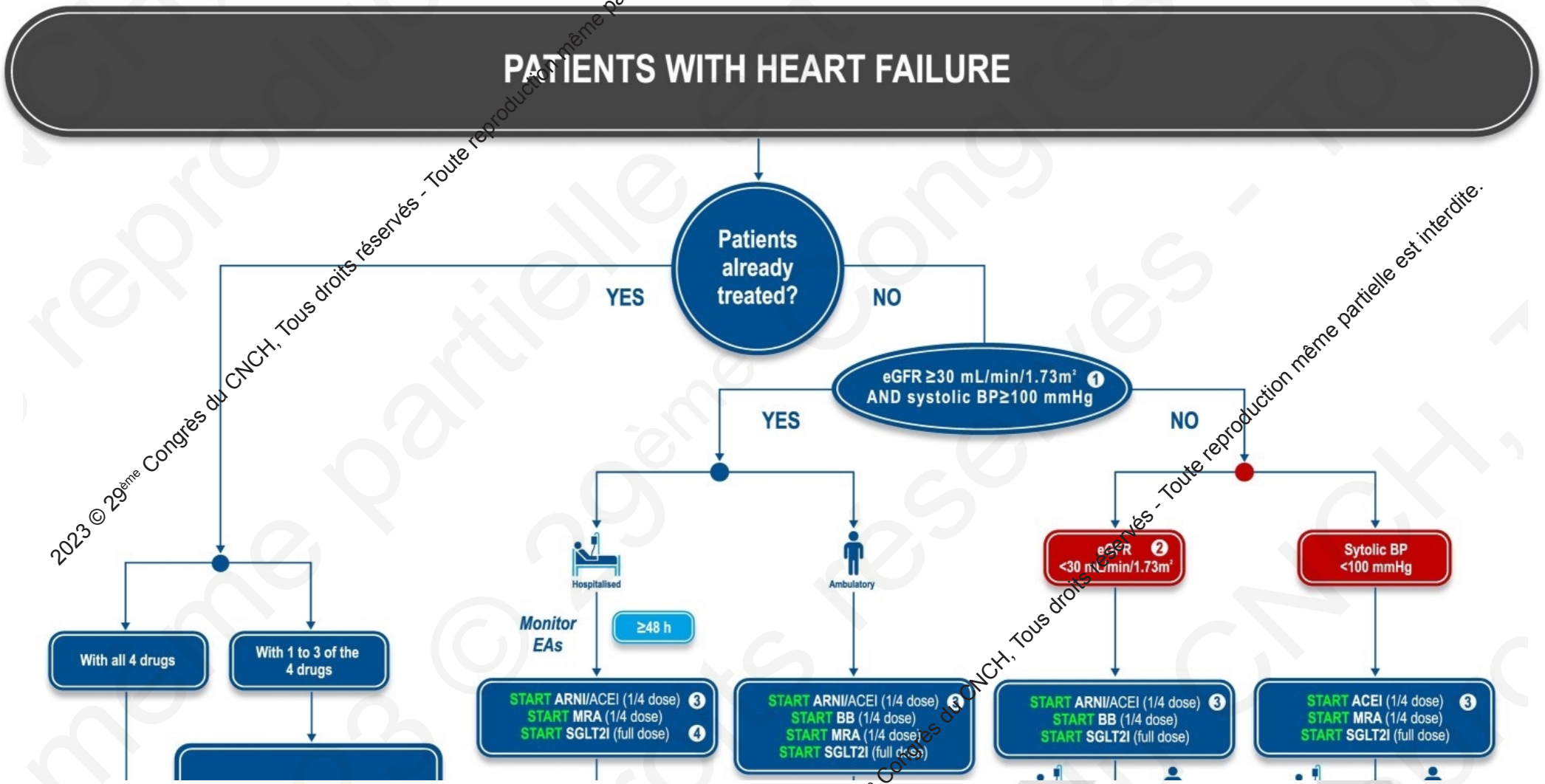
CENTRAL ILLUSTRATION Strategies to Facilitate Implementation of Guideline-Directed Medical Therapy for Heart Failure



Patolia H, et al. J Am Coll Cardiol. 2023;82(6):529-543.

There are a multitude of strategies that offer the potential to improve gaps in guideline-directed medical therapy (GDMT) prescription. A multimodal combination strategy may be best equipped to combat a culture of clinical inertia toward medication changes and maximally improve use of foundational GDMTs among all eligible patients with heart failure with reduced ejection fraction. EPIC-HF = Electronically Delivered, Patient-Activation Tool for Intensification of Medications for Chronic Heart Failure with Reduced Ejection Fraction; GWTG-HF = Get With The Guidelines Heart Failure; IMPROVE-HF = Registry to Improve the Use of Evidence-Based Heart Failure Therapies in the Outpatient Setting.

HOW TO DEAL WITH THESE ISSUES?



N.Girerd et al, Rev Esp Card 2023

HOW TO DEAL WITH THESE ISSUES?

TITRATION OF THE FOUR HF MEDICATIONS 6

- UP-TITRATE EVERY 1 - 2 WEEKS until maximum tolerated dose is reached.
- INCREASE 1 - 2 MEDICATIONS AT THE SAME TIME (exceptionally 3 for patients with good renal function and sufficiently high blood pressure).
- REDUCE DIURETICS whenever possible.
- CHECK RENAL FONCTION and SERUM POTASSIUM between each titration visit.
- CONSIDER TELEMONITORING for treatment optimisation.

Perform blood monitoring within SEVEN days of EACH drug introduction or escalation step.

Monitor heart rate and blood pressure following EACH medication change.

N.Girerd et al, Rev Esp Card 2023

Collège National des Cardiologues des Hôpitaux

LES QUESTIONS EN SUSPENS

- Initiation rapide d'une mono/bi/tri ?
- Toutes les cardiopathies se valent ? Les 4 pour tous ?
- Aide à la stratification du risque ?
- Comment s'organiser au mieux ? Programme dédié de titration rapide ?
- Aujourd'hui 4… et demain ?
- …

TAKE HOME MESSAGES

- Fantastic four for « all » HFrEF
- Initiate as soon as possible and be « strong »
- Avoid discontinuation/de-escalation/withdrawal
- Prefer 4 low-dose rather than 2 full-dose
- Therapeutic inertia still exist ++
- Health network is crucial

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FAUVEL Charles
Cardiologue – CHU de Rouen

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