CNCH, 2022

U1046 / UMR9214

PHYSIOLOGIE MEDECINE EXPERIMENTALE COEUR MUSCLES

L'insuffisance cardiaque en pratique : Optimisons la prise en charge!

Cas 2

Pr François Roubille

Cardiology Intensive Care Unit
francois.roubille@gmail.com

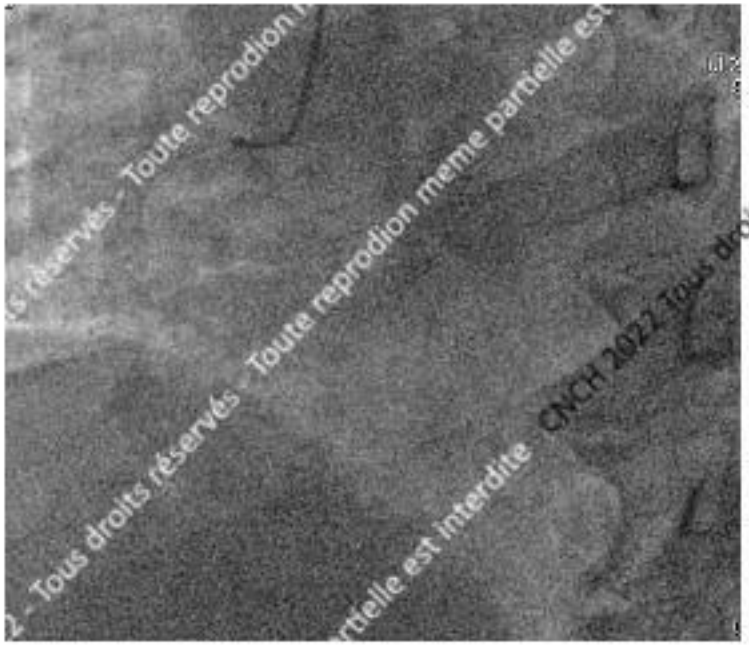
MUSE
MONTPELLIER UNIVERSITÉ D'EXCELLENCE

Conflits d'intérêt

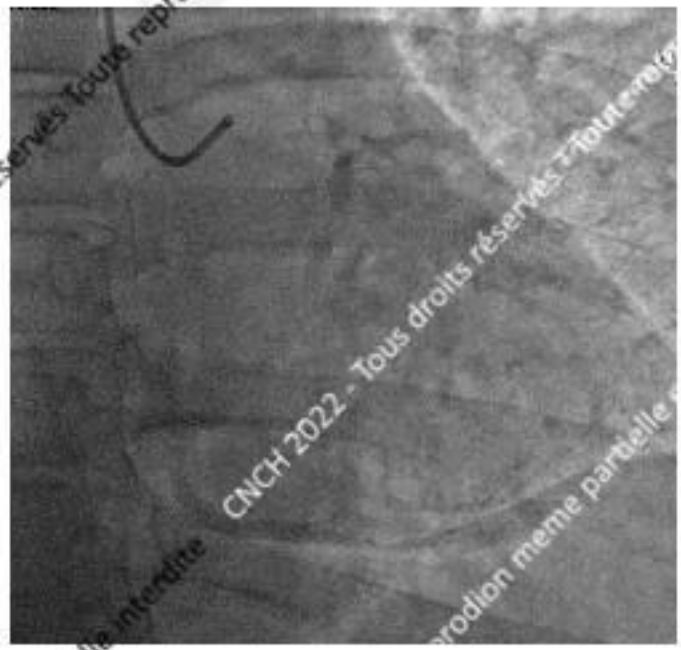
Affiliation/Financial Relationship	Company
• Grant/Research Support	• Servier, Medtronic, Astra-Zeneca
• Consulting Fees/Honoraria	• Air liquid, Medtronic, Novartis, AZ, MSD, Amgen, Sanofi, Pfizer, Mylan, Alliance Boehringer Ingelheim-Lilly
• Major Stock Shareholder/Equity	• 0
• Royalty Income	• 0
• Ownership/Founder	• 0
• Intellectual Property Rights	• 0
• Other Financial Benefit	• Abbott

Case report

19h22

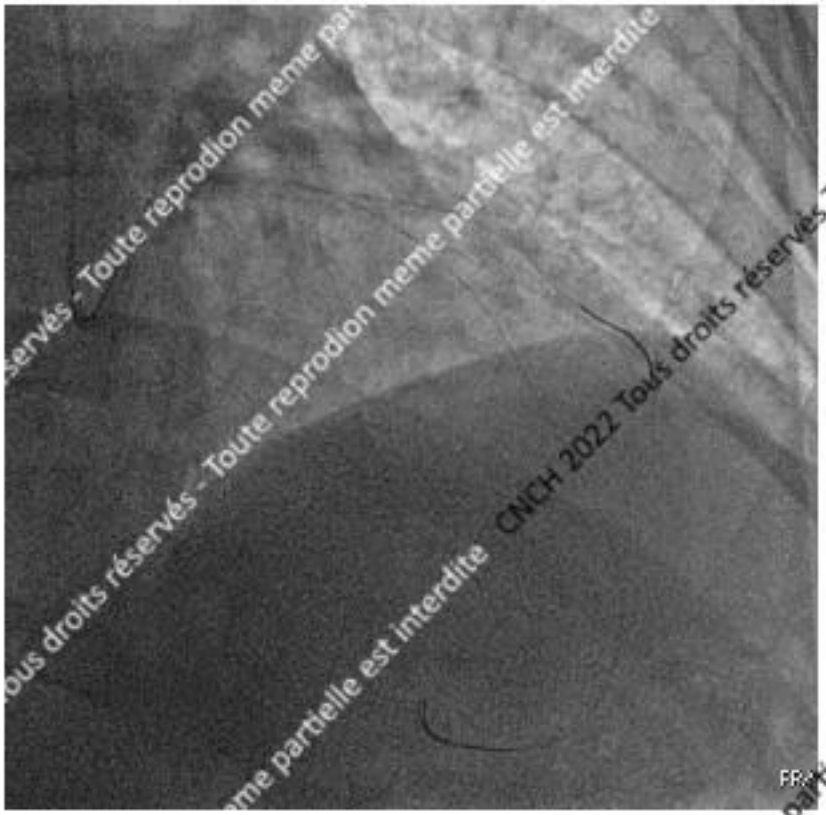


Right CA



Left CA

Case report



LDA is reperfused

But

Hypotension
Coronary flux?

Assist device? Transplantation?

Heart Failure

Homme de 64 ans, réhospitalisé à 6 mois de son IDM

Il vous dit qu'il allait bien, que cela a été brutal.
Depuis les quelques jours de sa nouvelle hospitalisation, il va mieux.
A l'examen: PA 105/60, pas de surcharge, FC 58 bpm, FEVG annoncée à 35%

Son <u>traitement comprend</u>:

Bêtabloquant	25% de la dose cible
IEC	50% de la dose cible
Furosémide	40 mg
Statine fortement dosée	
IPP	

Vous proposez:

A. Rééducation cardiaque

B. Optimisation du traitement médicamenteux

C. Renouvellement de l'ordonnance et consultation à 6 mois

D. Programme PRADO

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The PRADO system remains to be evaluated

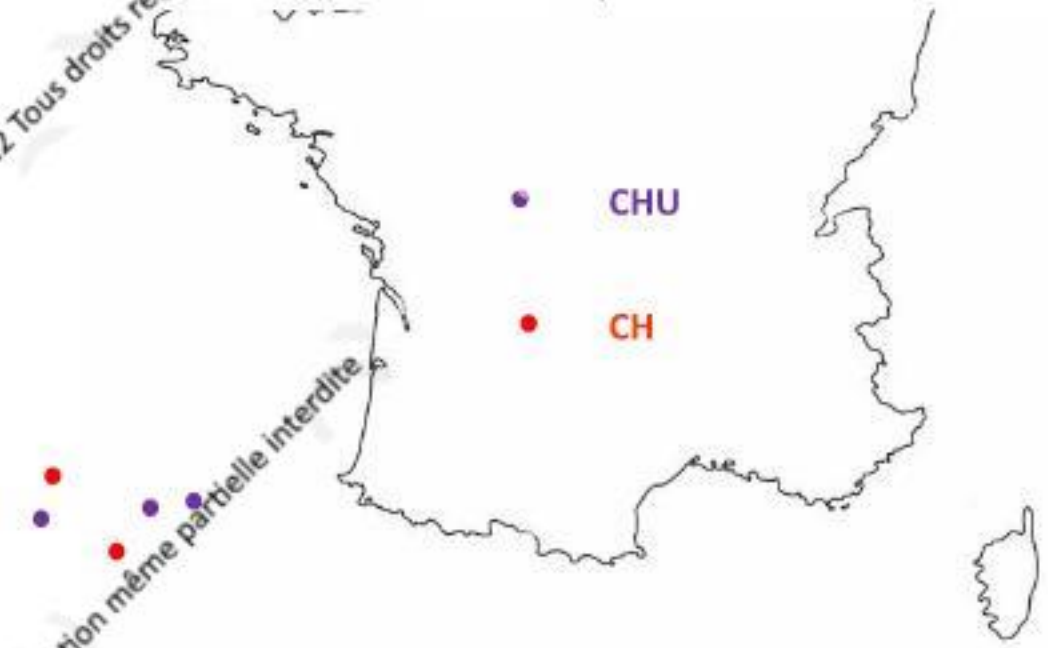
PRADOC trial
NCT03396081
N=404
Results expected in 2023

ESC HEART FAILURE
ESC Heart Failure 2021; 8: 1649–1655
Published online 25 December 2020 in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/ehf2.13086

STUDY DESIGN

PRADOC: a trial on the efficiency of a transition care management plan for hospitalized patients with heart failure in France

Claire Duflos[1], Jean-Philippe Labarre[2], Roxana Ologeanu[4], Marie Robin[1], Guillaume Cayla[6], Michel Galinier[7], Frédéric Georger[8], Thibaut Petroni[3], Clément Alarcon[9], Sylvain Aguilhon[3], Christine Delonca[5], Pascal Battistella[5], Audrey Agullo[3], Florence Leclercq[3], Jean-Luc Pasquie[5,10], Laurence Papinaud[11], Grégoire Mercier[12,2], Jean-Etienne Ricci[6] and François Roubille[3,10]*



Optimisation du traitement:

A. Augmentation du bêtabloquant

B. Augmentation de l'IEC

C. Augmentation du furosémide

D. Introduction d'une gliflozine 25 mg

E. Introduction de la spironolactone 75 mg

F. Ajout du sacubitril-valsartan au traitement précédent

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C. Augmentation du furosémide

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E. Introduction de la spironolactone 75 mg

F. Ajout du sacubitril-valsartan au traitement précédent

Optimisation du traitement:

A. Augmentation du bêtabloquant: non (FC basse, voir tolérance à l'effort)

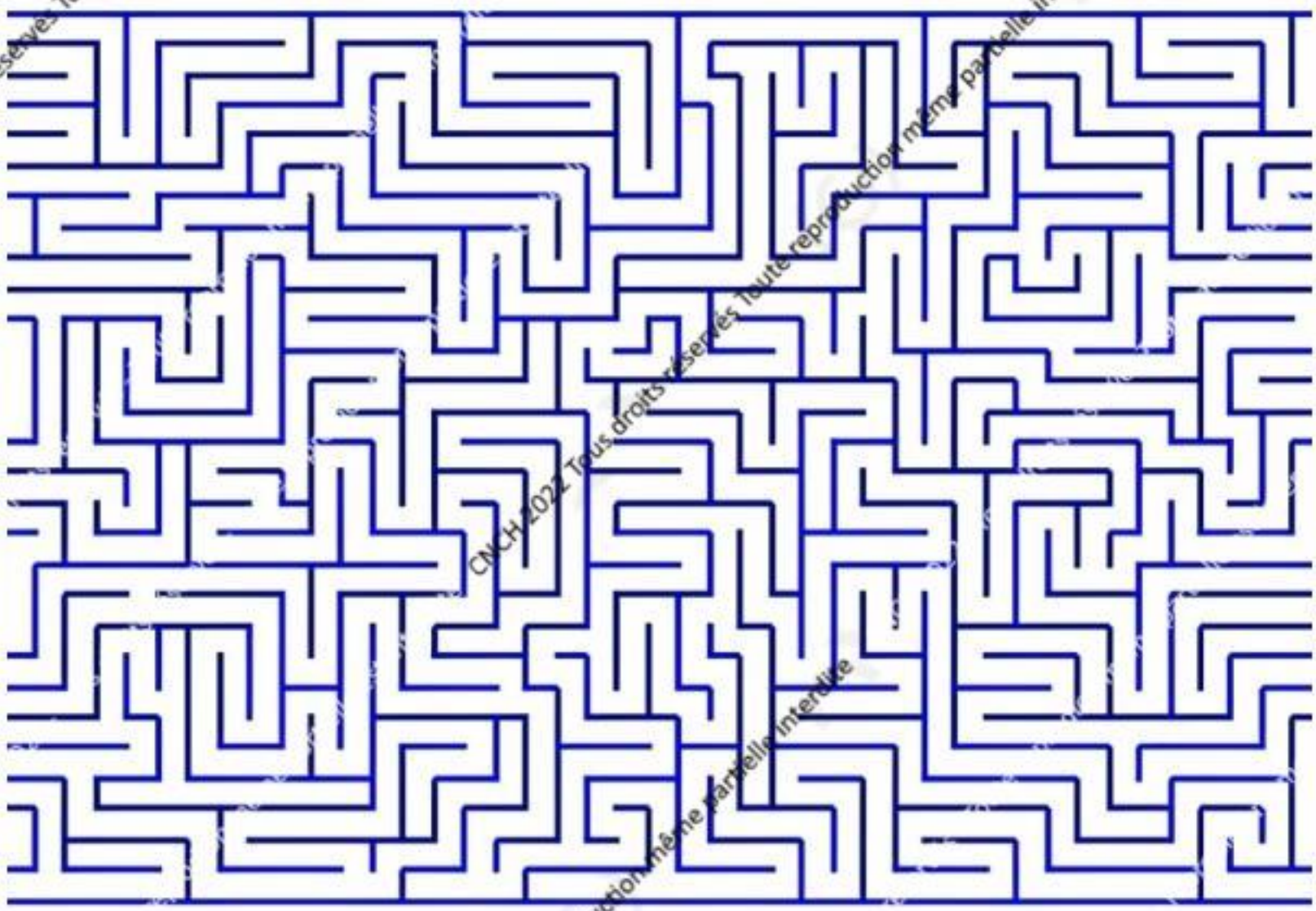
B. Augmentation de l'IEC ou switch vers le sacubitril-valsartan

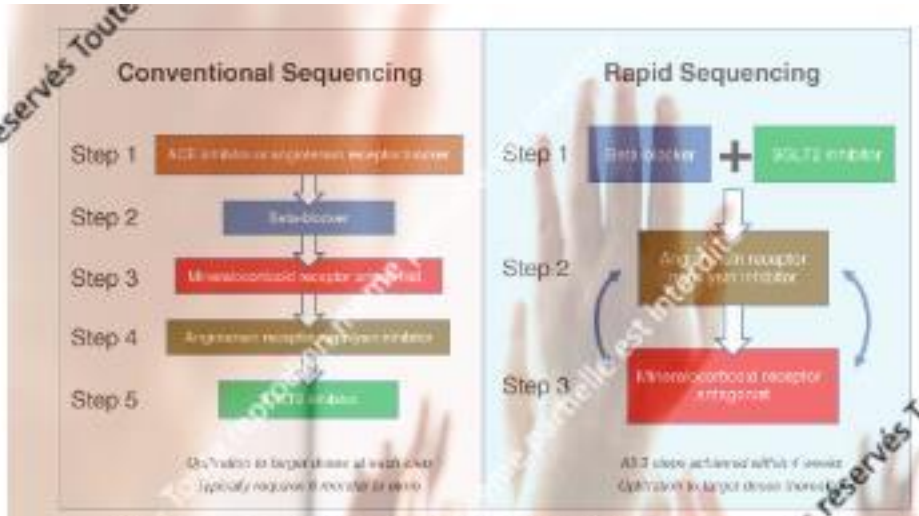
C. Augmentation du furosémide: dose minimale nécessaire

D. Introduction d'une gliflozine 10 mg

E. Introduction de la spironolactone 25 mg

F. Switch vers sacubitril-valsartan



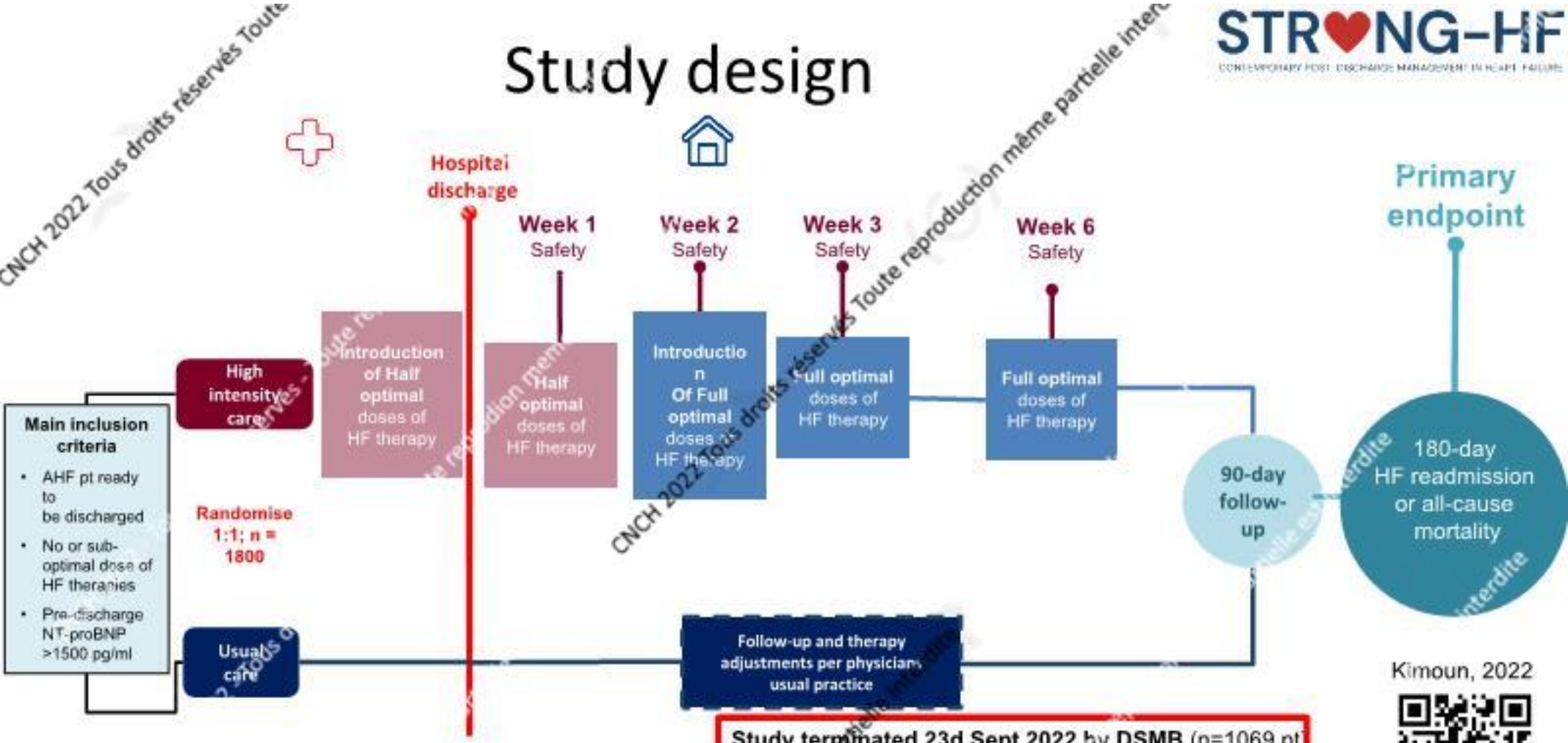


Eur J Heart Fail. 2021 Jun; 23(6): 882–894

Consensus submitted

Study design

STRONG-HF
CONTEMPORARY POST-DISCHARGE MANAGEMENT IN HEART FAILURE



Kimoun, 2022

Study terminated 23d Sept 2022 by DSMB (n=1069 pt)
- larger than expected difference in primary endpoint
- unethical to keep patients in usual care

HF therapy: combining ACEi/ARB/ARNi & BB & MRA
Safety = clinical exam & biology (NT-proBNP, K, Creat, hemoglobin)

ACEi, angiotensin converting enzyme inhibitors; AHF, acute heart failure; ARB, angiotensin receptor blockers; BB, beta blockers; HF, heart failure; MRA, mineralcorticoid receptor antagonists; NT-proBNP, N-terminal pro B-type natriuretic peptide

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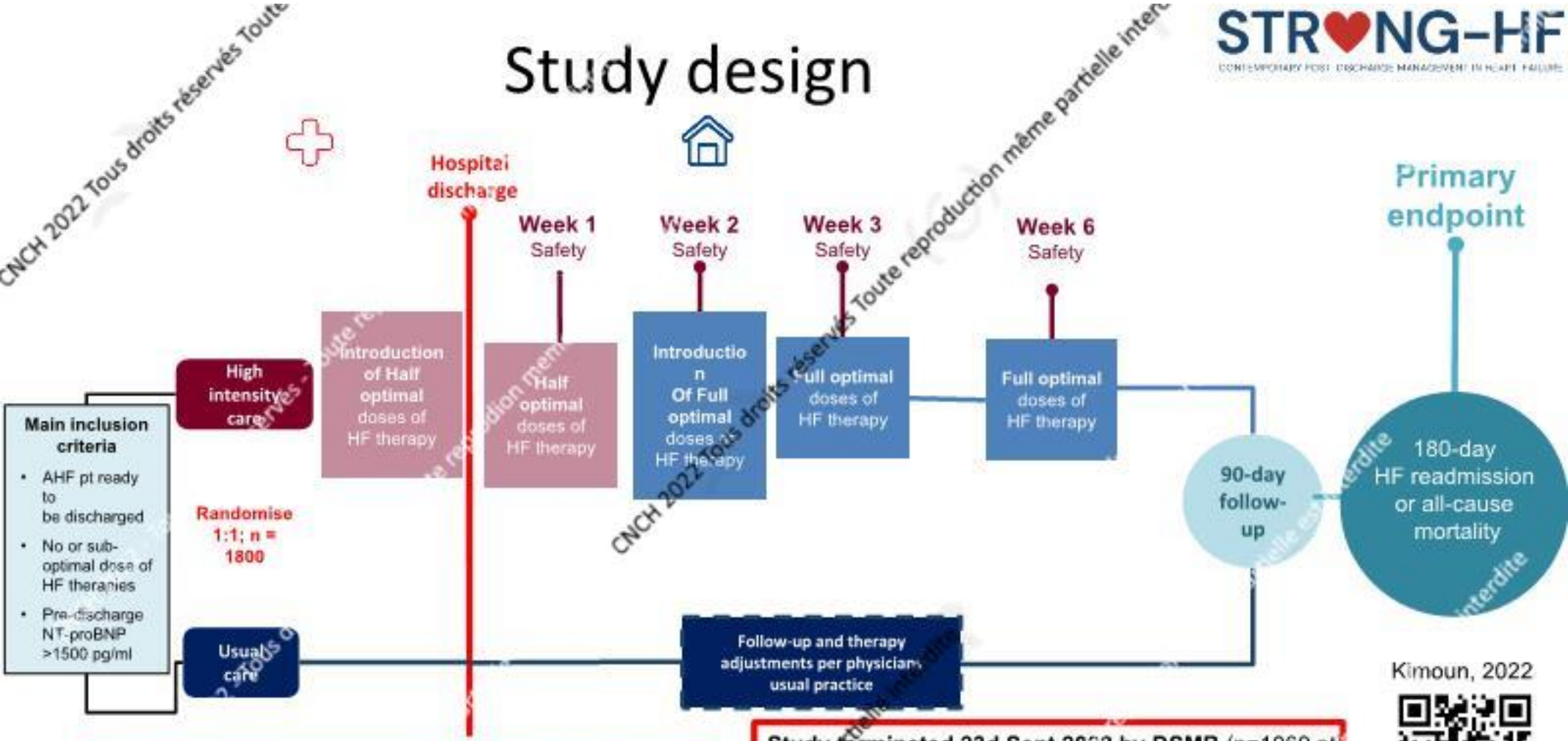

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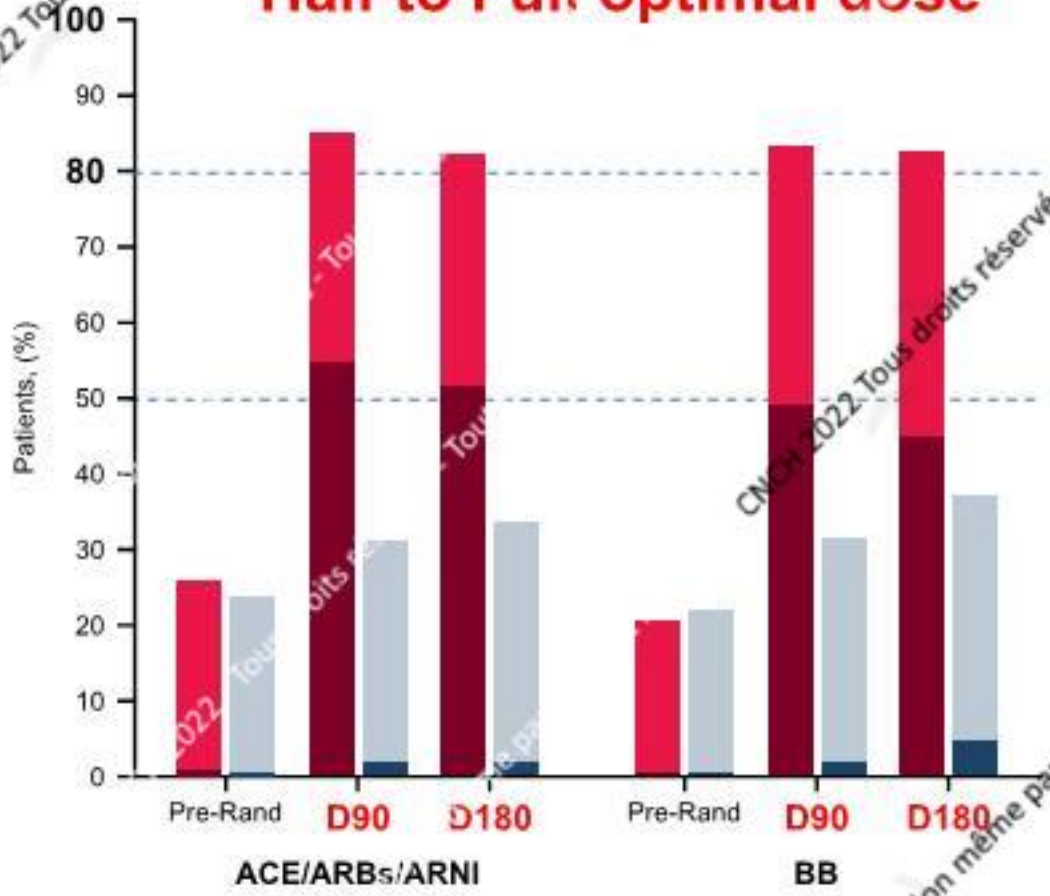
Oral HF therapies prescribed in high intensity and usual care

Half to Full optimal dose



High Intensity Care

½ –< Full optimal dose

≥ Full optimal dose

Usual Care

½ –< Full optimal dose

≥ Full optimal dose

Mebazaa, 2022

ACEI, angiotensin converting enzyme inhibitors; ARB, angiotensin receptor blockers; GDMT, guideline-directed medical therapies; MRA, mineralocorticoid receptor antagonists; Pre-Rand, pre-randomization

Patients will ❤ STRONG-HF

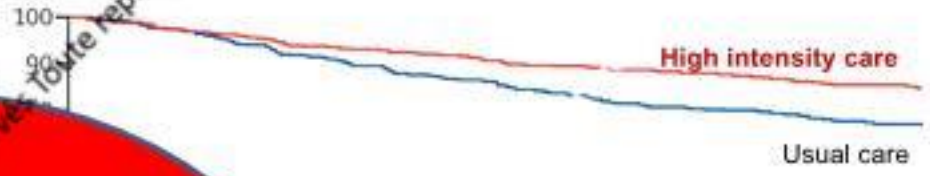
Improvement in all parameters of congestion at Day 90

Parameter	Adjusted Treatment Effect (95% CI)	P-value
Weight, kg	-1.36 (-1.91, 0.80)	<0.00
Respiratory Rate, breaths/min	-0.4 (-0.7, -0.1)	
Peripheral edema, grade	1.30 (1.17, 1.44)	
Jugular venous pressure, cm	1.13 (1.05, 1.21)	
NYHA, class	1.36 (1.22, 1.53)	
NT-proBNP, pg/mL*	0.77 (0.67, 0.89)	0.

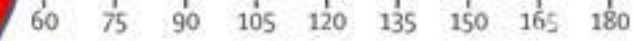
- No iSGLT2
- No impact on mortality!

Primary endpoint:

180-Day readmission for heart failure or all-cause death



t 8.1%, 95% CI 2·9 to 13·2; p=0·0021)



Time since randomisation (days)

Main secondary endpoint: Patient's QoL

	High intensity	Usual	Treatment effect	P value
EQ-5D VAS at Day 90	10.7 (0.9)	7.2 (0.9)	3.5 (1.7 to 5.2)	< 0.0001

Mebazaa, 2022

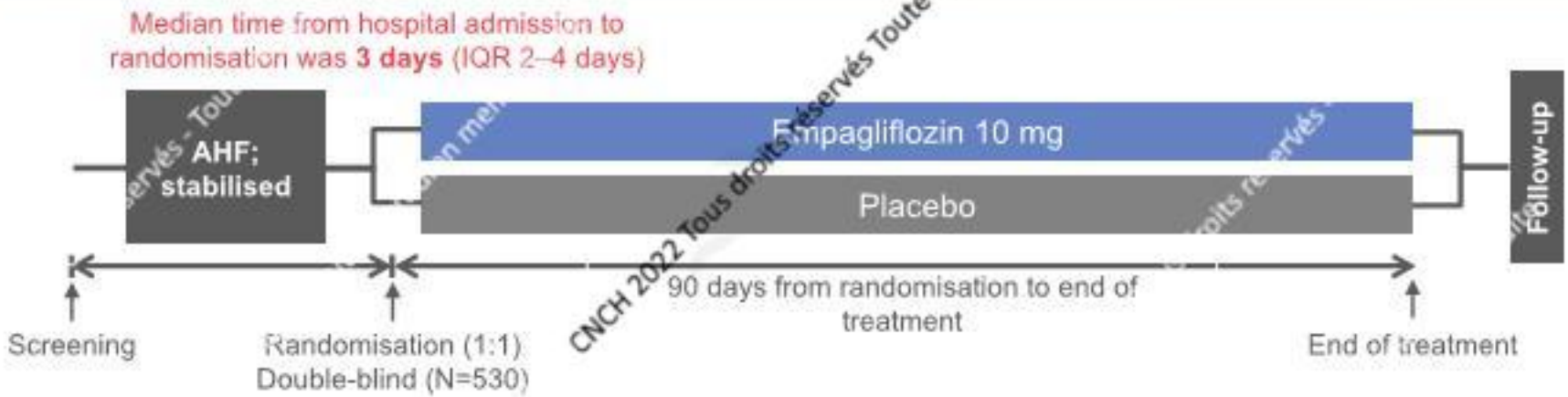
Safety

Treatment-emergent adverse events – day 90, n (%)	High intensity care (N=542)	Usual care (N=536)
Any adverse event	223 (41.1)	158 (29.5)
Any serious adverse event	88 (16.2)	92 (17.2)
Any fatal serious adverse event	25 (4.6)	32 (6.0)

Mebazaa, 2022

EMPULSE: a randomised, double-blind, placebo-controlled, superiority, phase III trial in patients hospitalised for AHF

Aim: to assess the clinical benefit and safety of **empagliflozin in patients hospitalised for AHF, once stabilised**



Primary endpoint	**Clinical benefit evaluated with a win ratio based on a composite of:** • Death • Number of HFEs (including HHFs, urgent HF visits and unplanned outpatient visits) • Time to first HFE • ≥5-point difference in the KCCQ-TSS change from baseline after 90 days of treatment

AHF, acute heart failure; HFE, heart failure event; HHF, hospitalisation for heart failure; IQR, interquartile range; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score

1. Tromp J et al. Eur J Heart Fail 2021;23:826; 2. Voors AA et al. Nat Med 2022; doi: 10.1038/s41591-021-01659-1

EMPULSE: criteria

Inclusion*	
Currently hospitalised for the primary diagnosis of AHF (de novo or decompensated chronic HF), regardless of EF	
Meets stabilisation criteria	
Randomisation ≥24 hours and no later than 5 days after admission, as early as possible after stabilisation and while still in hospital	
Elevated NT-proBNP or BNP:	
Without AF: NT-proBNP ≥1600 pg/ml or BNP ≥400 pg/ml	With AF: NT-proBNP ≥2400 pg/ml or BNP ≥600 pg/ml
Treatment with minimum dose of 40 mg of IV furosemide (or equivalent of other IV loop diuretic)	

Exclusion*
Cardiogenic shock
HHF triggered by secondary cause (e.g. acute MI, pulmonary embolism)
Planned or previous (within 30 days) cardiovascular revascularisation or major cardiac surgery/intervention/ device implantation
Prior ACS, MI, stroke or TIA within 90 days
eGFR <20 ml/min/1.73 m^2
Type 1 diabetes mellitus

*Further inclusion and exclusion criteria apply

ACS, acute coronary syndrome; AF, atrial fibrillation; AHF, acute heart failure; BNP, B-type natriuretic peptide; EF, ejection fraction; HHF, hospitalisation for heart failure; IV, intravenous; NT-proBNP, N-terminal pro-B-type natriuretic peptide

Tromp J *et al. Eur J Heart Fail* 2021;23:826

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Tromp J *et al. Eur J Heart Fail* 2021;23:826

EMPULSE: stabilisation criteria

All of the following criteria must apply for inclusion

1

Systolic BP ≥100 mmHg and no symptoms of hypotension in the preceding **6 hours**

2

No increase in IV diuretic dose for **6 hours** prior to randomisation

3

No IV vasodilators including nitrates within the last **6 hours** prior to randomisation

4

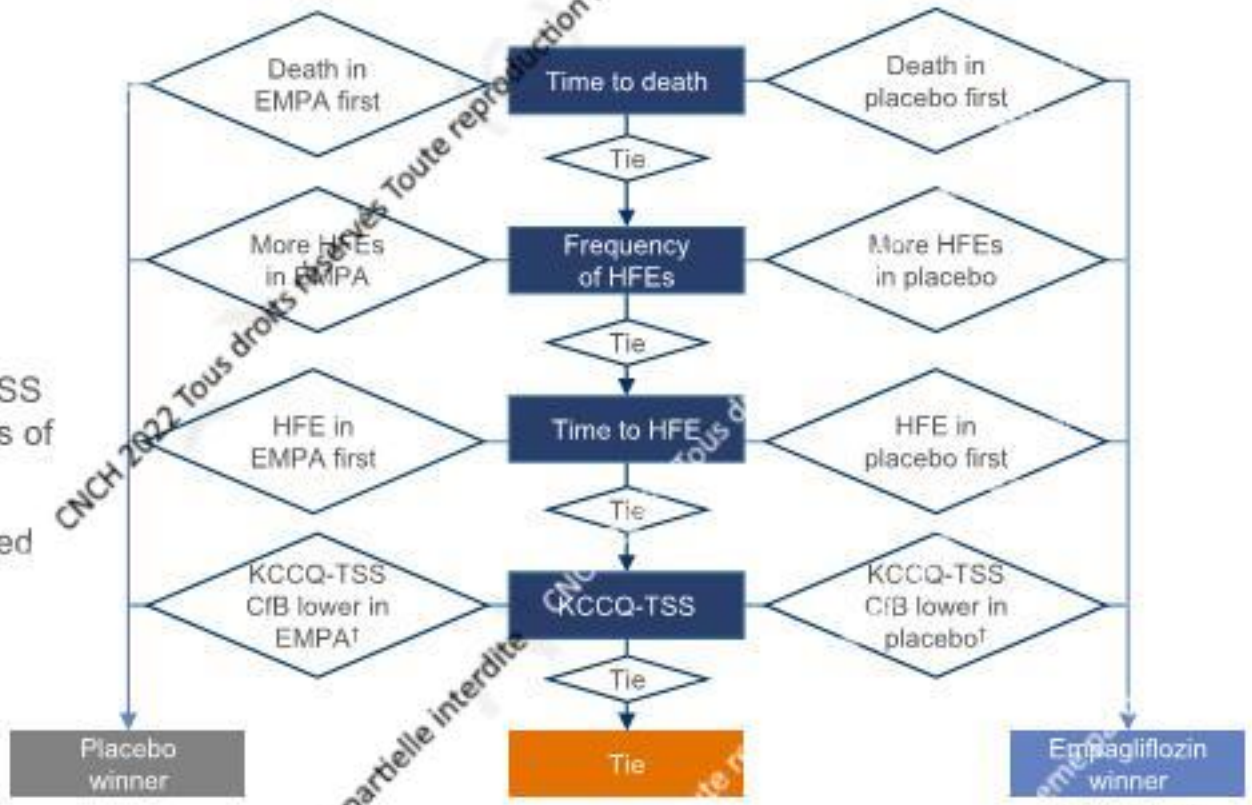
No IV inotropic drugs for **24 hours** prior to randomisation

IV, intravenous

Tromp J *et al. Eur J Heart Fail* 2021;23:826

EMPULSE: primary endpoint

- **Primary endpoint (clinical benefit), composite of:**
  - Death
  - Number of heart failure events (HFEs)*
  - Time to first HFE
  - ≥5-point difference in the KCCQ-TSS change from baseline after 90 days of treatment
- Primary analysis assessed by a stratified **win ratio**



Comparisons were stratified by HF status (i.e. de novo HF vs decompensated chronic HF)
*HFE includes hospitalisations for HF, urgent HF visits and unplanned outpatient visits †≥5-point threshold for a difference, otherwise recorded as a tie
CfB, change from baseline; EMPA, empagliflozin; HFE, heart failure event; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score
Voors AA *et al. Nat Med* 2022; doi: 10.1038/s41591-021-01659-1

EMPULSE: what is the win ratio??

Criteria

1. **Death**
   - If neither patient is superior based on death
2. **Number of HFEs**
   - If neither patient is superior based on death or number of HFEs
3. **Time to first HFE**
   - If neither patient is superior based on 1–3
4. **≥5-point difference in the KCCQ-TSS change from baseline after 90 days**

Pairwise comparison

Each patient in the empagliflozin group is compared against every patient in the placebo group

Calculation

Win ratio =

Total number of wins in the empagliflozin group / **Total number of wins in the placebo group**

Comparisons were stratified by HF status (i.e. de novo HF vs decompensated chronic HF)
HFE, heart failure event; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score
Voors AA *et al. Nat Med* 2022; doi: 10.1038/s41591-021-01659-1

EMPULSE: baseline characteristics (1/3)

	Placebo (n=265)	Empagliflozin (n=265)
Age, years, median (IQR)	70 (59, 78)	71 (62, 78)
Women, n (%)	93 (35.1)	86 (32.5)
Race, n (%)		
White	202 (76.2)	211 (79.6)
Black	33 (12.5)	21 (7.9)
Asian	25 (9.4)	32 (12.1)
Other/mixed race	4 (1.5)	1 (0.4)
Region, n (%)		
Europe	171 (64.5)	168 (63.4)
North America	69 (26.0)	66 (24.9)
Asia	25 (9.4)	31 (11.7)
NYHA functional class, n (%)		
Class I	6 (2.3)	8 (3.0)
Class II	91 (34.3)	95 (35.8)
Class III	145 (54.7)	134 (50.6)
Class IV	23 (8.7)	26 (9.8)

Missing data are not shown. IQR, interquartile range; NYHA, New York Heart Association

Voors AA *et al. Nat Med* 2022; doi: 10.1038/s41591-021-01659-1

EMPULSE: baseline characteristics (2/3)

	Placebo (n=265)	Empagliflozin (n=265)
KCCQ-TSS	39.6 (22.4, 58.3)	37.5 (20.8, 58.3)
NT-proBNP, pg/ml	3106 (1588, 6013)	3299 (1843, 6130)
Blood pressure, mmHg		
Systolic	122 (110.0, 138.0)	120 (109.0, 135.0)
Diastolic	74.0 (67.0, 80.0)	72.0 (64.0, 82.0)
BMI, kg/m²	29.1 (24.7, 33.6)	28.4 (24.5, 32.5)
eGFR, ml/min/1.73 m²	54.0 (39.0, 70.0)	50.0 (36.0, 65.0)
<30 ml/min/1.73 m², n (%)	24 (9.1)	27 (10.2)
Haemoglobin, g/dl	13.4 (11.8, 14.8)	13.2 (11.8, 14.8)
LVEF, %	32.0 (22.5, 49.0)	31.0 (23.0, 45.0)
≤40%, n (%)	172 (64.9)	182 (68.7)
>40%, n (%)	93 (35.1)	76 (28.7)
HF status, n (%)		
Decompensated chronic HF	178 (67.2)	177 (66.8)
De novo	87 (32.8)	88 (33.2)

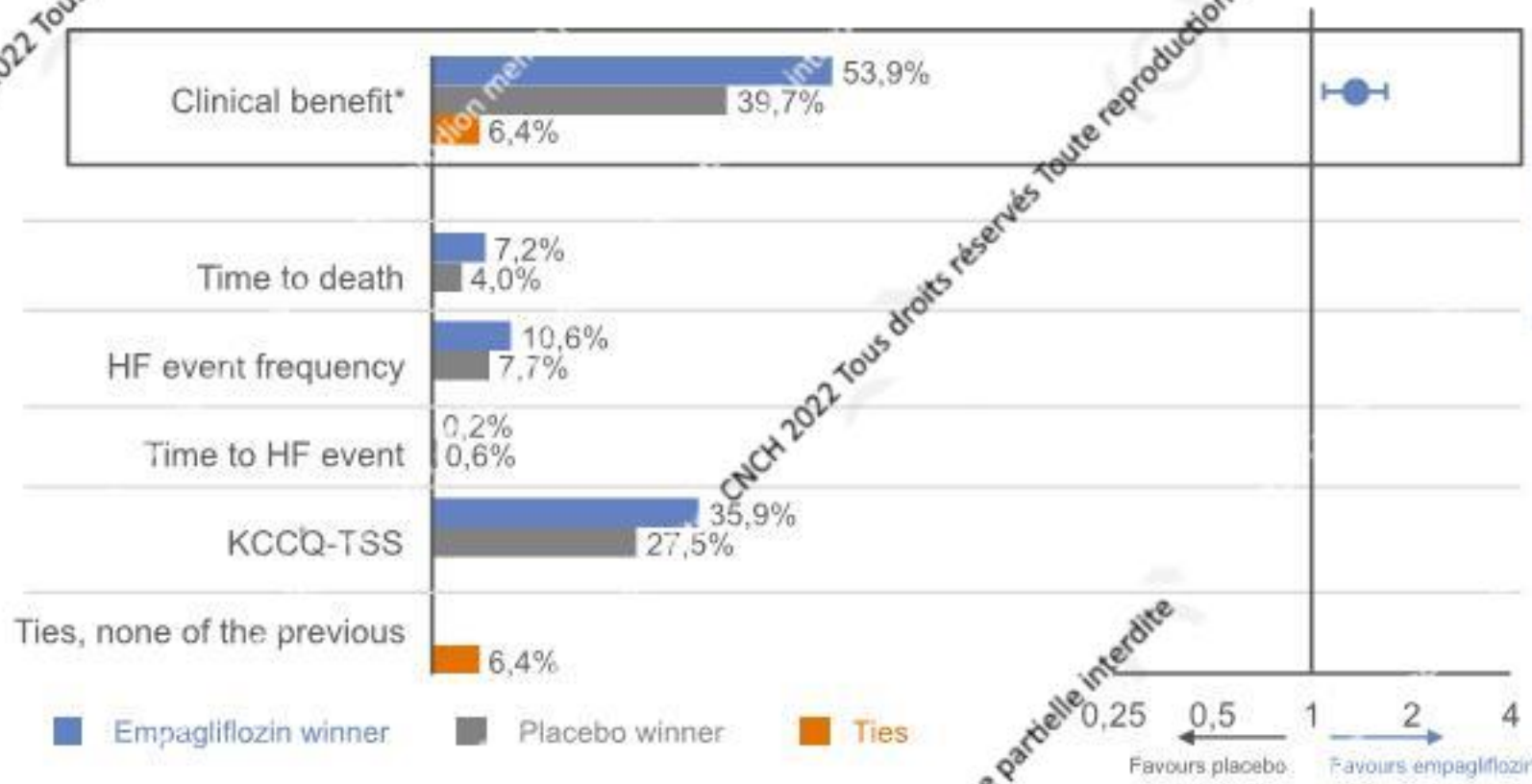
Values are median (IQR) unless stated otherwise. Missing data are not shown
IQR, interquartile range; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score; NT-proBNP, N-terminal pro-B-type natriuretic peptide
Voors AA *et al. Nat Med* 2022; doi: 10.1038/s41591-021-01659-1

EMPULSE: baseline characteristics (3/3)

	Placebo (n=265)	Empagliflozin (n=265)
Medical history, n (%)		
Diabetes	**116 (43.8)**	**124 (46.8)**
Hypertension	221 (83.4)	205 (77.4)
MI	62 (23.4)	66 (24.9)
Atrial fibrillation	128 (48.3)	134 (50.6)
CABG/PCI	78 (29.4)	78 (29.4)
Valvular heart disease	167 (63.0)	173 (65.3)
CV medications, n (%)		
ACEi/ARB/ARNi	185 (69.8)	186 (70.2)
ACEi	89 (33.6)	88 (33.2)
ARB	52 (19.6)	64 (24.2)
ARNi	45 (17.0)	36 (13.6)
MRA	125 (47.2)	151 (57.0)
Beta blocker	208 (78.5)	213 (80.4)
Loop diuretic	204 (77.0)	233 (87.9)

Missing data are not shown. CABG, coronary artery bypass graft; MRA, mineralocorticoid receptor antagonist; PCI, percutaneous coronary intervention
Voors AA *et al. Nat Med* 2022; doi: 10.1038/s41591-021-01659-1

EMPULSE: patients treated with empagliflozin were 36% more likely to experience a clinical benefit than those who received placebo



Stratified win ratio
1.36
(95% CI 1.09, 1.68)
p=0.0054

Death:
Empagliflozin: 4.2%
Placebo: 8.3%

HF event:
Empagliflozin 10.6%
Placebo 14.7%

Values are percentage of comparisons. For the components of the win ratio these values do not reflect randomised comparisons. *Composite of death, number of HFEs (including HHFs, urgent HF visits and unplanned outpatient visits), time to first HFE and change from baseline in KCCQ-TSS after 90 days of treatment; ≥5-point difference in the KCCQ-TSS change from baseline after 90 days of treatment. HFE, heart failure event; HHF, hospitalisation for heart failure; KCCQ-TSS, Kansas City Cardiomyopathy Questionnaire Total Symptom Score. Voors AA *et al. Nat Med* 2022; doi: 10.1038/s41591-021-01659-1

EMPULSE: primary endpoint first component

1 **Death**
- Death is worse than no death
- Earlier death is worse

11% of the comparisons
are decided based on
the first component

33 patients died
11 (4.2%) in the empagliflozin group
22 (8.3%) in the placebo group

Values are percentage of comparisons
Voors AA *et al. Nat Med* 2022, doi: 10.1038/s41591-021-01659-1

EMPULSE: the clinical benefits were consistent regardless of whether patients presented with de novo or decompensated chronic HF

	Empagliflozin	Placebo	Win ratio (95% CI)	Interaction *p*-value
	n with event/total N			
All patients	265	265	1.36 (1.09, 1.68)	
HF status				0.76
De novo	88	87	1.29 (0.89, 1.89)	
Decompensated chronic	177	178	1.39 (1.07, 1.81)	
Baseline diabetes status				0.57
Diabetic	124	116	1.47 (1.07, 2.02)	
Non-diabetic	141	149	1.30 (0.97, 1.73)	
Age				0.89
<70 years	116	129	1.38 (1.01, 1.90)	
≥70 years	149	136	1.43 (1.06, 1.92)	
Sex				0.69
Male	179	172	1.39 (1.06, 1.81)	
Female	86	93	1.27 (0.88, 1.83)	
Region				0.06
Asia	31	25	0.66 (0.34, 1.30)	
Europe	168	171	1.59 (1.20, 2.09)	
North America	66	69	1.32 (0.87, 2.00)	

Graph for the primary endpoint subgroup analysis
Voors AA *et al. Nat Med* 2022; doi: 10.1038/s41591-021-01659-1

EMPULSE: the clinical benefits were consistent regardless of LVEF (including in patients with HFrEF or HFpEF)

	Empagliflozin	Placebo	Win ratio (95% CI)	Interaction *p*-value
	n with event/total N			
All patients	265	265	1.36 (1.09, 1.68)	
NT-proBNP at baseline,* pg/ml				0.79
<Median	125	130	1.36 (0.99, 1.85)	
≥Median	130	126	1.44 (1.06, 1.96)	
eGFR (CKD-EPI) at baseline, ml/min/1.73 m²				0.76
<60	161	145	1.38 (1.04, 1.83)	
≥60	88	106	1.48 (1.04, 2.13)	
Atrial fibrillation/flutter at baseline				0.11
No	123	133	1.68 (1.22, 2.32)	
Yes	142	132	1.18 (0.88, 1.59)	
Baseline LVEF, %				0.90
≤40	182	172	1.35 (1.04, 1.75)	
>40	76	93	1.39 (0.95, 2.03)	

Graph for the primary endpoint subgroup analysis
*At baseline, median NT-proBNP was 3299 pg/ml and 3106 pg/ml for the empagliflozin and placebo groups, respectively
CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; NT-proBNP, N-terminal pro–B-type natriuretic peptide
Voors AA *et al. Nat Med* 2022; doi: 10.1038/s41591-021-01659-1

Vous pourriez sécuriser les adaptations en vous appuyant sur

A. Télésurveillance du poids

B. IPA

C. IDE avec délégation de tâche

D. Pharmacien clinicien

E. Autres systèmes de télésurveillance

Vous pourriez sécuriser les adaptations en vous appuyant sur

A. Télésurveillance du poids

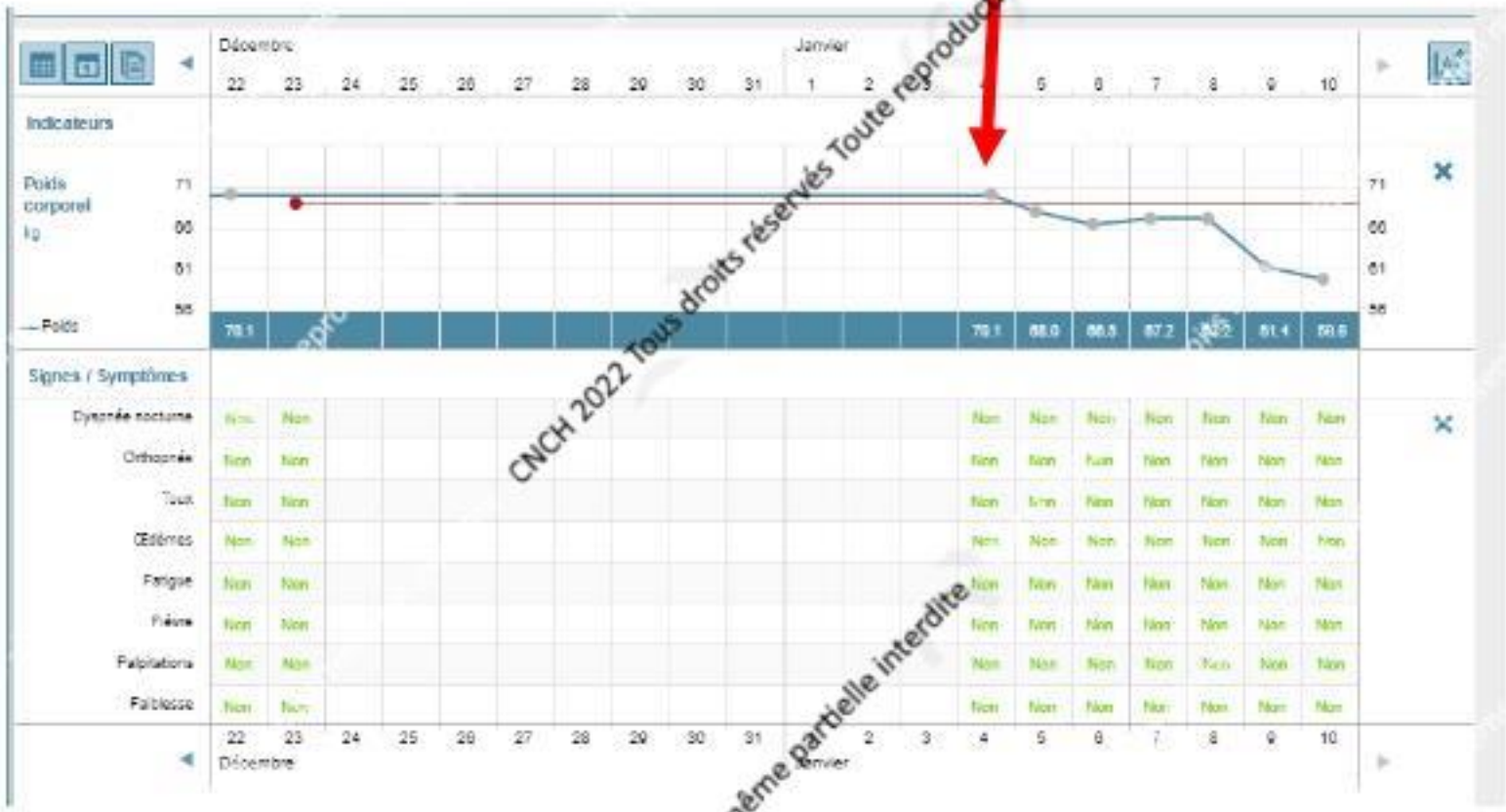
B. IPA

C. IDE avec délégation de tâche

D. Pharmacien clinicien

E. Autres systèmes de télésurveillance

Admission for



« To infinity and beyond »: ambulatory, personnalized approach

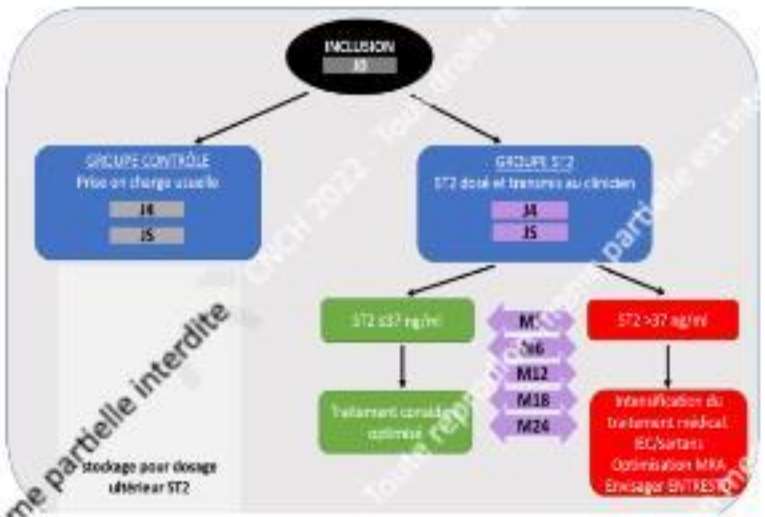
ESC European Society of Cardiology
European Journal of Heart Failure (2022) 24, 750–761
doi:10.1002/ejhf.2503
REVIEW

Practical outpatient management of worsening chronic heart failure

Nicolas Girerd[1]*, Nathan Mewton[2], Jean-Michel Tartière[3], Damien Guijarro[4], Patrick Jourdain[5,6], Thibaud Damy[7], Nicolas Lamblin[8], Antoni Bayes-Génis[9], Pierpaolo Pellicori[10], James L. Januzzi[11], Patrick Rossignol[1], and François Roubille[12], on behalf of a panel of multidisciplinary experts and the Heart Failure Working Group of the French Society of Cardiology

Médico-economic Evaluation of Therapeutic Adaptation Guided by the sST-2 Biomarker in the Management of Patients With Acute HF (ICAME)

NCT04554277



Comment faire en 2 mots?