Insuffisance cardiaque: nouvelles recommandations
Télémeeting du 5 octobre 2022

PD Dr Philippe Meyer
Responsable de l'unité d'insuffisance cardiaque et de réadaptation cardiaque
Service de Cardiologie
Philippe.meyer@hcuge.ch

Conflits d’intérêt potentiels

- Participations à des présentations ou à des conseils consultatifs parrainés par les entreprises **AstraZeneca, Novartis, Abbott, Vifor, Bayer, Servier, Boehringer Ingelheim**

- **Aucun hononaire personnel**

- Honoraires versés **intégralement** à la **Fondation** pour la recherche de la cardiologie universitaire de Genève (**GEcor**) depuis 2015

ESC European Society of Cardiology

European Heart Journal (2021) **00**, 1–128
doi:10.1093/eurheartj/ehab368

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)

With the special contribution of the Heart Failure Association (HFA) of the ESC

McDonagh TA et al. Eur Heart J. 2021 Aug 27:ehab368. doi: 10.1093/eurheartj/ehab368. Online ahead of print.

Plan

1) Clinical vignette
2) Classification
3) New evidence since 2016 (last ESC recommendations)
4) How to treat patients in 2022?

Plan

1) **Clinical vignette**
2) Classification
3) New evidence since 2016 (last ESC recommendations)
4) How to treat patients in 2022?

Clinical vignette #1: Mr P. B. 72 yo, outpatient visit

Diagnoses	• Chronic HFrEF due to stable ischemic heart disease, LVEF 30%, CRT-D • Type 2 NIR diabetes • No complaints, NYHA II
Physical exam	• Sitting blood pressure 116/68 mmHg (standing 113/70 mmHg) • Heart rate 62 bpm. • No signs of congestion.
ECG	• Sinus rhythm at 62 bpm with resynchronised ventricular pacing
Labs	• Na 137 mmol/l, K 4.7 mmol/l, creatinine 123 µmol/l, (eGFR 57 ml/min/1.73m^2), NT-proBNP 535 ng/l, HbA1c 7.5%

How would you optimize therapy?

Medications	• Aspirin 100 mg 1-0-0 • Atorvastatin 40 mg 1-0-0 • Lisinopril 20 mg 1-0-1 • Carvedilol 12.5 mg 1-0-1 • Spironolactone 25 mg 1-0-0 • Metformin 500 mg 1-0-1

Plan

1) Clinical vignette
2) **Classification**
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2021 classification of heart failure

Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF ≤40%	LVEF 41–49%[b]	LVEF ≥50%
	3	-	-	Objective evidence of cardiac structural and/or functional abnormalities consistent with the presence of LV diastolic dysfunction/raised LV filling pressures, including raised natriuretic peptides[c]
RATE (HUG)		35%	15%	**50%**

McDonagh TA et al. Eur Heart J. 2021 Aug 27:ehab368. doi: 10.1093/eurheartj/ehab368. Online ahead of print.

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European Heart Journal Advance Access published May 20, 2016

European Heart Journal
doi:10.1093/eurheartj/ehw128

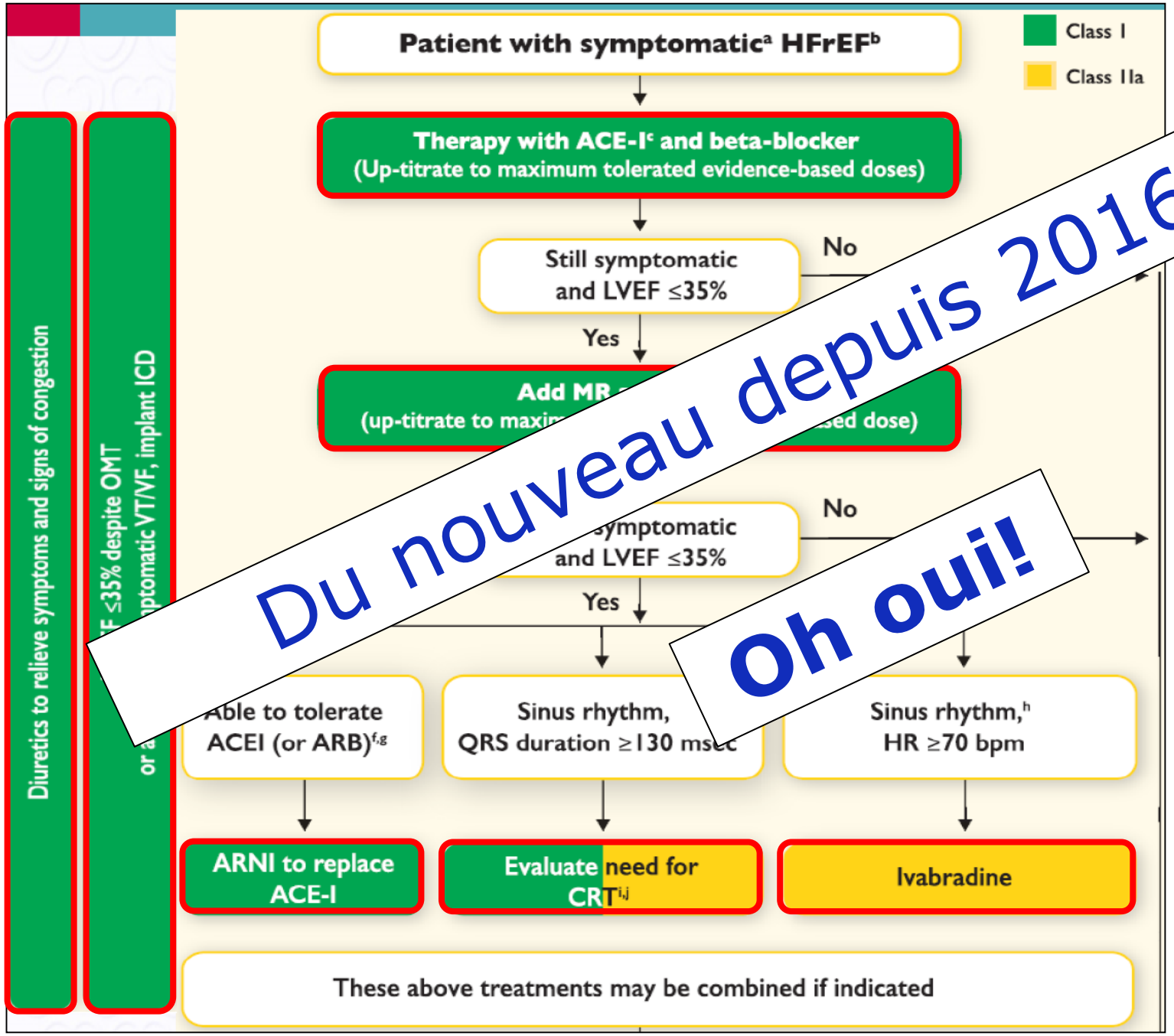
ESC GUIDELINES

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)

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

Authors/Task Force Members: Piotr Ponikowski* (Chairperson) (Poland), Adriaan A. Voors* (Co-Chairperson) (The Netherlands), Stefan D. Anker (Germany), Héctor Bueno (Spain), John G. F. Cleland (UK), Andrew J. S. Coats (UK), Volkmar Falk (Germany), José Ramón González-Juanatey (Spain), Veli-Pekka Harjola (Finland), Ewa A. Jankowska (Poland), Mariell Jessup (USA), Cecilia Linde (Sweden), Petros Nihoyannopoulos (UK), John T. Parissis (Greece), Burkert Pieske (Germany), Jillian P. Riley (UK), Giuseppe M. C. Rosano (UK/Italy), Luis M. Ruilope (Spain), Frank Ruschitzka (Switzerland), Frans H. Rutten (The Netherlands), Peter van der Meer (The Netherlands)



Du nouveau depuis 2016?

Oh oui!

ligne: IEC, BB, diurétique

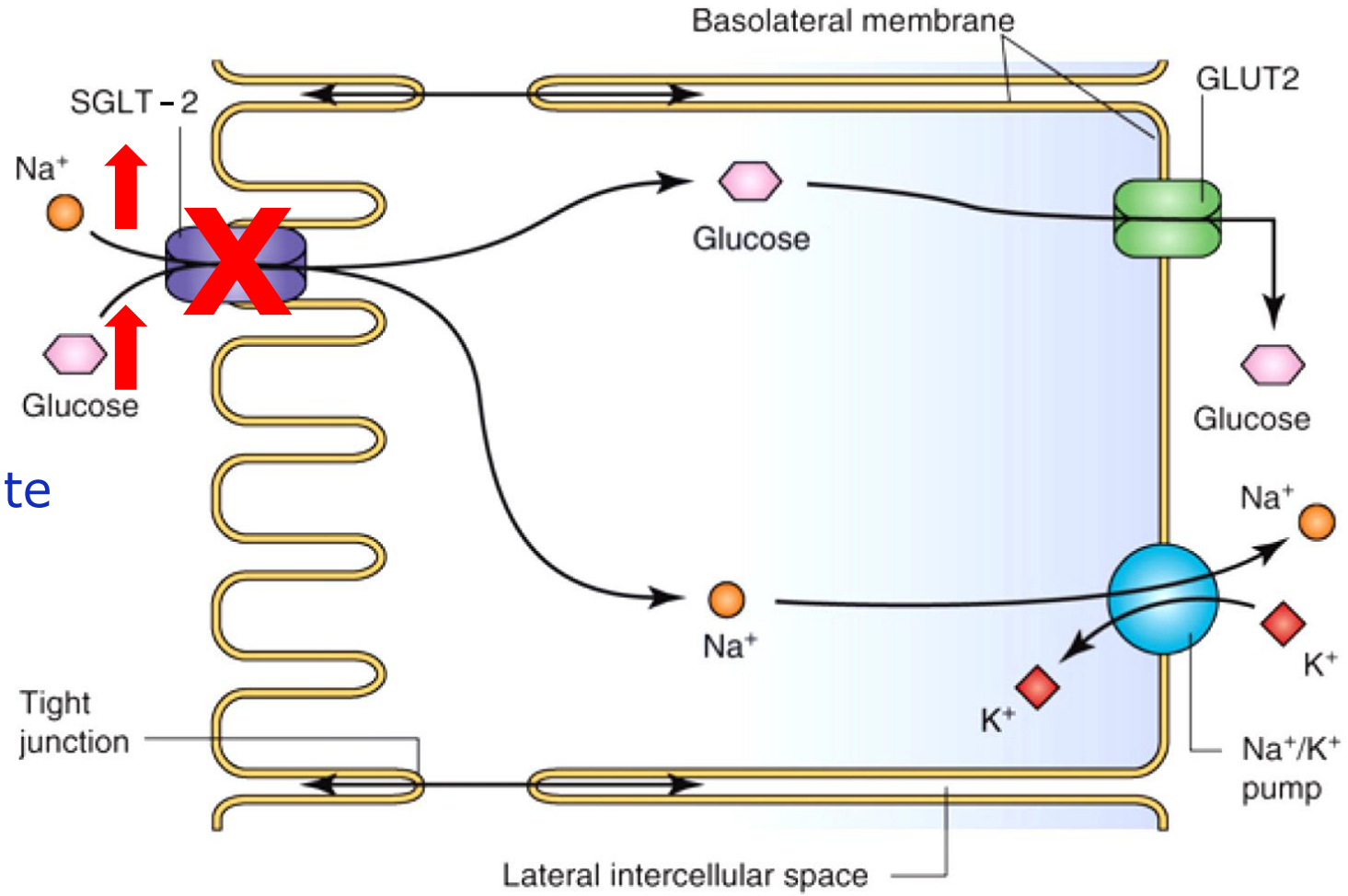
- **2ème ligne:** antagonistes aldostérone

- **3ème ligne:**
  - Switch IEC → ARNI *et/ou*
  - Considérer CRT *et/ou*
  - Considérer ivabradine

Ponikowski P et al. Eur Heart J 2016;37:2129–2200.

Sodium-glucose co-transporter 2 inhibition in the proximal tubule

Glomerular filtrate



Interstitial fluid

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

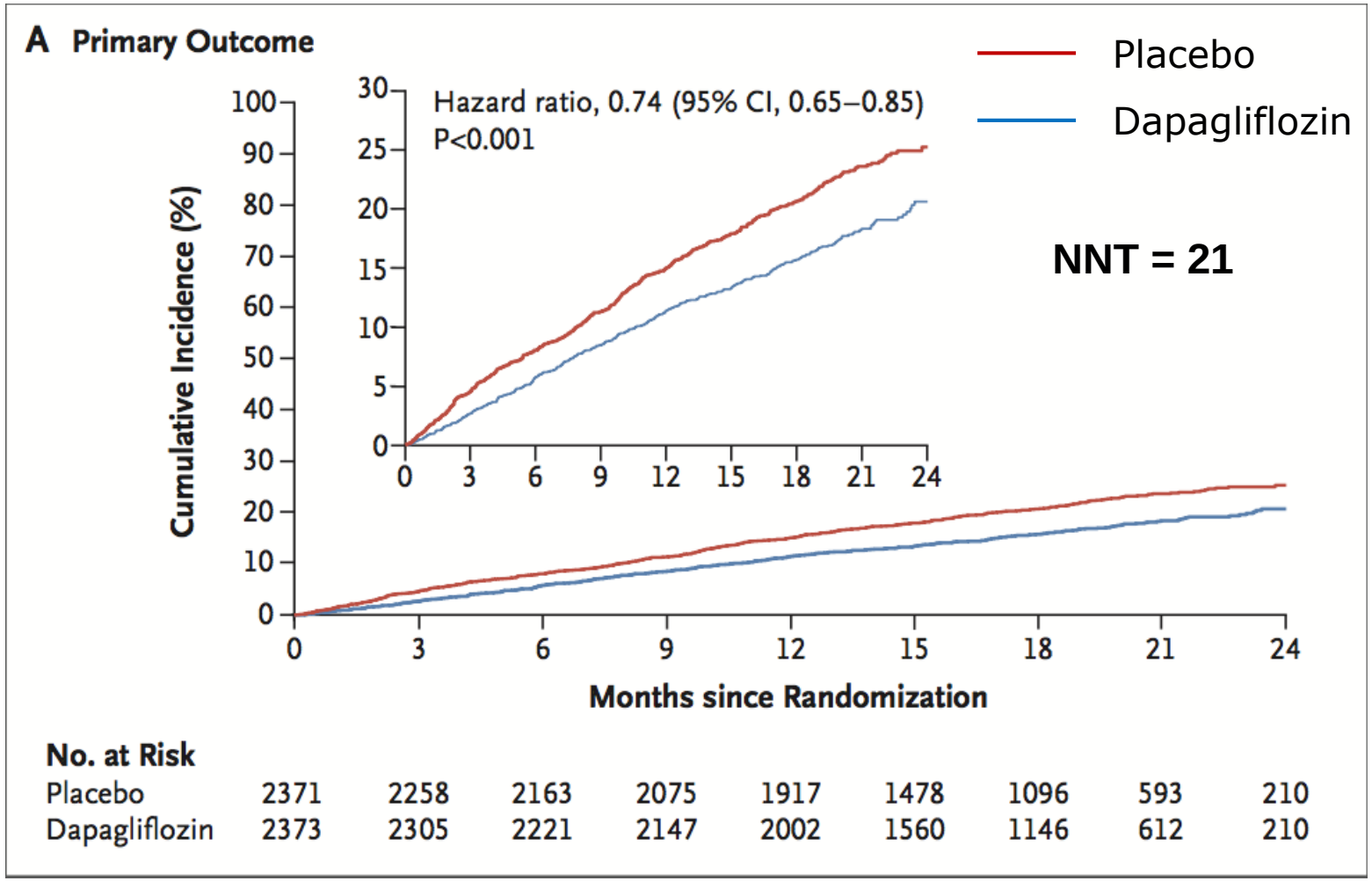
J.J.V. McMurray, S.D. Solomon, S.E. Inzucchi, L. Køber, M.N. Kosiborod, F.A. Martinez, P. Ponikowski, M.S. Sabatine, I.S. Anand, J. Bělohlávek, M. Böhm, C.-E. Chiang, V.K. Chopra, R.A. de Boer, A.S. Desai, M. Diez, J. Drozdz, A. Dukát, J. Ge, J.G. Howlett, T. Katova, M. Kitakaze, C.E.A. Ljungman, B. Merkely, J.C. Nicolau, E. O'Meara, M.C. Petrie, P.N. Vinh, M. Schou, S. Tereshchenko, S. Verma, C. Held, D.L. DeMets, K.F. Docherty, P.S. Jhund, O. Bengtsson, M. Sjöstrand, and A.-M. Langkilde, for the DAPA-HF Trial Committees and Investigators*

N Engl J Med 2019;380:347-357.

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

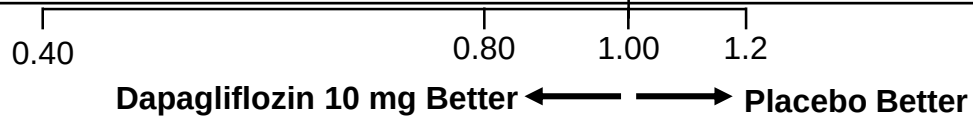
- **4744** stable HFrEF NYHA ≥2
- Mean age 66 yrs, **Mean LVEF 31%**
- **58% of patients without DM2**
- Optimal baseline medical therapy
- **eGFR >30**
- Randomization to dapagliflozin or placebo
- Primary endpoint: CV death or hHF or urgent HF visit
- Median follow-up: 18.2 months

Primary outcome: CV death or hHF or an urgent HF Visit



Summary of the main CV endpoints

Outcome, n (%)	Dapagliflozin 10 mg (n=2373)	Placebo (n=2371)	HR (95% CI)	HR (95% CI)	p-value
CV death, hHF, or urgent HF visit	386 (16.3)	502 (21.2)		0.74 (0.65, 0.85)	<0.001
hHF or urgent HF visit	237 (10.0)	326 (13.7)		0.70 (0.59, 0.83)	0.00003
Hospitalization for HF	231 (9.7)	318 (13.4)		0.70 (0.59, 0.83)	0.0001
CV death	227 (9.6)	273 (11.5)		0.82 (0.69, 0.98)	0.029
CV death or hHF	382 (16.1)	495 (20.9)		0.75 (0.65, 0.85)	<0.001
Death from any cause	276 (11.6)	329 (13.9)		0.83 (0.71, 0.97)	0.022



Safety outcomes

Event, n (%)	Dapagliflozin 10 mg (n=2368)	Placebo (n=2368)	p-value
AE leading to treatment discontinuation	111 (4.7)	116 (4.9)	0.79
AE of interest			
Volume depletion	178 (7.5)	162 (6.8)	0.40
Renal AE	153 (6.5)	170 (7.2)	0.36
Fracture	49 (2.1)	50 (2.1)	1.00
Amputation	13 (0.5)	12 (0.5)	1.00
Major hypoglycemia	4 (0.2)	4 (0.2)	-
Diabetic ketoacidosis	3 (0.1)	0 (0)	-
Fournier's gangrene	0	1 (<0.1)	-
Genital infection			
Serious	0	1 (0.0)	-
Leading to treatment discontinuation	7 (0.3)	0	-
Urinary tract infection			
Serious	14 (0.6)	17 (0.7)	-
Leading to treatment discontinuation	5 (0.2)	5 (0.2)	-

The NEW ENGLAND JOURNAL of MEDICINE

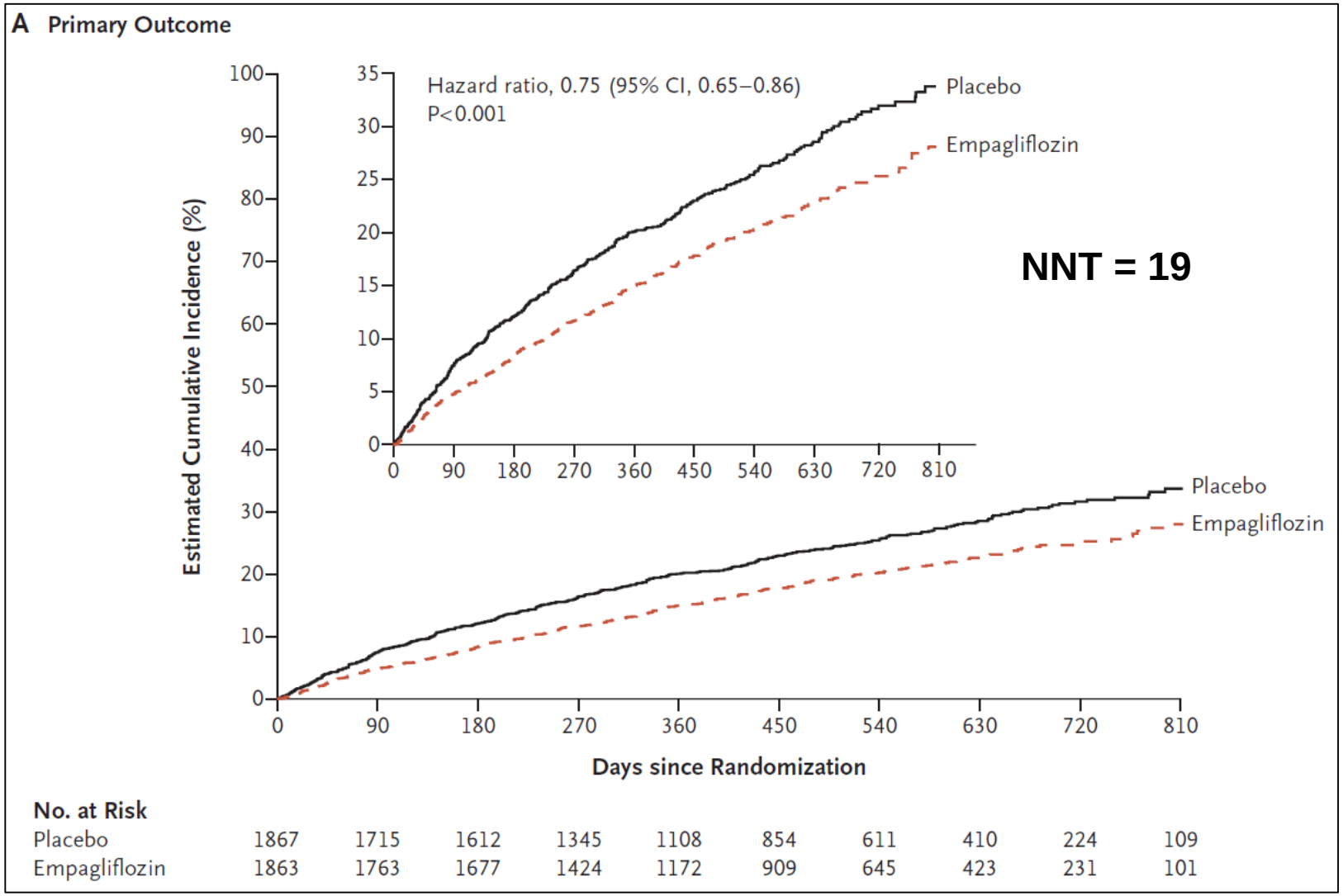
ORIGINAL ARTICLE

Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

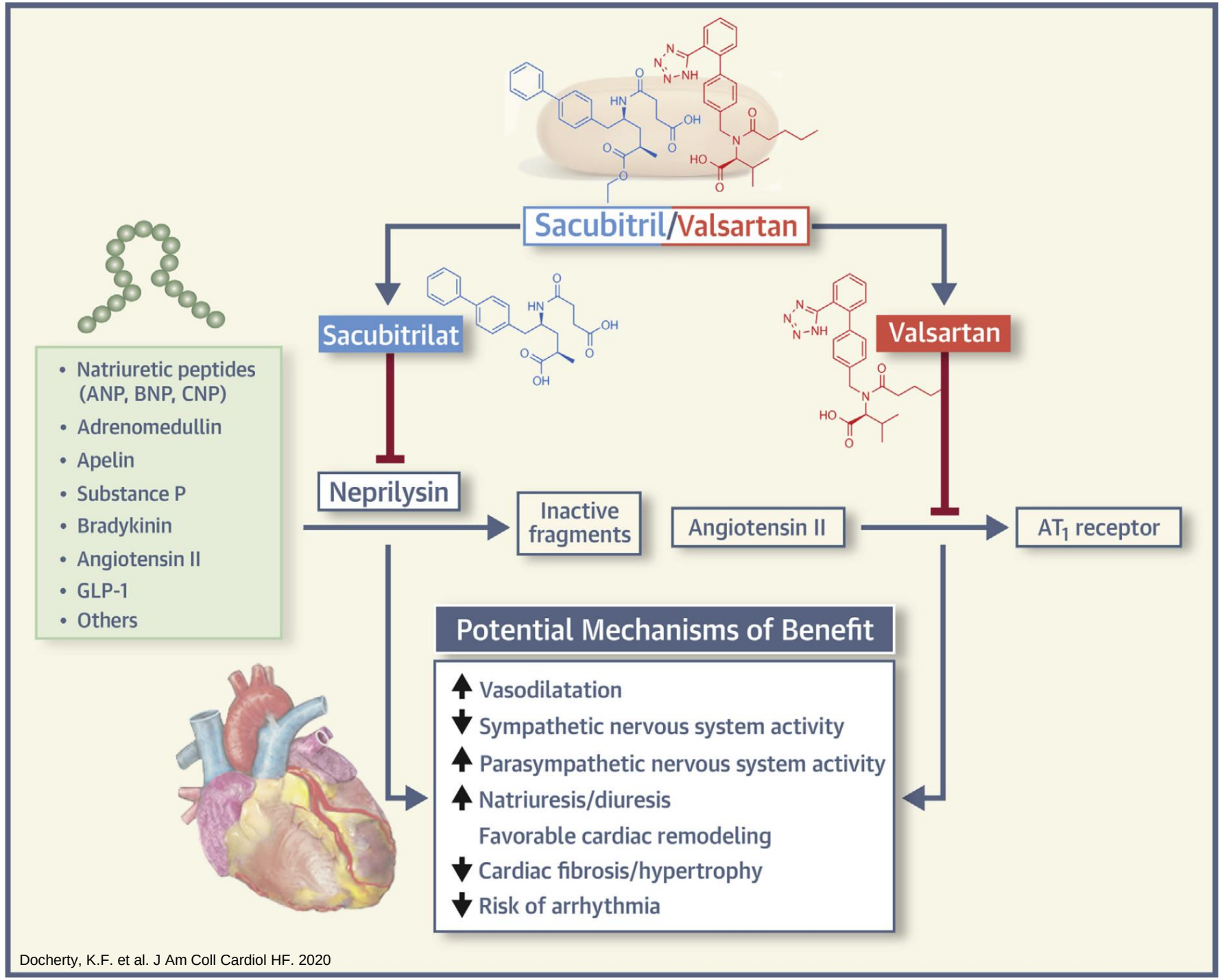
M. Packer, S.D. Anker, J. Butler, G. Filippatos, S.J. Pocock, P. Carson, J. Januzzi, S. Verma, H. Tsutsui, M. Brueckmann, W. Jamal, K. Kimura, J. Schnee, C. Zeller, D. Cotton, E. Bocchi, M. Böhm, D.-J. Choi, V. Chopra, E. Chuquiure, N. Giannetti, S. Janssens, J. Zhang, J.R. Gonzalez Juanatey, S. Kaul, H.-P. Brunner-La Rocca, B. Merkely, S.J. Nicholls, S. Perrone, I. Pina, P. Ponikowski, N. Sattar, M. Senni, M.-F. Seronde, J. Spinar, I. Squire, S. Taddei, C. Wanner, and F. Zannad, for the EMPEROR-Reduced Trial Investigators*

N Engl J Med 2020; 383:1413-1424.

Primary outcome: CV death or hospitalization for HF



N Engl J Med 2020; 383:1413-1424



Docherty, K.F. et al. J Am Coll Cardiol HF. 2020

Angiotensin–Neprilysin Inhibition in Acute Decompensated Heart Failure

Eric J. Velazquez, M.D., David A. Morrow, M.D., M.P.H., Adam D. DeVore, M.D., M.H.S., Carol I. Duffy, D.O., Andrew P. Ambrosy, M.D., Kevin McCague, M.A., Ricardo Rocha, M.D., and Eugene Braunwald, M.D., for the PIONEER-HF Investigators*

881 patients hospitalized for **acute decompensated HF**

Randomized after a mean of 2.8 days to enalapril or sacubitril/valsartan

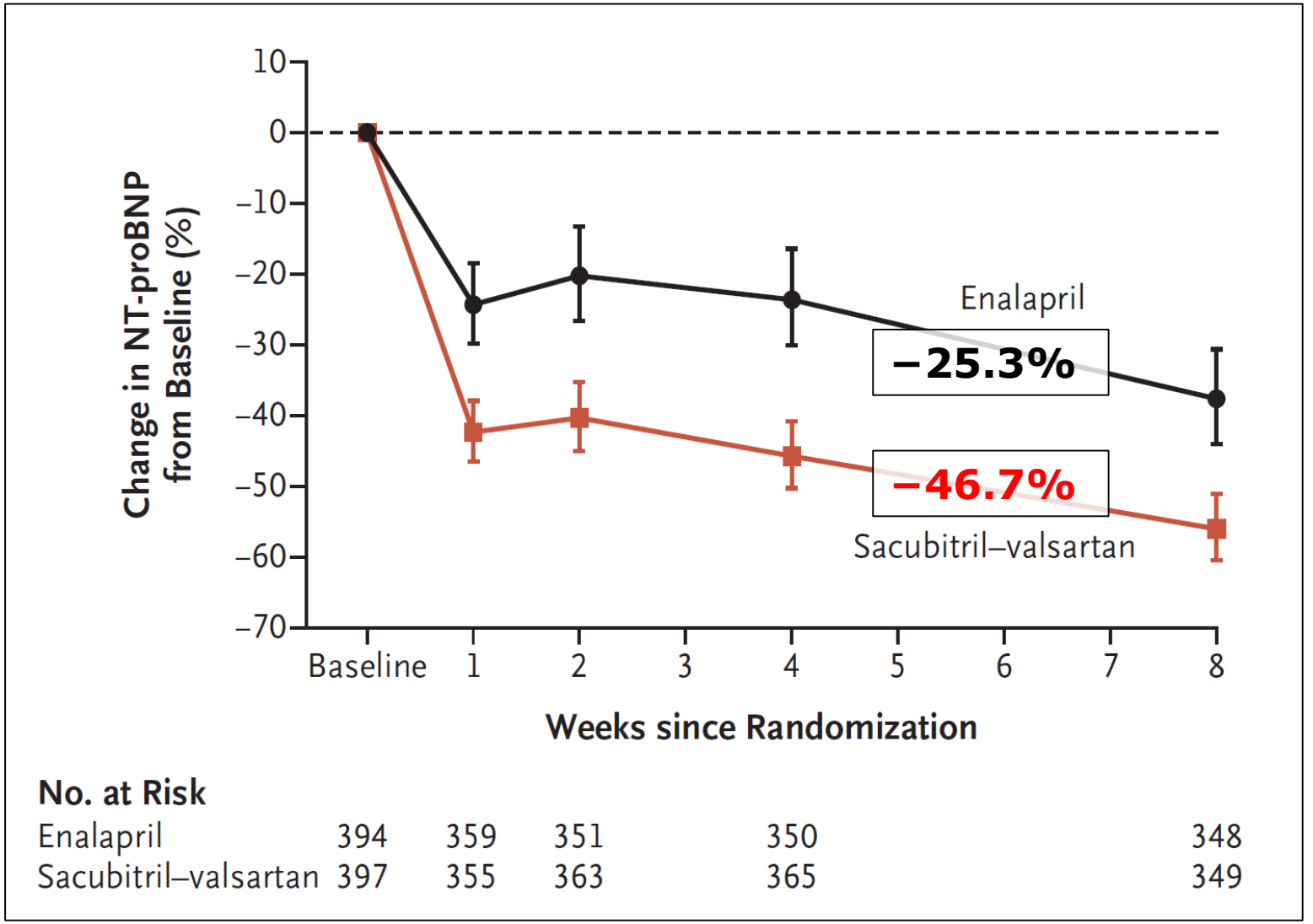
Median LVEF 25%

Median NT-proBNP: 2700 pg/mL

Stabilized (SBP ≥100 mmHg, no recent increase in iv diuretics, no iv vasodilators/inotropes)

N Engl J Med 2019; 380:539-548.

Primary endpoint: % change in NT-proBNP

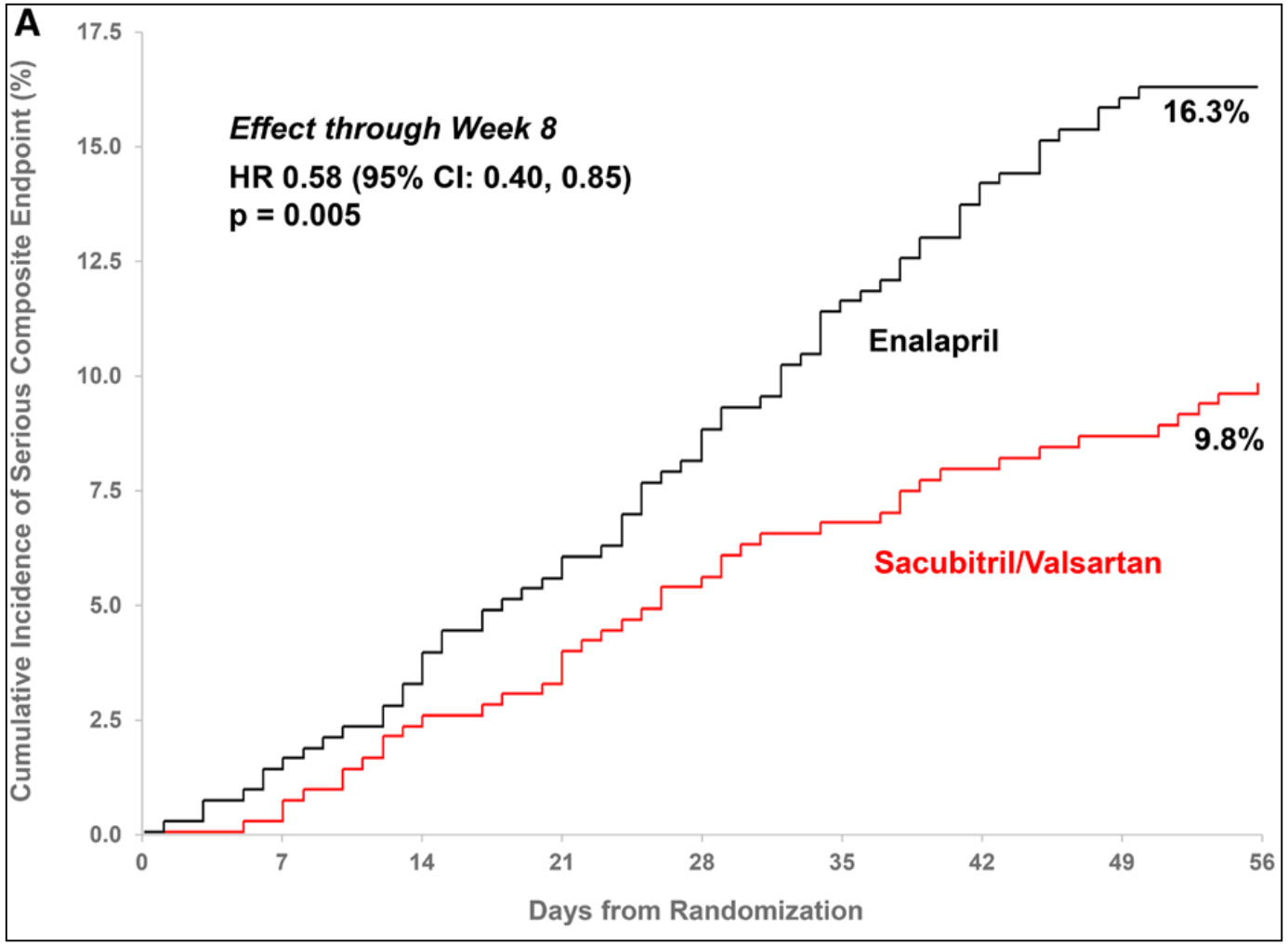


(P<0.001)

Safety events

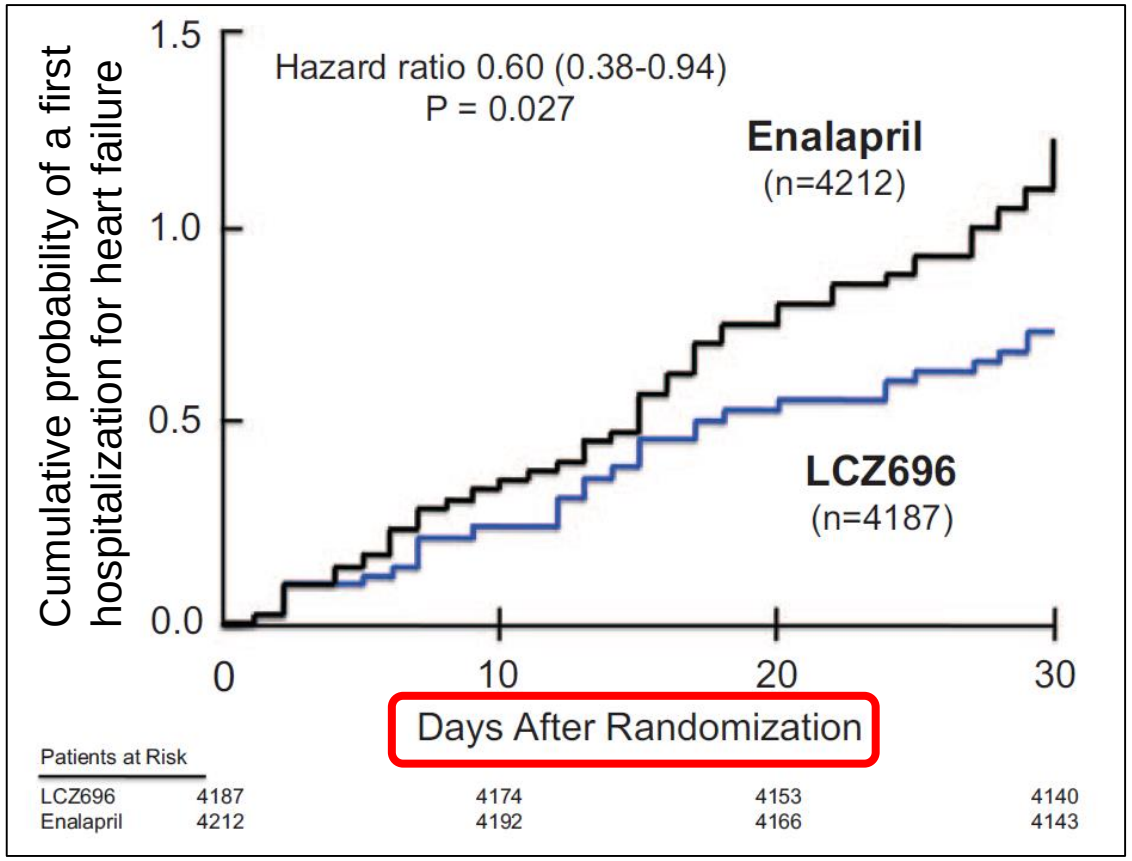
Safety Events (%)	Sacubitril/ Valsartan (n=440) (%)	Enalapril (n=441) (%)	RR (95% CI)
Worsening renal function[a]	13.6	14.7	0.93 (0.67-1.28)
hyperkalaemia	11.6	9.3	1.25 (0.84-1.84)
Symptomatic hypotension	15.0	12.7	1.18 (0.85-1.64)
Angioedema events[b]	0.2	1.4	0.17 (0.02-1.38)

Clinical composite of death from any cause, rehospitalization for HF, LVAD implantation, or listing for cardiac transplant



Morrow DA et al. Circulation. 2019;139:2285–2288.

Angiotensin Receptor Neprilysin Inhibition Compared With Enalapril on the Risk of Clinical Progression in Surviving Patients With Heart Failure



Packer M et al. Circulation. 2015;131:54–61 et al.

Plan

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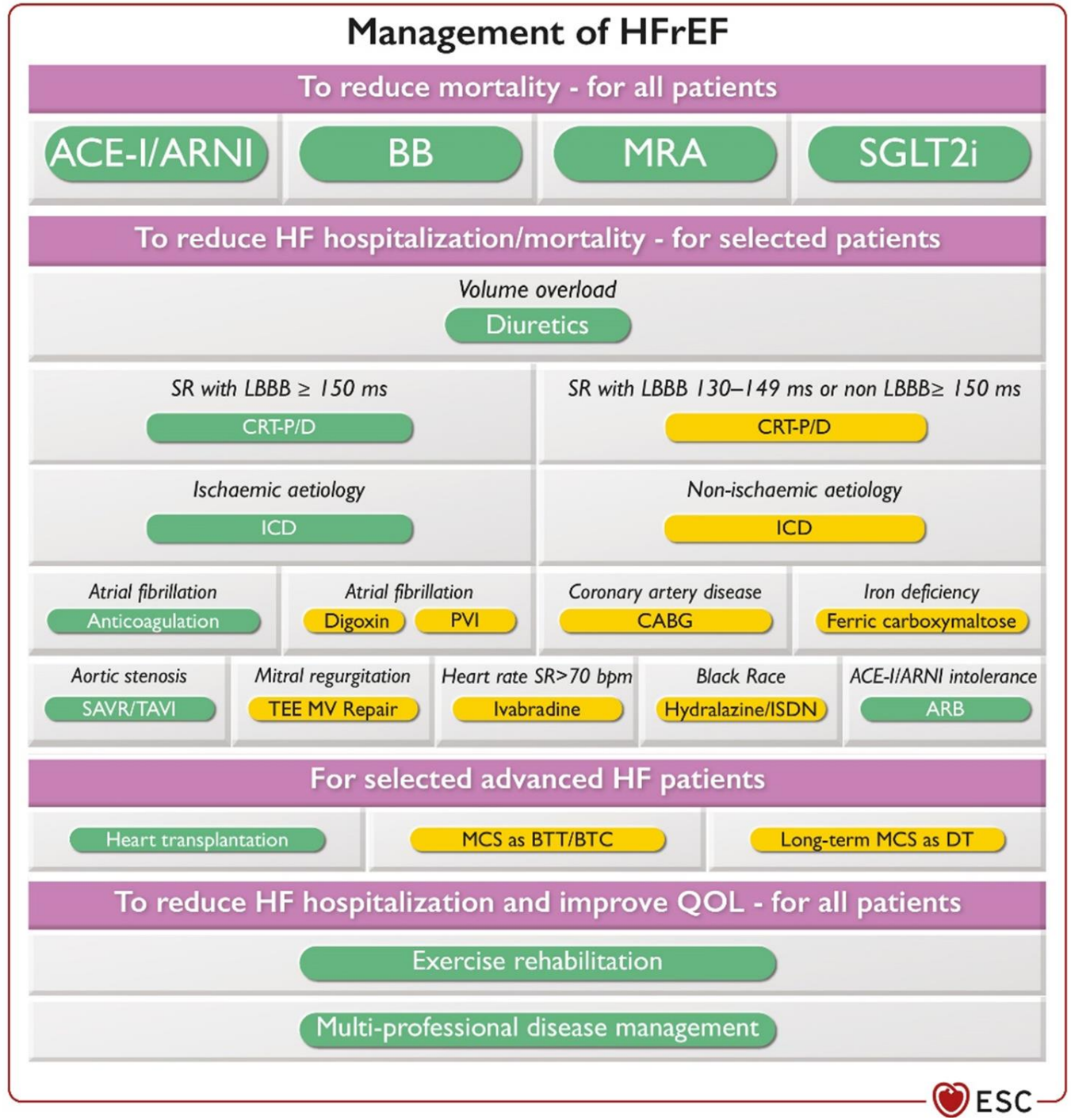
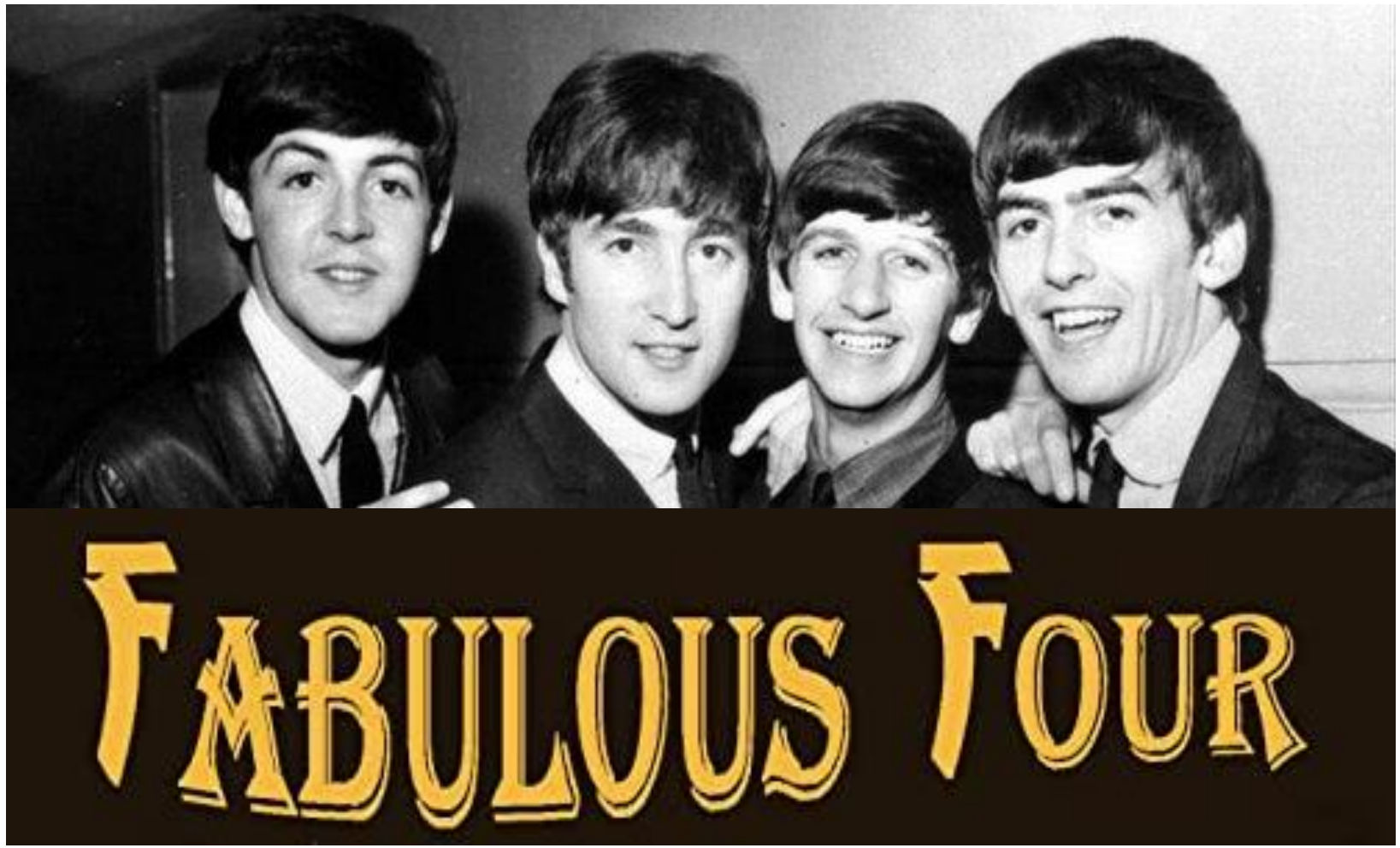
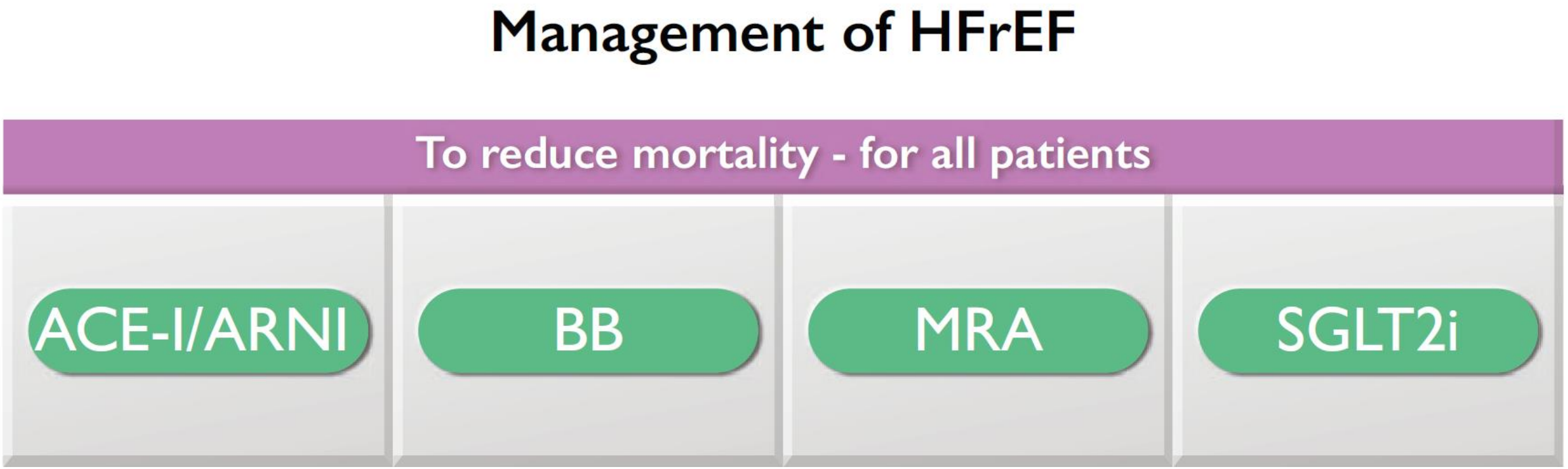

Management of HFrEF
To reduce mortality - for all patients
ACE-I/ARNI
BB
MRA
SGLT2i
To reduce HF hospitalization/mortality - for selected patients
Volume overload
Diuretics
SR with LBBB ≥ 150 ms
CRT-P/D
SR with LBBB 130–149 ms or non LBBB≥ 150 ms
CRT-P/D
Ischaemic aetiology
ICD
Non-ischaemic aetiology
ICD
Atrial fibrillation
Anticoagulation
Atrial fibrillation
Digoxin
PVI
Coronary artery disease
CABG
Iron deficiency
Ferric carboxymaltose
Aortic stenosis
SAVR/TAVI
Mitral regurgitation
TEE MV Repair
Heart rate SR>70 bpm
Ivabradine
Black Race
Hydralazine/ISDN
ACE-I/ARNI intolerance
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
ESC

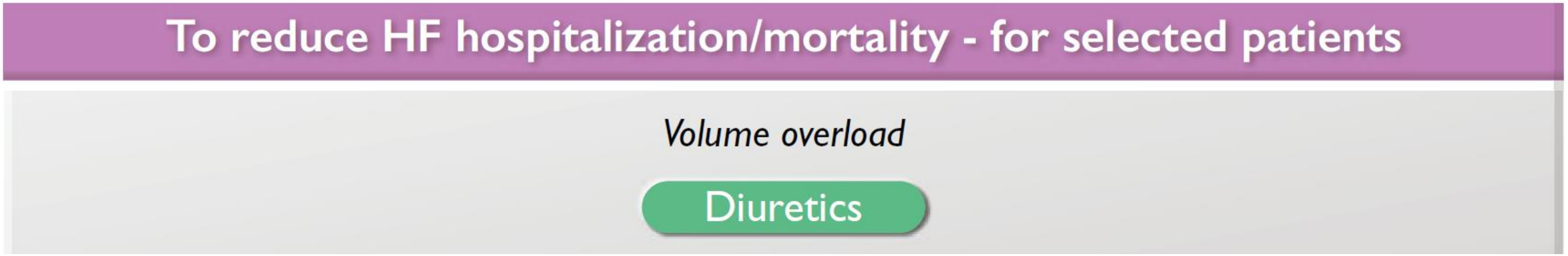

FANTASTIC FOUR


FABULOUS FOUR

Algorithme ESC de traitement de l'insuffisance cardiaque (1)



Algorithme ESC de traitement de l'insuffisance cardiaque (2)



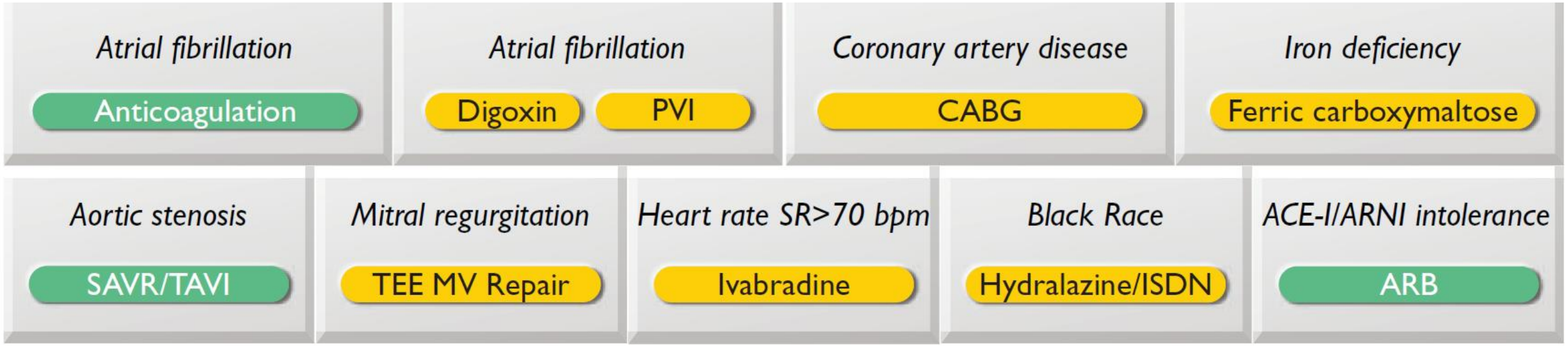
«Start low, go slow, aim high»

Neuro-hormonal antagonists (ARNI / ACE-I, BB, and MRA) should be **gradually up-titrated** to **target doses** or **maximally tolerated doses** to achieve the benefits on morbidity/mortality demonstrated in clinical trials

Algorithme ESC de traitement de l'insuffisance cardiaque (3)

SR with LBBB ≥ 150 ms CRT-P/D	*SR with LBBB 130–149 ms or non LBBB≥ 150 ms* CRT-P/D
Ischaemic aetiology ICD	*Non-ischaemic aetiology* ICD

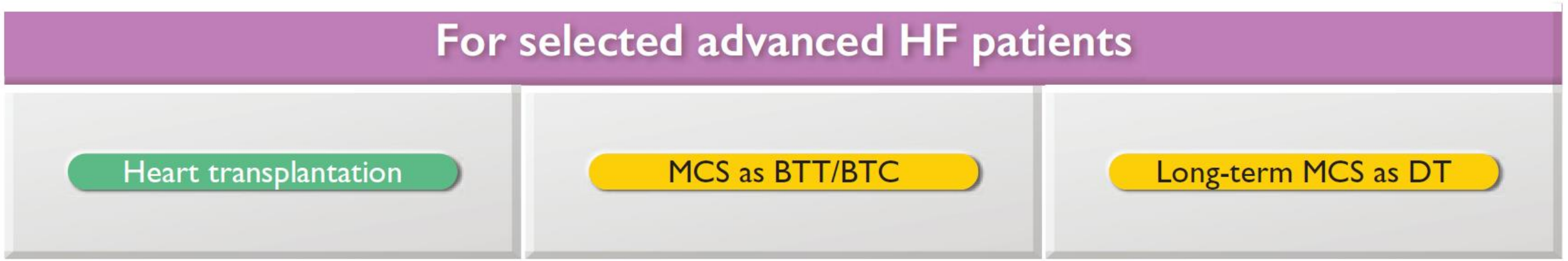
Algorithme ESC de traitement de l'insuffisance cardiaque (4)



Definition of iron deficiency (ID) in heart failure

- Different as in the general population
- Absolute ID = Serum ferritin <100 µg/l
- Functional ID = Ferritin 100-299 µg/l + transferrin saturation <20%

Algorithme ESC de traitement de l'insuffisance cardiaque (5)



Algorithme ESC de traitement de l'insuffisance cardiaque (6)

Clinical vignette #1: Mr P. B. 72 yo, outpatient visit

Diagnoses	• Chronic HFrEF due to stable ischemic heart disease, LVEF 30%, CRT-D • Type 2 NIR diabetes • No complains, NYHA II
Physical exam	• Sitting blood pressure 116/68 mmHg (standing 113/70 mmHg) • Heart rate 62 bpm. • No signs of congestion.
ECG	• Sinus rhythm at 62 bpm with resynchronised ventricular pacing
Labs	• Na 137 mmol/l, K 4.7 mmol/l, creatinine 123 µmol/l, (eGFR 57 ml/min/1.73m^2), NT-proBNP 535 ng/l, HbA1c 7.5%

How would you optimize therapy?

Medications	• Aspirin 100 mg 1-0-0 • Atorvastatin 40 mg 1-0-0 • Lisinopril 20 mg 1-0-1 • Carvedilol 12.5 mg 1-0-1 • Spironolactone 25 mg 1-0-0 • Metformin 500 mg 1-0-1

1) Keep the same treatment
2) Switch lisinopril to sacubitril/valsartan 100 mg b.i.d.
3) Add dapagliflozin or empagliflozin 10 mg o.d.
4) 2) + 3)

How would you optimize therapy?

Medications	• Aspirin 100 mg 1-0-0 • Atorvastatin 40 mg 1-0-0 • Lisinopril 20 mg 1-0-1, **switch to sac/val 100 mg bid after 36 h** • Carvedilol 12.5 mg 1-0-1 • Spironolactone 25 mg 1-0-0 • Metformin 500 mg 1-0-1 **+ dapagliflozin 10 mg/d**

1) Keep the same treatment
2) Switch lisinopril to sacubitril/valsartan 100 mg b.i.d.
3) Add dapagliflozin or empagliflozin 10 mg o.d.
4) 2) + 3)

Merci !

PD Dr Philippe Meyer
Responsable de l'unité d'insuffisance cardiaque et de réadaptation cardiaque
Service de Cardiologie
Philippe.meyer@hcuge.ch

Telemeeting 04.10.2022

European Society of Cardiology guidelines: recommendations in HFpEF

2012 ESC guidelines

- No treatment has yet been shown, convincingly, to reduce morbidity or mortality in patients with HFpEF

2016 ESC guidelines

- No treatment has yet been shown, convincingly, to reduce morbidity or mortality in patients with HFpEF

2021 ESC guidelines

- To date, no treatment has been shown to convincingly reduce mortality and morbidity in patients with HFpEF, although improvements have been seen for some specific phenotypes of patients within the overall HFpEF umbrella

Recommendations for the treatment of patients with heart failure with preserved ejection fraction

Recommendations	Class[a]	Level[b]
Screening for, and treatment of, aetiologies, and cardiovascular and non-cardiovascular comorbidities is recommended in patients with HFpEF (see relevant sections of this document).	I	C
Diuretics are recommended in congested patients with HFpEF in order to alleviate symptoms and signs.[137]	I	C

The NEW ENGLAND JOURNAL of MEDICINE

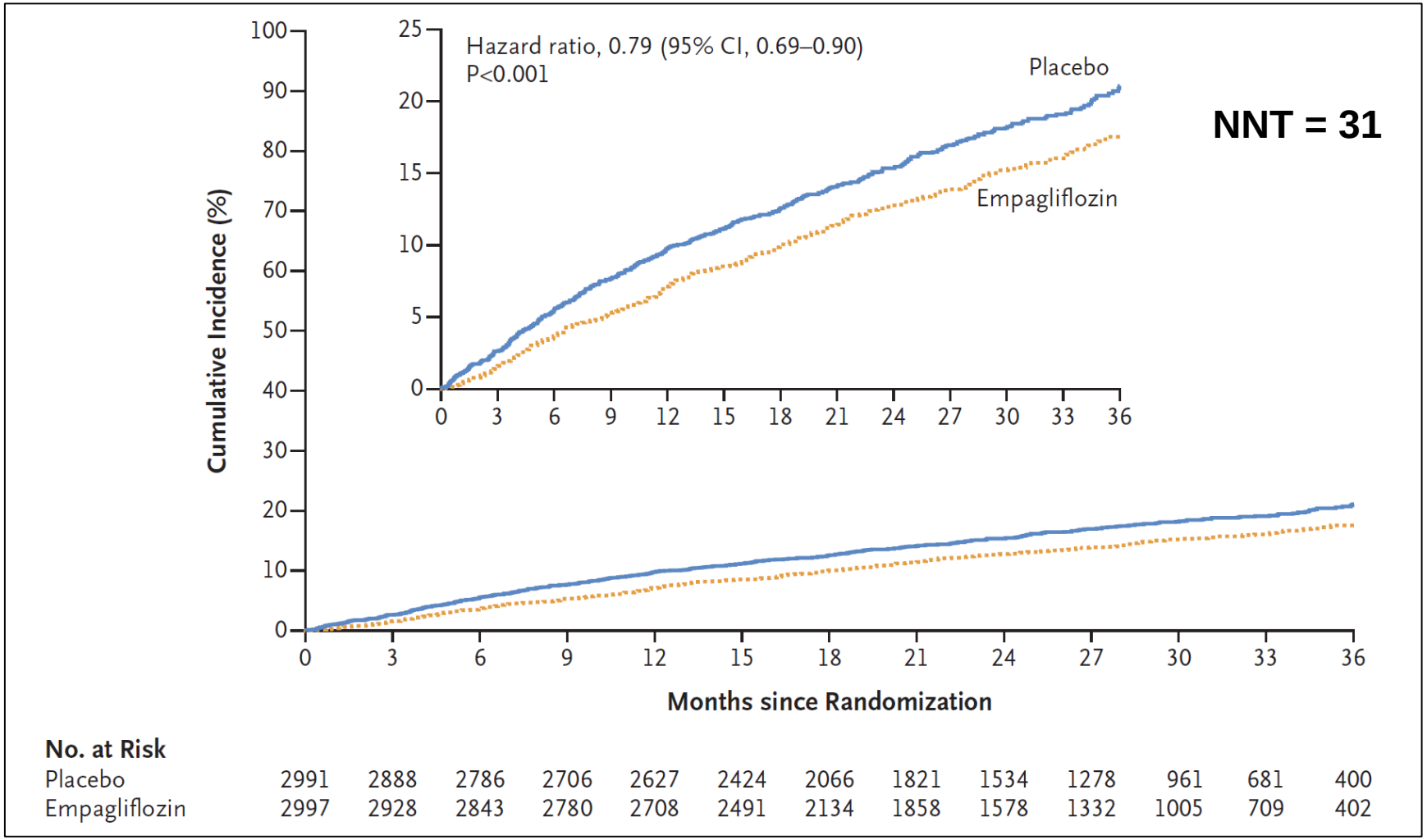
ORIGINAL ARTICLE

Empagliflozin in Heart Failure with a Preserved Ejection Fraction

S.D. Anker, J. Butler, G. Filippatos, J.P. Ferreira, E. Bocchi, M. Böhm, H.-P. Brunner–La Rocca, D.-J. Choi, V. Chopra, E. Chuquiure-Valenzuela, N. Giannetti, J.E. Gomez-Mesa, S. Janssens, J.L. Januzzi, J.R. Gonzalez-Juanatey, B. Merkely, S.J. Nicholls, S.V. Perrone, I.L. Piña, P. Ponikowski, M. Senni, D. Sim, J. Spinar, I. Squire, S. Taddei, H. Tsutsui, S. Verma, D. Vinereanu, J. Zhang, P. Carson, C.S.P. Lam, N. Marx, C. Zeller, N. Sattar, W. Jamal, S. Schnaidt, J.M. Schnee, M. Brueckmann, S.J. Pocock, F. Zannad, and M. Packer, for the EMPEROR-Preserved Trial Investigators*

N Engl J Med. 2021 Aug 27. doi: 10.1056/NEJMoa2107038. Online ahead of print.

Primary endpoint: cardiovascular death or hospitalization for heart failure



The NEW ENGLAND JOURNAL of MEDICINE

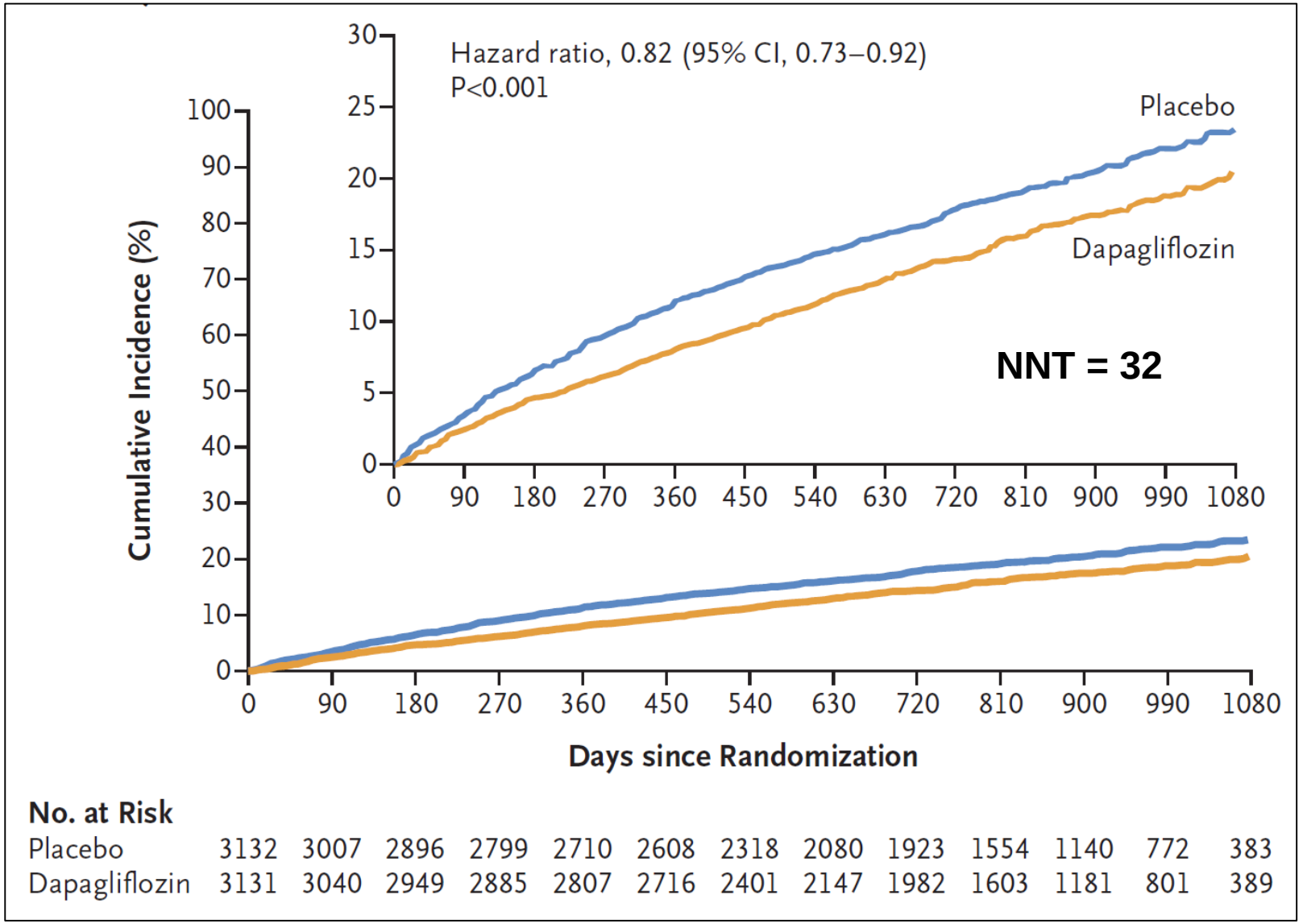
ORIGINAL ARTICLE

Dapagliflozin in Heart Failure with Mildly Reduced or Preserved Ejection Fraction

S.D. Solomon, J.J.V. McMurray, B. Claggett, R.A. de Boer, D. DeMets, A.F. Hernandez, S.E. Inzucchi, M.N. Kosiborod, C.S.P. Lam, F. Martinez, S.J. Shah, A.S. Desai, P.S. Jhund, J. Belohlavek, C.-E. Chiang, C.J.W. Borleffs, J. Comin-Colet, D. Dobreanu, J. Drozdz, J.C. Fang, M.A. Alcocer-Gamba, W. Al Habeeb, Y. Han, J.W. Cabrera Honorio, S.P. Janssens, T. Katova, M. Kitakaze, B. Merkely, E. O'Meara, J.F.K. Saraiva, S.N. Tereshchenko, J. Thierer, M. Vaduganathan, O. Vardeny, S. Verma, V.N. Pham, U. Wilderäng, N. Zaozerska, E. Bachus, D. Lindholm, M. Petersson, and A.M. Langkilde, for the DELIVER Trial Committees and Investigators*

N Engl J Med. 2022 Aug 27. doi: 10.1056/NEJMoa2206286. Online ahead of print.

Primary endpoint: worsening heart failure (unplanned HF hospitalization or urgent HF visit) or cardiovascular death



No. at Risk

Placebo	3132	3007	2896	2799	2710	2608	2318	2080	1923	1554	1140	772	383
Dapagliflozin	3131	3040	2949	2885	2807	2716	2401	2147	1982	1603	1181	801	389