SGLT2 e scompenso cardiaco: punto di vista del cardiologo

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OSPEDALE POLICLINICO SAN MARTINO
Sistema Sanitario Regione Liguria

Speaker and/or advisory board fees from:

Novartis, AstraZeneca, Bayer, and Vifor Pharma

HF with reduced EF (HFrEF):

- HF with LVEF ≤40%

HF with mildly reduced EF (HFmrEF):

- HF with LVEF 41–49%

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- HF with LVEF ≥50%

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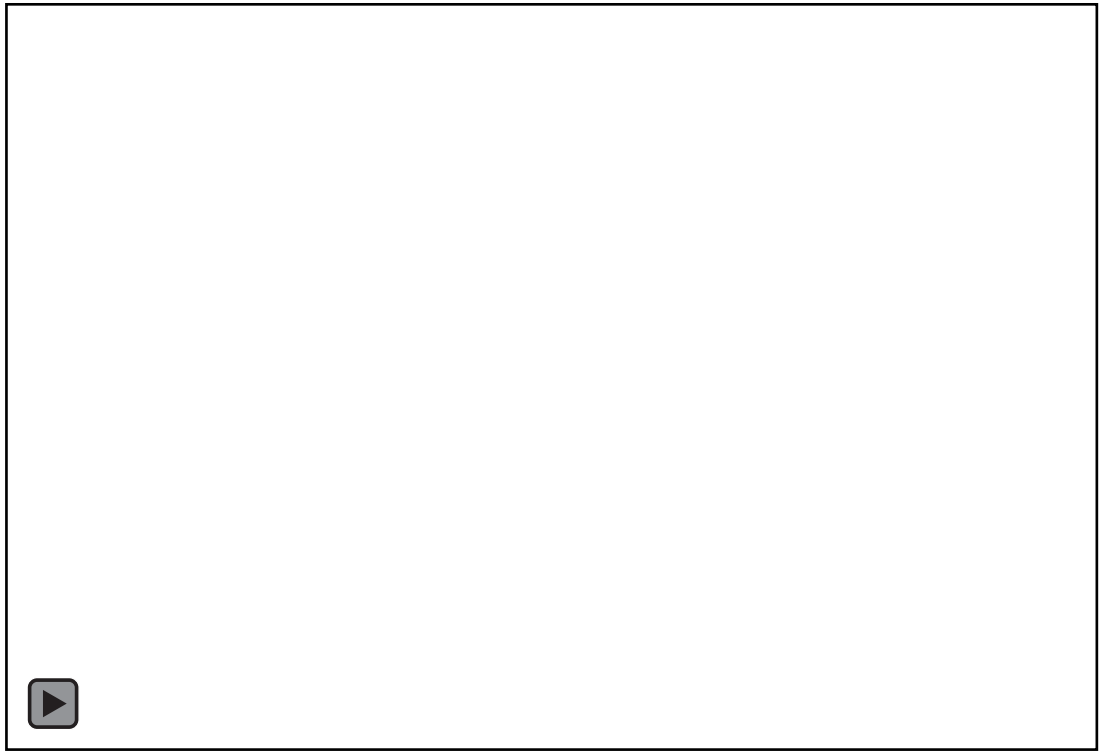
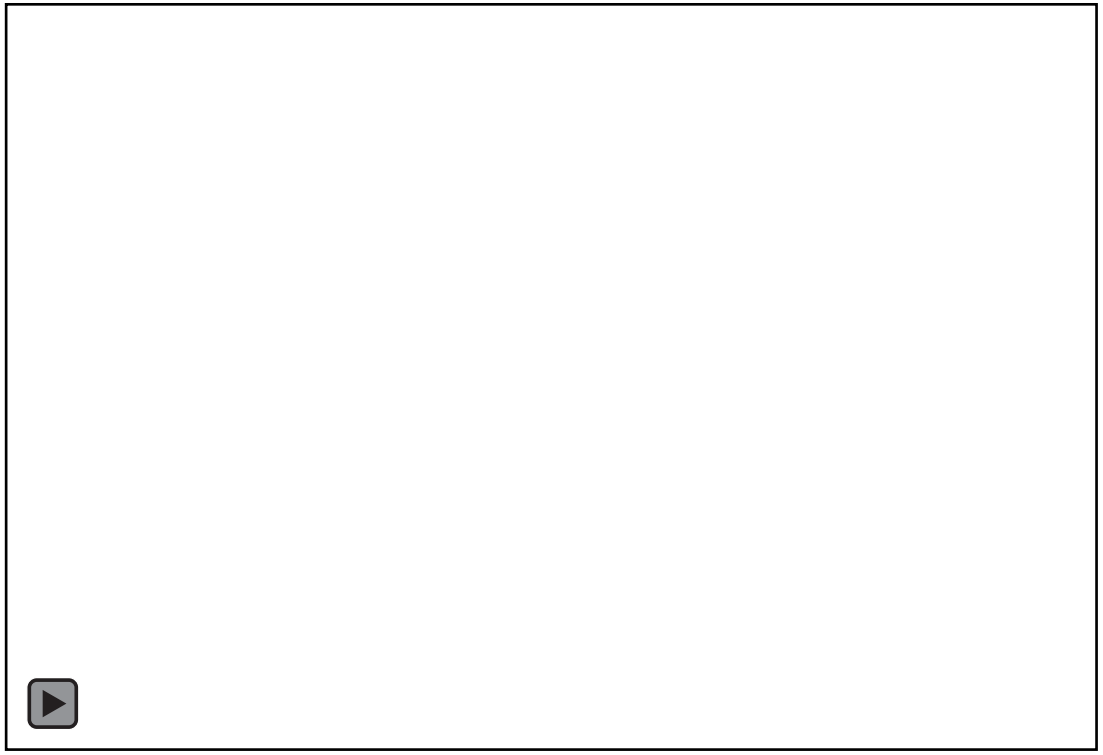
- HF with a baseline LVEF ≤40%, a ≥10 point increase from baseline LVEF, and a second measurement of LVEF >40%

Bozkurt B et al. Eur J Heart Fail. 2021;23:352-80

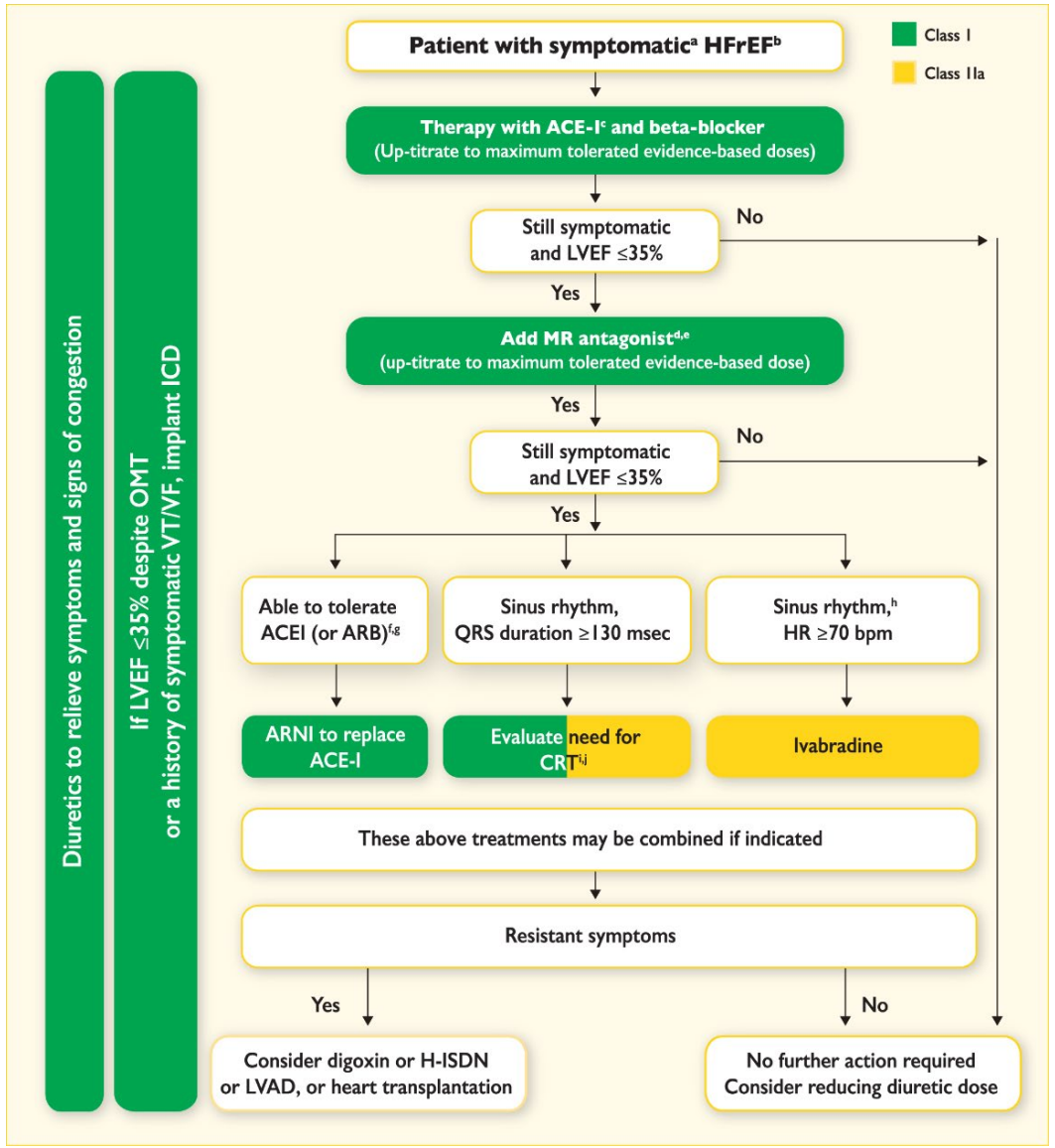
Uomo, 71 anni

Insufficienza cardiaca cronica con ridotta FEVS in cardiopatia ischemica; DM2





	Mattina	Pranzo	Pomeriggio	Sera
Bisoprololo 5 mg	1 + ½ cp			
Sacubitril-valsartan 97/103 mg	1 cp			1 cp
Spironolattone 25 mg			1 cp	
Ivabradina 5 mg	1 cp			1 cp
Furosemide 25 mg	½ cp			
ASA 100 mg		1 cp		
Ticagrelor 60 mg	1 cp			1 cp
Alirocumab 75 mg	1 fiala ogni 15 giorni			
Ezetimibe 10 mg				1 cp
Pantoprazolo 40 mg	1 cp			
Metformina 1000/alogliptin 12,5 mg				1 cp



- Bisoprololo 5 mg
- Spironolattone 25 mg
- Sacubitril-valsartan 97/103 mg
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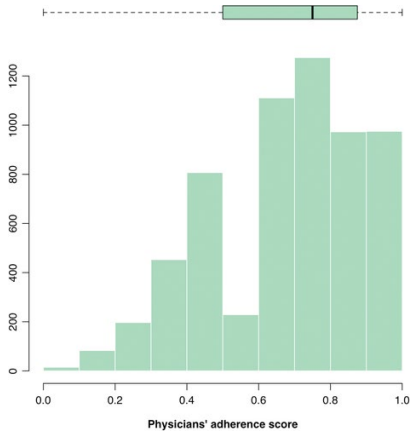
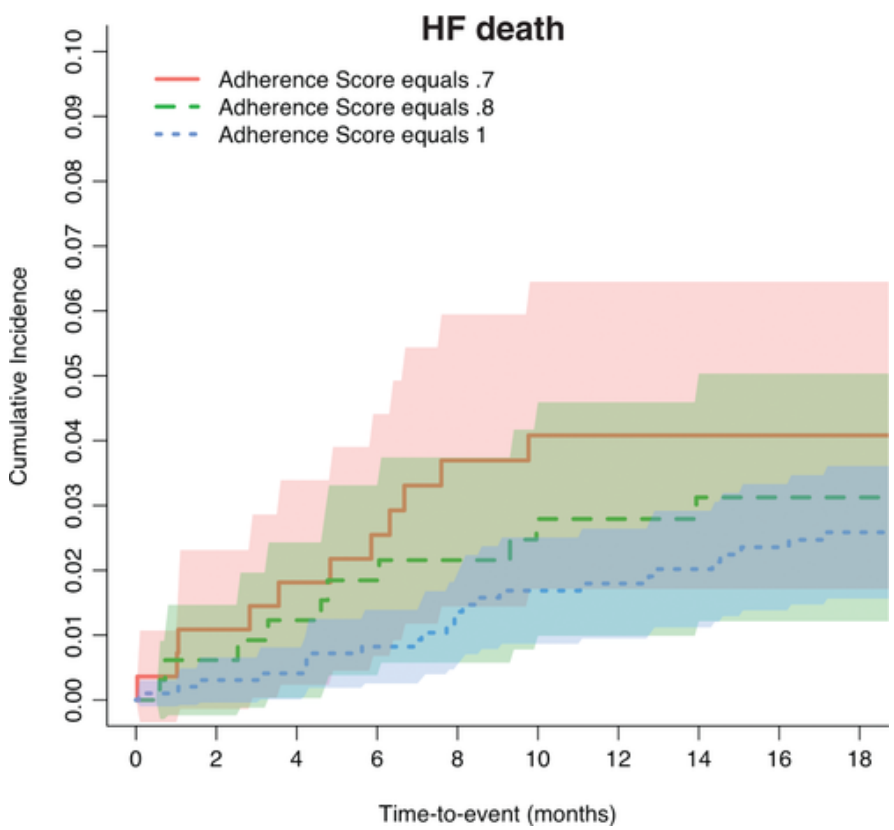
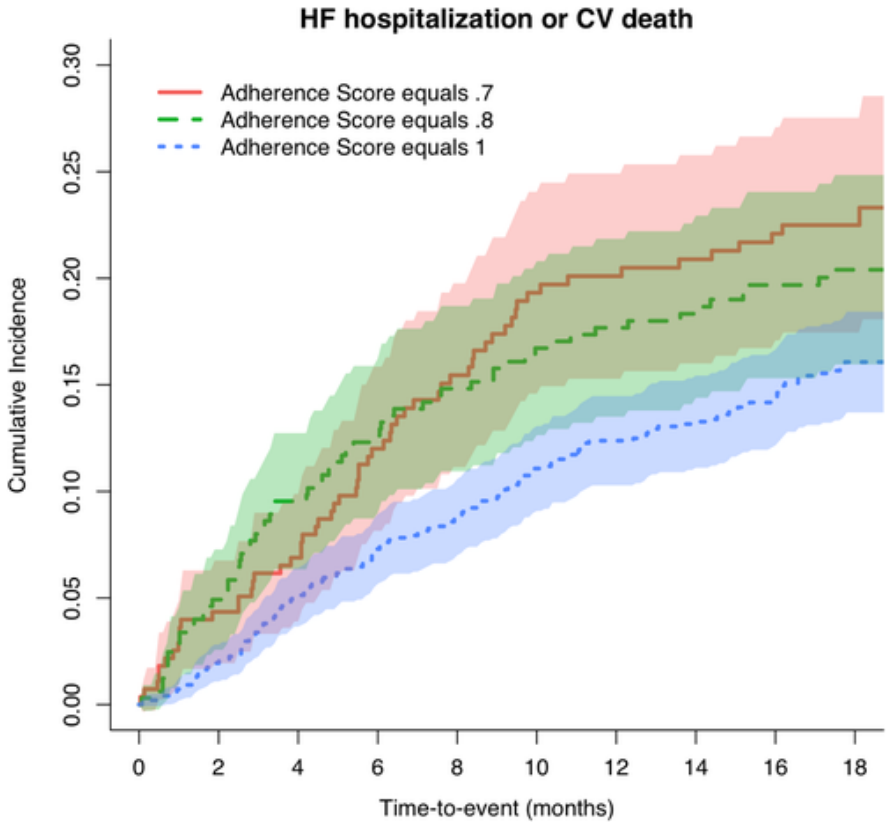
- Furosemide 25 mg

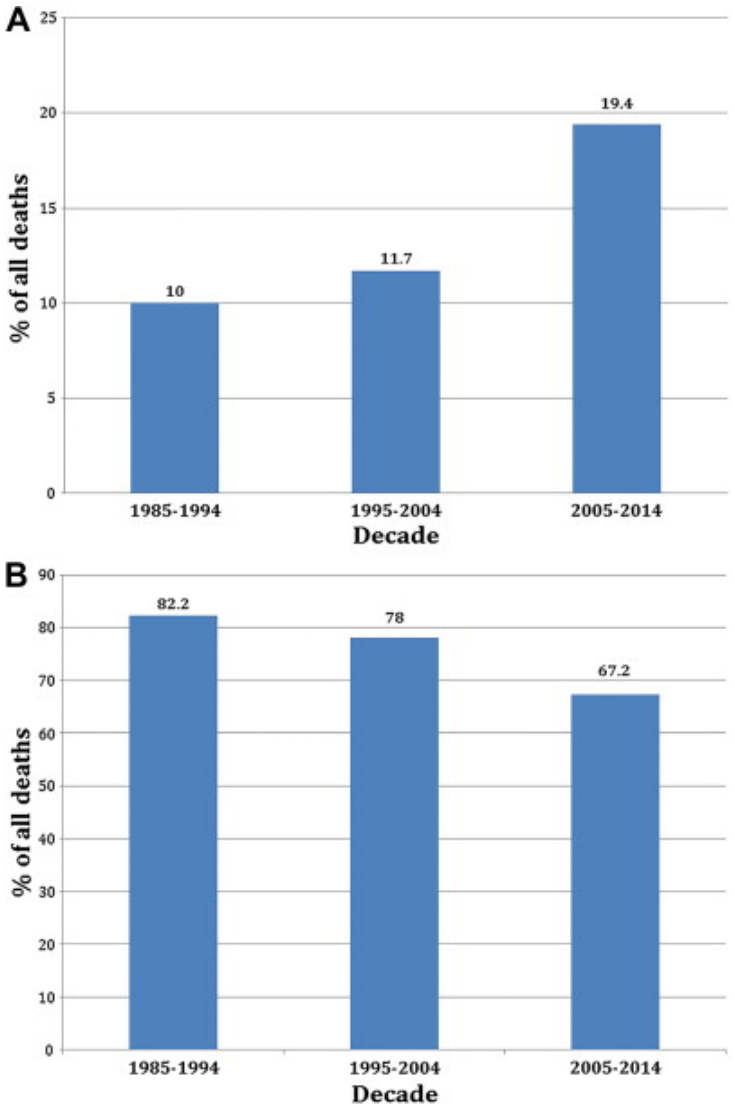
Ponikowski P et al. Eur J Heart Fail 2016;18:891-975







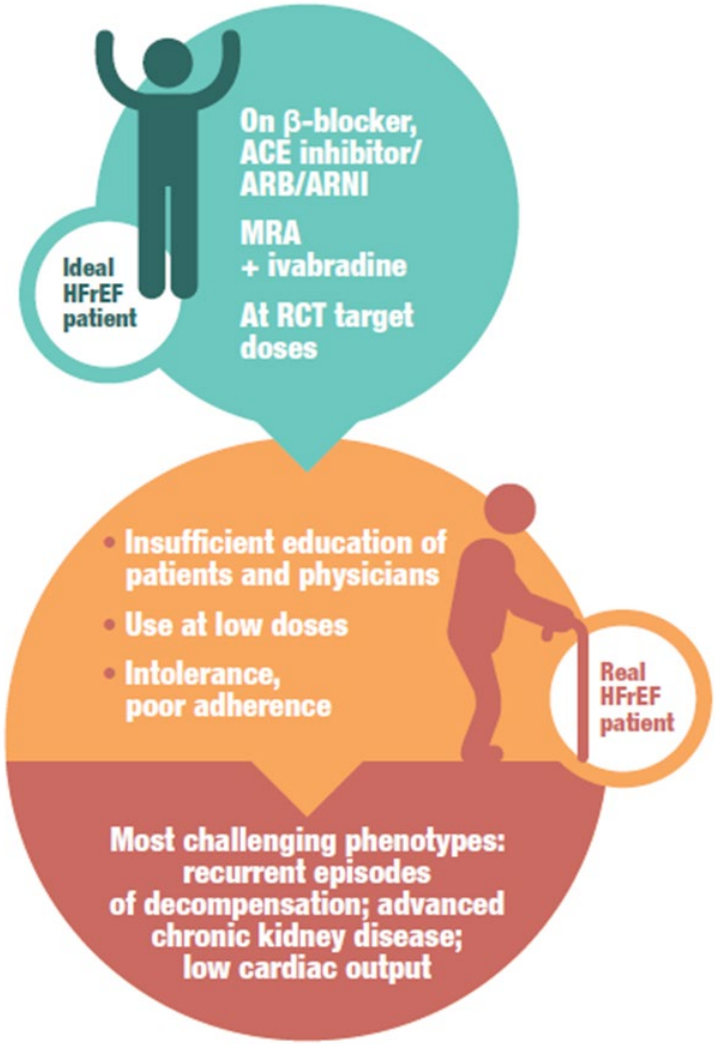
Komajda M et al. Eur J Heart Fail. 2019;21:921-9



Rush CJ et al. JACC Heart Fail. 2015;3:603-14

PARADIGM-HF

- ✓ 14.5% of the participants died from CV causes, mainly sudden cardiac death and worsening HF
- ✓ 12.8% of the patients receiving sacubitril-valsartan and 15.6% of those allocated to enalapril were hospitalized for HF, and 12.4% and 14.3%, respectively, needed intensification of the outpatient therapy



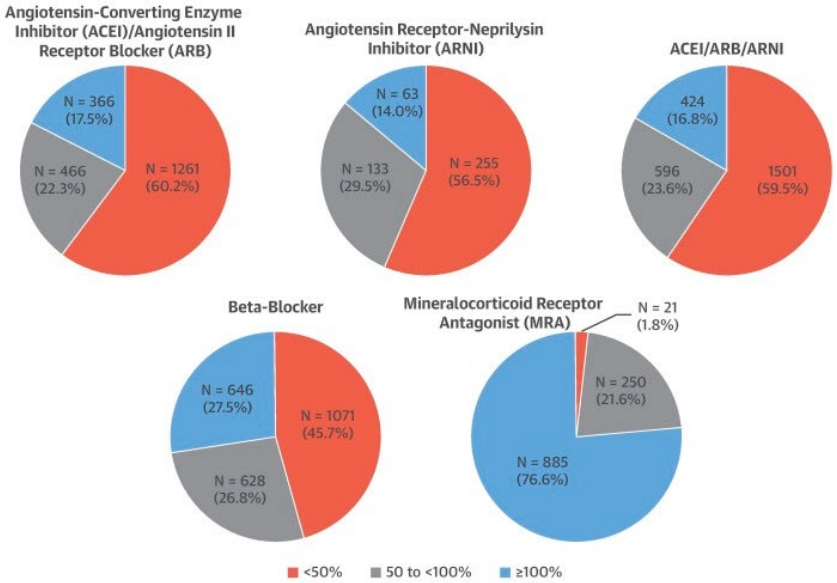
Ameri P et al. Eur Heart J Cardiovasc Pharmacother. 2021 May 26:pvab033.

CENTRAL ILLUSTRATION: Use and Dosing of Guideline-Directed Medical Therapy Among Patients With Chronic HFrEF in Contemporary U.S. Outpatient Practice

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



Greene, S.J. et al. J Am Coll Cardiol. 2018;72(4):351-66.

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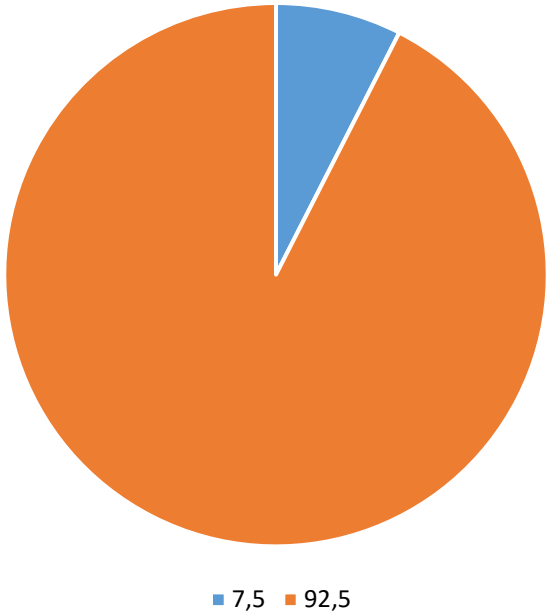
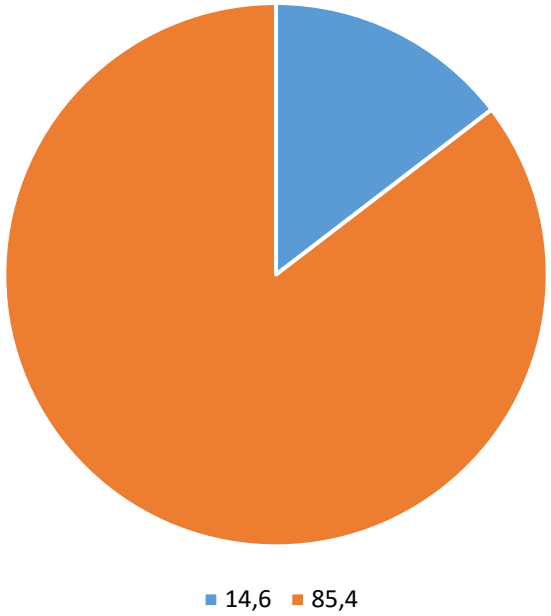
Outpatient HF Unit, Ospedale Policlinico San Martino, Genova, Italy

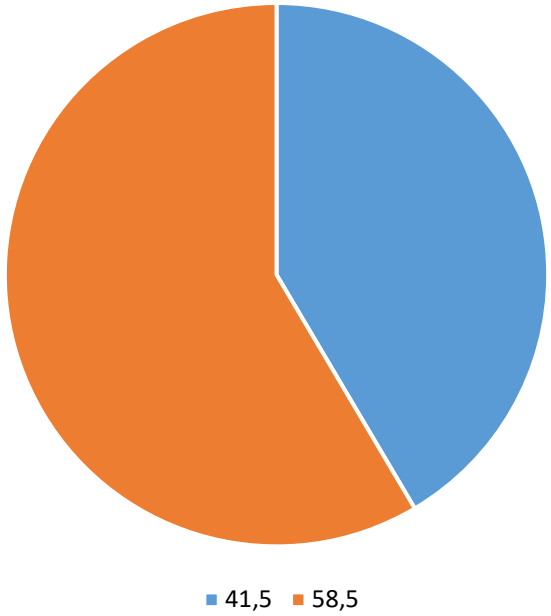
beta-blocker



ACEi/ARB/ARNI



MRA



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ORIGINAL ARTICLE

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

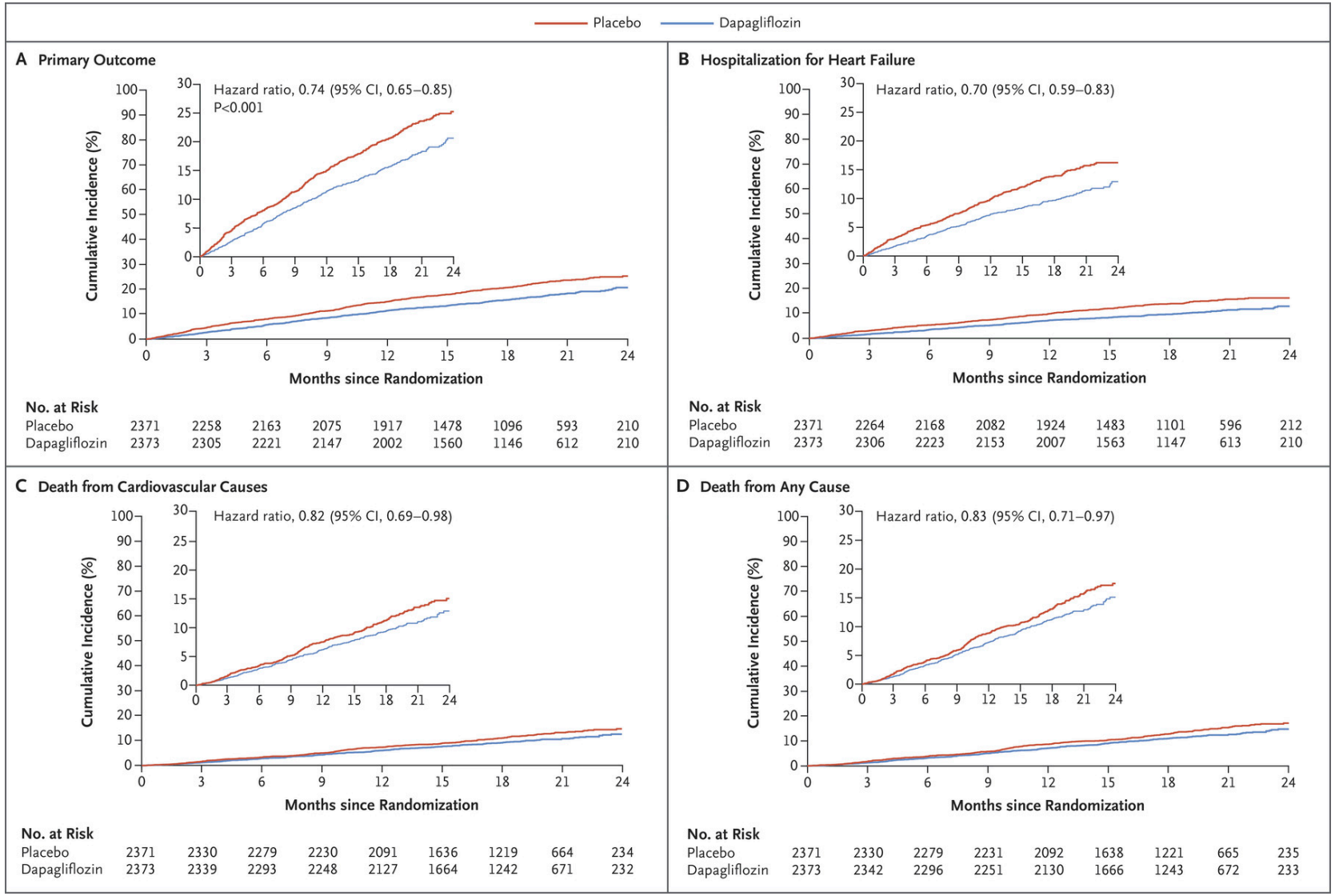
J.J.V. McMurray, S.D. Solomon, S.E. Inzucchi, L. Køber, M.N. Kosiborod, F.A. Martinez, P. Ponikowski, M.S. Sabatine, I.S. Anand, J. Bělohlávek, M. Böhm, C.-E. Chiang, V.K. Chopra, R.A. de Boer, A.S. Desai, M. Diez, J. Drozdz, A. Dukát, J. Ge, J.G. Howlett, T. Katova, M. Kitakaze, C.E.A. Ljungman, B. 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*

ORIGINAL ARTICLE

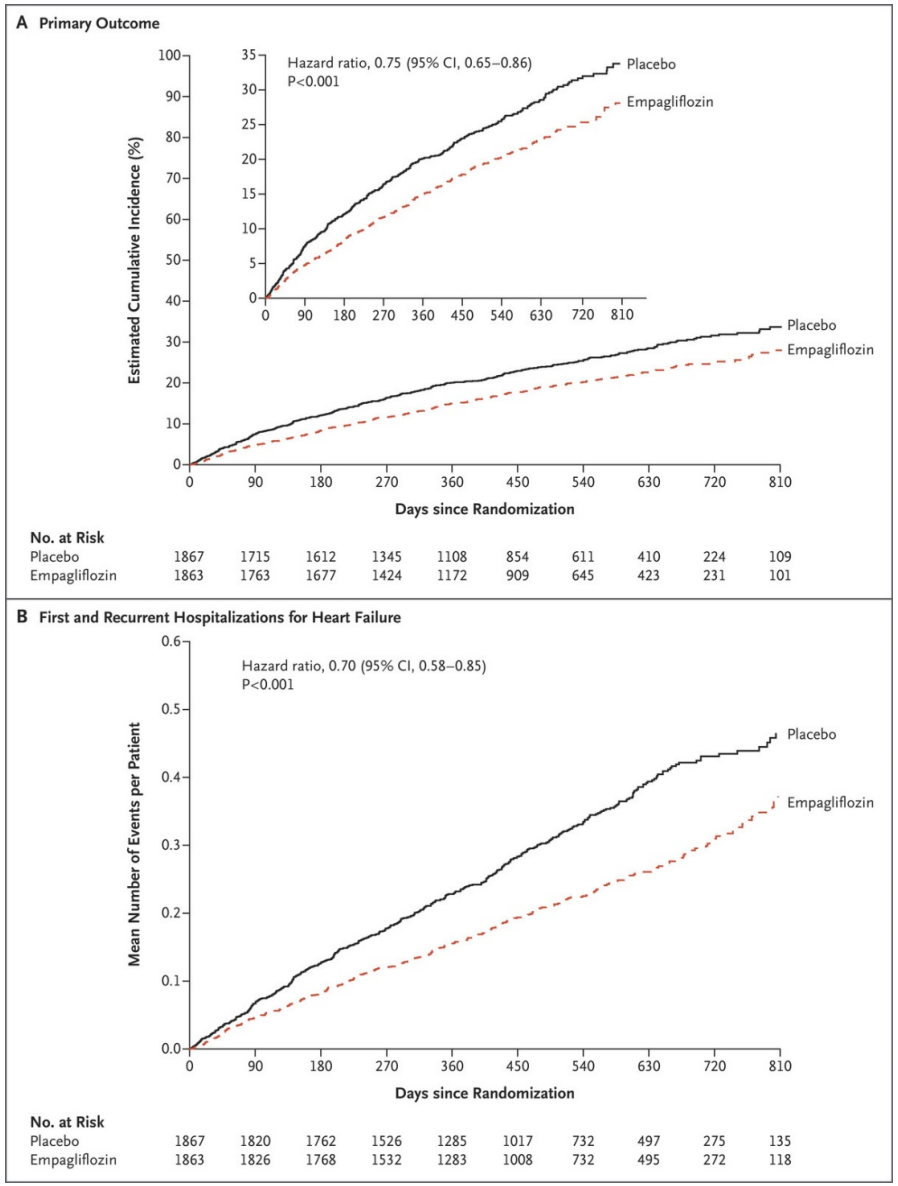
Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure

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*

	DAPA-HF	EMPEROR-Reduced
Beta-blocker (%)	96	94.7
RASi (%)	84.6	70.5
ARNI (%)	10.8	18.3
MRA (%)	71.5	70.1
CRT (%)	26.2	31
ICD (%)	8	11.8

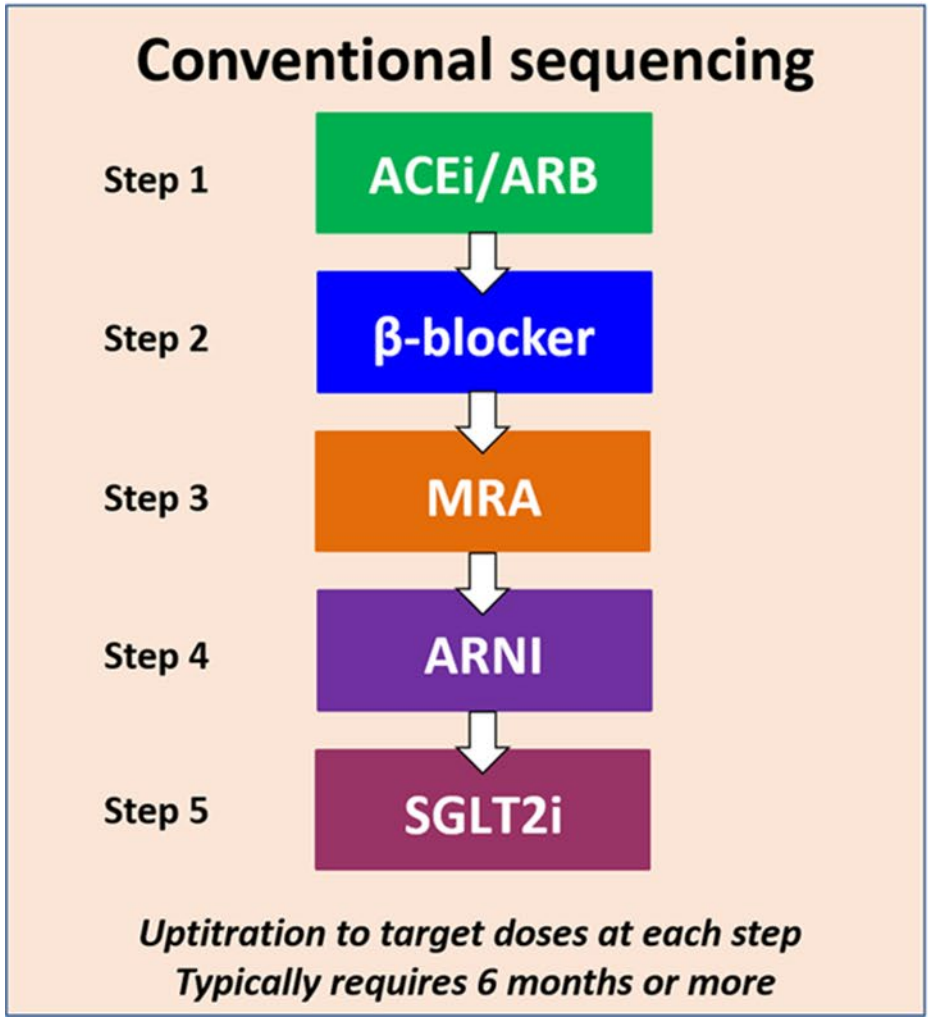


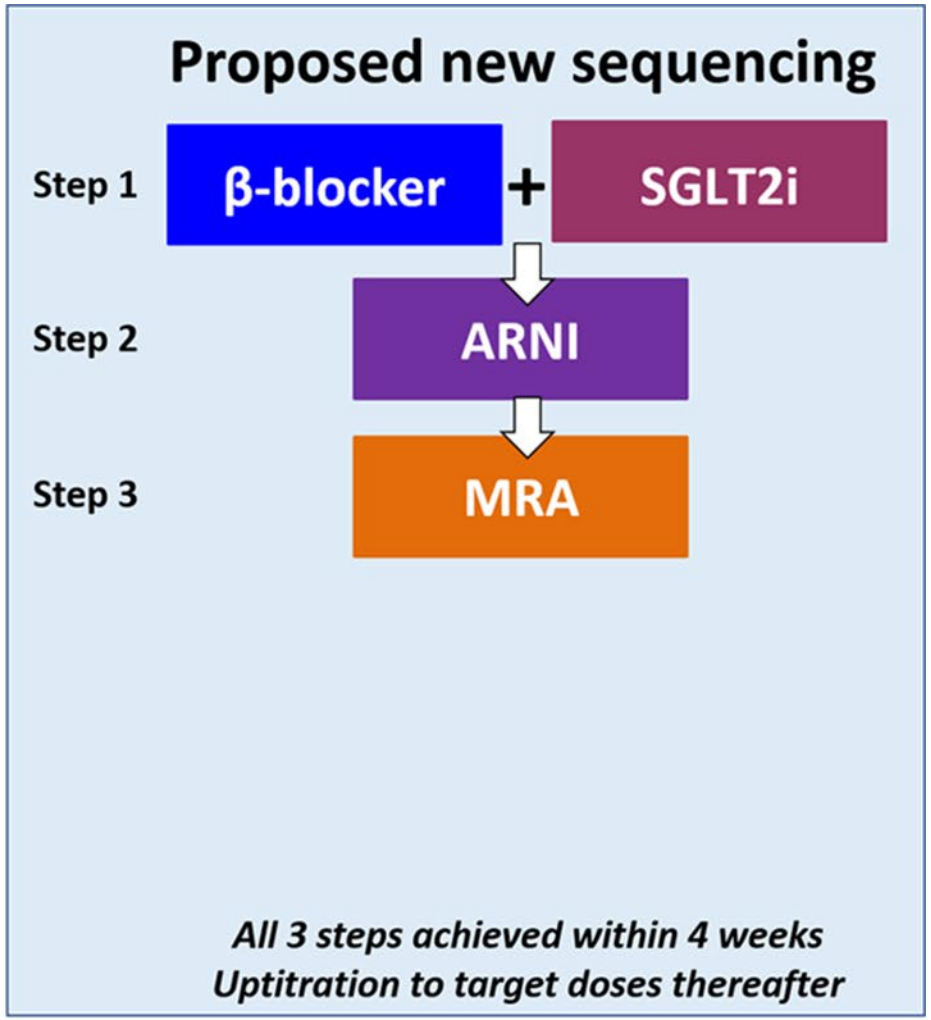
McMurray JJV et al. N Engl J Med. 2019;381:1995-2008



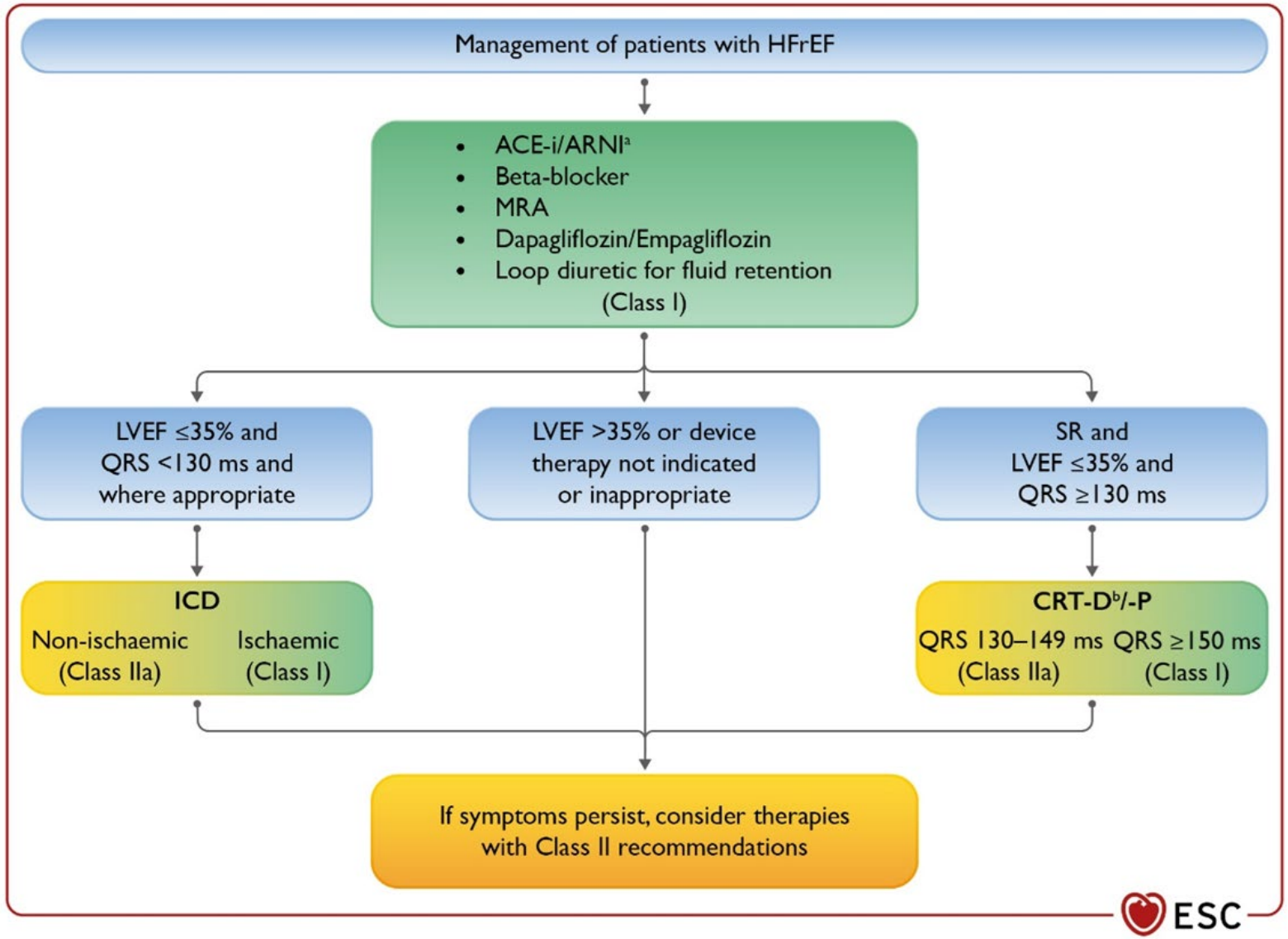
Trial	Median follow-up (months)	Arm	HHF or CV death (events/100 patient-year)
PARADIGM-HF	27	Sacubitril-valsartan	10.5
		Enalapril	13.2
DAPA-HF	18.2	Dapagliflozin	11.4
		Placebo	15.3
EMPEROR-Reduced	16	Empagliflozin	15.8
		Placebo	21.0

Packer M et al. N Engl J Med 2020;383:1413-24





McMurray JJV, Packer M. Circulation. 2021;143:875-7



Mc Donagh T, Metra M et al. Eur Heart J. 2021;42:3599-3726

HF with reduced EF (HFrEF):

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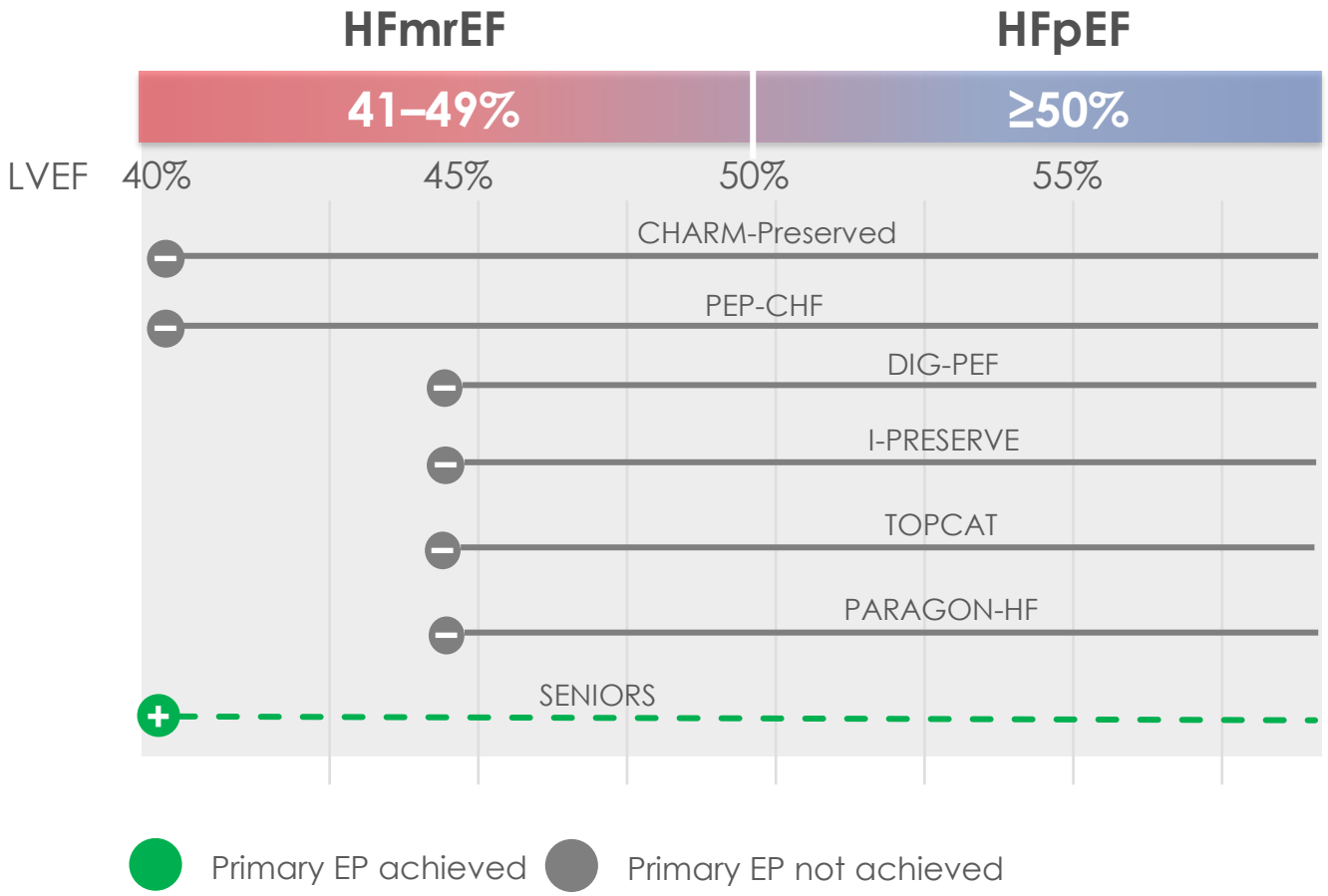
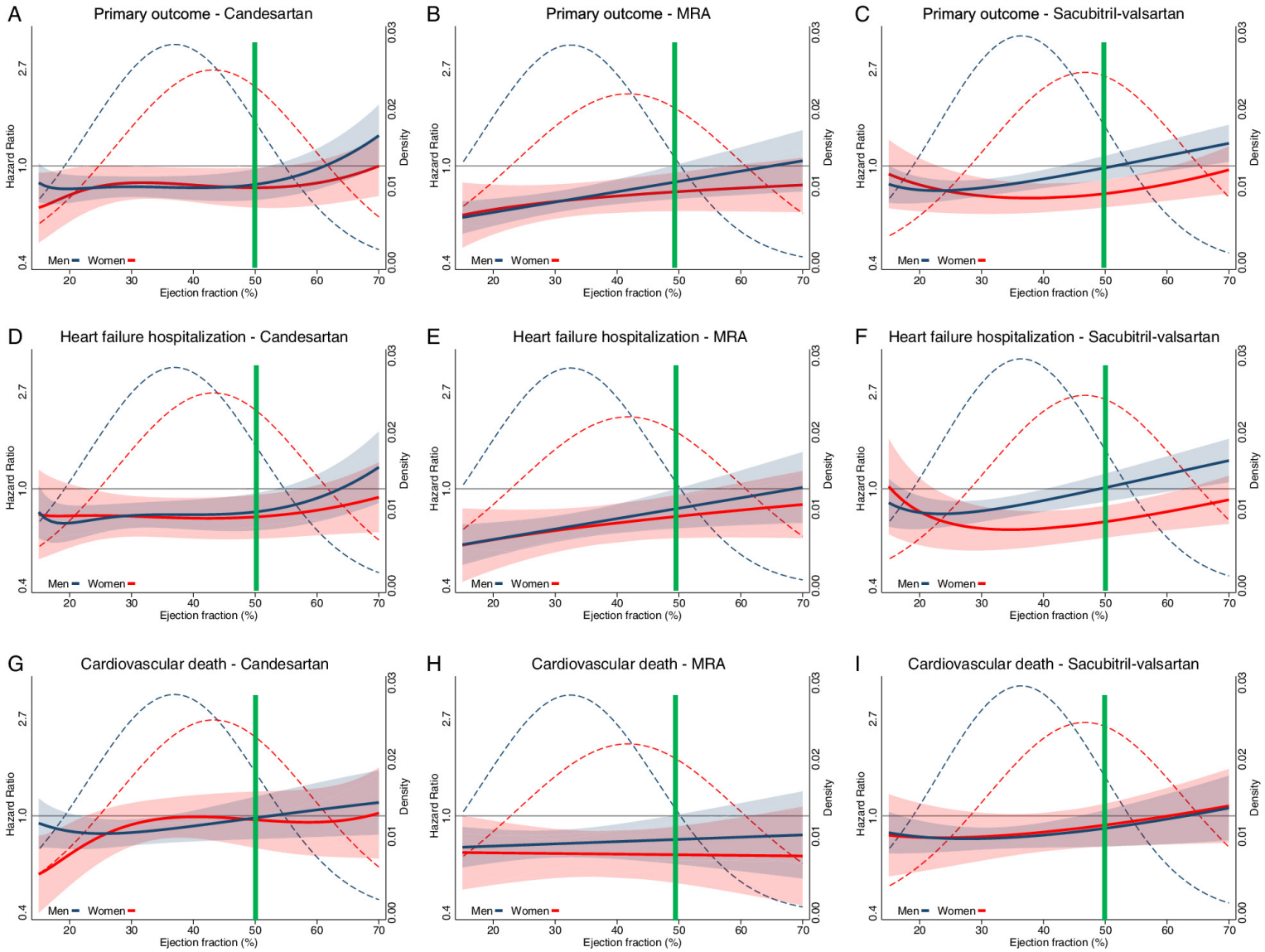
Bozkurt B et al. Eur J Heart Fail. 2021;23:352-80

THE LANCET

HFpEF ≠ HF with LVEF <40%

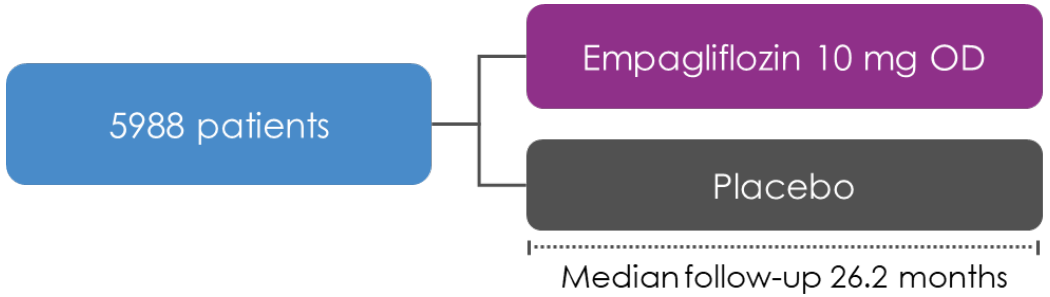

HFmrEF
HFpEF
41–49%
≥50%
LVEF 40%
45%
50%
55%
CHARM-Preserved
PEP-CHF
DIG-PEF
I-PRESERVE
TOPCAT
PARAGON-HF
SENIORS
Primary EP achieved
Primary EP not achieved



Dewan P et al. Eur J Heart Fail. 2020;22:898-901

EMPEROR-Preserved

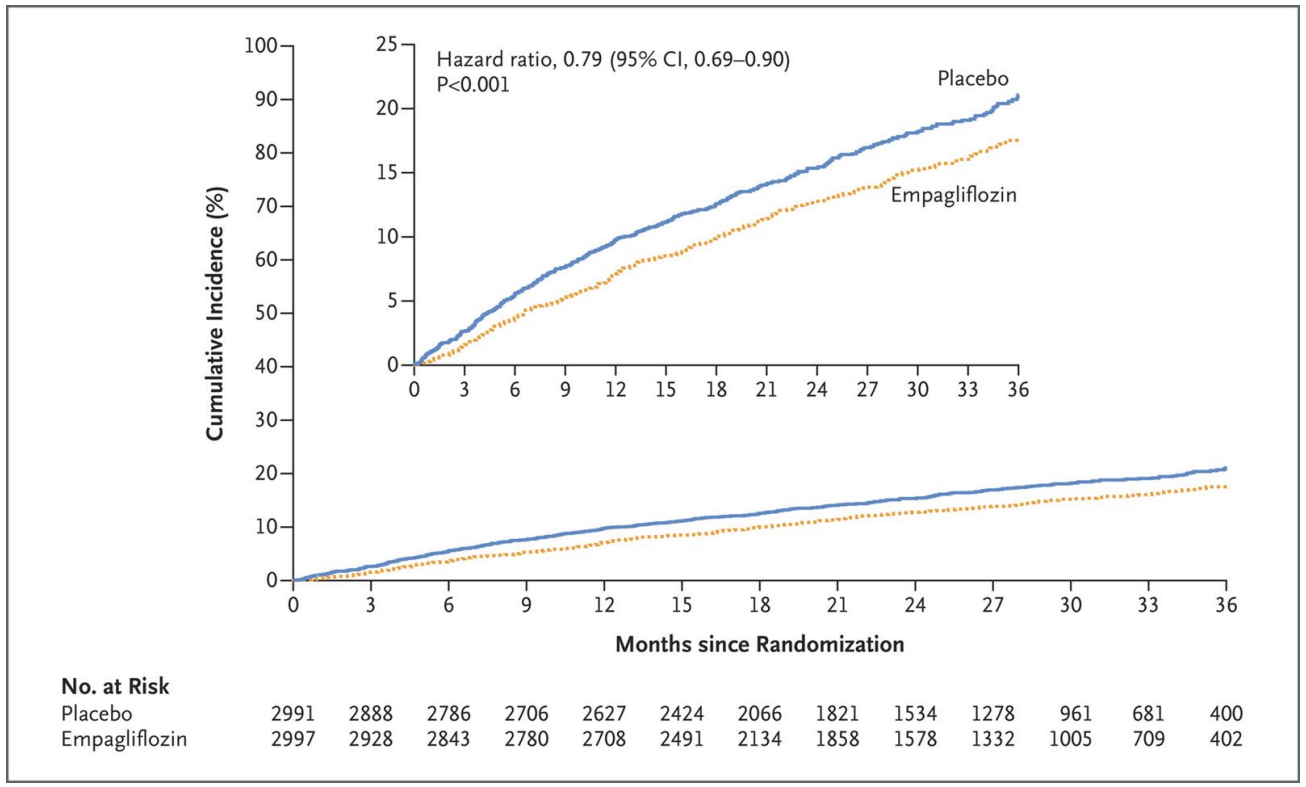
- age ≥18 years
- NYHA class II−IV
- LVEF >40%
- NT-proBNP >300 pg/mL (>900 pg/mL if AF)
- stable oral diuretic for ≥1 week
- structural changes in the heart (increases in left atrial size or LV mass) or HHF within 12 months of screening
- eGFR ≥20 mL/min/1.73 m^2
- SBP ≥180 mmHg or 151-179 mmHg with <3 antihypertensive drugs
- symptomatic hypotension and/or SBP<100 mmHg

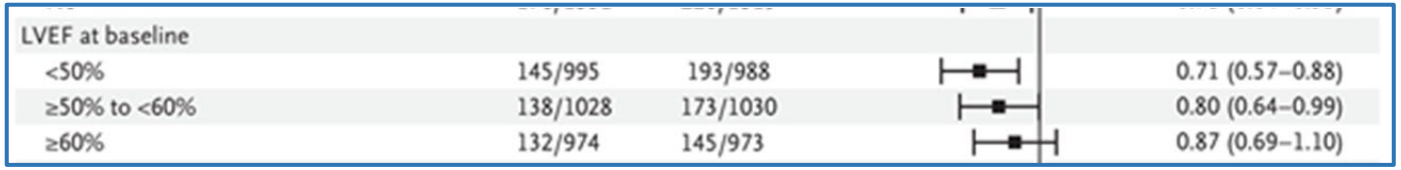


Anker SD et al. N Engl J Med 2021;385:1451-61

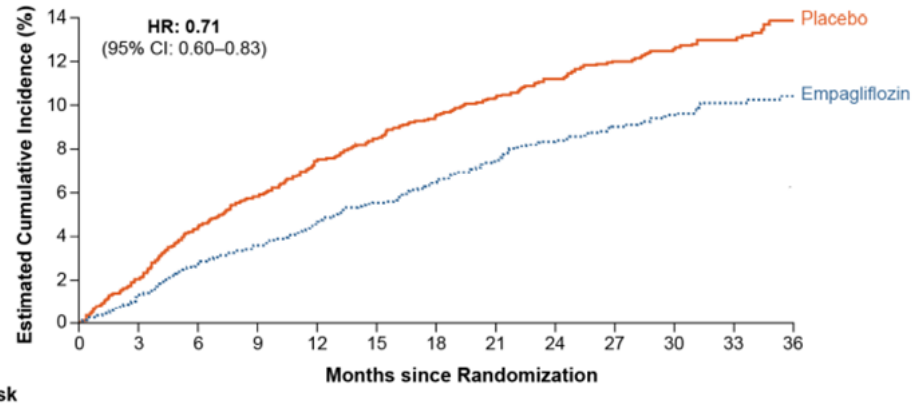
	Empagliflozin (n=2997)	Placebo (n=2991)
Age, years	71.8±9.3	71.9±9.6
Women, n (%)	1338 (44.6)	1338 (44.7)
Race, n (%)		
White / Asian	2286 (76.3) / 413 (13.8)	2256 (75.4) / 411 (13.7)
Black / Other or missing	133 (4.4) / 165 (5.5)	125 (4.2) / 199 (6.7)
BMI, kg/m^2	29.77±5.8	29.90±5.9
Hypertension, n (%)	2721 (90.8)	2703 (90.4)
Diabetes mellitus, n (%)	1466 (48.9)	1472 (49.2)
eGFR, mL/min/1.73 m^2	60.6±19.8	60.6±19.9
eGFR <60 mL/min/1.73 m^2, n (%)	1504/2997 (50.2)	1484/2989 (49.6)
Atrial fibrillation, n (%)	1543 (51.5)	1514 (50.6)
Ischemic HF, n (%)	1079 (36.0)	1038 (34.7)
HHF <12 months, n (%)	699 (23.3)	670 (22.4)

	Empagliflozin (n=2997)	Placebo (n=2991)
NYHA II / III, n (%)	2432 (81.1) / 552 (18.4)	2451 (81.9) / 531 (17.8)
Heart rate, bpm	70.4±12.0	70.3±11.8
Systolic BP, mmHg	131.8±15.6	131.9±15.7
LVEF, %	54.3±8.8	54.3±8.8
>40 to <50%, n (%)	995 (33.2)	988 (33.0)
≥50 to <60%, n (%)	1028 (34.3)	1030 (34.4)
≥60%, n (%)	974 (32.5)	973 (32.5)
NT-proBNP, pg/mL	994 (501-1740)	946 (498-1725)
RAASi ± neprilysin inhibitor, n (%)	2428 (81.0)	2404 (80.4)
MRA, n (%)	1119 (37.3)	1125 (37.6)
Beta blocker, n (%)	2598 (86.7)	2569 (85.9)
Digitalis glycosides, n (%)	293 (9.8)	263 (8.8)
Aspirin / statin, n (%)	1240 (41.4) / 2042 (68.1)	1272 (42.5) / 2089 (69.8)





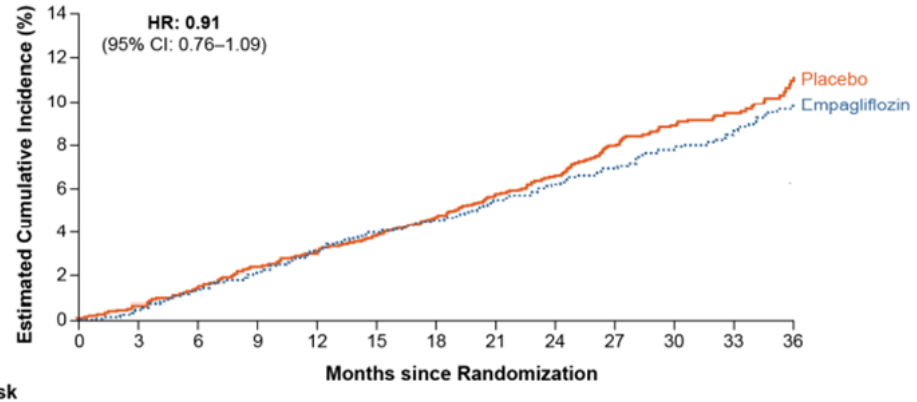
A First Hospitalizations for Heart Failure



No. at Risk

Placebo	2991	2888	2786	2706	2627	2424	2066	1821	1534	1278	961	681	400
Empagliflozin	2997	2928	2843	2780	2708	2491	2134	1858	1578	1332	1005	709	402

B Cardiovascular Death



No. at Risk

Placebo	2991	2960	2923	2883	2849	2656	2302	2046	1738	1459	1107	781	471
Empagliflozin	2997	2974	2930	2891	2847	2641	2287	2022	1725	1469	1118	794	462

- more uncomplicated genital and urinary tract infections with EMPA than with placebo

SGLT2i

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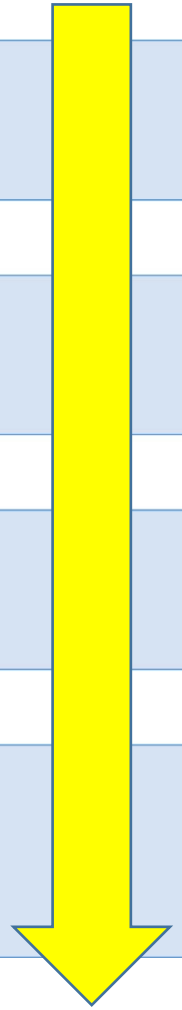

Bozkurt B et al. Eur J Heart Fail. 2021;23:352-80