I PERCORSI APPROPRIATI
ASSISTENZIALI E TERAPEUTICI
IN PREVENZIONE SECONDARIA

Approccio al paziente
ad alto rischio cardiovascolare

10 GIUGNO
2022

TERAPIA DI ASSOCIAZIONE NEL PAZIENTE AD ALTO RISCHIO CARDIOVASCOLARE: DALLE LINEE GUIDA ESC AL MONDO REALE.

COME RAGGIUNGERE I TARGET?

Diabete mellito tipo 2: il punto di vista del cardiologo

Vito Altamura (Roma)

La più grande crisi sanitaria del XXI secolo.

Il Diabete Tipo 2 rappresenta circa il 90% di tutti i casi di diabete.

Gli eventi cardiovascolari in questa popolazione rappresentano la causa principale di complicanze, **portando a morte precoce almeno il 50% dei pazienti**.
Nel periodo 2000–2016, la mortalità prematura per diabete è aumentata del 5%.

Le principali malattie cardiovascolari associate al T2DM sono:

- cardiopatia ischemica,
- insufficienza cardiaca,
- ictus,
- malattia coronarica
- arteriopatia periferica.

Systematic Review

Economic Burden of Cardiovascular Disease in Type 2 Diabetes: A Systematic Review

Thomas R. Einarson, PhD[1,a], Annabel Acs, MPH[2], Craig Ludwig, MSc[2,], Ulrik H. Panton, PhD[3]*

[1]*Leslie Dan Faculty of Pharmacy, University of Toronto, Toronto, Ontario, Canada;* [2]*Last Mile, Holte, Denmark;* [3]*Novo Nordisk A/S, Søborg, Denmark*

Table 4 – Additional burden of T2DM complications by event.

Complication	Studies	N	Average health care costs* ($)		Percent increase costs due to treating CVD complications	
			T2DM patients without CVD complications	T2DM patients with CVD complications	Median (%)	Range (%)
CVD	4	30,447	8,310	15,105	112	47–196
CAD	4	179,812	3,698	7,386	107	59–128
Heart failure	3	388,308	8,066	16,872	59	11–150
Stroke	3	16,609	3,755	13,460	322	100–545

CAD, coronary artery disease; CVD, cardiovascular disease; T2DM, type 2 diabetes mellitus.

* All costs are per patient per year, expressed in 2016 US dollars.


Medications
Inactive
Obesity
Aging
Genetics
Rare disorders
Insulin Resistance
Hypertension
PCOS
Type 2 diabetes
Dyslipidemia
Atherosclerosis

HF, CKD, and T2D Are Often Comorbid

CKD = chronic kidney disease; HF = heart failure; M = million; T2D = type 2 diabetes.

1. GBD 2017 Disease and Injury Incidence and Prevalence Collaborators. *Lancet.* 2018;392:1789-1858; 2. Ronco C et al. *J Am Coll Cardiol.* 2008;52:1527-1539; 3. Jager KJ et al. *Nephrol Dial Transplant.* 2019;34:1803-1805; 4.Birkeland KI et al. *Diabetes Obes Metab.* 2020:22:1607-1618; 5. IDF Diabetes Atlas, 9th edition. www.diabetesatlas.org. Accessed September 1, 2021; 6. Parving HH et al. *Kidney Int.* 2006;69:2057-2063.

ESC European Society of Cardiology

European Heart Journal (2022) **43**, 1029–1030
https://doi.org/10.1093/eurheartj/ehab765

CARDIOPULSE

Braunwald's Corner

SGLT2 inhibitors: the statins of the 21st century

Eugene Braunwald [1,2]*

[1]TIMI Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital, Hale Building for Transformative Medicine, Suite 7022, 60 Fenwood Road, Boston, MA 02115, USA; and [2]Department of Medicine, Harvard Medical School, Boston, MA, USA

A relatively small number of drugs have been responsible for major advances in medical practice. The discovery, development, and elucidation of the mechanisms of action of aspirin, penicillin, and statins are remarkable success stories, each with some surprises and each crowned by a Nobel Prize. The sodium glucose co-transporter inhibitors have been proven effective in the treatment of type 2 diabetes mellitus, various forms of heart failure, and kidney failure and represent *the, or one of the,* major pharmacological advances in cardiovascular medicine in the 21st century.

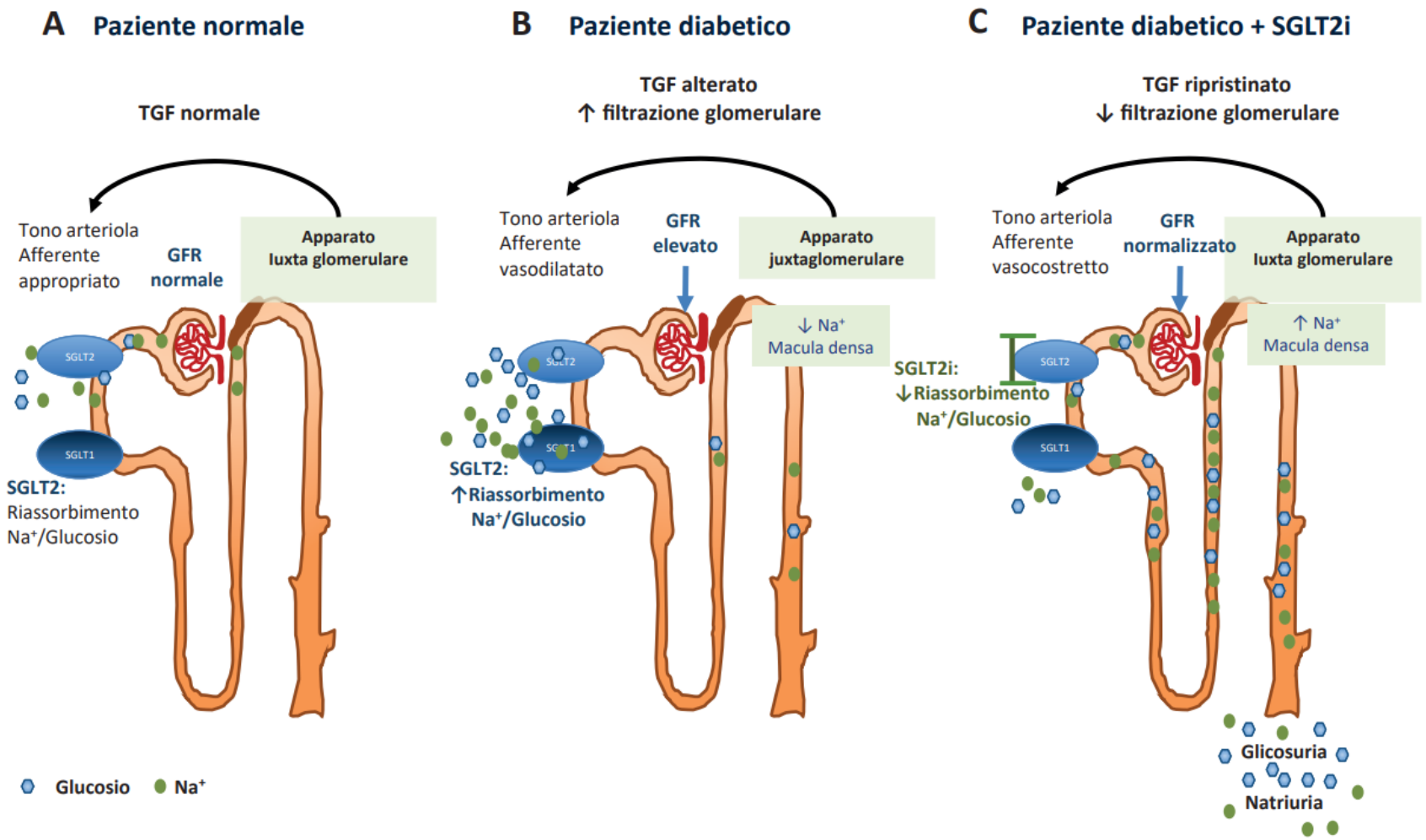
Glifozine, AIFA estende la prescrivibilità anche al cardiologo

Redazione

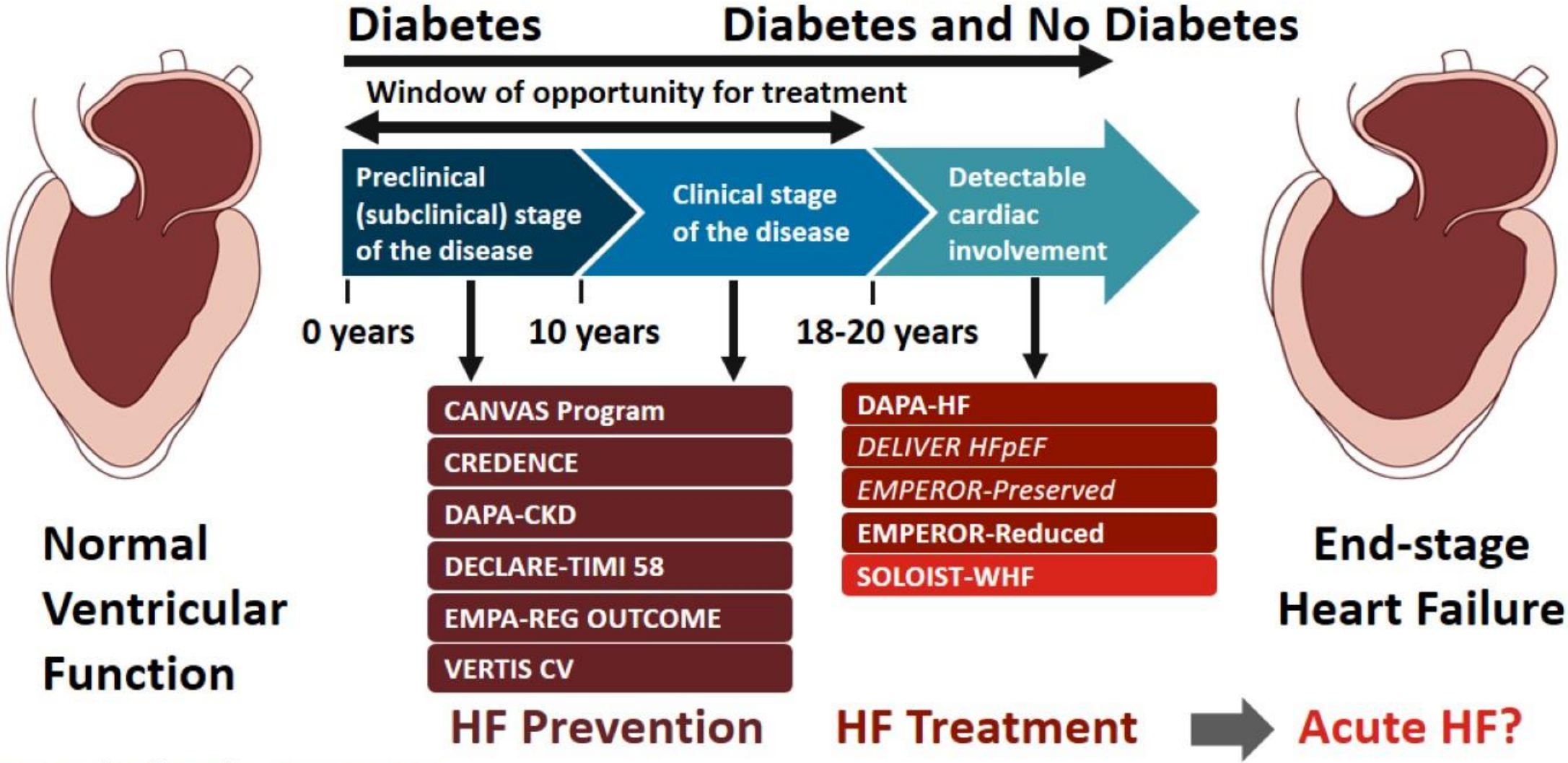
18 Gennaio 2022

Position paper ANMCO: L'impiego degli inibitori del co-trasportatore sodio-glucosio di tipo 2 nella prevenzione e cura dell'insufficienza cardiaca nei soggetti diabetici e nei portatori di insufficienza cardiaca, diabetici e non diabetici

Edoardo Gronda[1], Claudio Napoli[2], Massimo Iacoviello[3], Stefano Urbinati[4], Pasquale Caldarola[5], Edoardo Mannucci[6], Furio Colivicchi[7], Domenico Gabrielli[8]

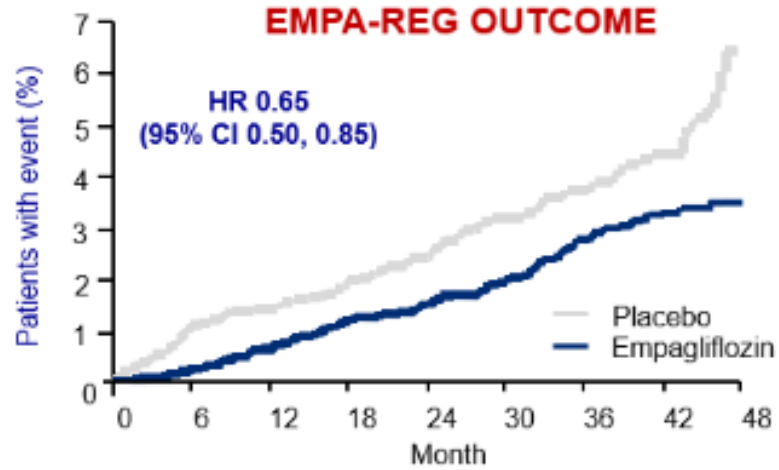


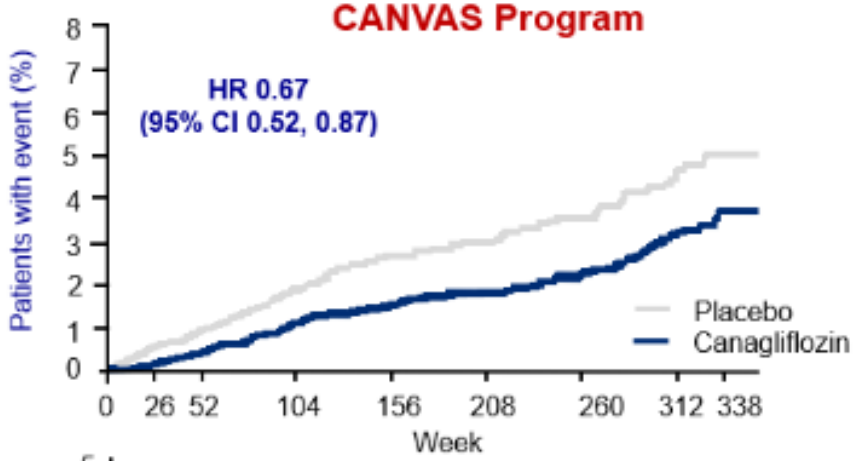
The Evolution of SGLT2 Inhibitors in HF Management

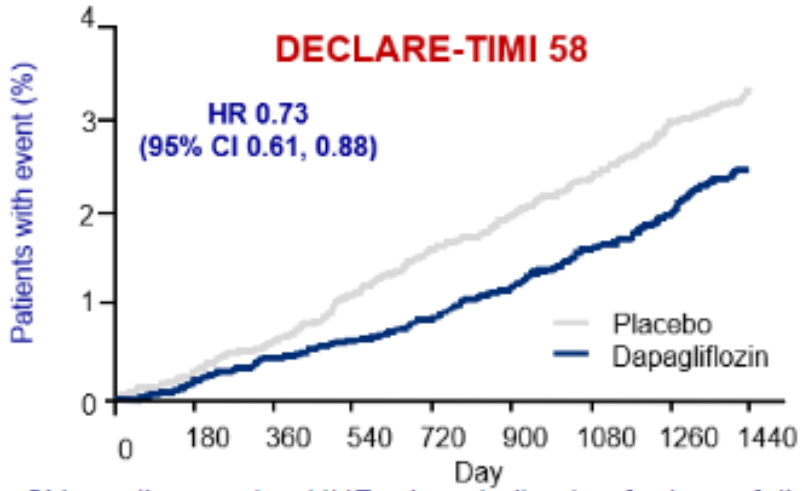


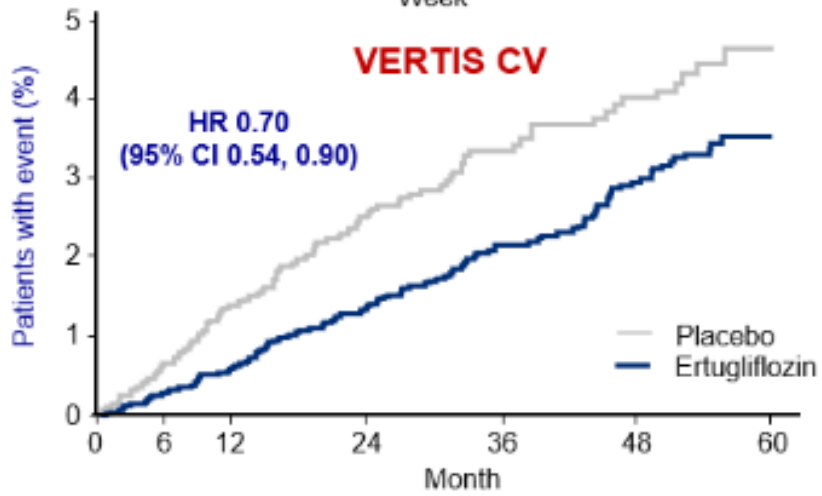
Bhatt DL, et al. *Cell Metab*. 2019;30:847-849.

HHF outcomes in SGLT2-inhibitor CV outcomes trials







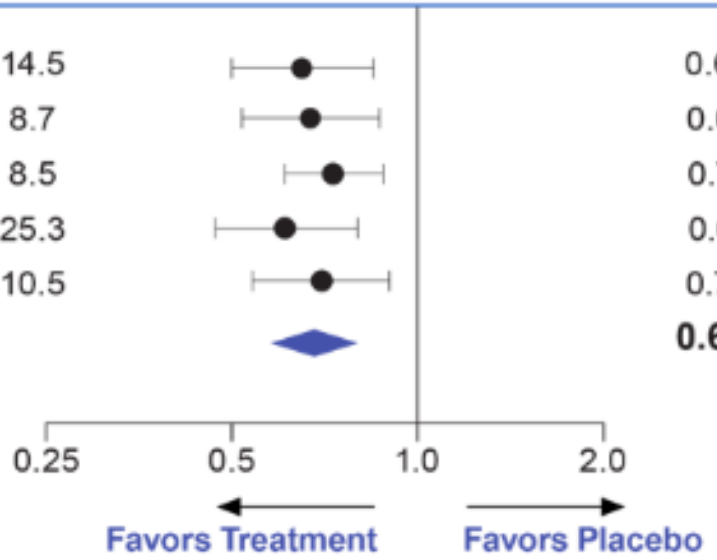


CV, cardiovascular; HHF = hospitalization for heart failure

Time to first hospitalization for Heart Failure (HHF)

HHF

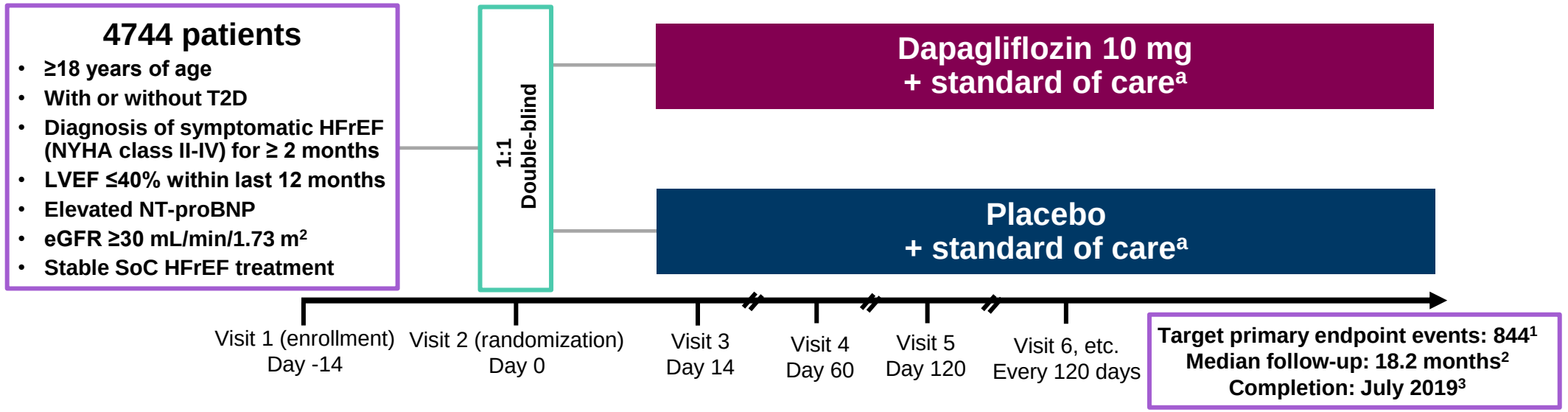
	Treatment Rate/1000 patient-years	Placebo Rate/1000 patient-years	Hazard ratio (95% CI)
EMPA-REG OUTCOME	9.4	14.5	0.65 (0.50-0.85)
CANVAS Program	5.5	8.7	0.67 (0.52-0.87)
DECLARE-TIMI 58	6.2	8.5	0.73 (0.61-0.88)
CREDENCE	15.7	25.3	0.61 (0.47-0.80)
VERTIS CV	7.3	10.5	0.70 (0.54-0.90)
Pooled estimate			**0.68 (0.61-0.76)**
(Q statistic P = 0.85; I^2= 0.0%)			



McGuire DG *et al.* JAMA Cardiology 2020

ASSESSING DAPAGLIFLOZIN IN PATIENTS WITH CHRONIC HFREF WITH OR WITHOUT T2D[1-4]

DAPAHF



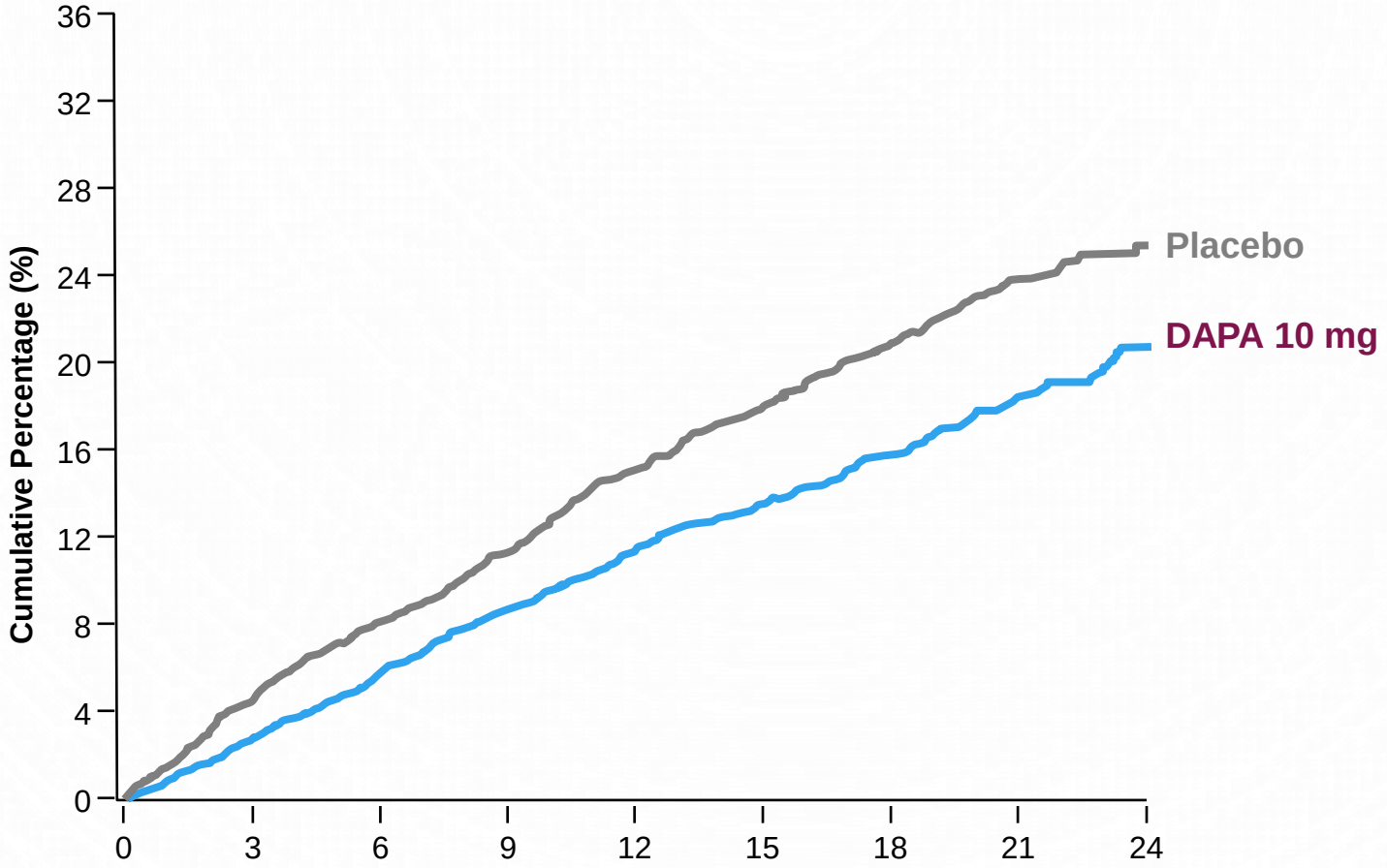
Primary Endpoint

- Time to first occurrence of any of the components of the composite: CV death or hHF or an urgent HF visit

Secondary Endpoints

- Time to first occurrence of either of the components of the composite: CV death or hHF
- Total number of (first and recurrent) hHF and CV death
- Change from baseline measured at 8 months in the total symptom score of the KCCQ
- Time to first occurrence of any of the components of the composite: ≥50% sustained decline in eGFR or reaching ESRD[b] or renal death
- Time to death from any cause

PRIMARY ENDPOINT: CV DEATH OR HHF OR AN URGENT HF VISIT[1,2]



26% RRR

HR 0.74 (0.65, 0.85)
p=0.00001

NNT = 21

Number at Risk									
DAPA 10 mg	2373	2305	2221	2147	2002	1560	1146	612	210
Placebo	2371	2258	2163	2075	1917	1478	1096	593	210

DAPAHF

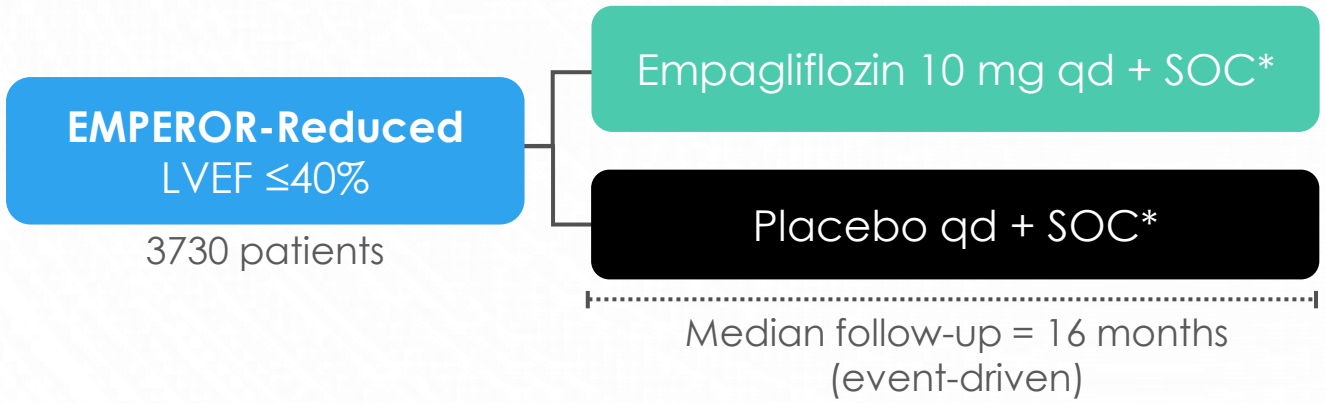
EMPEROR-REDUCED

Phase III randomised double-blind placebo-controlled trial

Aim: To investigate the safety and efficacy of empagliflozin versus placebo on top of guideline-directed medical therapy in patients with HF with **reduced ejection fraction**

Population: T2D and non-T2D, aged ≥18 years, chronic HF (NYHA class II–IV)

Study design[1–3]



Confirmatory endpoints[1,2]

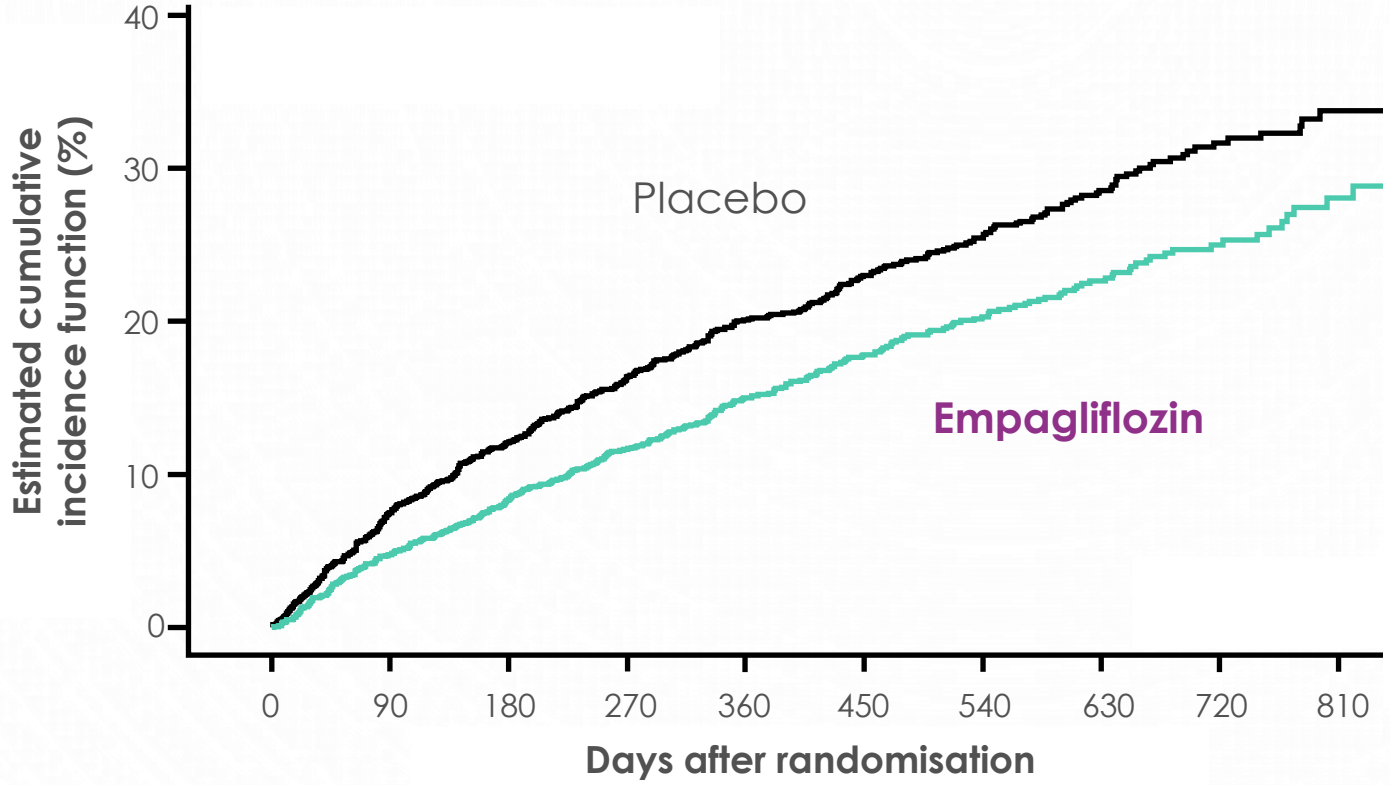
COMPOSITE PRIMARY ENDPOINT

Time to first event of adjudicated CV death or adjudicated HHF

SECONDARY ENDPOINTS

- **First and recurrent adjudicated HHF events**
- **eGFR slope: change from baseline**

PRIMARY ENDPOINT: FIRST ADJUDICATED CV DEATH OR HOSPITALISATION FOR HEART FAILURE



Patients at risk										
Placebo	1867	1715	1612	1345	1108	854	611	410	224	109
Empagliflozin	1863	1763	1677	1424	1172	909	645	423	231	101

RRR 25%

ARR 5.2%

NNT = 19

HR 0.75
(95% CI 0.65, 0.86)
p<0.001

Empagliflozin:
361 patients with event
Rate: 15.8/100 patient-years
Placebo:
462 patients with event
Rate: 21.0/100 patient-years

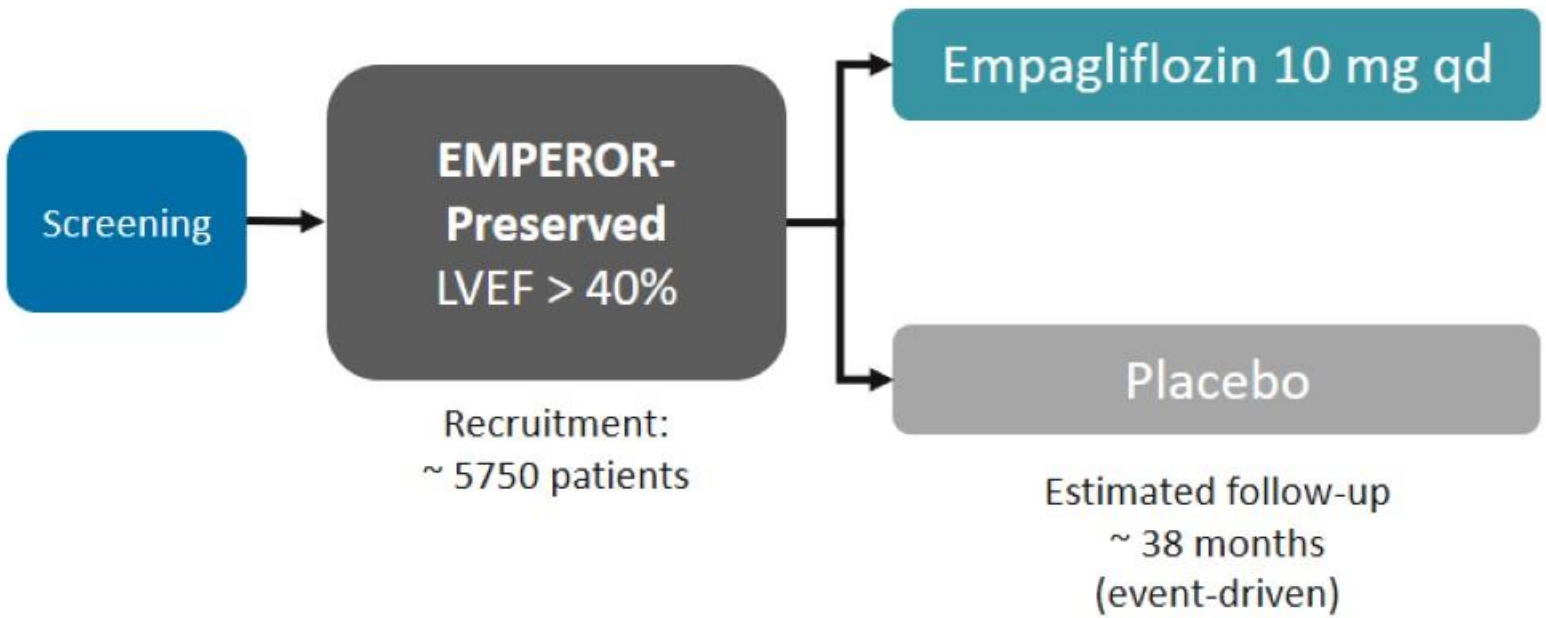
Cox regression model including covariates age, baseline eGFR, geographic region, baseline diabetes status, sex, LVEF and treatment
LVEF, left ventricular ejection fraction; RRR, relative risk reduction. NNT: Number needed to treat

Packer M et al. New England Journal of Medicine 2020 DOI: 10.1056/NEJMoa2022190

EMPEROR-Preserved in HFpEF

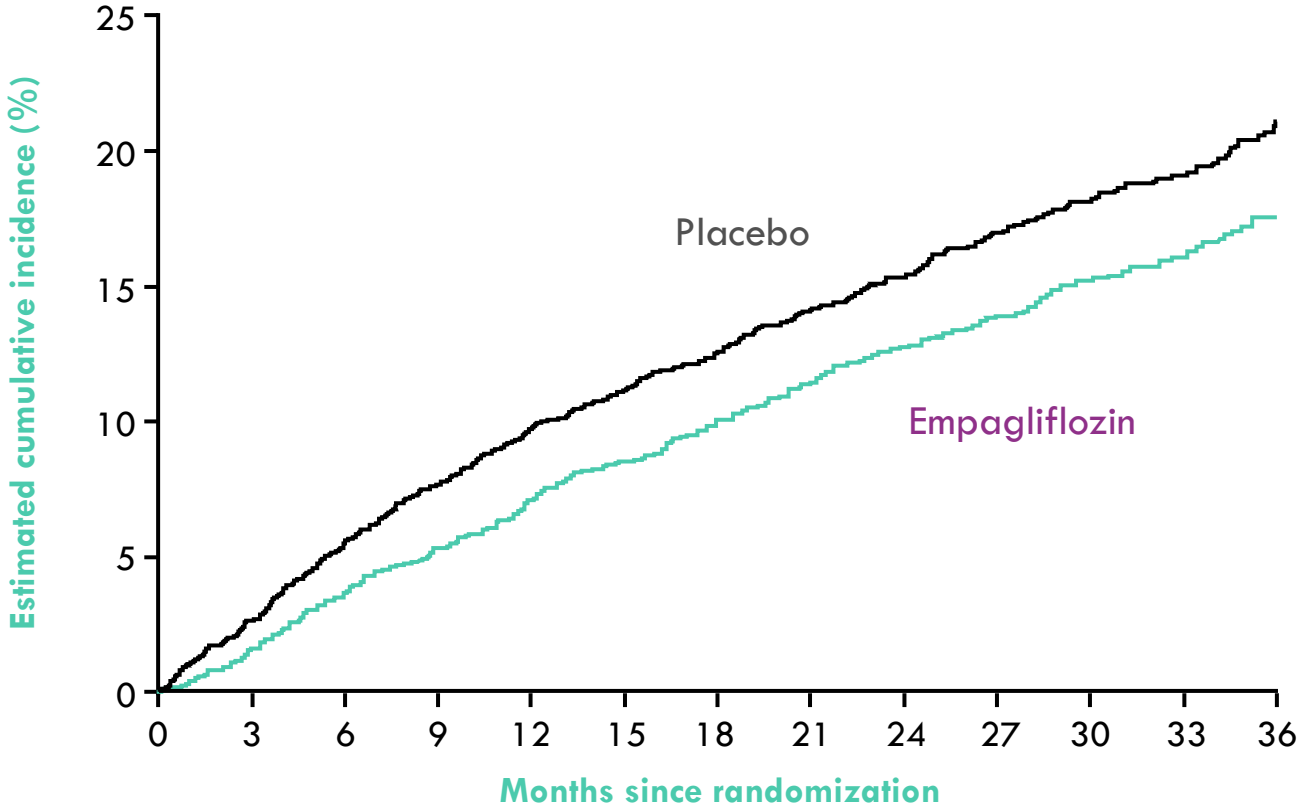
EMPEROR-Preserved: Patients with HFpEF randomized to receive empagliflozin 10 mg or placebo once daily up to 38 months

Primary endpoint: Time to first event of adjudicated CV death or adjudicated HHF



Clinicaltrials.gov: NCT03057951.

Empagliflozin demonstrated a clinically meaningful 21% RRR in the composite primary endpoint of CV death or HHF



Patients 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

RRR 21%

ARR 3.3%

NNT*=31

HR: 0.79
(95% CI: 0.69, 0.90)
$p<0.001$

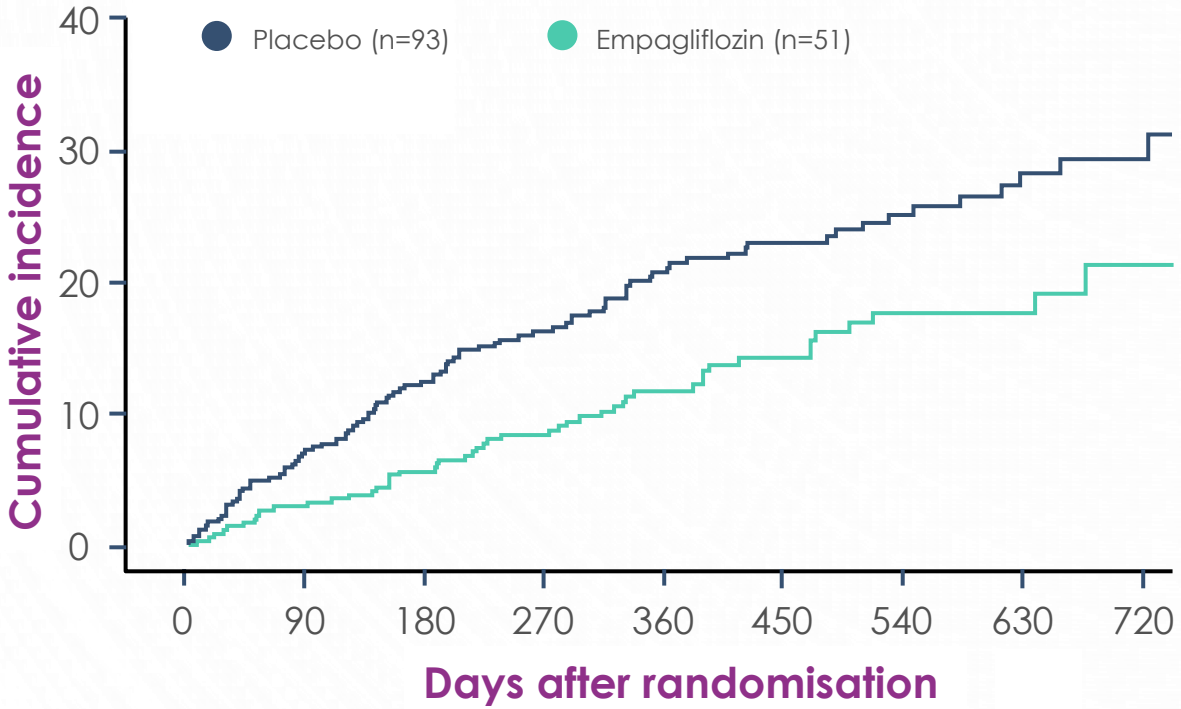
Empagliflozin:
415 (13.8%) patients with event
Rate: 6.9/100 patient-years
Placebo:
511 (17.1%) patients with event
Rate: 8.7/100 patient-years

***During a median trial period of 26 months.** ARR, absolute risk reduction; CI, confidence interval; CV, cardiovascular; HHF, hospitalization for heart failure; HR, hazard ratio; NNT, number needed to treat; RRR, relative risk reduction. Anker S *et al. N Engl J Med.* 2021; 10.1056/NEJMoa2107038.

EMPEROR-REDUCED: TIME TO CV DEATH OR HF HOSPITALISATION

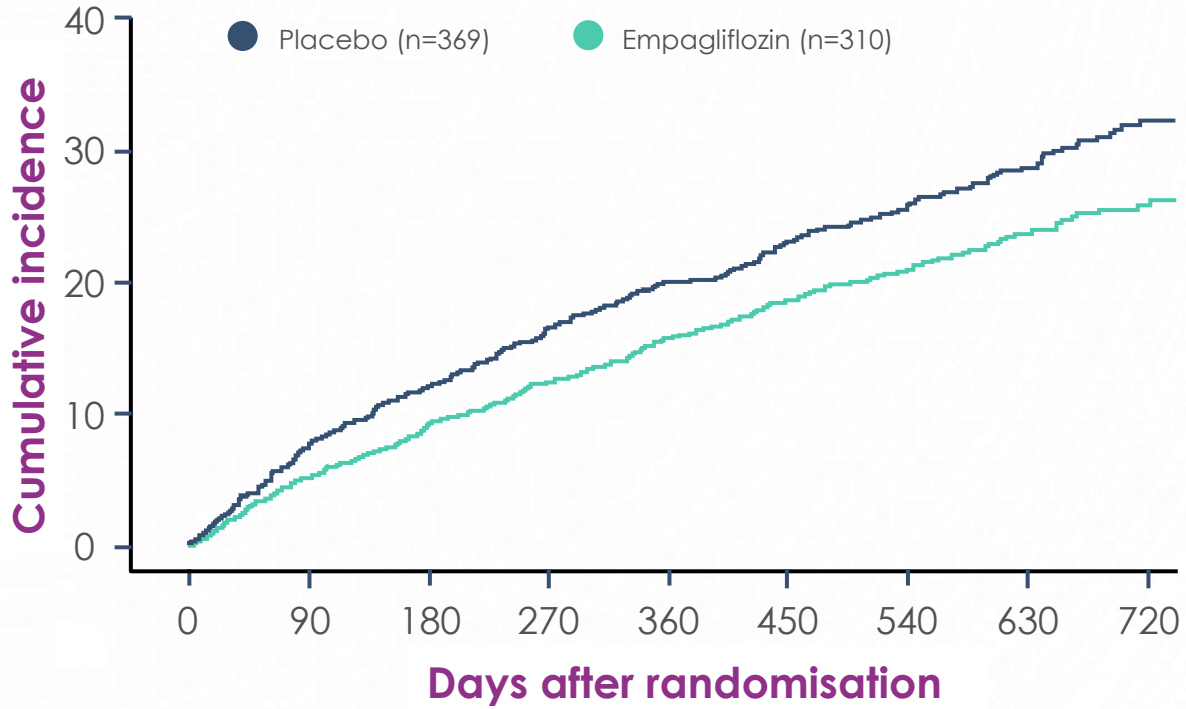
Neprilysin inhibitor

HR 0.64 (0.45, 0.89)



No neprilysin inhibitor

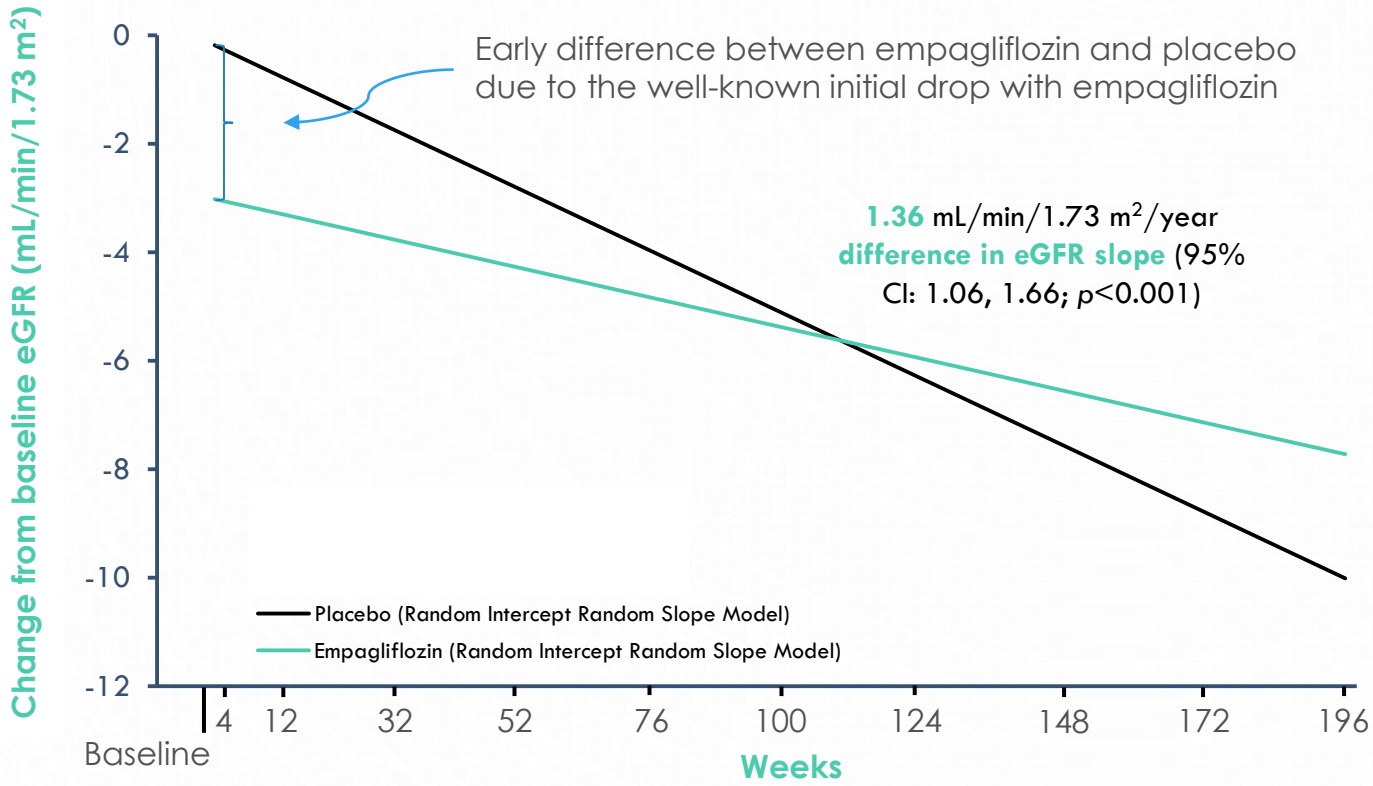
HR 0.77 (0.66, 0.90)



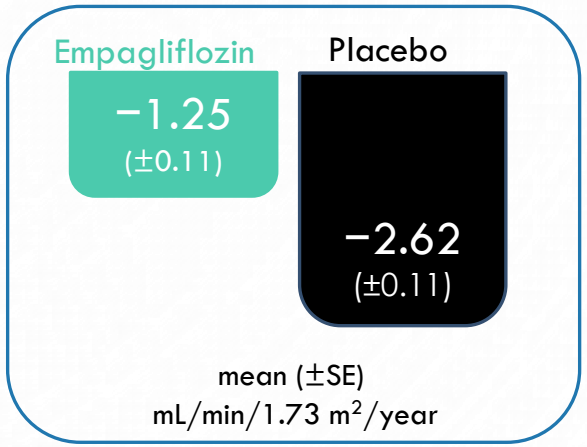
Treatment by neprilysin inhibitor interaction: *p*=0.31

Packer M *et al. Eur Heart J* 2021; DOI: 10.1093/eurheartj/ehaa968

EMPAGLIFLOZIN PROTECTED THE KIDNEY BY SIGNIFICANTLY SLOWING THE DECLINE IN KIDNEY FUNCTION



The rate of eGFR decline in patients treated with empagliflozin was half that of patients treated with placebo



eGFR slope = rate of decline (and is a measure for long-term renal function). eGFR slope is analysed based on on-treatment data using a random coefficient model including age, baseline eGFR and baseline LVEF as linear covariates and sex, region, baseline diabetes status, and baseline by time and treatment by time interactions as fixed effects; the model allows for randomly varying slope and intercept between patients.
eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; SE, standard error.
Developed from data reported in Anker S *et al. N Engl J Med.* 2021; 10.1056/NEJMoa2107038.

SOLOIST - WHF TRIAL

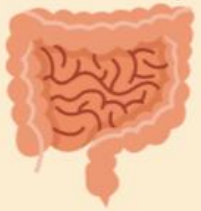
Bhatt DL et al. Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure. N Engl J Med. 2021;384(2):117-128.

SOTAGLIFLOZIN

inhibits

SGLT-2 → increases urinary glucose excretion

SGLT-1 → delays intestinal glucose absorption



QUESTION

In patients with diabetes and recently worsening HF, does SOTAGLIFLOZIN:
↓ CV mortality?
↓ HF urgent visits?
↓ HF hospitalizations?

INCLUSION

18 - 85 yo patients with diabetes hospitalized for signs or symptoms of HF and treatment with IV diuretics

1222 patients

TOTAL NO. OF EVENTS (RATE PER 100 PATIENT YEARS)

	PRIMARY OUTCOME: HF urgent visits + HF hospitalizations + CV Death	SECONDARY OUTCOME: HF urgent visits + HF hospitalizations	SECONDARY OUTCOME: CV Death
Sotagliflozin n=608	245 (51)	194 (40)	51 (11)
	HR 0.67 95% CI 0.52-0.85 p<0.001	HR 0.64 95% CI 0.49-0.83 p<0.001	HR 0.84 95% CI 0.58-1.22 p=0.36
Placebo n=614	355 (76)	297 (64)	58 (13)

CONCLUSION

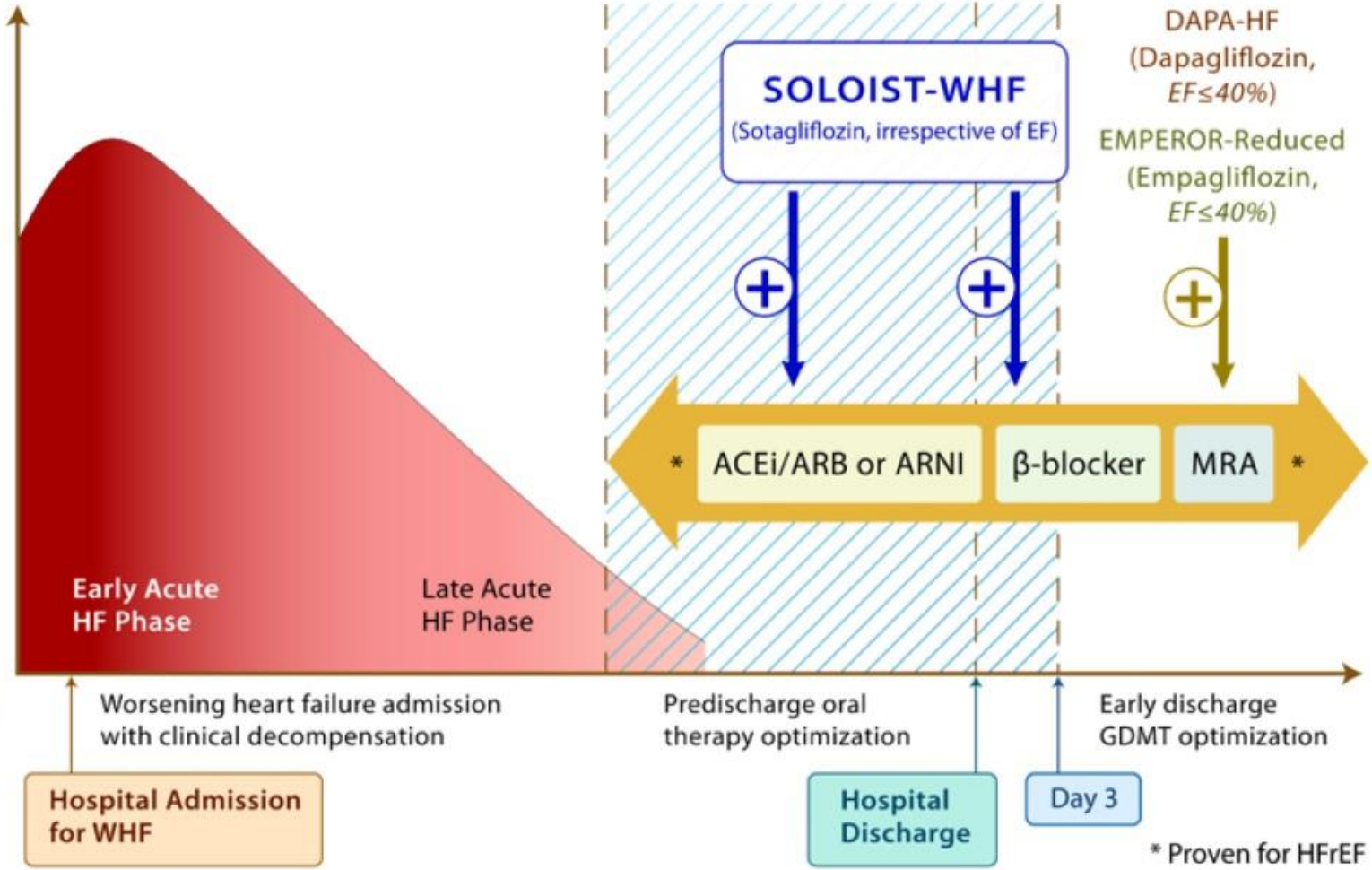
In patients with diabetes with worsening HF, sotagliflozin significantly decreased CV deaths, HF urgent visits, and HF hospitalizations

SOLOIST-WHF

Addressing the Vulnerable Period of an Admission for Worsening Heart Failure

Take-Home Message of SOLOIST-WHF:

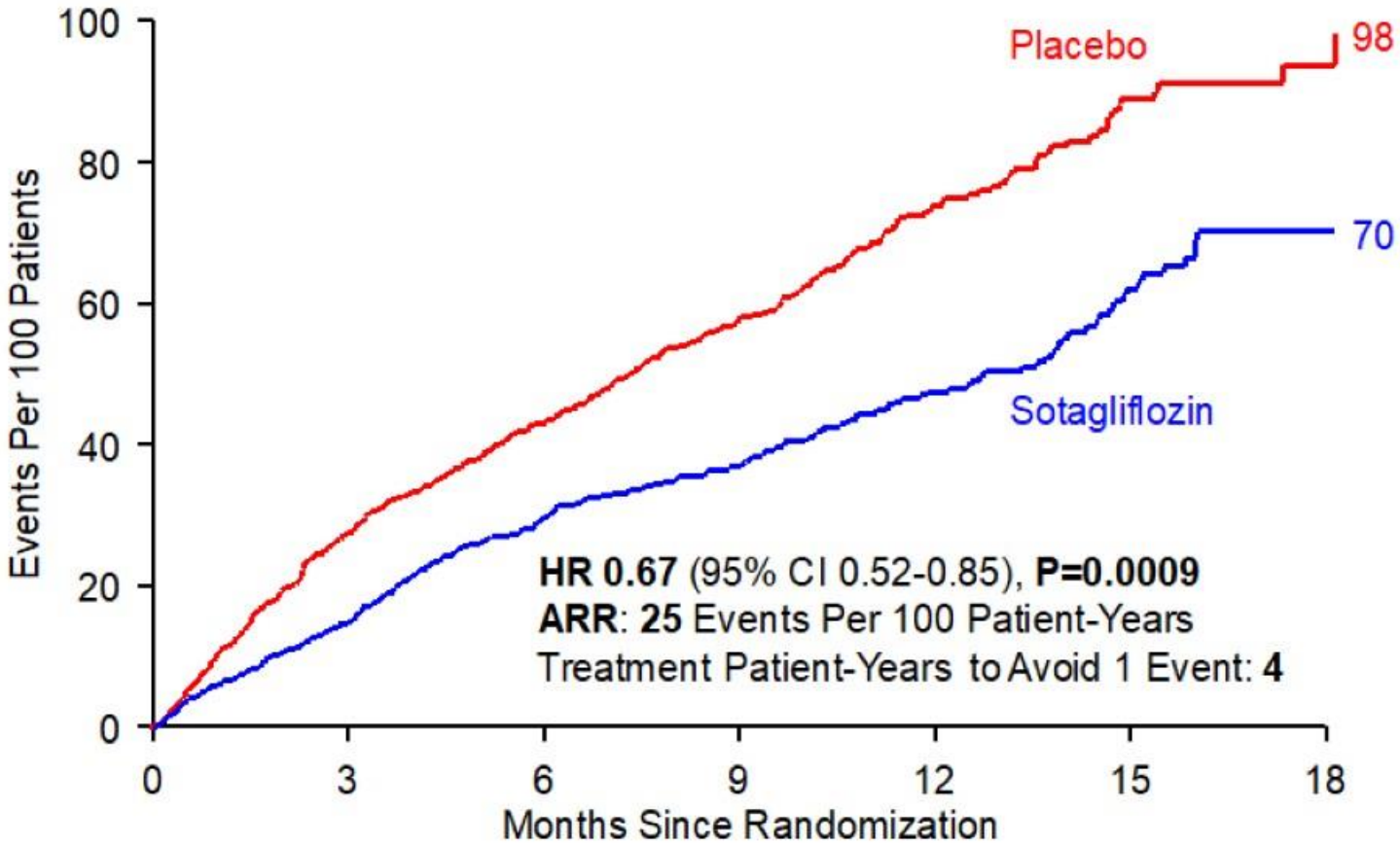
In patients with T2D and WHF, SGLT2 inhibitors should be initiated earlier, as soon as possible once the patient is clinically stable, preferably prior to discharge

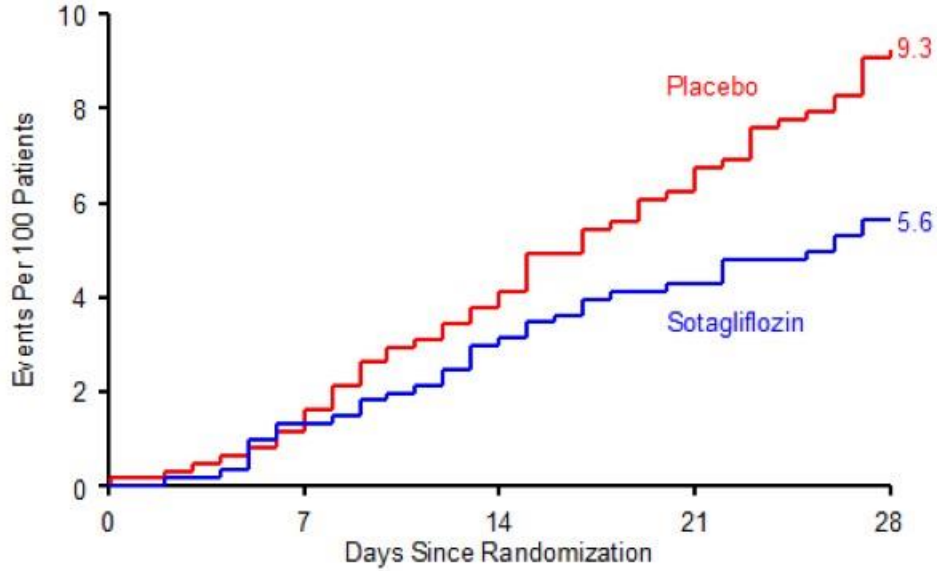


Verma S, et al. *ESC Heart Fail.* 2020;7:3261-3267.

Primary Endpoint

Total CV Death, HHF, and Urgent HF Visit





There was an early effect of sotagliflozin that was significant by 28 days: HR = 0.61, *P* = .035

Bhatt DL, et al. *N Engl J Med. N Engl J Med.* 2021;384:117-128; Bhatt DL, et al. AHA 2020.

SOLOIST-WHF Subgroups Analysis

Events Per 100 Patient-Years

Subgroup	Patients	Sotagliflozin	Placebo	HR (95% CI)
Overall	1222	51.0	76.3	0.67 (0.52, 0.85)
LVEF (%)				
< 50	966	56.9	79.9	0.72 (0.56, 0.94)
≥ 50	256	30.6	64.0	0.48 (0.27, 0.86)
First Study Drug Dose				
Before Discharge	596	52.1	76.6	0.71 (0.51, 0.99)
After Discharge	626	50.0	76.1	0.64 (0.45, 0.90)

The effect of sotagliflozin was observed across all subgroups, particularly according to different levels of LVEF and if treatment was administered before or after discharge

Bhatt DL, et al. *N Engl J Med. N Engl J Med.* 2021;384:117-128; Bhatt DL, et al. AHA 2020.

QUANDO NON USARE GLI SGLT2-I

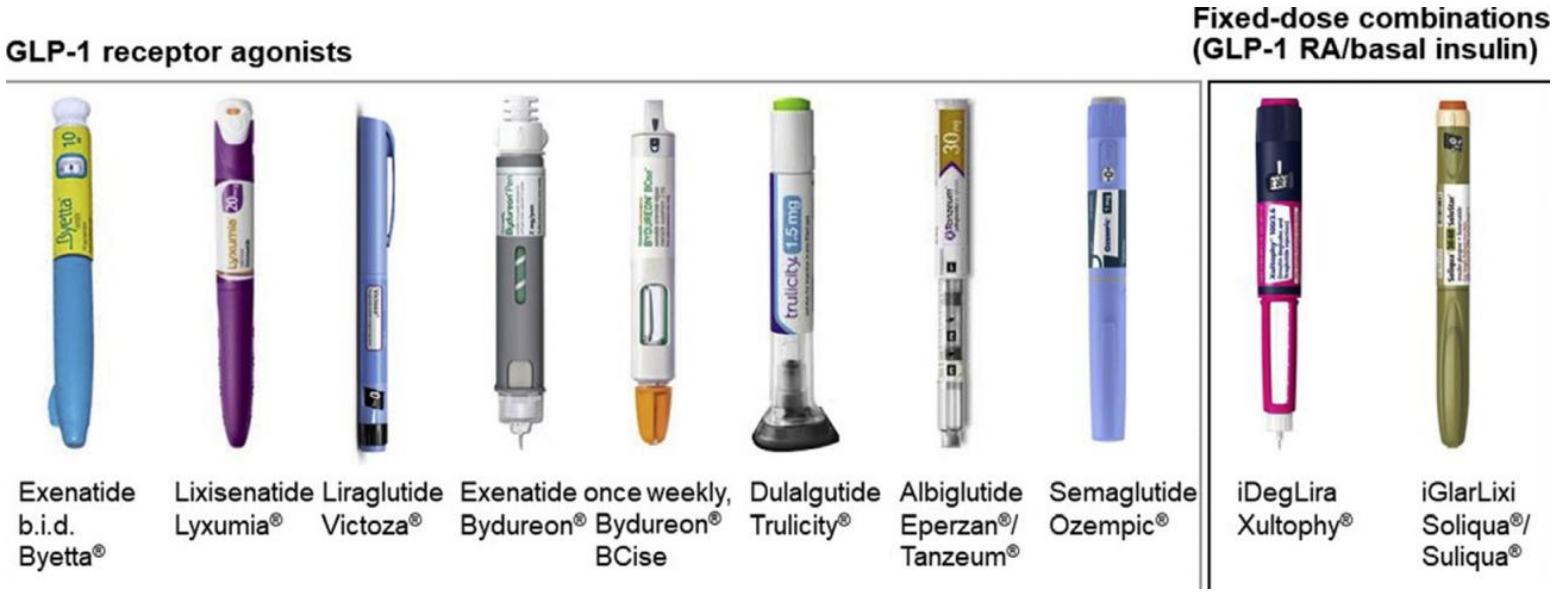
- ✓ Diabete mellito di tipo 1
- ✓ VFG < di 25 ml/minuto
- ✓ Candidosi Genitali Recidivanti

QUANDO SOSPENDERE L'SGLT2-I

- ✓ Patologie Acute ad alto rischio di Acidosi Metabolica(infezioni,digiuno,etc)
- ✓ Candidosi Recidivanti e resistenti alla Terapia
- ✓ Deplezione Di Volume

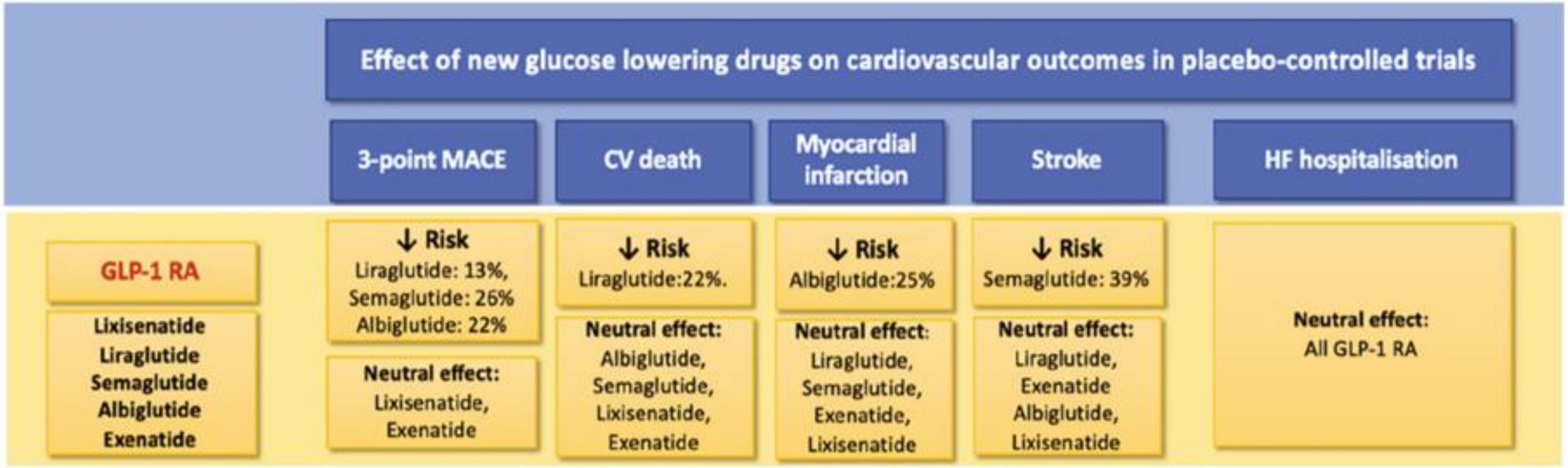
GLP-1 receptor agonists in the treatment of type 2 diabetes – state-of-the-art

INCRETINE: Aumentano la secrezione di insulina durante il pasto
Soppressione dell'ipersecrezione di glucagone
Rallentano lo svuotamento gastrico.



MOLECULAR METABOLISM 46 (2021) 101102

RISULTATI DEI TRIALS CHE HANNO UTILIZZATO GLP1RA IN PZ DIABETICI.

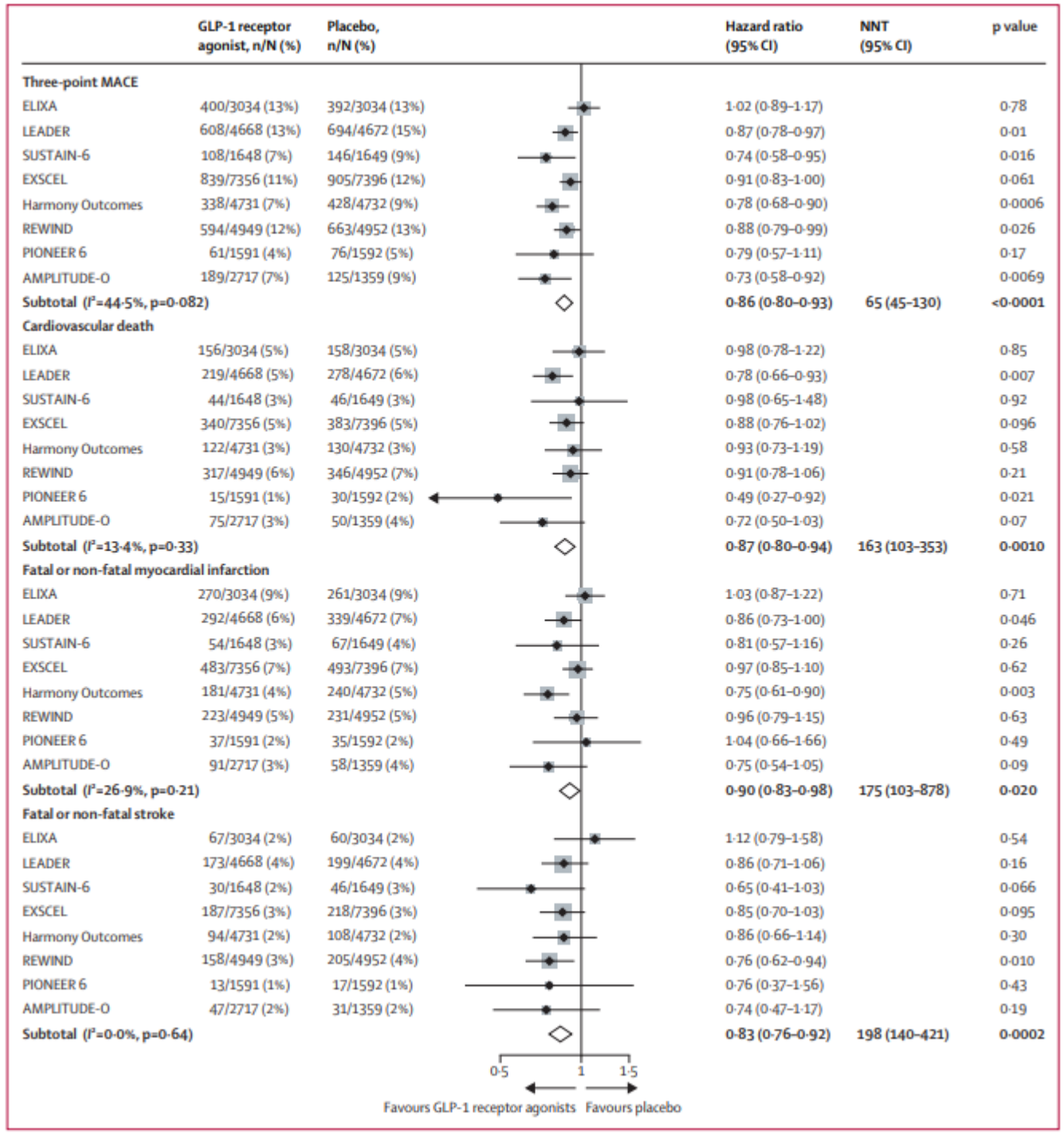


Seferovic PM et al. European Journal of Heart Failure (2020) 22, 196–213 POSITION PAPER
doi:10.1002/ejhf.1673

Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of randomised trials

Naveed Sattar, Matthew M Y Lee*, Søren L Kristensen*, Kelley R H Branch, Stefano Del Prato, Nardev S Khurmi, Carolyn S P Lam, Renato D Lopes, John J V McMurray, Richard E Pratley, Julio Rosenstock, Hertzel C Gerstein*

Findings Of 98 articles screened, eight trials comprising 60 080 patients fulfilled the prespecified criteria and were included. Overall, GLP-1 receptor agonists reduced MACE by 14% (HR 0·86 [95% CI 0·80–0·93]; p<0·0001), with no significant heterogeneity across GLP-1 receptor agonist structural homology or eight other examined subgroups (all $p_{interaction} \geq 0·14$). GLP-1 receptor agonists reduced all-cause mortality by 12% (HR 0·88 [95% CI 0·82–0·94]; p=0·0001), hospital admission for heart failure by 11% (HR 0·89 [95% CI 0·82–0·98]; p=0·013), and the composite kidney outcome by 21% (HR 0·79 [95% CI 0·73–0·87]; p<0·0001), with no increase in risk of severe hypoglycaemia, retinopathy, or pancreatic adverse effects. In sensitivity analyses removing the only trial restricted to patients with an acute coronary syndrome (ELIXA), all benefits marginally increased, including the outcome of worsening of kidney function, based on eGFR change (HR 0·82 [95% CI 0·69–0·98]; p=0·030).


GLP-1 receptor agonist, n/N (%)
Placebo, n/N (%)
Hazard ratio (95% CI)
NNT (95% CI)
p value
Three-point MACE
ELIXA 400/3034 (13%) 392/3034 (13%) 1·02 (0·89–1·17) 0·78
LEADER 608/4668 (13%) 694/4672 (15%) 0·87 (0·78–0·97) 0·01
SUSTAIN-6 108/1648 (7%) 146/1649 (9%) 0·74 (0·58–0·95) 0·016
EXSCEL 839/7356 (11%) 905/7396 (12%) 0·91 (0·83–1·00) 0·061
Harmony Outcomes 338/4731 (7%) 428/4732 (9%) 0·78 (0·68–0·90) 0·0006
REWIND 594/4949 (12%) 663/4952 (13%) 0·88 (0·79–0·99) 0·026
PIONEER 6 61/1591 (4%) 76/1592 (5%) 0·79 (0·57–1·11) 0·17
AMPLITUDE-O 189/2717 (7%) 125/1359 (9%) 0·73 (0·58–0·92) 0·0069
Subtotal (I²=44·5%, p=0·082) 0·86 (0·80–0·93) 65 (45–130) <0·0001
Cardiovascular death
ELIXA 156/3034 (5%) 158/3034 (5%) 0·98 (0·78–1·22) 0·85
LEADER 219/4668 (5%) 278/4672 (6%) 0·78 (0·66–0·93) 0·007
SUSTAIN-6 44/1648 (3%) 46/1649 (3%) 0·98 (0·65–1·48) 0·92
EXSCEL 340/7356 (5%) 383/7396 (5%) 0·88 (0·76–1·02) 0·096
Harmony Outcomes 122/4731 (3%) 130/4732 (3%) 0·93 (0·73–1·19) 0·58
REWIND 317/4949 (6%) 346/4952 (7%) 0·91 (0·78–1·06) 0·21
PIONEER 6 15/1591 (1%) 30/1592 (2%) 0·49 (0·27–0·92) 0·021
AMPLITUDE-O 75/2717 (3%) 50/1359 (4%) 0·72 (0·50–1·03) 0·07
Subtotal (I²=13·4%, p=0·33) 0·87 (0·80–0·94) 163 (103–353) 0·0010
Fatal or non-fatal myocardial infarction
ELIXA 270/3034 (9%) 261/3034 (9%) 1·03 (0·87–1·22) 0·71
LEADER 292/4668 (6%) 339/4672 (7%) 0·86 (0·73–1·00) 0·046
SUSTAIN-6 54/1648 (3%) 67/1649 (4%) 0·81 (0·57–1·16) 0·26
EXSCEL 483/7356 (7%) 493/7396 (7%) 0·97 (0·85–1·10) 0·62
Harmony Outcomes 181/4731 (4%) 240/4732 (5%) 0·75 (0·61–0·90) 0·003
REWIND 223/4949 (5%) 231/4952 (5%) 0·96 (0·79–1·15) 0·63
PIONEER 6 37/1591 (2%) 35/1592 (2%) 1·04 (0·66–1·66) 0·49
AMPLITUDE-O 91/2717 (3%) 58/1359 (4%) 0·75 (0·54–1·05) 0·09
Subtotal (I²=26·9%, p=0·21) 0·90 (0·83–0·98) 175 (103–878) 0·020
Fatal or non-fatal stroke
ELIXA 67/3034 (2%) 60/3034 (2%) 1·12 (0·79–1·58) 0·54
LEADER 173/4668 (4%) 199/4672 (4%) 0·86 (0·71–1·06) 0·16
SUSTAIN-6 30/1648 (2%) 46/1649 (3%) 0·65 (0·41–1·03) 0·066
EXSCEL 187/7356 (3%) 218/7396 (3%) 0·85 (0·70–1·03) 0·095
Harmony Outcomes 94/4731 (2%) 108/4732 (2%) 0·86 (0·66–1·14) 0·30
REWIND 158/4949 (3%) 205/4952 (4%) 0·76 (0·62–0·94) 0·010
PIONEER 6 13/1591 (1%) 17/1592 (1%) 0·76 (0·37–1·56) 0·43
AMPLITUDE-O 47/2717 (2%) 31/1359 (2%) 0·74 (0·47–1·17) 0·19
Subtotal (I²=0·0%, p=0·64) 0·83 (0·76–0·92) 198 (140–421) 0·0002
0·5
1
1·5
Favours GLP-1 receptor agonists
Favours placebo

Guidelines for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes

JACC Guideline Comparison

Michelle D. Kelsey, MD,[a,b] Adam J. Nelson, MBBS, PhD,[b] Jennifer B. Green, MD,[b,c] Christopher B. Granger, MD,[a,b] Eric D. Peterson, MD, MPH,[d] Darren K. McGuire, MD, MHSc,[d] Neha J. Pagidipati, MD, MPH[a,b]

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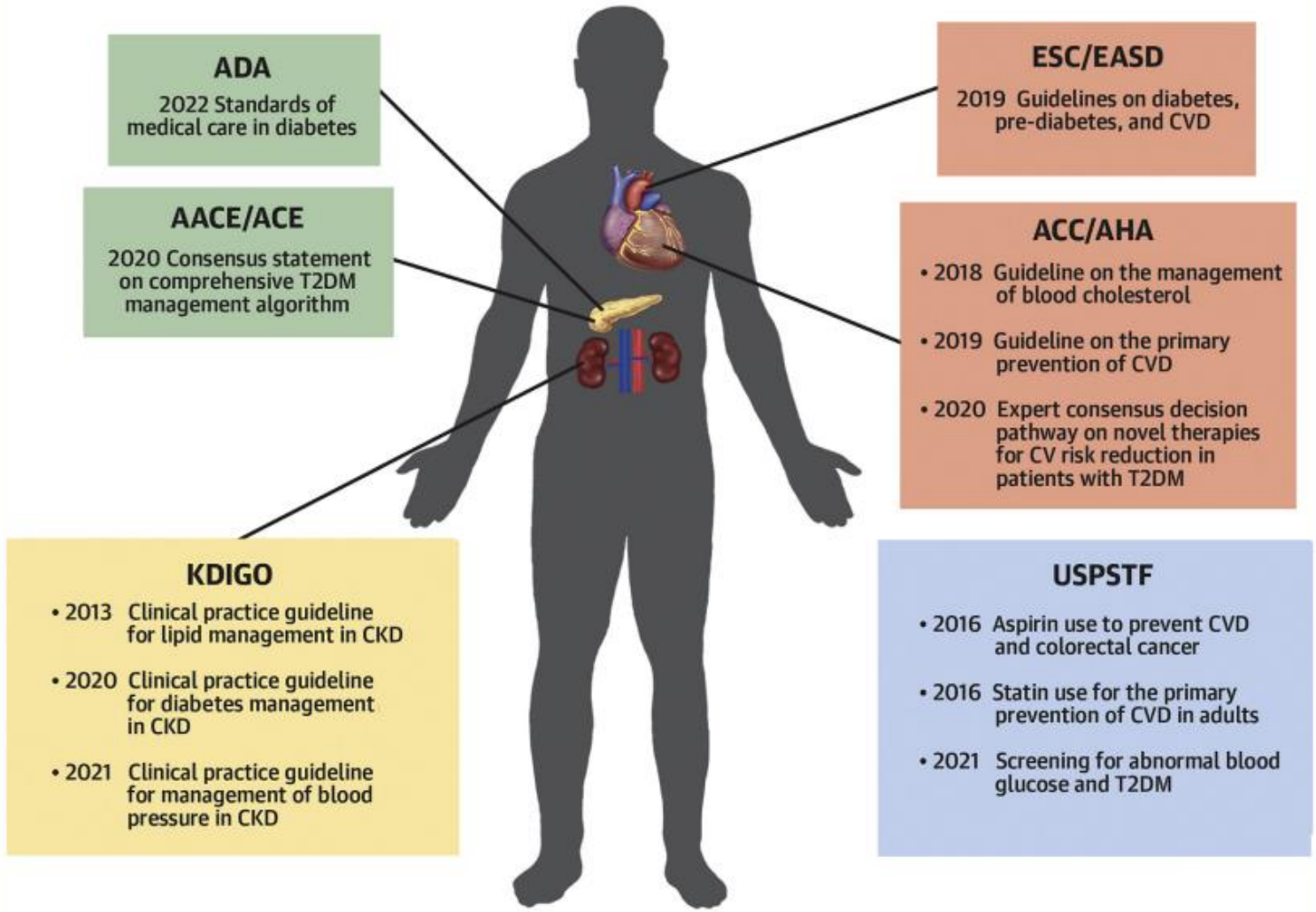
CENTRAL ILLUSTRATION Cardiovascular Risk Reduction in Type 2 Diabetes Mellitus Guidelines and Consensus Recommendations



Kelsey MD, et al. J Am Coll Cardiol. 2022;79(18):1849-1857.

Guideline documents and consensus statements across general medical, CV, kidney, and endocrine professional societies with recommendations for CV risk reduction in T2DM. AACE = American Association of Clinical Endocrinology; ACE = American College of Endocrinology; ADA = American Diabetes Association; ACC = American College of Cardiology; AHA = American Heart Association; CKD = chronic kidney disease; CV = cardiovascular; CVD = CV disease; ESC = European Society of Cardiology; EASD = European Association for the Study of Diabetes; KDIGO = Kidney Disease: Improving Global Outcomes; T2DM = type 2 diabetes mellitus; USPSTF = U.S. Preventive Services Task Force.

Guidelines for Cardiovascular Risk Reduction in Patients With Type 2 Diabetes

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TABLE 1 Comparison of Type 2 Diabetes Guideline Recommendations

	ACC/AHA[8,13,39]	ADA[4,17,38,43]	AACE/ACE[5,6]	ESC/EASD[7]	USPSTF[1-3]	KDIGO[10,11,33]
Risk assessment						
Method	Pooled Cohort Equation and diabetes-specific risk enhancers	Pooled Cohort Equation and diabetes-specific risk enhancers	Framingham Risk Assessment Tool and risk factors	Moderate, high, very high risk	Pooled Cohort Equation	No recommendation
Lifestyle recommendations						
Exercise	150 min of moderate-intensity activity per week	150 min of moderate-intensity activity per week	150 min of moderate-intensity activity per week	150 min of moderate-intensity activity per week	No specific recommendation	150 min of moderate-intensity activity per week
Diet	Individualized nutrition assessment; Mediterranean Diet	Individualized nutrition assessment; Mediterranean Diet	Individualized nutrition assessment; Mediterranean Diet	Individualized nutrition assessment; Mediterranean Diet	No specific recommendation	Individualized nutrition assessment; Mediterranean Diet, 0.8 g protein/day if CKD
Vitamin use	No recommendation	No recommendation	No recommendation	Avoid vitamin supplementation to reduce ASCVD risk in T2DM	No recommendation	No recommendation
Blood pressure management						
BP target	<130/80 mm Hg	<130/80 mm Hg if 10-y ASCVD risk ≥15%; <140/90 if 10-y ASCVD risk <15%	<130/80 mm Hg	<130/80 mm Hg, (but not <120/70 mm Hg), and 130-139 mm Hg in those older than 65 y	<120/80 mm Hg only for stroke risk reduction	<120/80 mm Hg if concurrent CKD
First-line treatment of hypertension	Angiotensin-converting enzyme/ARB if albuminuria	Angiotensin-converting enzyme/ARB if albuminuria	Angiotensin-converting enzyme/ARB	Angiotensin-converting enzyme/ARB if albuminuria or LVH	No recommendation	Angiotensin-converting enzyme/ARB if albuminuria
Indication for combination therapy	If BP >140/90 mm Hg	Dual therapy first line regardless of BP	If BP >150/100 mm Hg	If BP >160/100 mm Hg	No recommendation	No recommendation
LDL-C management						
Primary prevention treatment targets	50% LDL-C lowering for those at high risk	50% LDL-C lowering for those at high risk	Numeric goal (LDL-C <55, 70, or 100 mg/dL)	Numeric goal (LDL-C <55, 70, or 100 mg/dL)	N/A	N/A
Primary prevention in young patients	Treat if longstanding disease, end-organ damage, risk factors	Treat if longstanding disease, end-organ damage, risk factors	No recommendation	Treat if LDL-C > 100 mg/dL	N/A	N/A
Secondary prevention treatment targets	Goal 50% LDL-C reduction, start meds LDL-C <70 mg/dL	Goal 50% LDL-C reduction, start meds at LDL-C <70 mg/dL	LDL-C <55 mg/dL	LDL-C < 55mg/dL	N/A	N/A
Secondary prevention second-line therapy	Ezetimibe	Ezetimibe or PCSK9i	No recommendation	Ezetimibe	N/A	N/A
Hyperglycemia treatment and novel agents						
First line	SGLT2i/GLP-1RA may be beneficial regardless of background metformin	SGLT2i/GLP-1RA may be beneficial regardless of background metformin	SGLT2i/GLP-1RA may be beneficial regardless of background metformin	SGLT2i/GLP-1RA first line	No recommendation	Metformin and SGLT2i in combination for those with CKD
Relative priority of SGLT2/GLP-1RA	SLGT2i >GLP-1RA for HF, renal disease, weight loss	SLGT2i >GLP-1RA for HF and renal disease	SLGT2i >GLP-1RA for HF and renal disease	No specific recommendation	No recommendation	SGLT2 inhibitor first, GLP-1RA second line
Aspirin recommendations						
Primary prevention	May be considered if elevated ASCVD risk without increased bleeding risk	May be considered if elevated ASCVD risk without increased bleeding risk	No recommendation	Not in moderate risk, but can be considered in high or very high risk	No significant risk reduction with aspirin in individuals with T2DM	May be considered if elevated ASCVD risk without increased bleeding risk
CKD						
Type 2 diabetes treatment	SGLT2i	SGLT2i, specifically canagliflozin	SGLT2i	SGLT2i	No recommendation	SGLT2i

ESC European Society of Cardiology
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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

Authors/Task Force Members: Theresa A. McDonagh* (Chairperson) (United Kingdom), Marco Metra * (Chairperson) (Italy), Marianna Adamo (Task Force Coordinator) (Italy), Roy S. Gardner (Task Force Coordinator) (United Kingdom), Andreas Baumbach (United Kingdom), Michael Böhm (Germany), Haran Burri (Switzerland), Javed Butler (United States of America), Jelena Čelutkienė (Lithuania), Ovidiu Chioncel (Romania), John G.F. Cleland (United Kingdom), Andrew J.S. Coats (United Kingdom), Maria G. Crespo-Leiro (Spain), Dimitrios Farmakis (Greece), Martine Gilard (France), Stephane Heymans

Recommendations for the primary prevention of heart failure in patients with risk factors for its development

Recommendations	Class[a]	Level[b]
Treatment of hypertension is recommended to prevent or delay the onset of HF, and to prevent HF hospitalizations.[287–290]	I	A
Treatment with statins is recommended in patients at high risk of CV disease or with CV disease in order to prevent or delay the onset of HF, and to prevent HF hospitalizations.[291,292]	I	A
SGLT2 inhibitors (canagliflozin, dapagliflozin, empagliflozin, ertugliflozin, sotagliflozin) are recommended in patients with diabetes at high risk of CV disease or with CV disease in order to prevent HF hospitalizations.[293–297]	I	A
Counselling against sedentary habit, obesity, cigarette smoking, and alcohol abuse is recommended to prevent or delay the onset of HF.[298–302]	I	C

CV = cardiovascular; HF = heart failure; SGLT2 = sodium-glucose co-transporter 2.
[a]Class of recommendation.
[b]Level of evidence.

GRAZIE DELL'ATTENZIONE