Società Italiana dell'Ipertensione Arteriosa
Lega Italiana contro l'Ipertensione Arteriosa

EVENTO FORMATIVO INTERREGIONALE SIIA
PIEMONTE | LIGURIA | VALLE D'AOSTA
Torino, 29 novembre 2025

La nefroprotezione con gli SGLT2i nel paziente iperteso a rischio cardiovascolare

Roberto Pontremoli

Università degli Studi e IRCCS Ospedale Policlinico San Martino - Genova

Il sottoscritto Roberto PONTREMOLI

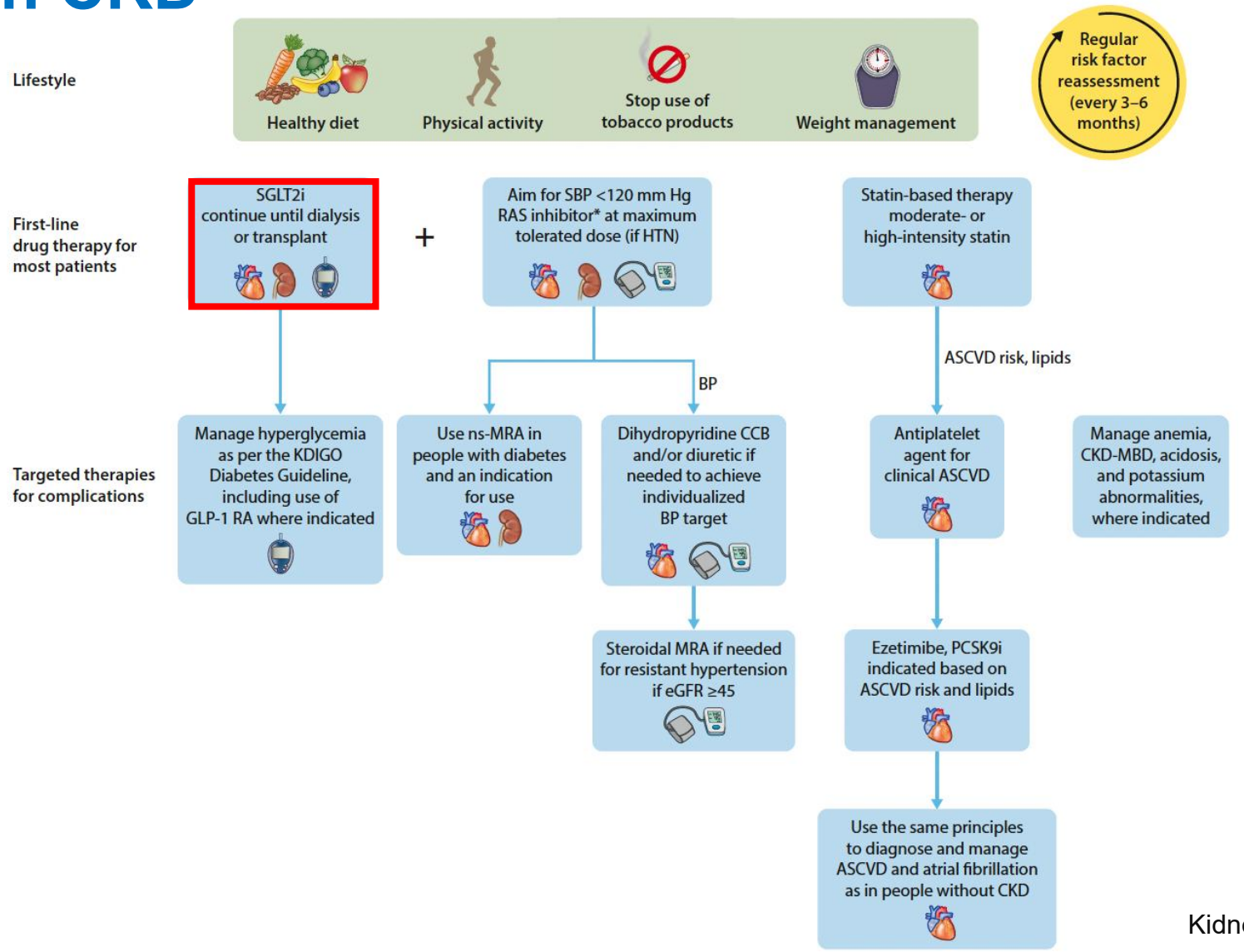
ai sensi dell’art. 76, comma 4 dell’Accordo Stato-Regioni del 2 febbraio 2017 e del paragrafo 4.5. del Manuale nazionale di accreditamento per l'erogazione di eventi ECM

dichiara che

negli ultimi due anni ha avuto i seguenti rapporti con soggetti portatori di interessi commerciali in ambito sanitario

- ASTRAZENECA
- BAYER
- BOEHRINGER-INGELHEIM
- GUIDOTTI
- LILLY
- MENARINI
- NOVONORDISK
- RECORDATI
- VIFOR

KDIGO now recommend SGLT2 inhibitors as a SOC for all patients with CKD



Kidney International, march 14 2024

ESC European Society of Cardiology
European Heart Journal (2021) **00**, 1–2
doi:10.1093/eurheartj/ehab765
CARDIOPULSE

Braunwald's Corner

SGLT2 inhibitors: the statins of the 21st century

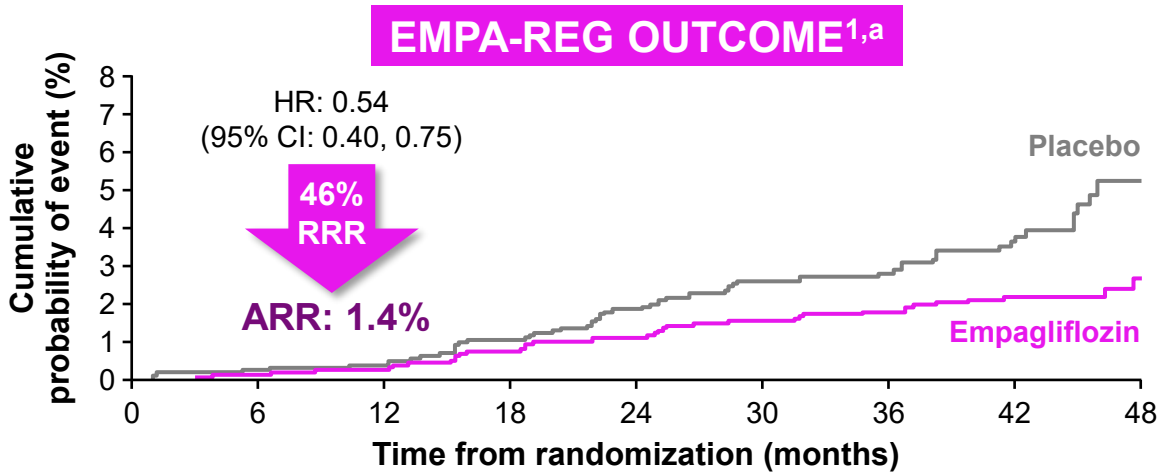
Eugene Braunwald [1,2]*

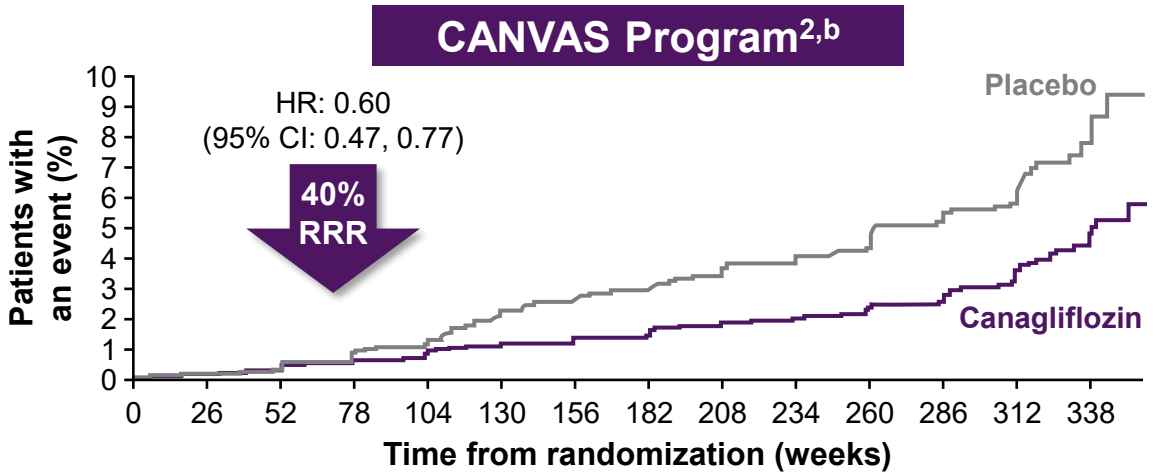
[1]TIMI Study Group, Division of Cardiovascular Medicine, Brigham and Women's Hospital, Hale Building for Transformative Medicine, Suite 7022, 60 Fenwood Road, Boston, MA 02115, USA; and [2]Department of Medicine, Harvard Medical School, Boston, MA, USA

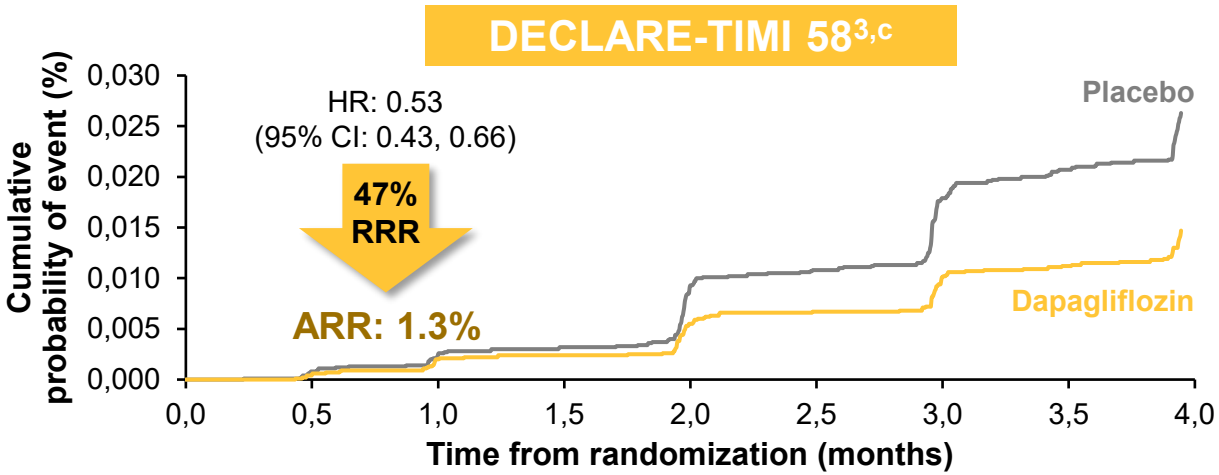
A relatively small number of drugs have been responsible for major advances in medical practice. The discovery, development, and elucidation of the mechanisms of action of aspirin, penicillin, and statins are remarkable success stories, each with some surprises and each crowned by a Nobel Prize. The 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.

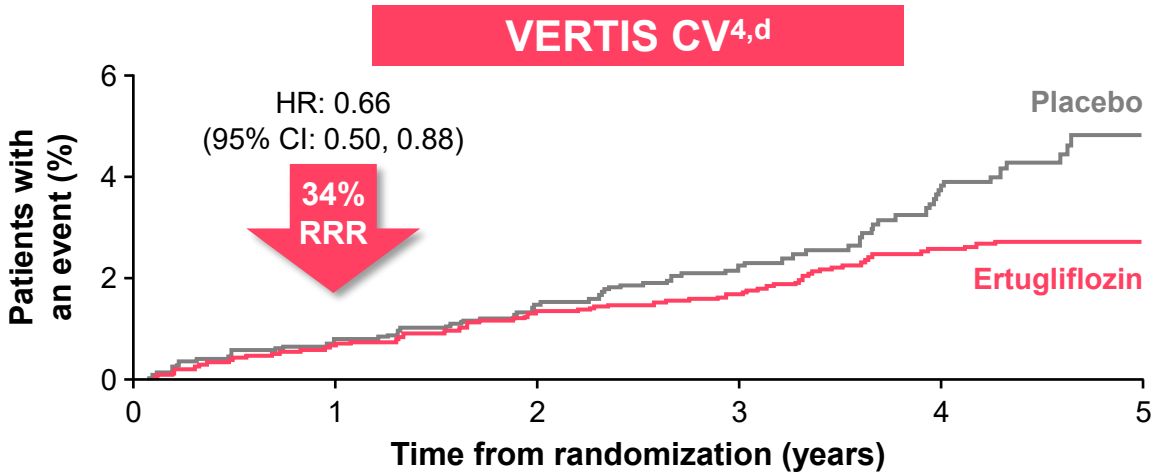
The 2008 FDA regulatory policy statement led to a landslide of CVOTs that opened up new therapeutic opportunities beyond GLT

SGLT2 inhibitors in CVOTs consistently reduced the risk of kidney composite endpoints compared with placebo









1. Wanner C, et al. *N Engl J Med* 2016;375:323–334; 2. Neal B, et al. *N Engl J Med* 2017;377:644–657; 3. Mosenzon O, et al. *Lancet Diabetes Endocrinol* 2019;7:606–617;
4. Cherney DZI, et al. *Diabetologia* 2021;64:1256–1267

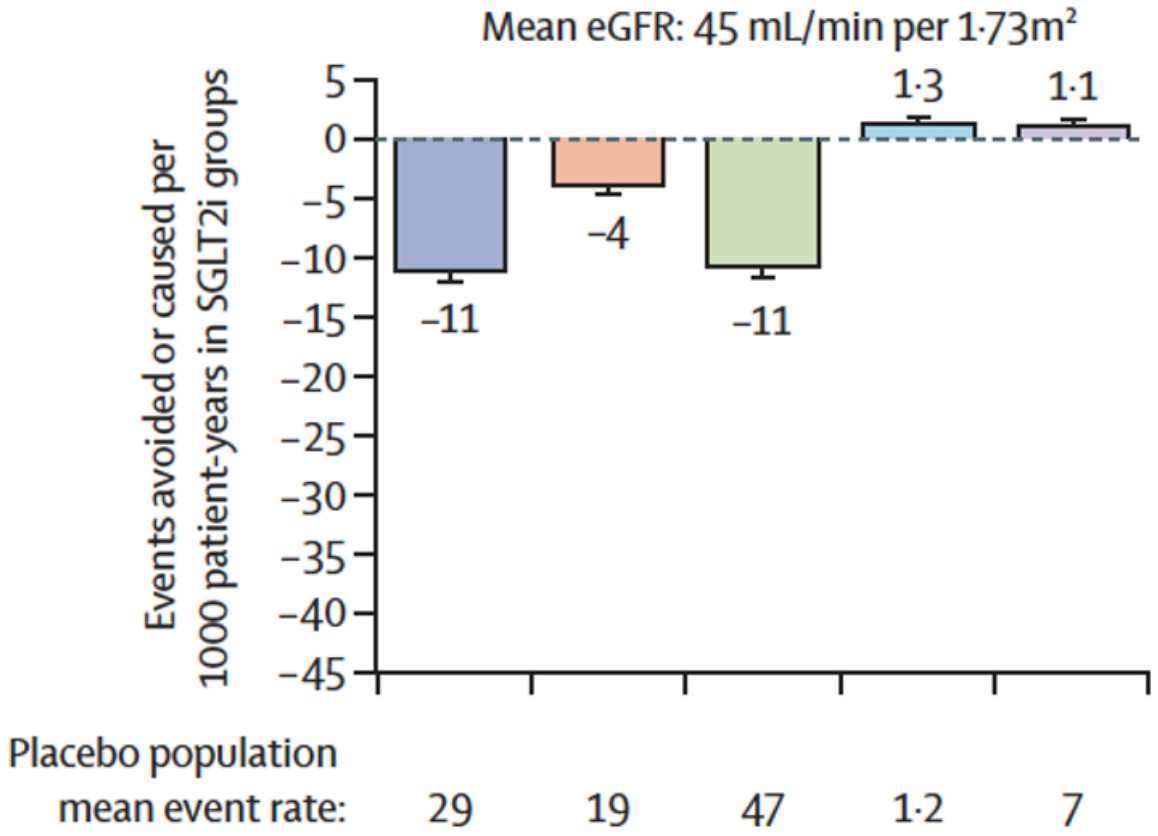
Kidney outcomes using generally consistent definitions: Sustained ≥40% decline in eGFR, ESKD or renal death

	Kidney composite outcomes	HR (95% CI)	
EMPA-REG OUTCOME[1]	Sustained ≥40% reduction in eGFR, renal-replacement therapy (dialysis or transplantation), or death from renal causes	0.55 (0.41, 0.73)	***RRR ≈45 %***
CANVAS Program[2]	Sustained ≥40% reduction in eGFR, renal-replacement therapy (dialysis or transplantation), or death from renal causes	0.60 (0.47, 0.77)	***RRR ≈40 %***
DECLARE-TIMI 58[3]	Sustained ≥40% decrease in eGFR to <60 mL/min/1.73 m^2 and/or end-stage renal disease and/or renal death	0.53 (0.43, 0.66)	***RRR ≈47 %***
VERTIS CV*	Sustained ≥40% reduction in eGFR, renal-replacement therapy (dialysis or transplantation), or death from renal causes	0.66 (0.50, 0.88)	***RRR ≈44 %***

*Pre-specified exploratory, intention-to-treat analysis set, 95.0% CI. CV, cardiovascular; CI, confidence interval; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; HR, hazard ratio. [1]Post-hoc exploratory, Perkovic V et al. Nephrol Dial Transplant (2019) 1–9; [2]Pre-specified exploratory, Neal B et al. N Engl J Med 2017;377:644-657; [3]Pre-specified secondary, Wiviott SD et al. N Engl J Med 2019;380:347-357.

Benefits and harms of SGLT2i in patients with CKD

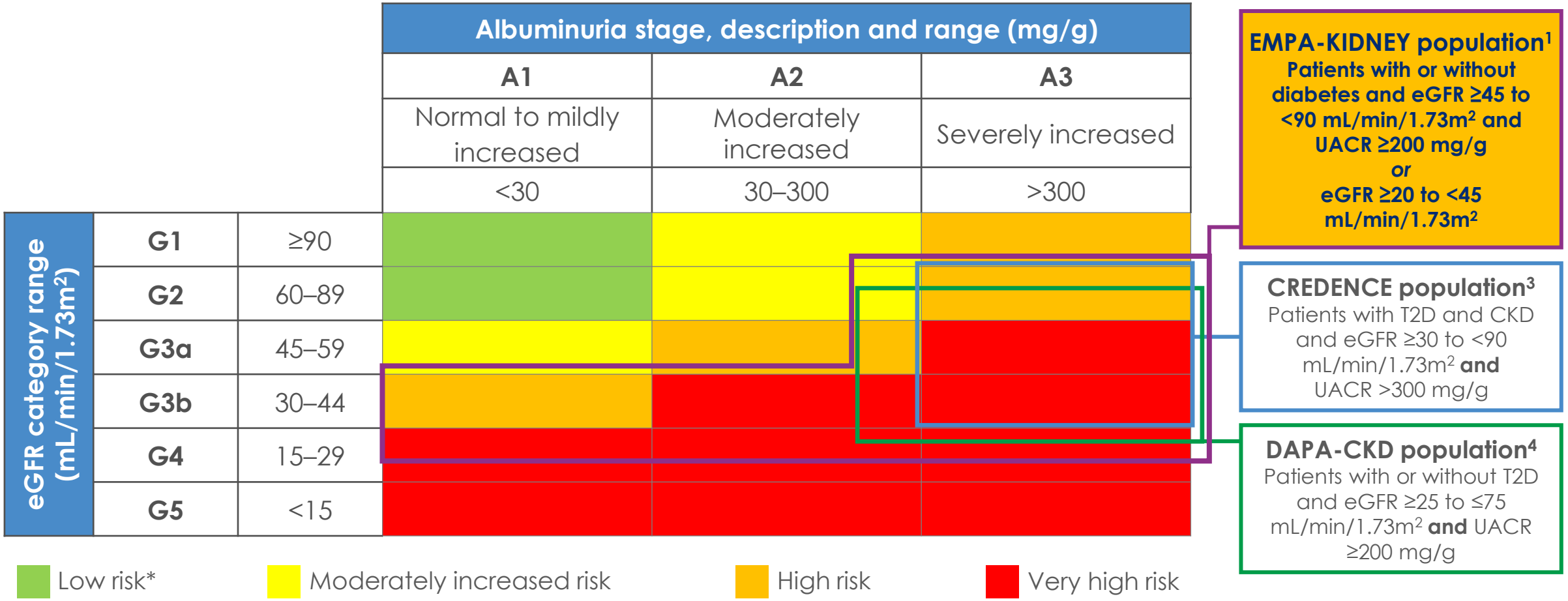
Diabetes



The Nuffield Department of Population Health Renal Studies Group and the SGLT2 inhibitor Meta-Analysis Cardio-Renal Trialists' Consortium, Lancet nov 5 2022*

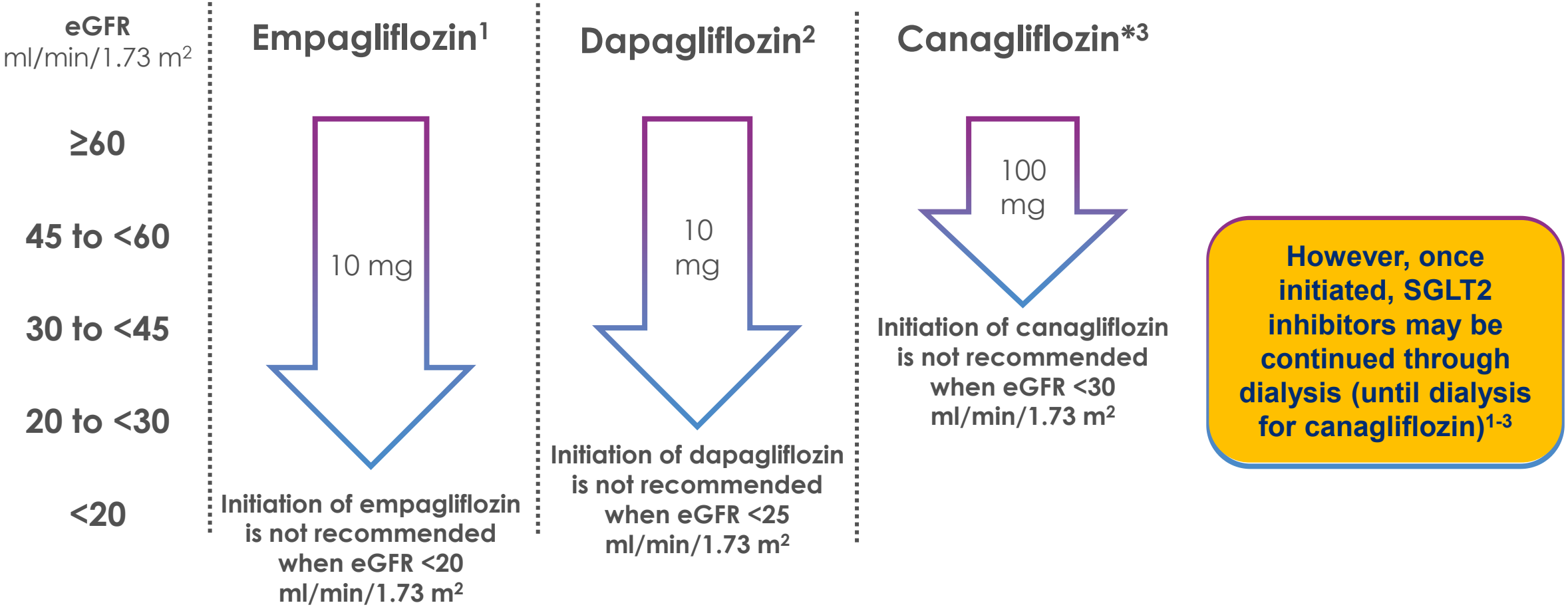
Trials with SGLT2is across the spectrum of renal risk

Prognosis of CKD by eGFR and albuminuria categories[2]



*If no other markers of kidney disease, no CKD.
CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; T2D, type 2 diabetes.
1. The EMPA-KIDNEY Collaborative Group. [Published online ahead of print March 3 2022]. *Nephrol Dial Transplant*. 2022. DOI:10.1093/ndt/gfac054 2. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl*. 2013;3(1):1–150. 3. Perkovic V, *et al. N Engl J Med*. 2019; 380:2295-2306 4. Wheeler DC, *et al. Nephrol Dial Transplant* 2020;35:1700.

Empagliflozin can be initiated with an eGFR as low as 20 ml/min/1.73 m^2 in people with CKD[1]



Please refer to local prescribing information for each compound

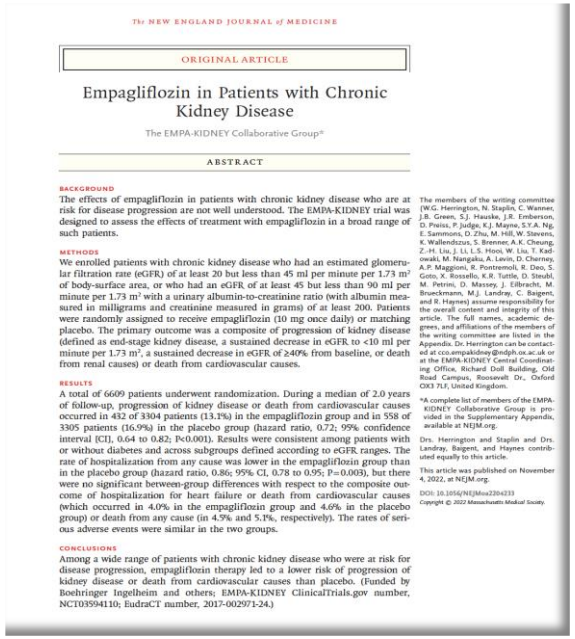
*In individuals tolerating 100 mg who have an eGFR ≥60 ml/min/1.73 m^2 and requiring additional glycaemic control, the dose can be increased to 300 mg.

SGLT2, sodium-glucose co-transporter-2

1. Empagliflozin summary of product characteristics; 2. Dapagliflozin summary of product characteristics; 3. Canagliflozin summary of product characteristics

SGLT2is

Effectiveness in low albuminuria phenotype



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Empagliflozin in Patients with Chronic Kidney Disease

The EMPA-KIDNEY Collaborative Group*

ABSTRACT

BACKGROUND

The effects of empagliflozin in patients with chronic kidney disease who are at risk for disease progression are not well understood. The EMPA-KIDNEY trial was designed to assess the effects of treatment with empagliflozin in a broad range of such patients.

METHODS

We enrolled patients with chronic kidney disease who had an estimated glomerular filtration rate (eGFR) of at least 20 but less than 45 ml per minute per 1.73 m^2 of body-surface area, or who had an eGFR of at least 45 but less than 90 ml per minute per 1.73 m^2 with a urinary albumin-to-creatinine ratio (with albumin measured in milligrams and creatinine measured in grams) of at least 200. Patients were randomly assigned to receive empagliflozin (10 mg once daily) or matching placebo. The primary outcome was a composite of progression of kidney disease (defined as end-stage kidney disease, a sustained decrease in eGFR to <10 ml per minute per 1.73 m^2, a sustained decrease in eGFR of ≥40% from baseline, or death from renal causes) or death from cardiovascular causes.

RESULTS

A total of 6609 patients underwent randomization. During a median of 2.0 years of follow-up, progression of kidney disease or death from cardiovascular causes occurred in 432 of 3304 patients (13.1%) in the empagliflozin group and in 558 of 3305 patients (16.9%) in the placebo group (hazard ratio, 0.72; 95% confidence interval [CI], 0.64 to 0.82; P<0.001). Results were consistent among patients with or without diabetes and across subgroups defined according to eGFR ranges. The rate of hospitalization from any cause was lower in the empagliflozin group than in the placebo group (hazard ratio, 0.86; 95% CI, 0.78 to 0.95; P=0.003), but there were no significant between-group differences with respect to the composite outcome of hospitalization for heart failure or death from cardiovascular causes (which occurred in 4.0% in the empagliflozin group and 4.6% in the placebo group) or death from any cause (in 4.5% and 5.1%, respectively). The rates of serious adverse events were similar in the two groups.

CONCLUSIONS

Among a wide range of patients with chronic kidney disease who were at risk for disease progression, empagliflozin therapy led to a lower risk of progression of kidney disease or death from cardiovascular causes than placebo. (Funded by Boehringer Ingelheim and others; EMPA-KIDNEY ClinicalTrials.gov number, NCT03594110; EudraCT number, 2017-002971-24.)

The members of the writing committee (W.G. Herrington, N. Staplin, C. Wanner, J.B. Green, S.J. Hauske, J.R. Emberson, D. Preiss, P. Judge, K.J. Mayne, S.Y.A. Ng, E. Sammons, O. Zhu, M. Hill, W. Stevens, K. Wallendszus, S. Brenner, A.K. Cheung, Z.-H. Liu, J. Li, L.S. Hooi, W. Liu, T. Kadowaki, M. Nangaku, A. Levin, D. Cherney, A.P. Maggioni, R. Pontremoli, R. Deo, S. Goto, X. Rossello, K.R. Tuttle, D. Steubl, M. Petrini, D. Massey, J. Eilbracht, M. Brueckmann, M.J. Landray, C. Baigent, and R. Haynes) assume responsibility for the overall content and integrity of this article. The full names, academic degrees, and affiliations of the members of the writing committee are listed in the Appendix. Dr. Herrington can be contacted at cco.empakidney@ndph.ox.ac.uk or at the EMPA-KIDNEY Central Coordinating Office, Richard Doll Building, Old Road Campus, Roosevelt Dr., Oxford OX3 7LF, United Kingdom.

*A complete list of members of the EMPA-KIDNEY Collaborative Group is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Herrington and Staplin and Drs. Landray, Baigent, and Haynes contributed equally to this article.

This article was published on November 4, 2022, at NEJM.org.

DOI: 10.1056/NEJMoa2204233

Benefit independent of diabetes status and baseline eGFR

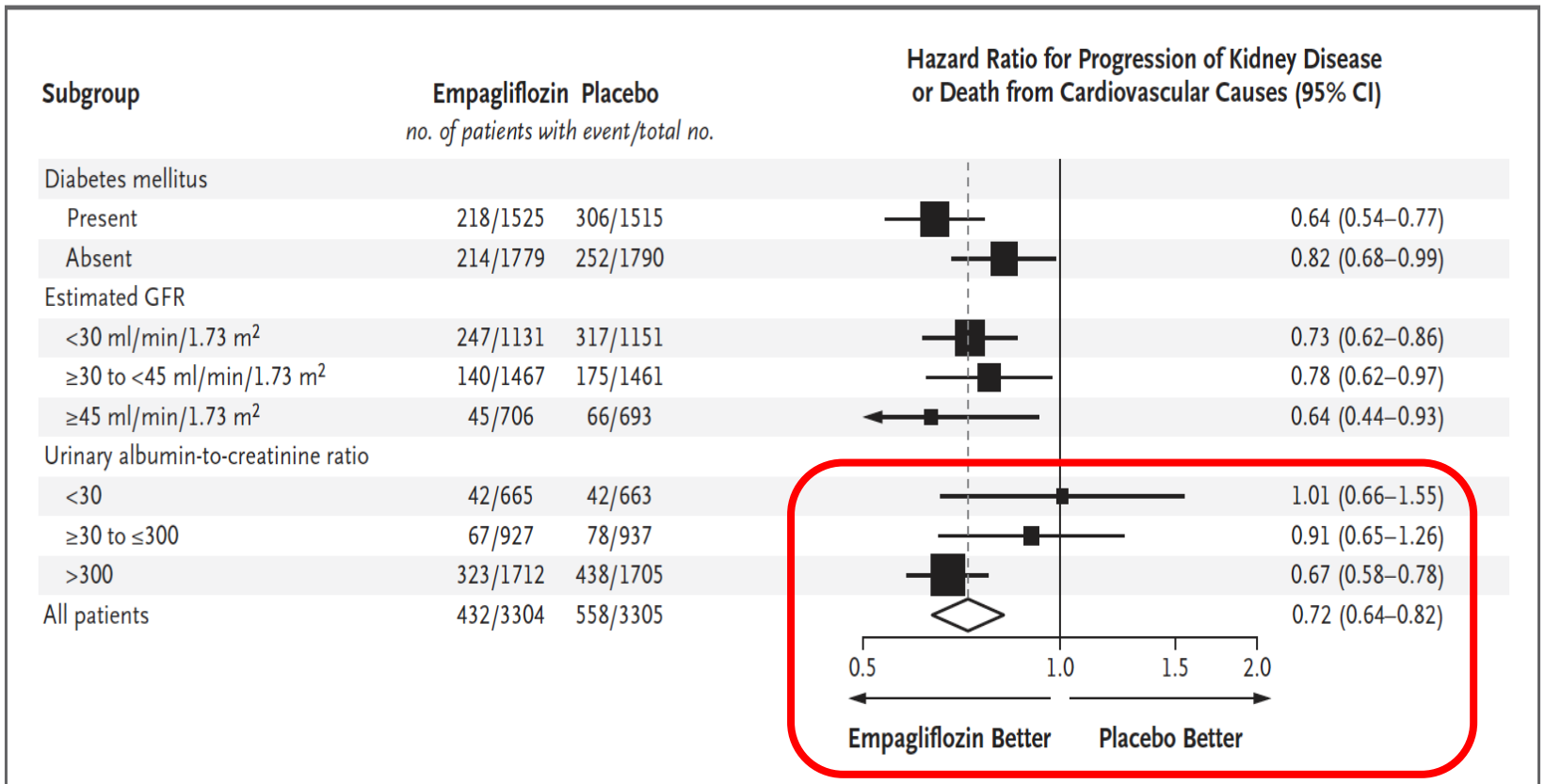


Figure 2. Primary Outcome in Key Prespecified Subgroups.

Shown are the hazard ratios for the primary outcome in key prespecified subgroups defined according to baseline characteristics. Hazard ratios and confidence intervals were estimated with the use of Cox proportional-hazards regression models, with adjustment for age, sex, history of diabetes, estimated glomerular filtration rate (GFR), urinary albumin-to-creatinine ratio (with albumin measured in milligrams and creatinine measured in grams), and geographic region. The area of each box is proportional to the inverse of the variance of the log hazard ratios. The arrow indicates that the boundary of the 95% confidence interval is outside the graphed area. The diamond represents the result of the primary analysis, with the width of the diamond indicating the 95% confidence interval. The dashed line indicates the hazard ratio in the overall population.

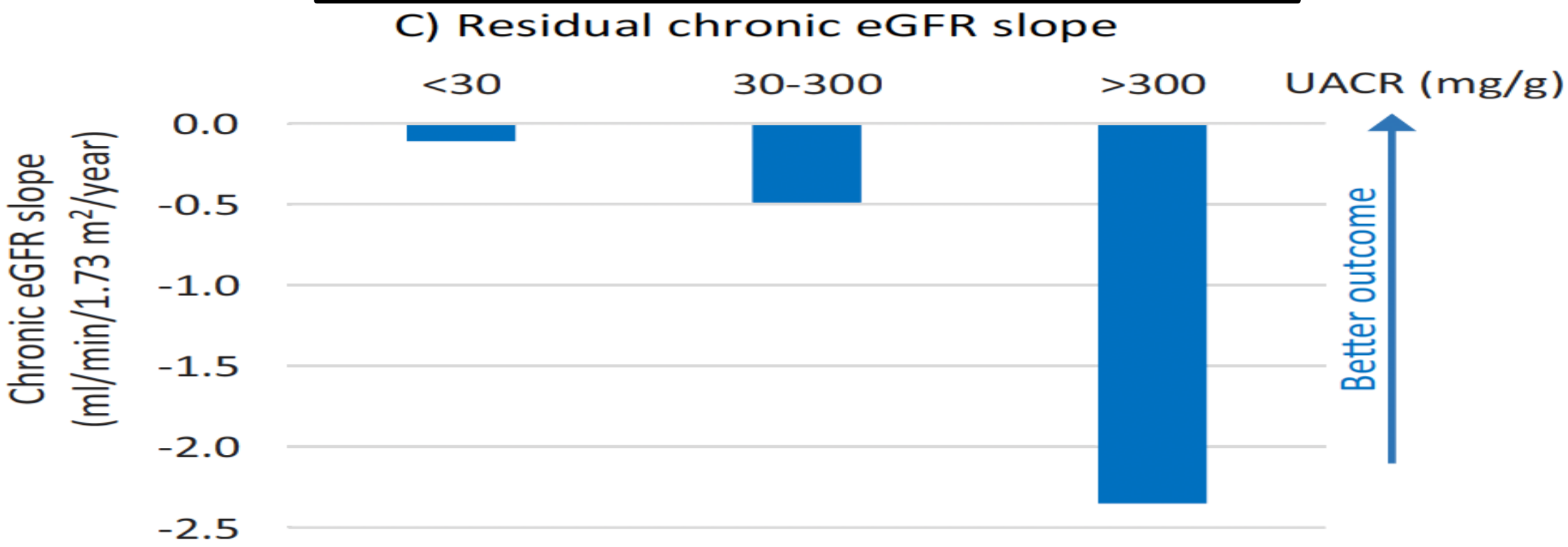
Clinical Kidney Journal, 2023, vol. 16, no. 8, 1187–1198

EDITORIAL COMMENT

EMPA-KIDNEY: expanding the range of kidney protection by SGLT2 inhibitors

Beatriz Fernández-Fernandez[1,2,3,4], Pantelis Sarafidis[5], Maria José Soler[2,4,6] and Alberto Ortiz[1,2,3,4]

Chronic eGFR slopes according to baseline UACR category in EMPAKIDNEY



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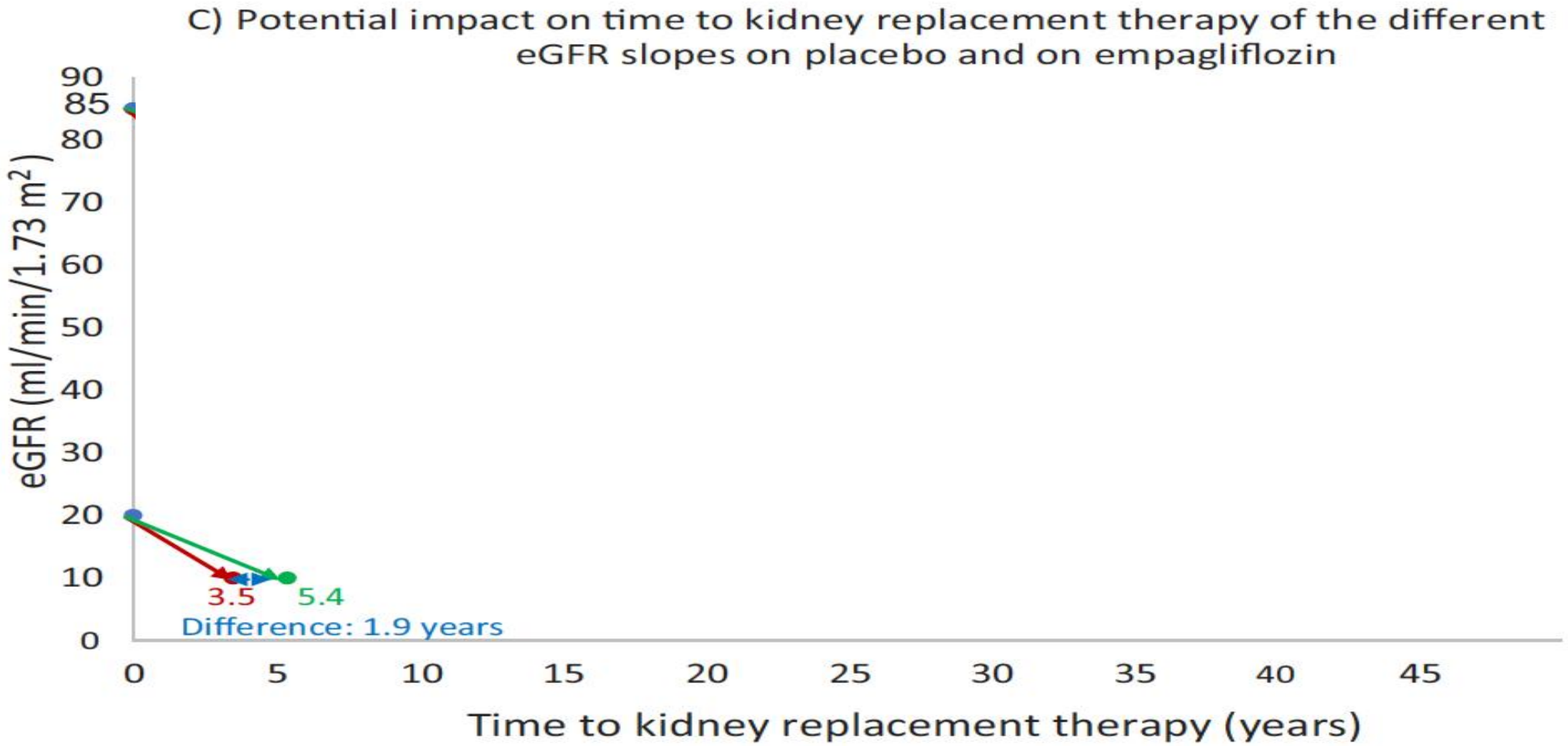
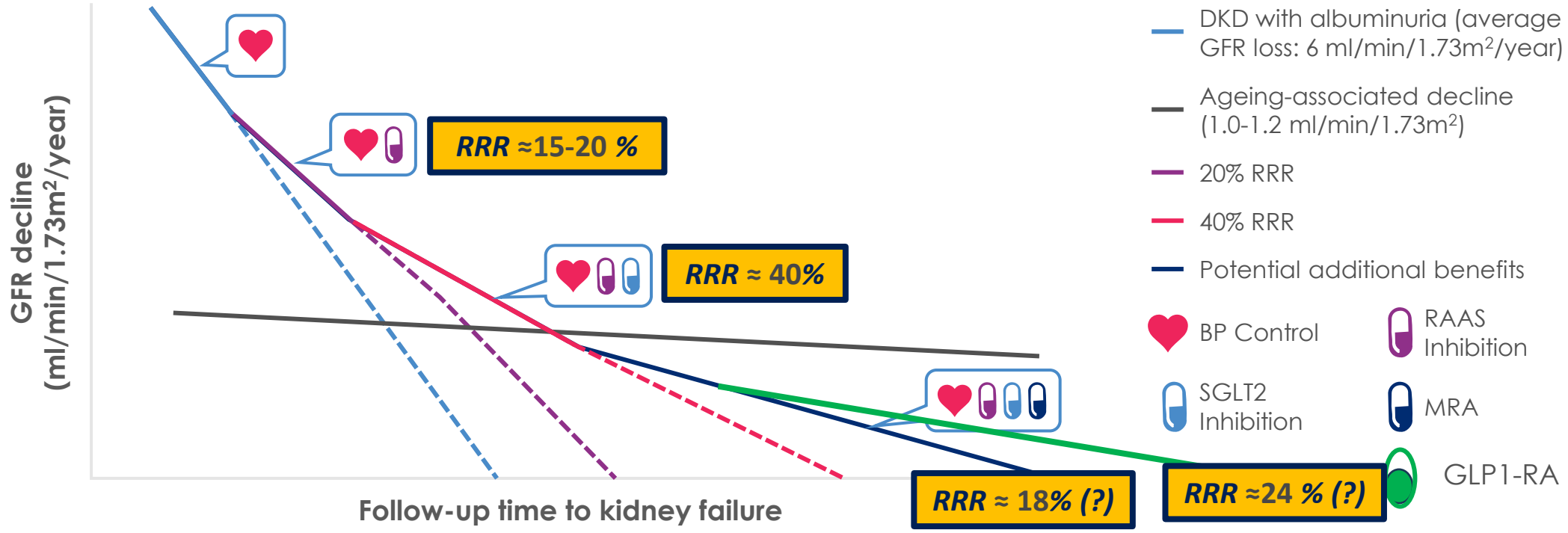
https:/doi.org/10.1093/ckj/sfad082
Advance Access Publication Date: 16 June 2023
Editorial Comment

Hypothetical transformation of chronic eGFR slopes into time to kidney failurein the EMPAKIDNEY Trial



With multifactorial intervention, the course of CKD has changed considerably

Incremental Benefit of Multifactorial Intervention on GFR Decline in Patients with CKD and T2D



BP, blood pressure; CKD, chronic kidney disease; DKD, diabetic kidney disease; GFR, glomerular filtration rate; MRA, mineralocorticoid receptor antagonist; RAAS, renin–angiotensin–aldosterone system; RRR, relative risk reduction; SGLT2, sodium-glucose co-transporter-2; T2D, type 2 diabetes. Fioretto P & Pontremoli R. Nat Rev Nephrol 2022;18:78

Take-Home messages

- **SGLT2-inhibition is mandatory for renal protection in CKD patients and its effectiveness is far greater as compared to other disease-modifying drug classes**

- **SGLT2is are effective also in *low albuminuria - low eGFR patients*, a very prevalent phenoytype in clinical practice**

- **Absolute benefit of SGLT2is treatment is greatest in fast progressors. A larger relative benefit is observed in non-albuminuric patients: the earlier treatment is started, the better the outcome.**