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LETTER TO THE EDITOR

Relook at DPP-4 inhibitors in the era of SGLT-2 inhibitors

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Abstract

SGLT-2 inhibitors (SGLT-2Is) have significantly improved cardio-renal outcomes and are preferred agents in people with cardiovascular diseases, heart failure, and diabetic kidney disease. Similarly, GLP-1 receptor agonists (GLP-1RAs) have significantly improved atherosclerotic cardiovascular outcomes. To this end, DPP-4 inhibitors (DPP-4Is) are cardiac-neutral drugs. While long-acting GLP-1RAs have shown a favorable HbA1c lowering compared to DPP-4Is, there is no clinically meaningful HbA1c lowering difference between SGLT-2Is *vs* DPP-4Is. Moreover, the glucose-lowering potential of SGLT-2Is gets compromised with a progressive decline in renal functions, unlike DPP-4Is. Furthermore, the HbA1c lowering potential of DPP-4Is is favorable in people with T2DM having a modest baseline HbA1c (8.0%-8.5%) compared with SGLT-2Is which lowers HbA1c larger in a background of higher baseline HbA1c (> 8.5%-9.0%). These findings suggest that the role of DPP-4Is in the management of type 2 diabetes mellitus cannot be completely ignored even in the era of SGLT-2Is.

Key Words: DPP-4 inhibitors; SGLT-2 inhibitors; GLP-1 receptor agonists; Cardiovascular outcomes; Renal outcomes

Core Tip: Despite the newer anti-diabetic agents such as SGLT-2 inhibitors (SGLT-2Is) and GLP-1 receptor agonists have taken the center stage in the management of type 2 diabetes mellitus due to additional cardiac and renal benefits, the role of DPP-4 inhibitors (DPP-4Is) cannot be undermined. HbA1c lowering potential of DPP-4Is are nearly similar to SGLT-2Is and surprisingly larger in a background of modest baseline HbA1c compared with SGLT-2Is. Moreover, the HbA1c lowering abilities of SGLT-2Is are compromised with declining renal function while DPP-4Is reduce HbA1c favorably in people with chronic kidney disease regardless of impaired kidney functions.

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TO THE EDITOR

We read with interest a minireview by Florentin *et al*[1] putting their arguments in favor of DPP-4 inhibitors (DPP-4Is) as a second-line drug after metformin in people with type 2 diabetes mellitus (T2DM) in particular who are elderly and have chronic kidney disease (CKD) stage 3A or lower. This wonderfully written minireview discusses the role of DPP-4Is in the era of two other novel anti-diabetic agents such as SGLT-2 inhibitors (SGLT-2Is) and GLP-1 receptor agonists (GLP-1RAs) that have shown a remarkably beneficial effect on cardiovascular (CV) and renal endpoints making them an ideal second or arguably even first-line drug in people with T2DM having established CV disease (CVD), heart failure (HF) and CKD. While authors have discussed the pharmacological differences amongst different DPP-4Is and put a perspective on the CV outcome trials in the era of SGLT-2Is and GLP-1RAs, few vital details seem to be missing and some of the statements appear rather ambiguous that need clarification. The most important area that is surprisingly missing in this review is the efficacy comparison between DPP-4Is *vs* SGLT-2Is or GLP-1RAs. Expectedly, the HbA1c lowering effect of DPP-4Is would be inferior to GLP-1RAs owing to their mechanism of action that causes a physiological *vs* pharmacological rise of GLP-1 respectively and indeed, several head-to-head studies of long-acting GLP-1RAs have shown a superior HbA1c lowering beside a significant reduction in weight and systolic blood pressure (SBP) when compared with DPP-4Is. However, the HbA1c lowering effect of DPP-4Is is not clinically meaningful different from SGLT-2Is. To this end, several studies have evaluated the HbA1c lowering effect of SGLT-2Is *vs* DPP4Is in the past decade[2-8]. Although in most of these SGLT-2Is head-to-head studies with DPP-4Is, HbA1c reduction was similar between the two drug classes; DPP-4Is were used as an open-label active comparator arm only for exploratory analysis. One study that compared empagliflozin 10 and 25 mg with 100 mg sitagliptin as an active comparator in a double-blind randomized fashion found no difference in HbA1c lowering[3]. However, two studies that compared canagliflozin 100 and 300 mg with sitagliptin 100 mg as an active comparator in a double-blind randomized fashion, found 300 mg canagliflozin to be superior to 100 mg sitagliptin in HbA1c lowering, though no difference was noted with 100 mg canagliflozin (Table 1)[6,7]. Meta-analyses that compared HbA1c lowering with DPP-4Is *vs* SGLT-2Is yielded discordant results[9-12]. While some found no difference in HbA1c lowering, others showed a small but significant HbA1c lowering with SGLT-2Is compared to DPP-4Is (Table 1). Notably, weight and SBP reduction were consistently superior with SGLT-2I *vs* DPP-4I in all these head-to-head studies including meta-analyses. Another interesting piece of missing information that needs discussion is the differential HbA1c lowering effect of DPP-4Is vs. SGLT-2Is stratified on baseline HbA1c. While the SGLT-2Is appear to lower the HbA1c more favorably compared with DPP-4Is in the background of higher baseline value (HbA1c 8.5%-9.0%), DPP-4Is lowered HbA1c more favorably compared with SGLT-2I in people having a modest baseline HbA1c value (< 8%-8.5%) (Table 1)[13-15]. This finding suggests DPP-4Is may have a favorable effect on HbA1c lowering compared to SGLT-2Is in people with T2DM having a modest baseline HbA1c, in absence of high CV risk. Although a reduction in HbA1c is always larger when baseline HbA1c is high, we do not know exactly why DPP-4Is reduce HbA1c larger compared to the SGLT-2Is when the baseline value is modest. Since SGLT-2Is HbA1c lowering ability is dependent on the renal threshold of glucose excretion (RT_G), modest baseline HbA1c may not produce further lowering of RT_G.

Nevertheless, we humbly disagree with the author's conclusion about "the lack of evidence with SGLT-2Is and GLP-1RAs in elderly patients with diabetes as well as the contraindication of SGLT-2Is in patients with CKD, grade 3A and lower, make DPP-4Is a safe choice in such populations." Let us recall that: (1) About one-fourth patients population (24.2%) in HF trial of SGLT-2I dapagliflozin were elderly [≥ 75 years, median age 79 years (76-82 years)] and they benefitted equally [Hazard ratio (HR), 0.68; 95% Confidence interval (CI), 0.53-0.88] when compared to the overall population (HR, 0.74; 95%CI, 0.65-0.85) in terms of reduction of the primary composite endpoint of CV death or HF hospitalization (HHF) or urgent HF visits ($P_{interaction}$ = 0.76)[16]; (2) Mean age of the population in CV-, HF- and renal-outcome trials of SGLT-2Is varied from as low as 62 years in renal outcome trial of dapagliflozin (DAPA-CKD) to as high as 72 years in HF trial of empagliflozin (EMPEROR-Preserved) that found a significantly beneficial renal and CV effect respectively[17]; (3) Current guidelines recommend using SGLT-2Is in patients with CKD if eGFR is ≥ 30 mL/min/1.73 m^2 and in addition, empagliflozin has been granted an additional label of use up to eGFR ≥ 20 mL/min/m^2 in patients with HF with reduced ejection fraction and CKD[18]; (4) The latest Kidney Disease: Improving Global Outcomes 2022 guideline which is currently under public review recommend using SGLT-2Is in patients with CKD if eGFR ≥ 20 mL/min/1.73 m^2 regardless of background HF. Moreover, once SGLT-2Is are initiated it is reasonable to continue even if the eGFR falls below 20 mL/min per 1.73 m^2 unless it is not tolerated or kidney

Table 1 HbA1c reduction with SGLT-2 inhibitors *vs* DPP-4 inhibitors

Ref.	Study duration (wk)	Background therapy	*n* (Active drug)	Baseline HbA1c	SGLT-2I (A) (% HbA1c reduction)	DPP-4I (B) (% HbA1c reduction)	Δ A minus B (95%CI)
HbA1c reduction with SGLT-2Is *vs* DPP-4Is in head-to-head randomized controlled trials							
Rosenstock *et al*[2], 2012	12	Metformin	193	7.6%-7.8%	-0.76 (Cana 100 mg) -0.92 (Cana 300 mg)	-0.74 (Sita 100 mg)	NC, (B) exploratory
Roden *et al*[3], 2013	24	Drug naïve	671	7.9%	-0.66 (Empa 10 mg) -0.78 (Empa 25 mg)	-0.66 (Sita 100 mg)	0.0 (-0.15, 0.14) -0.12 (-0.26, 0.03)
Rosenstock *et al*[4], 2013	12	Metformin	212	7.9%-8.1%	-0.56 (Empa 10 mg) -0.55 (Empa 25 mg)	-0.45 (Sita 100 mg)	NC, (B) exploratory
Ferrannini *et al*[5], 2013	90	Metformin	332	7.9%-8%	-0.34 (Empa 10 mg) -0.63 (Empa 25 mg)	-0.40 (Sita 100 mg)	NC, (B) exploratory
Lavalle-González *et al*[6], 2013	52	Metformin	1079	7.9%	-0.73 (Cana 100 mg) -0.88 (Cana 300 mg[a])	-0.73 (Sita 100 mg)	-0.15[a] (-0.27, -0.03)
Schernthaner *et al*[7], 2013	52	Metformin + SU	755	8.1%	-1.03 (Cana 300 mg[a])	-0.66 (Sita 100 mg)	-0.37[a] (-0.50, -0.25)
Amin *et al*[8], 2015	12	Metformin	328	8.1%	-0.80 (Ertu 5 mg)	-0.87 (Sita 100 mg)	NC, (B) exploratory
Difference in HbA1c reduction with SGLT-2Is *vs* DPP-4Is in meta-analyses							
Pinto *et al*[9], 2015	≥ 12	LSM, Metformin, SU	NR (6 studies)	-	SGLT-2Is	DPP-4Is	-0.15[a] (-0.21, -0.08)
Maruthur *et al*[10], 2016	≤ 52	Metformin	1278 (4 studies)	-	SGLT-2Is	DPP-4Is	(B) minus (A) = +0.17[a] (0.08, 0.26)
Wang *et al*[11], 2018	12-78	Metformin	3454 (7 studies)	-	SGLT-2Is	DPP-4Is	(B) minus (A) = +0.11 (-0.03, 0.25)
Mishriky *et al*[12], 2018	≤ 26	Metformin	2462 (6 studies)	-	SGLT-2Is	DPP-4Is	(B) minus (A) = +0.05 (-0.05, 0.16)
	≥ 52	Metformin	1872 (3 studies)	-	SGLT-2Is	DPP-4Is	(B) minus (A) = +0.11[a] (0.03, 0.20)
HbA1c reduction with SGLT-2Is *vs* DPP-4Is in head-to-head randomized controlled trial stratified on baseline HbA1c							
Rosenstock *et al*[13], 2015	24	Metformin	190	> 9%	-1.87 (Dapa 10 mg)	-1.32 (Saxa 5 mg)	NC
			103	< 8%	-0.45 (Dapa 10 mg)	-0.69 (Saxa 5 mg)	
Lewin *et al*[14], 2015	24	LSM	116	≥ 8.5%	-1.66 (Empa 25 mg) -1.54 (Empa 10 mg	-1.07 (Lina 5 mg)	NC
			473	< 8.5%	-0.66 (Empa 25 mg) -0.56 (Empa 10 mg)	-0.55 (Lina 5 mg)	NC
DeFronzo *et al*[15], 2015	24	Metformin	101	≥ 8.5%	-1.22 (Empa 25 mg) -1.29 (Empa 10 mg)	-0.99 (Lina 5 mg)	NC
			508	< 8.5%	-0.43 (Empa 25 mg) -0.46 (Empa 10 mg)	-0.62 (Lina 5 mg)	NC

[a](A) superior over (B).

SGLT-2Is: SGLT-2 inhibitors; DPP-4Is: DPP4 inhibitors; Cana: Canagliflozin; Empa: Empagliflozin; Dapa: Dapagliflozin; Ertu: Ertugliflozin; Sita: Sitagliptin; Saxa: Saxagliptin; Lina: Linagliptin; SU: Sulfonylureas; LSM: Life style modification; NC: Not compared.

replacement therapy is initiated[19]; (5) Although there are no head-to-head randomized controlled trials that compared CV outcomes between DPP-4Is *vs* DPP-4Is, several large real-world, propensity-matched studies showed a significant reduction in HHF with SGLT-2Is compared with DPP-4Is in patients with T2DM, regardless of baseline high CV risk[20]; and (6) Finally, the 2011 European Diabetes Working Party for Older People clinical guideline that recommended DPP-4I as a second-line drug of choice in elderly were made before the US Federal Drug Administration approval of first SGLT-2I

canagliflozin in 2013 and first positive CV outcome with empagliflozin in 2015. These findings suggest author's conclusion is discordant with the available evidence[21].

FOOTNOTES

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REFERENCES

1 **Florentin M**, Kostapanos MS, Papazafiropoulou AK. Role of dipeptidyl peptidase 4 inhibitors in the new era of antidiabetic treatment. *World J Diabetes* 2022; **13**: 85-96 [PMID: 35211246 DOI: 10.4239/wjd.v13.i2.85]
2 **Rosenstock J**, Aggarwal N, Polidori D, Zhao Y, Arbit D, Usiskin K, Capuano G, Canovatchel W; Canagliflozin DIA 2001 Study Group. Dose-ranging effects of canagliflozin, a sodium-glucose cotransporter 2 inhibitor, as add-on to metformin in subjects with type 2 diabetes. *Diabetes Care* 2012; **35**: 1232-1238 [PMID: 22492586 DOI: 10.2337/dc11-1926]
3 **Roden M**, Weng J, Eilbracht J, Delafont B, Kim G, Woerle HJ, Broedl UC; EMPA-REG MONO trial investigators. Empagliflozin monotherapy with sitagliptin as an active comparator in patients with type 2 diabetes: a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Diabetes Endocrinol* 2013; **1**: 208-219 [PMID: 24622369 DOI: 10.1016/S2213-8587(13)70084-6]
4 **Rosenstock J**, Seman LJ, Jelaska A, Hantel S, Pinnetti S, Hach T, Woerle HJ. Efficacy and safety of empagliflozin, a sodium glucose cotransporter 2 (SGLT2) inhibitor, as add-on to metformin in type 2 diabetes with mild hyperglycaemia. *Diabetes Obes Metab* 2013; **15**: 1154-1160 [PMID: 23906374 DOI: 10.1111/dom.12185]
5 **Ferrannini E**, Berk A, Hantel S, Pinnetti S, Hach T, Woerle HJ, Broedl UC. Long-term safety and efficacy of empagliflozin, sitagliptin, and metformin: an active-controlled, parallel-group, randomized, 78-week open-label extension study in patients with type 2 diabetes. *Diabetes Care* 2013; **36**: 4015-4021 [PMID: 24186878 DOI: 10.2337/dc13-0663]
6 **Lavalle-González FJ**, Januszewicz A, Davidson J, Tong C, Qiu R, Canovatchel W, Meininger G. Efficacy and safety of canagliflozin compared with placebo and sitagliptin in patients with type 2 diabetes on background metformin monotherapy: a randomised trial. *Diabetologia* 2013; **56**: 2582-2592 [PMID: 24026211 DOI: 10.1007/s00125-013-3039-1]
7 **Schernthaner G**, Gross JL, Rosenstock J, Guarisco M, Fu M, Yee J, Kawaguchi M, Canovatchel W, Meininger G. Canagliflozin compared with sitagliptin for patients with type 2 diabetes who do not have adequate glycemic control with metformin plus sulfonylurea: a 52-week randomized trial. *Diabetes Care* 2013; **36**: 2508-2515 [PMID: 23564919 DOI: 10.2337/dc12-2491]
8 **Amin NB**, Wang X, Jain SM, Lee DS, Nucci G, Rusnak JM. Dose-ranging efficacy and safety study of ertugliflozin, a sodium-glucose co-transporter 2 inhibitor, in patients with type 2 diabetes on a background of metformin. *Diabetes Obes Metab* 2015; **17**: 591-598 [PMID: 25754396 DOI: 10.1111/dom.12460]
9 **Pinto LC**, Rados DV, Remonti LR, Kramer CK, Leitao CB, Gross JL. Efficacy of SGLT2 inhibitors in glycemic control, weight loss and blood pressure reduction: a systematic review and meta-analysis. *Diabetol Metab Syndr* 2015; **7**: A58 [DOI: 10.1186/1758-5996-7-s1-a58]
10 **Maruthur NM**, Tseng E, Hutfless S, Wilson LM, Suarez-Cuervo C, Berger Z, Chu Y, Iyoha E, Segal JB, Bolen S. Diabetes Medications as Monotherapy or Metformin-Based Combination Therapy for Type 2 Diabetes: A Systematic Review and Meta-analysis. *Ann Intern Med* 2016; **164**: 740-751 [PMID: 27088241 DOI: 10.7326/M15-2650]
11 **Wang Z**, Sun J, Han R, Fan D, Dong X, Luan Z, Xiang R, Zhao M, Yang J. Efficacy and safety of sodium-glucose cotransporter-2 inhibitors *vs* dipeptidyl peptidase-4 inhibitors as monotherapy or add-on to metformin in patients with type 2 diabetes mellitus: A systematic review and meta-analysis. *Diabetes Obes Metab* 2018; **20**: 113-120 [PMID: 28656707 DOI: 10.1111/dom.13047]
12 **Mishriky BM**, Tanenberg RJ, Sewell KA, Cummings DM. Comparing SGLT-2 inhibitors to DPP-4 inhibitors as an add-on therapy to metformin in patients with type 2 diabetes: A systematic review and meta-analysis. *Diabetes Metab* 2018; **44**: 112-120 [PMID: 29477373 DOI: 10.1016/j.diabet.2018.01.017]
13 **Rosenstock J**, Hansen L, Zee P, Li Y, Cook W, Hirshberg B, Iqbal N. Dual add-on therapy in type 2 diabetes poorly

controlled with metformin monotherapy: a randomized double-blind trial of saxagliptin plus dapagliflozin addition *vs* single addition of saxagliptin or dapagliflozin to metformin. *Diabetes Care* 2015; **38**: 376-383 [PMID: 25352655 DOI: 10.2337/dc14-1142]

14 **Lewin A**, DeFronzo RA, Patel S, Liu D, Kaste R, Woerle HJ, Broedl UC. Initial combination of empagliflozin and linagliptin in subjects with type 2 diabetes. *Diabetes Care* 2015; **38**: 394-402 [PMID: 25633662 DOI: 10.2337/dc14-2365]

15 **DeFronzo RA**, Lewin A, Patel S, Liu D, Kaste R, Woerle HJ, Broedl UC. Combination of empagliflozin and linagliptin as second-line therapy in subjects with type 2 diabetes inadequately controlled on metformin. *Diabetes Care* 2015; **38**: 384-393 [PMID: 25583754 DOI: 10.2337/dc14-2364]

16 **Martinez FA**, Serenelli M, Nicolau JC, Petrie MC, Chiang CE, Tereshchenko S, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Ponikowski P, Sabatine MS, DeMets DL, Dutkiewicz-Piasecka M, Bengtsson O, Sjöstrand M, Langkilde AM, Jhund PS, McMurray JJV. Efficacy and Safety of Dapagliflozin in Heart Failure With Reduced Ejection Fraction According to Age: Insights From DAPA-HF. *Circulation* 2020; **141**: 100-111 [PMID: 31736328 DOI: 10.1161/CIRCULATIONAHA.119.044133]

17 **Singh AK**, Singh R. Similarities and differences in cardio-renal outcome trials with SGLT-2 inhibitors: call for pharmacogenomic studies? *Pharmacogenomics Res Pers Med* 2022 [DOI: 10.21037/prpm-22-2]

18 **Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group**. . KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. *Kidney Int* 2020; **98**: S1-S115 [PMID: 32998798 DOI: 10.1016/j.kint.2020.06.019]

19 KDIGO 2022 Clinical Practice Guidelines for Diabetes Management in Chronic Kidney Disease. [Accessed March 5, 2022]. Available from: https://kdigo.org

20 **Singh AK**, Singh R. Heart failure hospitalization with SGLT-2 inhibitors: a systematic review and meta-analysis of randomized controlled and observational studies. *Expert Rev Clin Pharmacol* 2019; **12**: 299-308 [PMID: 30817235 DOI: 10.1080/17512433.2019.1588110]

21 **Sinclair AJ**, Paolisso G, Castro M, Bourdel-Marchasson I, Gadsby R, Rodriguez Mañas L; European Diabetes Working Party for Older People. European Diabetes Working Party for Older People 2011 clinical guidelines for type 2 diabetes mellitus. Executive summary. *Diabetes Metab* 2011; **37** Suppl 3: S27-S38 [PMID: 22183418 DOI: 10.1016/S1262-3636(11)70962-4]

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