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### Paper:

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## **Dapagliflozin and renal function**

Letter related to:

Diabetes and kidney disease: the role of Sodium-Glucose Cotransporter-2 (SGLT-2) and SGLT-2 inhibitors in modifying disease outcomes. Mende CW. *Curr Med Res Opin.* 2016 Dec 15:1-37. [Epub ahead of print].

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Dear Sir

We read with interest the recently published review published by Mende entitled 'Diabetes and kidney disease: the role of Sodium-Glucose Cotransporter-2 (SGLT-2) and SGLT-2 inhibitors in modifying disease outcomes [1]. Of interest, there are isolated incidents of a deterioration in renal function associated with the use of SGLT-2 inhibitors in clinical trials [2, 3]. We agree with Mende and other publications [4] providing experimental evidence to support that SGLT-2 inhibitors are nephroprotective rather than nephrotoxic.

We have examined changes in renal function in our routine real-world clinic practice database before and during treatment with dapagliflozin. Dapagliflozin is recommended by NICE as monotherapy or in combination with other anti-diabetic medications including insulin in type 2 diabetes [5]. In our practice, dapagliflozin was added to concomitant anti-diabetic medications including insulin and GLP-1 agonists. We undertook a prospective audit of patients who had been initiated on dapagliflozin and had undergone at least one follow-up visit. A paired t-test was performed to examine changes in serum creatinine and estimated glomerular filtration rate (eGFR) before and during treatment with dapagliflozin. We identified 148 patients (63% male) with a mean age of  $57.8 \pm 9.0$  years who had received a mean duration of treatment of  $15.6 \pm 8.7$  months with dapagliflozin. We observed no significant changes in pre and post treatment serum creatinine ( $76 \pm 18$  vs  $77 \pm 21 \mu\text{mol/L}$ ,  $P=0.509$ ) and eGFR ( $92 \pm 23$  vs  $92 \pm 24$  mL/min per  $1.73 \text{ m}^2$ ,  $P=0.983$ ). A modest but significant reduction in systolic blood pressure ( $139 \pm 19$  vs  $134 \pm 19$  mmHg,  $P=0.002$ ) and diastolic blood pressure ( $79 \pm 10$  vs  $77 \pm 8$  mmHg,  $P=0.025$ ) was observed. Significant reduction in HbA1c, body weight and doby mass index (BMI) were also observed as shown in Table 1. In those individuals with a follow-up of less than 6

months (n=23), eGFR decreased from  $87 \pm 20$  to  $80 \pm 20$  mL/min per  $1.73 \text{ m}^2$ ,  $P=0.02$ ).

In conclusion, no significant change in renal function was observed in our cohort (n=148), who had been treated with dapagliflozin for a mean duration of 15.6 months. Our finding supported the idea that SGLT2 inhibitors are not nephrotoxic. Larger studies with long-term follow-up are warranted to confirm the nephroprotective effect of SGLT2 inhibitors.

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### **Declaration of financial and other interest**

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### **References**

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**Table 1** Mean change in renal function, blood pressure, HbA1c and body weight in patients receiving dapagliflozin

<b>Measurement</b>	<b>Baseline</b>	<b>Follow-up</b>	<b>Mean difference (95%CI)</b>	<b>P</b>
Creatinine ( $\mu\text{mol/L}$ )	76 $\pm$ 18	77 $\pm$ 21	1 (-2, 4)	0.509
eGFR ( $\text{mL/min per } 1.73\text{m}^2$ )	92 $\pm$ 23	92 $\pm$ 24	0 (-3, 3)	0.983
Weight (kg)	105 $\pm$ 18	102 $\pm$ 18	-3 (-4,-2)	<0.001
BMI ( $\text{kg/m}^2$ )	36 $\pm$ 6	35 $\pm$ 6	-1 (-1.4,-0.8)	<0.001
SBP (mmHg)	139 $\pm$ 19	134 $\pm$ 19	-5 (-8,-2)	0.002
DBP (mmHg)	79 $\pm$ 10	77 $\pm$ 8	-2 (-4, 0.2)	0.025
HbA1c (mmol/mol)	82 $\pm$ 18	69 $\pm$ 13	-13 (-16, -10)	<0.001

Unless indicated otherwise, data are given as the mean  $\pm$  SD.

eGFR: estimated glomerular filtration rate; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; CI: confidence interval.