Canagliflozin use in patients with reduced renal function at baseline is still associated with significant improvements in multiple parameters: results from the Association of British Clinical Diabetologists (ABCD) canagliflozin audit

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Introduction

Canagliflozin has been demonstrated to improve HbA1c, reduce weight, reduce cardiovascular disease risk and preserve renal function in people with diabetes(1,2).

Due to its mechanism of action on the sodium glucose linked transporter-2 (SGLT2) it is currently only licensed for initiation in those with an eGFR >60mL/min/1.73m^2. Although following commencement it can be used down to a lower eGFR, it is recommended to be discontinued in those with an eGFR<45mL/min/1.73m^2

The UK nationwide canagliflozin audit was launched in 2016 so clinicians could record routinely collected, anonymised patient data. More recently this has been added to with data being provided from clinical commissioning groups as well. The aim of the audit programme is to provide evidence of outcomes from canagliflozin in a real world cohort.

Methods

Data were extracted from the UK ABCD nationwide audit programme. Patients with a minimum dataset of a baseline eGFR (n=2,948) and then, for each variable, a baseline and subsequent follow-up measurement at 6-months and 12-months, were included in the analysis.

Patients were stratified into groups as follows:

- Group CKD1 – eGFR ≥90mL/min/1.73m^2 (n=1716)
- Group CKD2 – eGFR 60-89mL/min/1.73m^2 (n=1156)
- Group CKD3 – eGFR <60mL/min/1.73m^2 (n=76)

Data were analysed using paired t-tests and analysis of variance where the distribution was normal. For non-normally distributed variables (alanine aminotransferase) Wilcoxon-Signed Rank tests and Kruskal-Wallis tests were used. Analysis was performed in Stata SE 16.

Fig 1. Table showing the baseline characteristics of the entire population included in this analysis of the UK ABCD canagliflozin audit

Characteristic		n=2948
Age, years ± SD		60.0 ± 10.7
Male, %		61.8
Median diabetes duration, year (IQR)		8.0 (4-12.3)
Mean Hba1C,	% ± SD	9.23 ± 1.64
	mmol/mol ± SD	77.2 ± 17.7
Mean BMI, kg/m2 ± SD		33.9 ± 7.2
Mean weight, kg ± SD		98.2 ± 21.7
Median ALT, U/L (IQR)		73.2 ± 17.1
Mean eGFR, ml/min		95.7 ± 24.8
Mean Systolic BP, mmHg ± SD		132.8 ± 14.0
Mean Diastolic BP, mmHg ± SD		78.1 ± 9.0

ALT, alanine aminotransferase; BMI, body mass index; BP, blood pressure

eGFR, estimated glomerular filtration rate
IQR, interquartile range; SD, standard deviation

Results

A total of 2,948 patients were included, with baseline characteristics as displayed in **Fig 1.**

Significant reductions in were observed in all groups at both 6- and 12-months (P<0.05 for all). Across the population as a whole, Hba1c fell by 11.5mmol/mol (P<0.0001, 95% CI -10.7, -10.3) by 6 months. At 12-months HbA1c was observed to be 10.9mmol/mol lower than baseline (P<0.0001), showing relative stability.

Results (continued)

Weight loss across the population was 3.2kg at 6-months and 3.3kg at 12-months (P<0.001).

ANOVA revealed significant differences in HbA1c reductions between CKD groups (P<0.05), with smaller reductions from baseline apparent in the CKD3+ (-8.2mmol/mol, 95% CI -2.8, -13.5) vs CKD1 (-12.8, 95% CI -11.6, -13.9) at 6-months. These results are displayed in **Fig 2.**

There was no difference in weight loss between groups. See **Fig 3.**

Reductions in systolic and diastolic blood pressure (SBP and DBP) were not significant in the CKD3+ group at 6 or 12-months but were statistically significant (P<0.001) in the CKD1 and CKD2 groups at both intervals. For CKD1 SBP/DBP change at 6-months, -3.3/-1.2 (95% CI -2.3/-0.5, -4.3/-1.8)

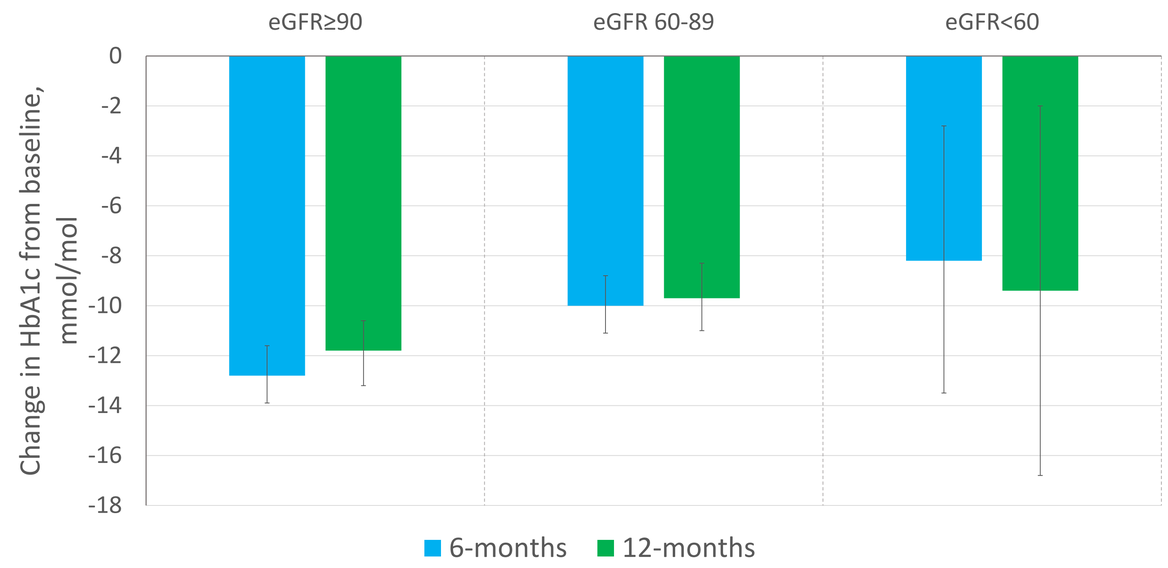
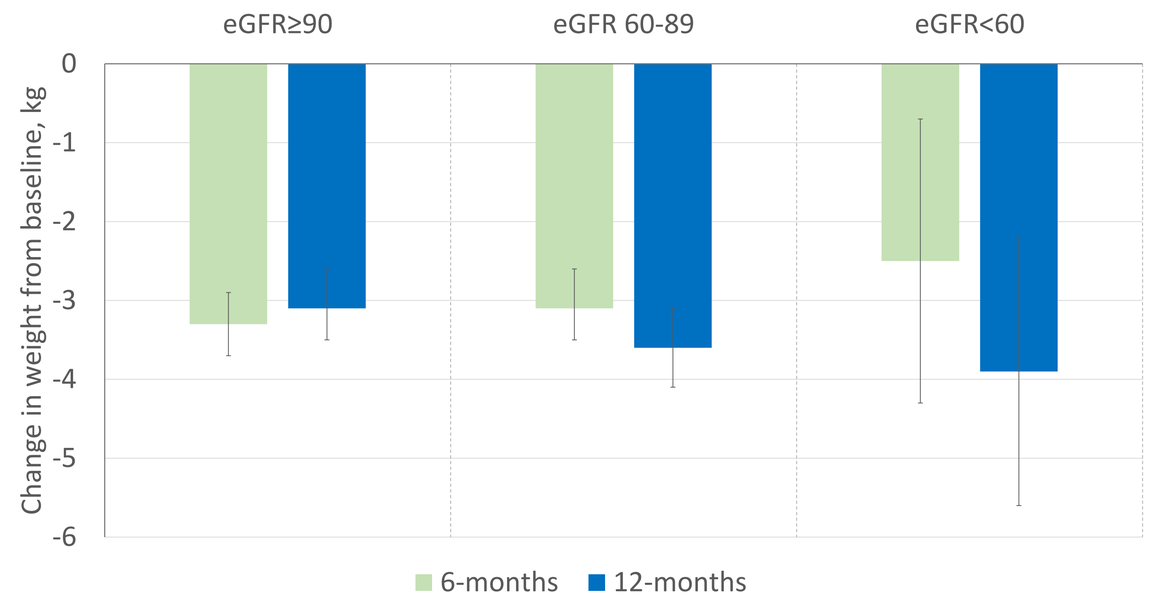


Figure 2. (above) Bar chart showing HbA1c change from baseline amongst canagliflozin users, stratified by baseline eGFR.
For both: Error bars showing 95% confidnece intervals All results P<0.05

Figure 3. (below) Bar chart showing weight change from baseline amongst canagliflozin users, stratified by baseline eGFR



Conclusion

Our results demonstrate the many of the effects of canagliflozin are still present even in those with reduced renal function at baseline in a real-world cohort of patients.

HbA1c reductions persist, but are of a smaller magnitude at lower eGFR levels. Effects on blood pressure also seem to diminish in those with lower eGFRs.

There was no difference in weight loss between groups – suggests some of the weight loss may be mediated via non-glycosuric mechanisms.

Further evidence is needed to support the use of canagliflozin at lower levels of eGFR for treatment of diabetes.

References

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