Which baseline characteristics predict response to canagliflozin? Updated results from the ABCD nationwide canagliflozin audit.

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Introduction

The ABCD nationwide audit programme has already demonstrated that significant improvements in HbA1c, weight, alanine aminotransferase (ALT) and blood pressure translate from randomised control trial evidence into our real-world cohort of patients. Previous audit data on Empagliflozin has suggested that those with different characteristics, namely the most elevated HbA1cs and most intact renal function, may have larger improvements in HbA1c and weight than others, and thus stand to gain the most benefit[1].

Recent real-world evidence shows similar results, although notably the only independent predictor of HbA1c reductions at 6-months was baseline HbA1c[2].

Methods

Data were extracted from the ABCD canagliflozin nationwide audit programme tool and combined with data submitted by ABCD members who collaborated with their clinical commissioning groups to obtain anonymised data extracted from Eclipse. Patients with a minimum dataset of a baseline and one follow-up visit. Then, for each variable, a baseline and subsequent follow-up measurement.

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. Predictors of change in weight and HbA1c (in mml/mol) were assessed using simple linear regression. Analysis was performed in Stata SE 16.

Due to multiplicity of measurement results were only considered significant at the P<0.01 level

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

Characteristic		n=2091
Age, years ± SD		58.4 ± 11.3
Male, %		66.6
Median diabetes duration, year (IQR)		7.4 (2.5-11.2)
Mean Hba1C,	% ± SD	9.74 ± 2.05
	mmol/mol ± SD	77.3 ± 21.2
Mean BMI, kg/m2 ± SD		33.5 ± 8.03
Mean weight, kg ± SD		99.2 ± 23.8
Median ALT, U/L (IQR)		29 (20-40)
Mean eGFR, ml/min		79.8 ± 13.2
Mean Systolic BP, mmHg ± SD		133.6 ± 14.4
Mean Diastolic BP, mmHg ± SD		78 .3± 9.6
Mean Total Cholesterol, mmol/L		4.2 ± 1.3
Mean Triglycerides, mmol/L		2.4 ± 1.8

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

eGFR, estimated glomerular filtration rate

IQR, interquartile range; SD, standard deviation

Fig 2. Table showing mean (or median) follow-up values changes from baseline in multiple variables following commencement of treatment with canagliflozin.

*results analysed by non-parametric methods; median difference given

Variable	Follow-up	Mean difference (95% CI)	P-value
HbA1c, mmol/mol	61.2	-17.2 (-15.9, -18.5)	<0.0001
HbA1c, %	8.17	-1.66 (-1.5, -1.78)	<0.0001
Weight, kg	97.7	-2.1 (-1.8, -2.4)	<0.0001
BMI, kg/m^2	32.8	-0.7 (-0.6, -0.8)	<0.0001
ALT, U/L*	25	-2 (-2, -2)	<0.0001
eGFR, mL/min/1.73m^2	78.2	-0.4 (-0.1, -0.8)	0.01
Systolic BP, mmHg	133.4	-0.2 (+0.5, -1.0)	0.55
Diastolic BP, mmHg	77.3	-0.5 (+0.05, -1.1)	0.07

Note: Since the acceptance of the abstract for this poster, further data has been received and so we are pleased to present the updated results including the most up-to-date data available from the audit programme.

Results

Complete datasets were extracted for 2,091 patients from the audit tool. The baseline characteristics or the cohort are described in **Fig 1.**

Significant HbA1c, weight, BMI, eGFR and ALT changes from baseline were noted across the cohort – results are displayed in **Fig 2.** No significant changes in blood pressure were noted. Median follow-up was 12 months (IQR 6-12).

Each variable assessed for predicting weight change or HbA1c change by linear regression including its R^2 value, coefficient and P-value is shown in **Fig 3.** below.

Fig 3. Tables showing the results of linear regression analysis for baseline characteristics predicting the magnitude of change in HbA1c and weight from baseline

	Predicting change in HbA1c, mmol/mol		
	R2	Coefficient	P-Value
HbA1c, mmol/mol	0.51	0.84	<0.0001
HbaA1c, %	0.51	8.72	<0.0001
Weight, kg	0.08	-0.30	<0.0001
BMI, kg/m2	0.14	-1.20	<0.0001
ALT, U/L	0.01	0.13	0.002
eGFR, ml/min/1.73m2	0.68	0.13	<0.0001

	Predicting change in weight, kg		
	R2	Coefficient	P-Value
HbA1c, mmol/mol	0.06	-0.06	<0.0001
HbaA1c, %	0.06	-0.64	<0.0001
Weight, kg	0.03	0.04	<0.0001
BMI, kg/m2	0.16	0.05	<0.0001
ALT, U/L	0.01	0.03	0.002
eGFR, ml/min/1.73m2	<0.01	-0.02	0.03

R^2 is the amount the difference between changes in weight that is predicted by the baseline variable

The coefficient is the direction and amount of extra change in weight or HbA1c associated with 1-unit change in the baseline variable

i.e. an increase of 1% in HbA1c, % reduces weight change by -0.64kg

Conclusion

Our results show multiple baseline characteristics which can predict response to canagliflozin therapy. Most of these predicting improved response but some predict lower levels of response – notably higher baseline HbA1c levels predicting less weight loss and increased baseline weight predicting smaller changes in HbA1c (in mmol/mol).

There was no significant association between preserved renal function and weight loss. This might suggest a non-glycosuria mediated mechanism that influence weight loss in users of canagliflozin, perhaps mediated via SGLT-1 inhibition.

This is the first analysis to show that baseline ALT level can predict metabolic response to canagliflozin therapy, albeit by very small amounts. Some of the significant relationships should be interpreted with caution due to the observational nature of this cohort and inability to adjust for some confounders e.g. alcohol use, other drugs.

This analysis highlights that these is still much to lean about sodium glucose link-transport inhibition and its effects in real-world use.

Declaration of interests/Funding

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Reference

1. Ken Y Thong et al. Predictors of glycaemic and weight response to empagliflozin treatment: the Association of British Clinical Diabetologists (ABCD) Nationwide Empagliflozin Audit; ADA 79th Scientific Sessions
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