

Dapagliflozin's impact on hormonal regulation and ketogenesis in type 1 diabetes: a randomised controlled crossover trial

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Electronic supplementary material

ESM Table 1: Analysis of area under the curves (AUC)

Outcome	Placebo ¹	Dapagliflozin ¹	Ratio ² (95%-CI)	p-value
AUC OGTTTC GLP-1 (pmol/l×min)	23668 (19099 - 26252)	24224 (18555 - 32349)	0.95 (0.82 - 1.10)	0.5
AUC HEC GLP-1 (pmol/l×min)	23213 (20346 - 35579)	25553 (17222 - 35265)	0.97 (0.79 - 1.20)	0.8
AUC OGTTTC Glucagon (ng/l×min)	167 (85 - 493)	189 (110 - 439)	0.96 (0.69 - 1.33)	0.8
AUC HEC Glucagon (ng/l×min)	170 (93 - 470)	209 (97 - 417)	0.95 (0.74 - 1.23)	0.7
AUC OGTTTC Somatostatin (pmol/l×min)	5270 (3711 - 9778)	6627 (4705 - 10496)	1.17 (0.83 - 1.64)	0.3
AUC HEC Somatostatin (pmol/l×min)	6940 (2828 - 8974)	5506 (3772 - 9318)	1.04 (0.76 - 1.43)	0.8
AUC OGTTTC Plasma Ketone (mmol/l×min)	4.95 (3.15 - 9.90)	11.55 (6.45 - 22.65)	1.69 (0.88 - 3.27)	0.11
AUC HEC Plasma Ketone (mmol/l×min)	6.45 (2.25 - 17.25)	29.10 (11.40 - 65.85)	3.91 (2.35 - 6.50)	<0.001

¹ Median (ICR)

² Geometric mean ratio (exponentiated model coefficient)

31 ESM Table 2: Per-protocol (PP) analysis of primary and secondary outcomes

32 The secondary per-protocol analysis is based on the PP set (9 patients)

Outcome	Placebo ¹	Dapagliflozin ¹	Ratio ² (95%-CI)	p-value
OGTTC GLP-1 (pmol/l)	192.4 (128.1 - 263.8)	193.2 (139.8 - 260.0)	0.93 (0.78 - 1.10)	0.4
HEC GLP-1 (pmol/l)	240.6 (144.4 - 328.3)	213.1 (145.6 - 309.7)	0.96 (0.84 - 1.08)	0.5
OGTTC Glucagon (ng/l)	2.05 (0.68 - 4.42)	1.52 (0.70 - 3.92)	1.08 (0.89 - 1.30)	0.4
HEC Glucagon (ng/l)	1.89 (0.77 - 3.80)	1.55 (0.74 - 4.47)	1.03 (0.88 - 1.22)	0.7
OGTTC Somatostatin (pmol/l)	40.3 (26.6 - 63.1)	51.8 (31.1 - 76.1)	1.02 (0.84 - 1.24)	0.8
HEC Somatostatin (pmol/l)	45.0 (21.6 - 76.5)	41.1 (27.7 - 81.2)	1.17 (0.94 - 1.46)	0.2
OGTTC Plasma Ketone (mmol/l)	0.05 (0.02 - 0.15)	0.11 (0.05 - 0.22)	1.98 (1.42 - 2.77)	<0.001
HEC Plasma Ketone (mmol/l)	0.06 (0.02 - 0.20)	0.19 (0.08 - 0.53)	2.88 (2.04 - 4.08)	<0.001

33 ¹ Median (IQR)

34 ² Geometric mean ratio (exponentiated model coefficient)

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37 ESM Table 3: The within-patient interclass correlation (ICC)

Outcome	ICC
OGTTC GLP-1 (pmol/l)	0.74
HEC GLP-1 (pmol/l)	0.84
OGTTC Glucagon (ng/l)	0.87
HEC Glucagon (ng/l)	0.88
OGTTC Somatostatin (pmol/l)	0.55
HEC Somatostatin (pmol/l)	0.47
OGTTC Plasma Ketone (mmol/l)	0.70
HEC Plasma Ketone (mmol/l)	0.72

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41 ESM Table 4: Glucose Level during HEC and OGTTTC

Outcome	Placebo ¹	Dapagliflozin ¹	Difference (95%-CI)	p-value
OGTTTC plasma glucose (mmol/l)	8.53 (6.94 - 10.54)	7.84 (6.08 - 9.40)	-1.08 (-1.48 - -0.68)	< 0.001
HEC plasma glucose (mmol/l)	6.75 (6.05 - 7.36)	6.70 (6.09 - 7.34)	0.01 (-0.16 - 0.17)	>0.9

42 ¹ Median (IQR)

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ESM Figure 1: Line plot of primary and secondary outcomes

Time course of primary and secondary outcomes. Each patient is shown and coloured individually

