

ESM Table 1. Summary of Efficacy Findings at Week 26 (LOCF)

Parameter	PBO (n = 183)	SITA 100 mg (n = 366)	CANA 100 mg (n = 368)	CANA 300 mg (n = 367)
HbA _{1c} , n	181	354	365	360
Mean ± SD baseline, % (mmol/mol)	8.0 ± 0.9 (64 ± 9.8)	7.9 ± 0.9 (63 ± 9.8)	7.9 ± 0.9 (63 ± 9.8)	8.0 ± 0.9 (64 ± 9.8)
LS mean ± SE change, % (mmol/mol)	-0.17 ± 0.06 (-1.9 ± 0.7)	-0.82 ± 0.04 (-9.0 ± 0.4)	-0.79 ± 0.04 (-8.6 ± 0.4)	-0.94 ± 0.04 (-10.3 ± 0.4)
Difference vs PBO (95% CI), %		-0.66 (-0.80, -0.52) ^a	-0.62 (-0.76, -0.48) ^b	-0.77 (-0.91, -0.64) ^b
Difference vs PBO (95% CI), mmol/mol		-7.2 (-8.7, -5.7) ^a	-6.8 (-8.3, -5.2) ^b	-8.4 (-9.9, -7.0) ^b
FPG, n	181	354	365	360
Mean ± SD baseline, mmol/l	9.1 ± 2.1	9.4 ± 2.3	9.4 ± 2.3	9.6 ± 2.5
LS mean ± SE change	0.1 ± 0.1	-1.1 ± 0.1	-1.5 ± 0.1	-2.1 ± 0.1
Difference vs PBO (95% CI)		-1.3 (-1.6, -0.9) ^a	-1.7 (-2.0, -1.3) ^b	-2.2 (-2.6, -1.9) ^b
2-hour PPG, n	129	295	298	288

Mean ± SD baseline, %	13.8 ± 3.6	14.2 ± 3.6	14.3 ± 3.8	14.5 ± 4.1
LS mean ± SE change	-0.6 ± 0.3	-2.7 ± 0.2	-2.7 ± 0.2	-3.2 ± 0.2
Difference vs PBO (95% CI)		-2.2 (-2.8, -1.6) ^a	-2.1 (-2.7, -1.5) ^b	-2.6 (-3.2, -2.0) ^b
Body weight, n	181	355	365	360
Mean ± SD baseline, kg	86.7 ± 22.5	87.6 ± 20.9	88.7 ± 22.3	85.4 ± 20.7
LS mean ± SE change, kg	-1.1 ± 0.2	-1.1 ± 0.2	-3.3 ± 0.2	-3.6 ± 0.2
LS mean ± SE percent change	-1.2 ± 0.3	-1.2 ± 0.2	-3.7 ± 0.2	-4.2 ± 0.2
Difference vs PBO (95% CI)		0.0 (-0.6, 0.6) ^a	-2.5 (-3.1, -1.9) ^b	-2.9 (-3.5, -2.3) ^b
Systolic BP, n	181	355	365	360
Mean ± SD baseline, mm Hg	128.0 ± 12.7	128.0 ± 13.5	128.0 ± 12.7	128.7 ± 13.0
LS mean ± SE change	1.5 ± 0.8	-1.8 ± 0.6	-3.8 ± 0.6	-5.1 ± 0.6
Difference vs PBO (95% CI)		-3.3 (-5.3, -1.4) ^a	-5.4 (-7.3, -3.4) ^b	-6.6 (-8.5, -4.7) ^b
Diastolic BP, n	181	355	365	360
Mean ± SD baseline, mm Hg	77.8 ± 8.0	77.5 ± 8.0	77.7 ± 8.4	77.9 ± 8.3
LS mean change ± SE	0.3 ± 0.5	-1.1 ± 0.4	-2.2 ± 0.4	-2.1 ± 0.4
Difference vs PBO (95% CI)		-1.4 (-2.6, -0.1) ^a	-2.5 (-3.7, -1.2) ^a	-2.4 (-3.6, -1.1) ^a

Triacylglycerol, n	171	338	358	341
Mean ± SD baseline, mmol/l	2.1 ± 1.3	2.0 ± 1.1	2.2 ± 1.6	2.1 ± 1.5
LS mean ± SE change	-0.03 ± 0.08	-0.08 ± 0.06	-0.10 ± 0.06	-0.27 ± 0.06
Median (IQR) percent change	-6.2 (-24.6, 22.4)	-3.7 (-24.4, 19.4)	-4.7 (-24.7, 21.4)	-13.5 (-30.6, 15.6)
LS mean ± SE percent change	3.2 ± 3.6	1.0 ± 2.7	1.6 ± 2.6	-1.4 ± 2.6
Difference vs PBO (95% CI)		-2.3 (-10.6, 6.1) ^a	-1.6 (-9.9, 6.7) ^c	-4.6 (-13.0, 3.7) ^c
LDL-C, n	170	335	354	335
Mean ± SD baseline, mmol/l	2.7 ± 0.9	2.8 ± 0.9	2.8 ± 0.8	2.8 ± 0.9
LS mean ± SE change	-0.11 ± 0.05	0.02 ± 0.04	0.08 ± 0.04	0.18 ± 0.04
Median (IQR) percent change	-3.4 (-16.8, 10.1)	-1.2 (-11.4, 11.6)	1.9 (-10.2, 19.4)	8.3 (-8.8, 22.8)
LS mean ± SE percent change	-1.5 ± 2.4	4.1 ± 1.8	6.5 ± 1.7	10.7 ± 1.8
Difference vs PBO (95% CI)		5.5 (-0.1, 11.2) ^a	7.9 (2.4, 13.5) ^a	12.2 (6.6, 17.8) ^a
HDL-C, n	171	336	357	336
Mean ± SD baseline, mmol/l	1.1 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	1.2 ± 0.3
LS ± SE mean change	0.04 ± 0.02	0.05 ± 0.01	0.11 ± 0.01	0.13 ± 0.01
Median (IQR) percent change	2.7 (-5.9, 14.4)	4.4 (-5.7, 14.0)	8.6 (-0.8, 19.3)	11.2 (0.0, 21.4)

LS mean ± SE percent change	3.7 ± 1.3	5.0 ± 1.0	10.3 ± 0.9	12.1 ± 1.0
Difference vs PBO (95% CI)		1.3 (−1.8, 4.3) ^a	6.6 (3.6, 9.7) ^b	8.4 (5.3, 11.5) ^b
LDL-C/HDL-C, n	170	335	354	335
Mean ± SD baseline, mol/mol	2.5 ± 1.0	2.6 ± 1.0	2.5 ± 0.9	2.4 ± 0.9
LS mean ± SE change	−0.16 ± 0.05	−0.08 ± 0.04	−0.13 ± 0.04	−0.09 ± 0.04
Median (IQR) percent change	−8.1 (−17.7, 6.3)	−3.5 (−16.7, 11.0)	−5.5 (−19.0, 10.5)	−2.6 (−18.0, 12.9)
LS mean ± SE percent change	−2.5 ± 2.3	0.5 ± 1.7	−1.3 ± 1.6	0.7 ± 1.7
Difference vs PBO (95% CI)		3.0 (−2.3, 8.4) ^a	1.2 (−4.1, 6.5) ^a	3.2 (−2.1, 8.6) ^a
Non-HDL-C, n	171	334	355	333
Mean ± SD baseline, mmol/l	3.7 ± 1.0	3.7 ± 1.0	3.8 ± 1.1	3.7 ± 1.0
LS mean ± SE change	−0.10 ± 0.06	−0.02 ± 0.04	0.02 ± 0.04	0.08 ± 0.04
Median (IQR) percent change	−2.8 (−13.6, 10.4)	−1.2 (−10.2, 9.5)	−0.7 (−9.6, 14.3)	3.6 (−9.3, 15.4)
LS mean ± SE percent change	−0.8 ± 1.8	1.6 ± 1.3	2.8 ± 1.3	4.5 ± 1.3
Difference vs PBO (95% CI)		2.5 (−1.7, 6.6) ^a	3.6 (−0.4, 7.7) ^a	5.4 (1.2, 9.5) ^a

LOCF, last observation carried forward; PBO, placebo; SITA, sitagliptin; CANA, canagliflozin; SD, standard deviation; LS, least squares; SE, standard error; CI, confidence interval; FPG, fasting plasma glucose; PPG, postprandial glucose; BP, blood pressure,

IQR, interquartile range; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; NS, not significant.

^aStatistical comparison vs PBO not performed (not pre-specified).

^b $P < 0.001$ vs PBO.

^c $P = \text{NS}$ vs PBO.