

SUPPLEMENTARY DATA

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Supplementary Table 1. Effects of canagliflozin from baseline to week 12 in fasting lipids in subjects with type 2 diabetes on metformin.

	CANA 50 mg QD (n=64)	CANA 100 mg QD (n=64)	CANA 200 mg QD (n=65)	CANA 300 mg QD (n=64)	CANA 300 mg BID (n=64)	SITA 100 mg QD (n=65)
Total cholesterol (mg/dL)						
Baseline	197.5±5.8	188.5±6.4	187.8±5.0	195.3±6.4	189.1 ±5.8	186.3±5.4
Change from baseline to week 12	-4.0 ± 5.6	-6.9 ± 5.6	2.8 ± 5.7	-5.0 ± 5.7	6.2 ± 5.6	-10.7 ± 5.6
HDL cholesterol (mg/dL)						
Baseline	44.4 ± 1.7	46.4 ± 1.4	43.9 ± 1.4	48.3 ± 1.5	44.2 ± 1.5	45.3 ± 1.3
Change from baseline to week 12	1.5 ± 1.2	0.1 ± 1.2	2.1 ± 1.2	2.0 ± 1.2	4.0 ± 1.2†	-0.8 ± 1.2
LDL cholesterol (mg/dL)						
Baseline	113.1 ± 4.6	110.3 ± 5.8	107.6 ± 4.7	110.7 ± 5.4	107.6 ± 5.3	104.4 ± 4.5
Change from baseline to week 12	-0.6 ± 5.0	-4.9 ± 5.0	3.2 ± 5.1	-1.1 ± 5.1	7.8 ± 5.0	-8.0 ± 5.0
Total cholesterol: HDL cholesterol ratio						
Baseline	4.72 ± 0.2	4.14 ± 0.1	4.47 ± 0.2	4.17 ± 0.2	4.56 ± 0.2	4.27 ± 0.2
Change from baseline to week 12	-0.15 ± 0.14	-0.09 ± 0.14	0.02 ± 0.15	-0.21 ± 0.15	-0.19 ± 0.14	-0.03 ± 0.14
Triglycerides (mg/dL)						
Baseline	198.9 ± 14.2	159.2 ± 8.2	182.6 ± 12.1	177.9 ± 11.4	195.0 ± 17.6	185.5 ± 14.0
Change from baseline to week 12	-21.9 ± 12.5	-17.3 ± 12.5	-17.0 ± 12.6	-28.5 ± 12.6*	-35.3 ± 12.5†	-11.4 ± 12.4

Results are PBO-subtracted least-squares mean change from baseline ± standard error.

* $P < 0.05$; † $P < 0.01$

PBO=placebo; CANA=canagliflozin; SITA=sitagliptin; QD=daily; BID= twice daily.

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Supplementary Table 2. Effects of canagliflozin from baseline to week 12 in HOMA2-%B in subjects with type 2 diabetes on metformin.

	PBO (n=53)	CANA 50 mg QD (n=54)	CANA 100 mg QD (n=54)	CANA 200 mg QD (n=50)	CANA 300 mg QD (n=51)	CANA 300 mg BID (n=53)	SITA 100 mg QD (n=55)
Baseline	54 ± 3	51 ± 3	52 ± 3	59 ± 5	56 ± 4	65 ± 4	68 ± 6
Change from baseline to week 12	2 ± 2	6 ± 2	14 ± 3*	15 ± 5*	18 ± 3*	16 ± 3*	10 ± 5*

Data are observed mean change from baseline ± standard error of the mean, and are shown only for subjects who had measurements at both visits. **P*<0.05 versus placebo by ANCOVA adjusted for baseline value and a stratification factor. PBO=placebo; CANA=canagliflozin; SITA=sitagliptin; QD=daily; BID= twice daily.

Supplementary Table 3. Effects of canagliflozin from baseline to week 12 in vital signs in subjects with type 2 diabetes on metformin.

	PBO (n=65)	CANA 50 mg QD (n=64)	CANA 100 mg QD (n=64)	CANA 200 mg QD (n=65)	CANA 300 mg QD (n=64)	CANA 300 mg BID (n=64)	SITA 100 mg QD (n=65)
Systolic blood pressure (mm Hg)							
Baseline	125.2 ± 9.8	126.8 ± 10.9	126.5 ± 13.3	124.3 ± 11.1	126.1 ± 11.6	128.5 ± 12.8	128.7 ± 13.4
Change from baseline to week 12	-1.3 ± 1.5	-0.9 ± 1.7	1.0 ± 1.3	-2.1 ± 1.8	-4.9 ± 1.5	-3.6 ± 1.4	-0.8 ± 1.4
Diastolic blood pressure (mm Hg)							
Baseline	77.8 ± 7.7	76.9 ± 7.6	77.6 ± 8.0	77.4 ± 8.9	79.8 ± 7.6	78.9 ± 8.2	78.7 ± 8.1
Change from baseline to week 12	-1.3 ± 1.0	-0.1 ± 1.0	-0.2 ± 1.0	-1.7 ± 1.3	-2.1 ± 1.1	-2.4 ± 1.0	-0.6 ± 1.0
Heart rate (bpm)							
Baseline	69.9 ± 12.0	69.9 ± 10.1	71.0 ± 12.4	70.8 ± 9.9	72.6 ± 0.5	71.8 ± 13.1	72.9 ± 10.8
Change from baseline to week 12	1.7 ± 1.2	-0.2 ± 1.0	-0.2 ± 1.1	0.6 ± 1.0	-1.7 ± 1.2	0.2 ± 1.2	-1.7 ± 0.9

PBO=placebo; CANA=canagliflozin; SITA=sitagliptin; QD=daily; BID= twice daily.

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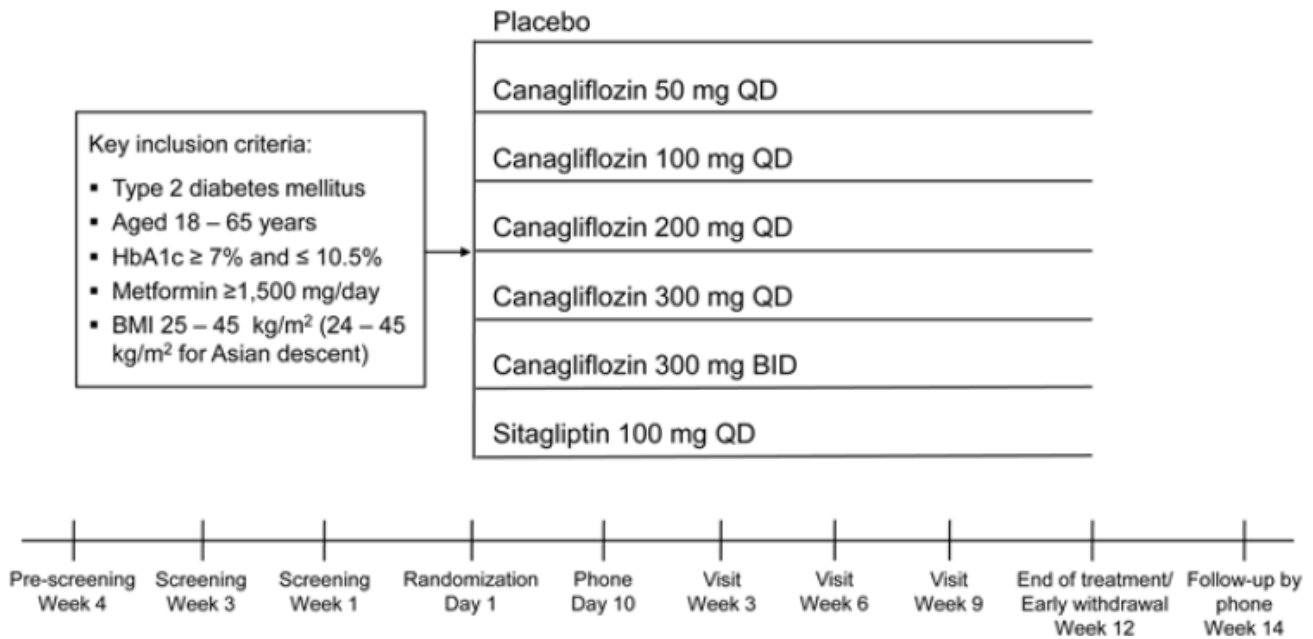
Supplementary Table 4. Effects of canagliflozin from baseline to week 12 in laboratory values in subjects with type 2 diabetes on metformin.

	PBO (n=65)	CANA 50 mg QD (n=64)	CANA 100 mg QD (n=64)	CANA 200 mg QD (n=65)	CANA 300 mg QD (n=64)	CANA 300 mg BID (n=64)	SITA 100 mg QD (n=65)
Blood urea nitrogen (mg/dL)	0.25 ± 0.43	1.00 ± 0.50	1.12 ± 0.43	0.93 ± 0.38	0.79 ± 0.48	2.00 ± 0.59	-0.17 ± 0.44
Serum creatinine (mg/dL)	0.016 ± 0.013	-0.005 ± 0.012	-0.010 ± 0.013	-0.002 ± 0.010	0.004 ± 0.012	0.019 ± 0.016	-0.005 ± 0.012
Serum calcium (mg/dL)	0.05 ± 0.06	-0.06 ± 0.08	-0.04 ± 0.05	0.09 ± 0.07	0.06 ± 0.06	0.08 ± 0.07	-0.02 ± 0.04
Serum magnesium (mg/dL)	-0.01 ± 0.02	0.12 ± 0.03	0.10 ± 0.03	0.14 ± 0.02	0.17 ± 0.02	0.20 ± 0.03	0.02 ± 0.02
Serum phosphate (mg/dL)	0.15 ± 0.06	-0.03 ± 0.07	0.03 ± 0.06	0.24 ± 0.06	0.03 ± 0.08	0.21 ± 0.07	0.03 ± 0.06
Serum uric acid (mg/dL)	-0.05 ± 0.09	-0.53 ± 0.13	-0.71 ± 0.12	-0.96 ± 0.14	-0.65 ± 0.11	-0.69 ± 0.11	-0.19 ± 0.13
Hematocrit (%)	-0.04 ± 0.32	1.11 ± 0.38	2.33 ± 0.35	2.09 ± 0.39	2.37 ± 0.43	2.60 ± 0.40	-0.75 ± 0.35
Hemoglobin (g/L)	-0.7 ± 0.78	3.2 ± 0.90	5.6 ± 0.90	6.0 ± 0.90	5.9 ± 1.36	8.1 ± 1.01	-2.7 ± 0.92
25-hydroxy vitamin D (ng/mL)	-2.26 ± 1.02	-0.55 ± 0.96	-0.74 ± 0.90	-1.11 ± 0.95	-3.27 ± 1.02	-1.15 ± 1.02	-2.02 ± 1.00
BSAP (µg/L)	0.51 ± 0.34	-0.32 ± 0.31	-0.41 ± 0.29	-0.48 ± 0.36	-0.35 ± 0.31	-0.43 ± 0.35	-1.12 ± 0.39
CTX (ng/mL)	0.03 ± 0.02	0.06 ± 0.03	0.07 ± 0.02	0.10 ± 0.02	0.10 ± 0.02	0.11 ± 0.02	-0.01 ± 0.02
Osteocalcin (µg/L)	1.06 ± 0.50	1.44 ± 0.40	1.21 ± 0.41	1.73 ± 0.41	0.74 ± 0.45	1.69 ± 0.41	1.03 ± 0.58
PTH (pg/mL)	1.17 ± 1.99	4.39 ± 2.58	0.79 ± 2.59	-2.59 ± 1.97	-0.87 ± 1.91	-2.65 ± 1.70	3.33 ± 2.09
P1NP (µg/L)	-1.28 ± 0.93	-1.53 ± 0.89	0.58 ± 0.94	1.34 ± 0.94	-0.69 ± 1.04	-0.11 ± 0.84	-1.37 ± 1.24
TRAP (U/L)	0.27 ± 0.10	0.34 ± 0.09	0.42 ± 0.08	0.33 ± 0.09	0.16 ± 0.07	0.36 ± 0.08	0.08 ± 0.09
Urinary NTX/creatinine ratio (nmol BCE/nmol Cr)	2.24 ± 2.54	-0.44 ± 3.17	4.45 ± 3.56	-1.78 ± 4.85	-2.52 ± 4.76	2.45 ± 2.35	-2.10 ± 3.05
Urinary calcium/creatinine ratio (mg/mg)	-0.01 ± 0.02	0.01 ± 0.11	0.00 ± 0.01	0.05 ± 0.01	-0.01 ± 0.02	-0.03 ± 0.01	0.01 ± 0.02
Urinary phosphate/creatinine ratio (mg/mg)	-0.05 ± 0.03	0.06 ± 0.03	0.09 ± 0.03	0.05 ± 0.02	0.04 ± 0.03	0.13 ± 0.02	-0.01 ± 0.03

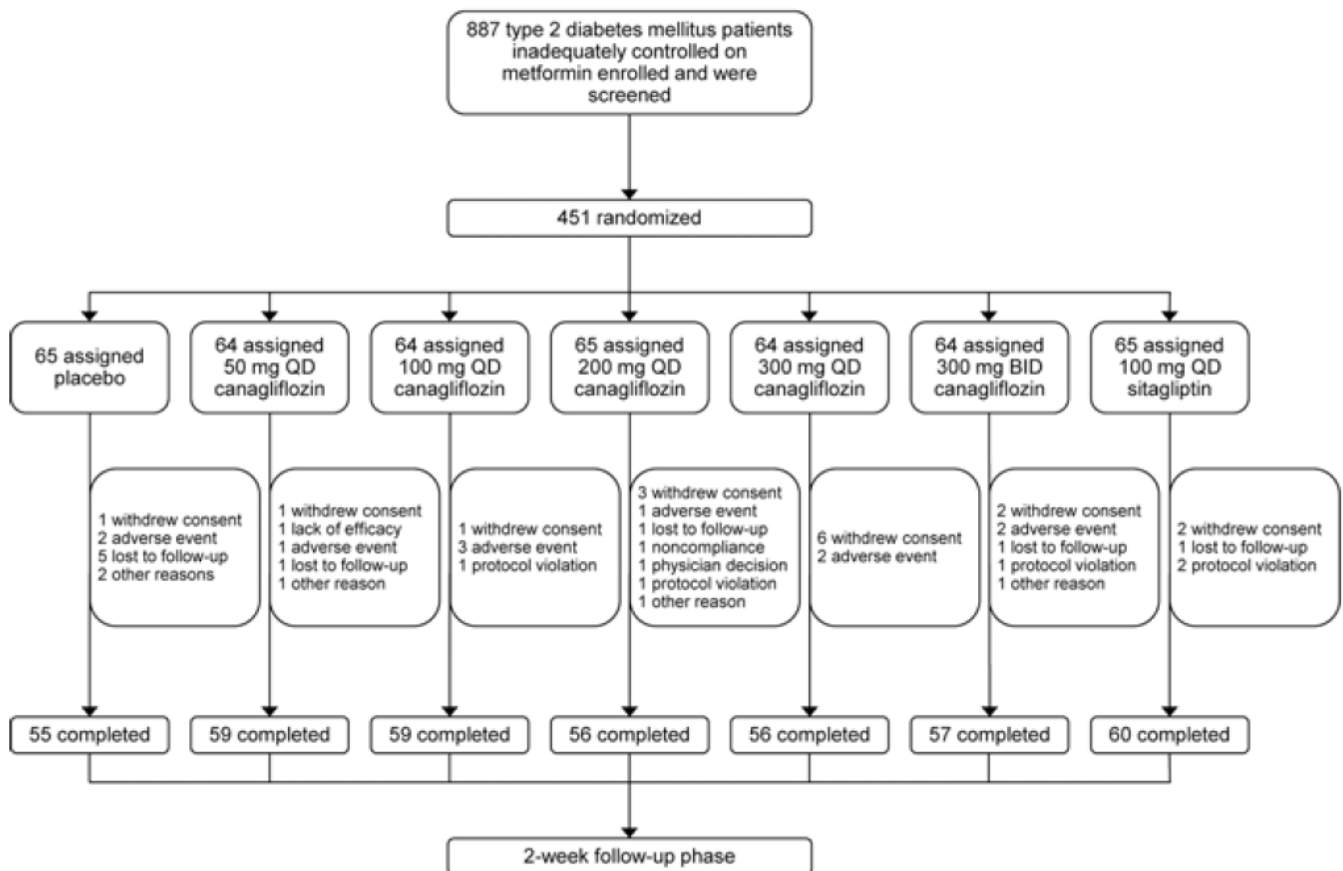
PBO=placebo; CANA=canagliflozin; SITA=sitagliptin; QD=daily; BID= twice daily; BSAP=bone specific alkaline phosphatase; CTX=collagen type 1 beta-carboxy telopeptide; PTH=parathyroid hormone; P1NP=propeptide amino-terminal type 1 procollagen; TRAP=tartrate resistant acid phosphatase; NTX=collagen type 1 amino-terminal telopeptide.

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Supplementary Figure 1. Study design.

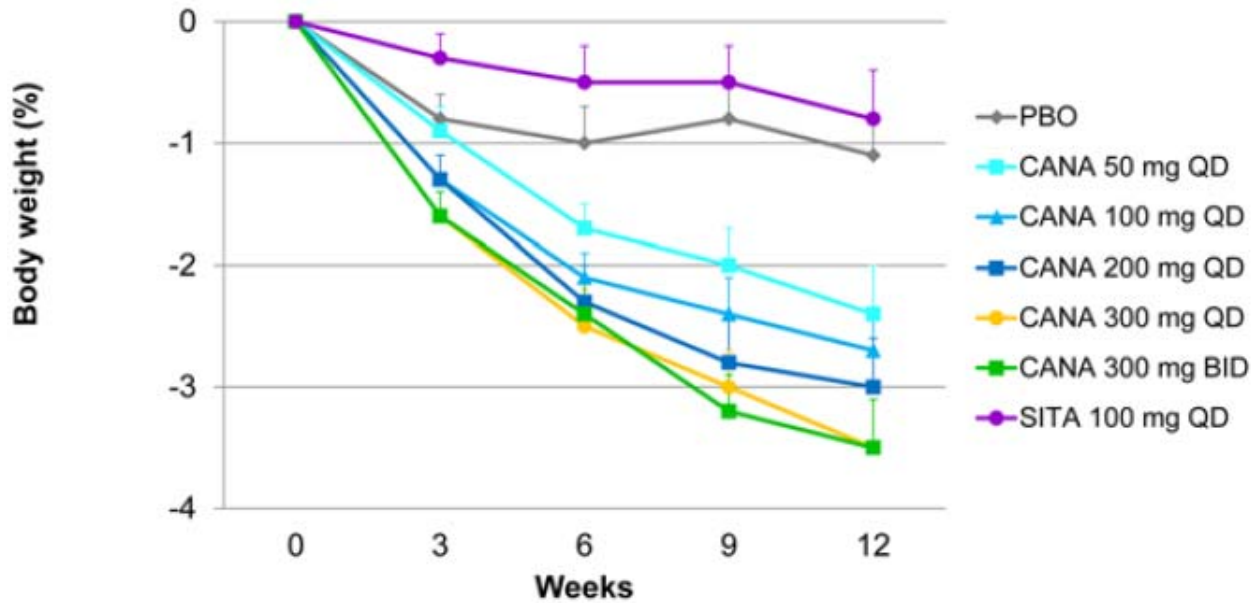


Supplementary Figure 2. Subject disposition.



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Supplementary Figure 3. Effect of canagliflozin on body weight over time in subjects with type 2 diabetes on metformin. Data are observed mean reductions from baseline. Error bars show standard error of the mean (observed population). PBO=placebo; CANA=canagliflozin; SITA=sitagliptin; QD=daily; BID= twice daily.



Supplementary Figure 4. Effect of canagliflozin on renal threshold over time in subjects with type 2 diabetes on metformin. Error bars show standard error of the mean (observed population). PBO=placebo; CANA=canagliflozin; SITA=sitagliptin; QD=daily; BID= twice daily.

