

SUPPLEMENTARY DATA

Supplementary Table 1.

SGLT2 Inhibitor Monotherapy

	Reference Number	Study Duration (Weeks)	Number of Subjects (n)	Mean Baseline HbA1C (%)	Placebo Adjusted Reduction in HbA1C (%)	Placebo Adjusted Reduction in FPG (mg/dl)
SGLT2 Inhibitor vs Placebo/Comparator						
Canagliflozin 100 mg		26	195	8.1	0.91	36.0
Canagliflozin 300 mg		26	197	8.0	1.16	43.2
Canagliflozin 100 mg		52	195	8.1	0.81*	27.4*
Canagliflozin 300 mg		52	197	8.0	1.11*	35.1*
Dapagliflozin 5 mg		24	132	~7.9	0.54	20.1
Dapagliflozin 10 mg		24	146	~8.0	0.66	24.4
Dapagliflozin 5 mg		24	203	9.1	1.19*	41.5*
Dapagliflozin 10 mg		24	219	9.1	1.45*	46.4*
Metformin XR		24	409	9.1	1.40*	34.0*
Empagliflozin 10 mg		24	224	7.9	0.74	31.1
Empagliflozin 25 mg		24	224	7.9	0.85	36.2
Sitagliptin 100 mg		24	223	7.9	0.73	16.7

* Change from baseline. Of note, because of different study populations and study conditions, accurate comparison of efficacy of various SGLT2 inhibitors is not possible without head-to-head studies which, to date have not been conducted.

SUPPLEMENTARY DATA

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SUPPLEMENTARY DATA

Supplementary Table 2.

SGLT2 Inhibitor + Metformin Dual Combination Therapy

	Reference Number	Study Duration (Weeks)	Number of Subjects	Mean Baseline HbA1C (%)	Placebo Adjusted↓ in HbA1C (%)	Placebo Adjusted↓ in FPG (mg/dl)
Metformin + SGLT2 Inhibitor vs Metformin + Placebo						
Metformin + Canagliflozin 100 mg		26	368	7.9	0.62	30.6
Metformin + Canagliflozin 300 mg		26	367	8.0	0.77	39.6
Metformin + Dapagliflozin 5 mg		24	137	8.2	0.40	15.5
Metformin + Dapagliflozin 10 mg		24	135	8.0	0.54	17.5
Metformin + Empagliflozin 10 mg		24	217	7.9	0.57	26.0
Metformin + Empagliflozin 25 mg		24	213	7.9	0.64	28.6
Metformin + SGLT2 Inhibitor vs Metformin + Sulfonylurea						
Metformin + Canagliflozin 100 mg		52	483	7.8	0.82*	25.2*
Metformin + Canagliflozin 300 mg		52	485	7.8	0.93*¥	27.0*
Metformin + Glimepiride 1mg titrated to 8 mg (mean Glimepiride dose 5.6 mg)		52	482	7.8	0.81*	18.0*
Metformin + Dapagliflozin titrated from 2.5-10 mg (mean Dapagliflozin dose 9.2mg)		52	400	7.7	0.52*	22.3*
Metformin + Glipizide titrated from 5-20 mg (mean Glipizide dose 16.4mg)		52	401	7.7	0.52*	18.7*
Metformin + Empagliflozin 25 mg		104	769	7.9	0.55*	19.4*
Metformin + Glimepiride titrated from 1- 4 mg		104	780	7.9	0.66*	8.6*

SUPPLEMENTARY DATA

(mean Glimperide dose 2.71 mg)						
Metformin + SGLT2 Inhibitor vs Metformin + DPP-4 Inhibitor						
Metformin + Canagliflozin 100 mg	52	368	7.9	0.73*	27.0*	
Metformin + Canagliflozin 300 mg	52	367	8.0	0.88*¥	36.0*	
Metformin + Sitagliptin 100 mg	52	366	7.9	0.73*	18.0*	

* Change from baseline. ¥ Glucose lowering with canagliflozin met superiority criteria

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SUPPLEMENTARY DATA

Supplementary Table 3.

SGLT2 Inhibitor + Sulfonylurea Dual Combination Therapy

	Reference Number	Study Duration (Weeks)	Number of Subjects	Mean Baseline HbA1C (%)	Placebo Adjusted Reduction in HbA1C (%)	Placebo Adjusted Reduction in FPG (mg/dl)
Glimepiride 4 mg + Dapagliflozin 5 mg (n=142)		48		8.1	0.52	0.0
Glimepiride 4 mg + Dapagliflozin 10 mg (n=151)		48		8.1	0.69	30.0

SGLT2 Inhibitor + DPP-4 Inhibitor Dual Combination Therapy

	Reference Number	Study Duration (Weeks)	Number of Subjects	Mean Baseline HbA1C (%)	Placebo Adjusted Reduction in HbA1C (%)	Placebo Adjusted Reduction in FPG (mg/dl)
Sitagliptin 100 mg + Dapagliflozin 10 mg (n=110)		24 48		8.0 8.0	0.60 0.90	24.0 39.9

SUPPLEMENTARY DATA

SGLT2 Inhibitor + Glitazone Dual Combination Therapy

	Reference Number	Study Duration (Weeks)	Number of Subjects	Mean Baseline HbA1C (%)	Placebo Adjusted Reduction in HbA1C (%)	Placebo Adjusted Reduction in FPG (mg/dl)
Pioglitazone 30/45 mg + Dapagliflozin 5 mg (n=141)		48		8.4	0.41	9.7
Pioglitazone 30/45 mg + Dapagliflozin 10 mg (n=140)		48		8.4	0.67	20.0
Pioglitazone 15-45 mg + Empagliflozin 10 mg (n=40)		24		8.1	0.70	NA
Pioglitazone 15-45 mg + Empagliflozin 25 mg (n=41)		24		8.1	0.80	NA

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SUPPLEMENTARY DATA

Supplementary Table 4.

SGLT2 Inhibitor + Metformin + DPP-4 Inhibitor Triple Combination Therapy

	Reference Number	Study Duration (Weeks)	Number of Subjects	Mean Baseline HbA1C (%)	Placebo Adjusted↓ in HbA1C (%)	Placebo Adjusted↓ in FPG (mg/dl)
Dapagliflozin 10 mg + Metformin + Sitagliptin (n=113)		48		7.8	0.40	29.2
Empagliflozin 25 mg + Metformin + Linagliptin (n=134)		52		7.9	1.19	35.3

SGLT2 Inhibitor + Metformin + Sulfonylurea Triple Combination Therapy

	Reference Number	Study Duration (Weeks)	Number of Subjects	Mean Baseline HbA1C (%)	Placebo Adjusted↓ in HbA1C (%)	Placebo Adjusted↓ in FPG (mg/dl)
Canagliflozin 100 mg + Metformin + SU* (n=157)		52		8.1	0.75	28.8
Canagliflozin 300 mg Metformin + SU* + (n=156)		52		8.1	0.97	37.8
Canagliflozin 300 mg + Metformin + SU* (n=377)		52		8.1	1.03**¥	30.6**
Sitagliptin 100 mg + Metformin + SU* (n=378)		52		8.1	0.66**	5.4**
Empagliflozin 10 mg + Metformin + SU* (n=226)		24		8.1	0.65	19.4***
Empagliflozin 25 mg + Metformin + SU* (n=218)		24		8.1	0.60	21.1***

SUPPLEMENTARY DATA

SGLT2 Inhibitor + Metformin + Glitazone Triple Combination Therapy

	Reference Number	Study Duration (Weeks)	Number of Subjects	Mean Baseline HbA1C (%)	Placebo Adjusted \downarrow in HbA1C (%)	Placebo Adjusted \downarrow in FPG (mg/dl)
Empagliflozin 10 mg + Metformin + Pioglitazone 15-45 mg + (n=125)		24		8.1	0.48	21.8
Empagliflozin 25 mg + Metformin + Pioglitazone 15-45 mg (n=127)		24		8.1	0.62	28.4

*Various SUs @ ½ maximal or higher dose ** Change from baseline

*** Change in mean daily glucose (MDG)

¥ Glucose lowering with canagliflozin met superiority criteria

(REFERENCES 47, 49, 50-53)

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SUPPLEMENTARY DATA

Supplementary Table 5.

SGLT2 Inhibitor + Insulin Combination Therapy

	Reference Number	Study Duration (Weeks)	Number of Subjects	Mean Baseline HbA1C (%)	Placebo Adjusted ↓ in HbA1C (%)	Placebo Adjusted ↓ in FPG (mg/dl)	Placebo Adjusted ↓ in Insulin dose (U/day)	Placebo Adjusted ↓ in body Wt. (Kg)
Combination with Insulin								
Dapagliflozin 5 mg (n=211)		48		8.62	0.49	12.2	10.2	1.82
Dapagliflozin 10 mg (n=194)		48		8.57	0.54	16.7	11.2	2.43
Dapagliflozin 5 mg (n=211)		104		8.62	0.39	16.0	16.8	2.86
Dapagliflozin 10 mg (n=194)		104		8.57	0.45	5.6	19.2	3.33
Canagliflozin 100 mg (n=692)		18		8.3	0.62	21.6	NA	1.9
Canagliflozin 300 mg (n=690)		18		8.3	0.73	43.2	NA	2.4
Canagliflozin 100 mg (n=692)		52		8.3	0.58	50.4	NA	2.8
Canagliflozin 300 mg (n=690)		52		8.3	0.73	63.0	NA	3.5
Empagliflozin 10 mg (n=186)		18		8.39	0.44	17.6	NA	1.31
Empagliflozin 25 mg (n=189)		18		8.29	0.52	24.5	NA	1.88
Empagliflozin 10 mg (n=186)		52		8.39	1.18	12.4	8.8	2.39
Empagliflozin 25 mg (n=189)		52		8.29	1.27	14.2	11.2	2.48

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