SUPPLEMENTARY MATERIAL

Fig. S1 Trial profile for the short-term and long-term treatment periods. The term "incorrect enrollment" was defined as patients not meeting inclusion criteria or meeting exclusion criteria during the enrollment process.

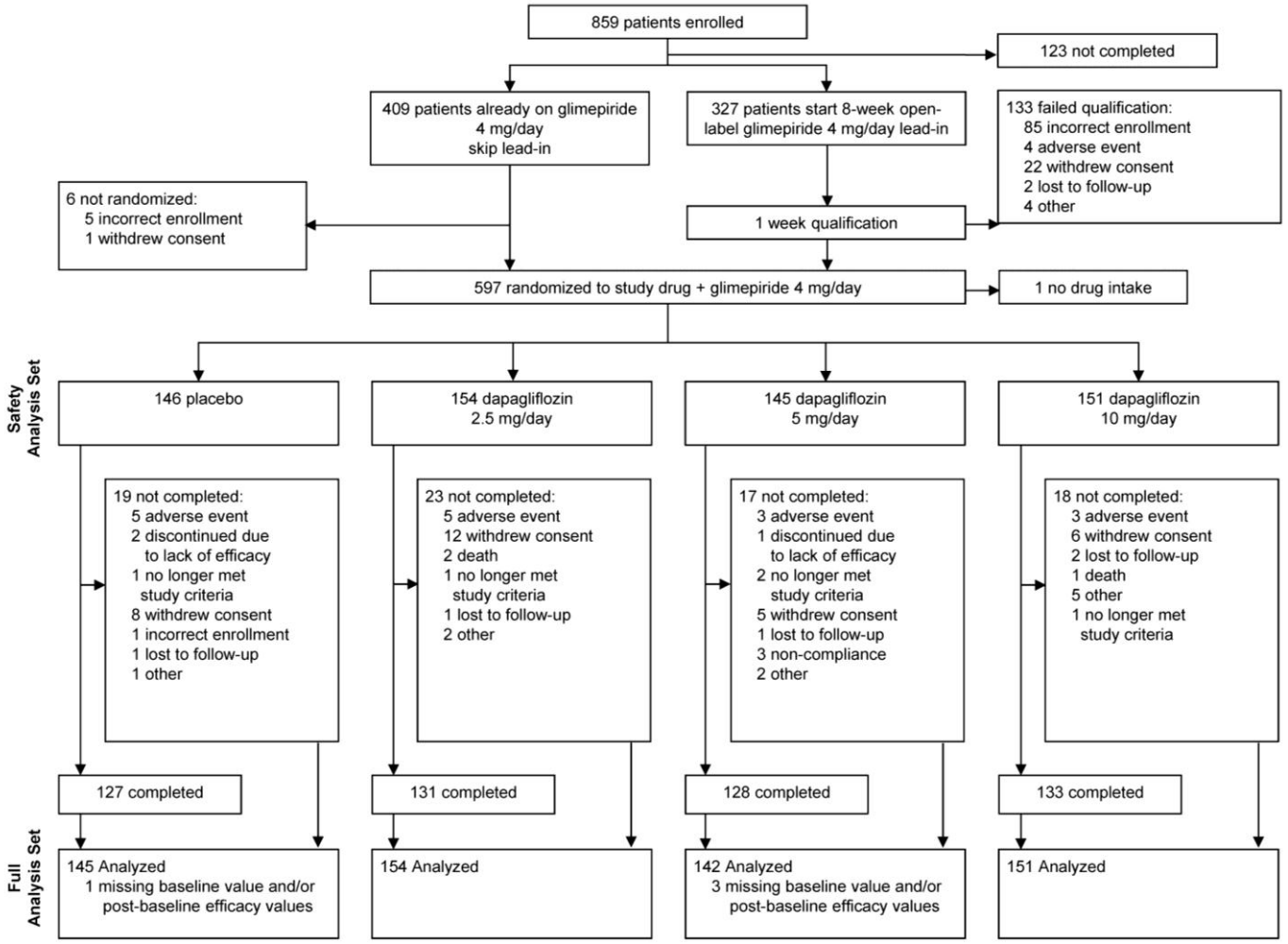


Fig. S2 Change in HbA_{1c} (%) with treatment over 48 weeks (full analysis set) including data after rescue therapy. *Data are adjusted mean changes from baseline ± 95% CI derived from a repeated-measures mixed model. *N* is the number of patients in the full analysis set, and *n* is the number of patients in the full analysis set with non-missing baseline and week (t) values. Treatment group symbols are shifted horizontally to prevent error bar overlapping. *CI* confidence interval, *DAPA* dapagliflozin, *GLI* glimepiride, *PLA* placebo. Placebo-corrected values for HbA_{1c} change from baseline at 48 weeks were −0.26 (95% CI, −0.44, −0.07), −0.34 (95% CI, −0.53, −0.15), and −0.50 (95% CI, −0.69, −0.31) in the dapagliflozin 2.5-, 5-, and 10-mg groups, respectively.

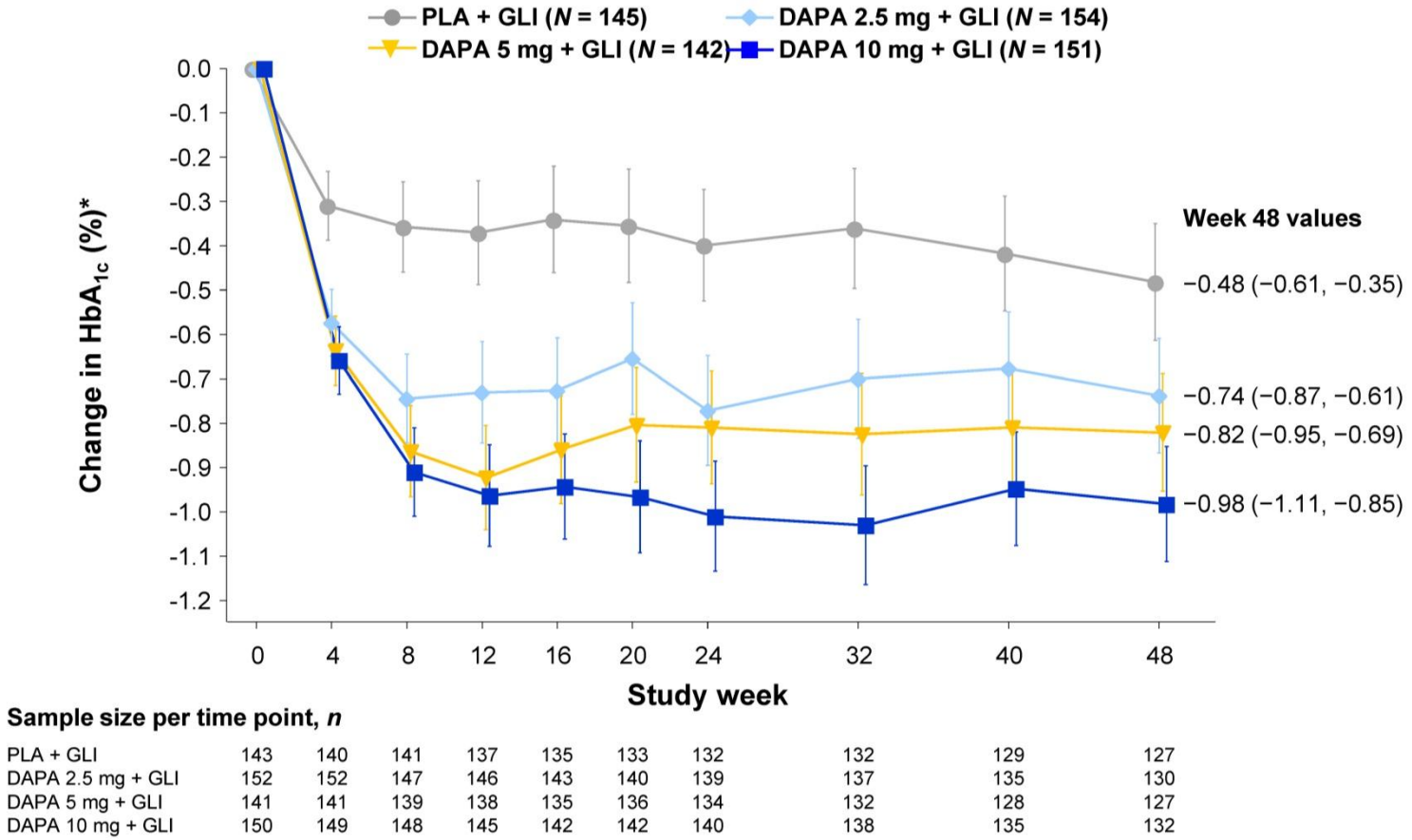
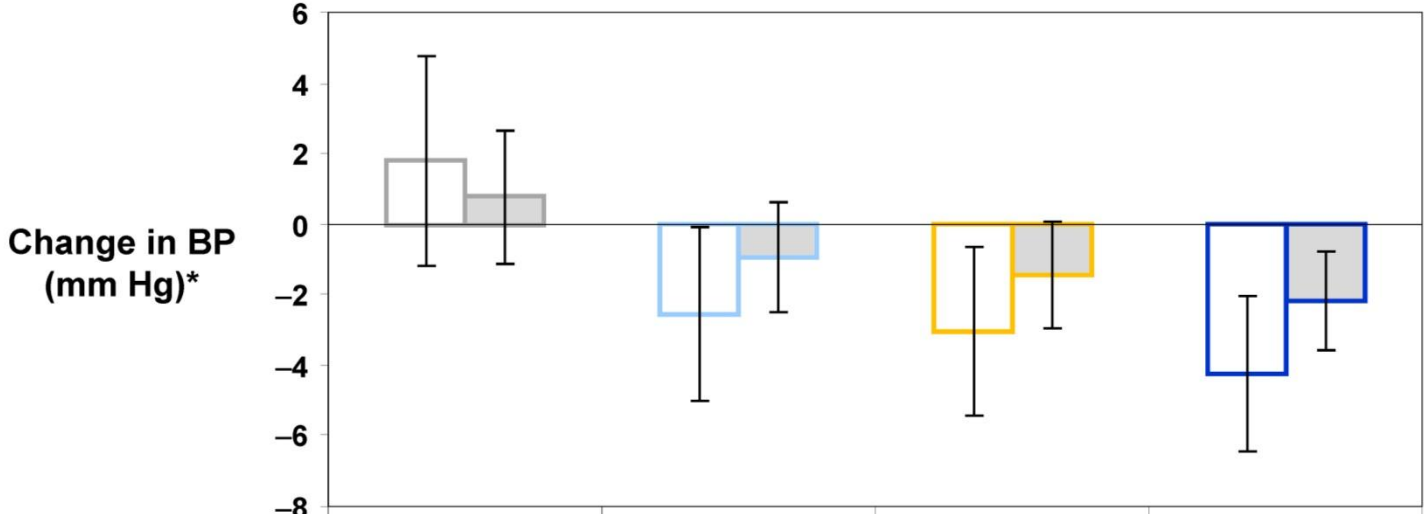


Fig. S3 Change in systolic BP (SBP) and diastolic BP (DBP) at week 48. Data are adjusted mean changes from baseline ± 95% confidence interval derived from repeated-measures analysis, and exclude data after rescue therapy. *n* is the number of patients with non-missing baseline and week 48 values. *BP* blood pressure, *DAPA* dapagliflozin, *GLI* glimepiride, *PLA* placebo.



	PLA + GLI (*n* = 55)	DAPA 2.5 mg + GLI (*n* = 83)	DAPA 5 mg + GLI (*n* = 90)	DAPA 10 mg + GLI (*n* = 107)
Seated SBP				
Baseline BP (mm Hg)	133.3	134.6	130.9	132.4
Change from baseline	1.81	−2.53	−3.01	−4.21
Difference vs. PLA		−4.33	−4.81	−6.02
95% CI of difference		−8.18 to −0.49	−8.62 to −1.01	−9.71 to −2.32
Seated DBP				
Baseline BP (mm Hg)	79.8	79.0	77.9	78.7
Change from baseline	0.79	−0.91	−1.41	−2.15
Difference vs. PLA		−1.70	−2.20	−2.94
95% CI of difference		−4.15 to 0.75	−4.62 to 0.22	−5.29 to −0.59

Fig. S4 Percentage of patients experiencing their first event of hypoglycemia from 0 to 24 weeks versus 24 to 48 weeks (safety analysis set and excluding data after rescue therapy). *DAPA* dapagliflozin, *GLI* glimepiride, *PLA* placebo.

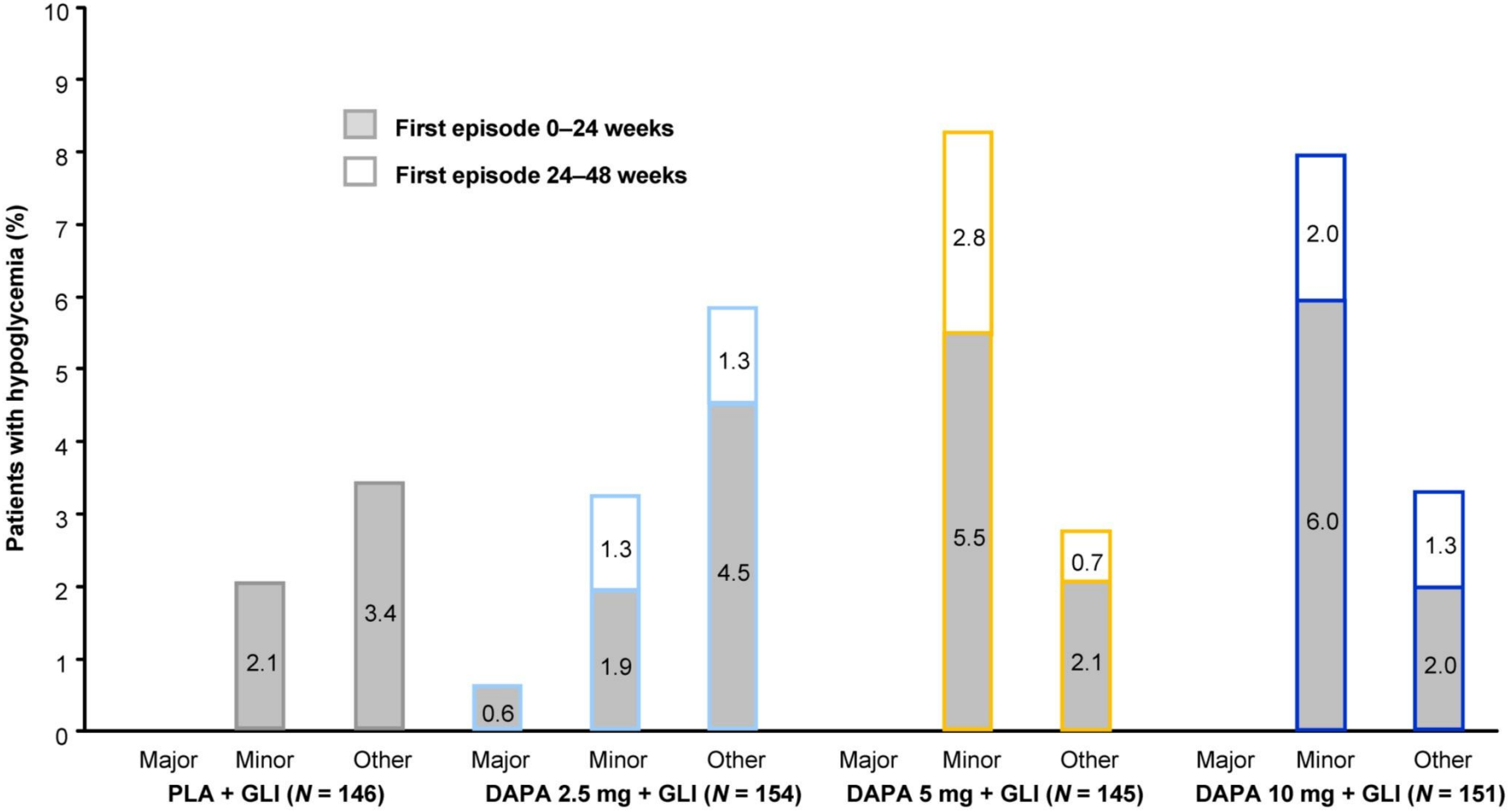


Table S1 Changes in HbA_{1c} (%) from week 24 at week 48[a]

	PLA + GLI (*N* = 111)	**DAPA 2.5 mg + GLI (*N* = 131)**	**DAPA 5 mg + GLI (*N* = 126)**	**DAPA 10 mg + GLI (*N* = 138)**
Week 24				
n	109	127	125	134
Mean ± SD	7.81 ± 0.78	7.42 ± 0.80	7.38 ± 0.87	7.25 ± 0.83
Week 48				
n	55	83	89	106
Mean ± SD	7.29 ± 0.66	7.21 ± 0.56	7.08 ± 0.75	7.11 ± 0.62
Adjusted change from week 24	0.20	0.22	0.10	0.08
95% CI for adjusted mean	0.07, 0.34	0.11, 0.34	−0.02, 0.21	−0.03, 0.19
Difference vs. PLA + GLI		0.02	−0.11	−0.12
95% CI for difference		−0.16, 0.20	−0.29, 0.07	−0.30, 0.05

N is the number of subjects in the short-term completers analysis set. At week 24, *n* corresponds to the number of patients in the short-term completers analysis set with non-missing week 24 value and at least one post-week 24 value. At week 48, *n* is the number of patients in the short-term completers analysis set with non-missing week 24 and week 48 values. *CI* confidence interval, *DAPA* dapagliflozin, *GLI* glimepiride, *PLA* placebo. [a]Longitudinal repeated measure analysis, excluding data after rescue therapy (short-term completers analysis set).

Table S2 Lipid parameters and fasting C-peptide levels at weeks 24 and 48 (full analysis set)[a]

	Placebo + glimepiride (*N* = 145)	**Dapagliflozin 2.5 mg + glimepiride (*N* = 154)**	**Dapagliflozin 5 mg + glimepiride (*N* = 142)**	**Dapagliflozin 10 mg + glimepiride (*N* = 151)**
Total cholesterol				
n	141	148	139	149
Baseline mean (mmol/L)	4.9	4.9	5.0	5.0
Mean percent change at week 24 (95% CI)	2.3 (–0.8, 5.3)	5.3 (1.8, 8.7)	3.4 (0.3, 6.5)	1.8 (–1.0, 4.7)
Mean percent change at week 48 (95% CI)	–0.5 (–4.7, 3.7)	5.6 (1.2, 10.1)	2.2 (–1.9, 6.3)	1.5 (–1.6, 4.6)
LDL cholesterol				
n	141	148	139	149
Baseline mean (mmol/L)	2.8	2.8	2.8	2.9
Mean percent change at week 24 (95% CI)	4.8 (–0.2, 9.8)	9.7 (4.4, 15.1)	6.3 (0.9, 11.7)	4.9 (0.1, 9.8)
Mean percent change at week 48 (95% CI)	–0.6 (–6.7, 5.6)	7.8 (1.0, 14.6)	5.7 (–1.8, 13.3)	3.9 (–1.1, 8.9)
HDL cholesterol				
n	141	148	139	149
Baseline mean (mmol/L)	1.2	1.2	1.2	1.2
Mean percent change at week 24 (95% CI)	4.9 (1.8, 7.9)	6.5 (3.8, 9.3)	6.0 (3.0, 9.0)	6.7 (3.8, 9.6)

	Placebo + glimepiride (*N* = 145)	**Dapagliflozin 2.5 mg + glimepiride (*N* = 154)**	**Dapagliflozin 5 mg + glimepiride (*N* = 142)**	**Dapagliflozin 10 mg + glimepiride (*N* = 151)**
Mean percent change at week 48 (95% CI)	5.5 (1.4, 9.6)	10.8 (7.0, 14.6)	7.9 (4.3, 11.5)	10.4 (6.8, 14.0)
Triglycerides				
n	141	148	139	149
Baseline mean (mmol/L)	2.1	1.9	2.1	2.2
Mean percent change at week 24 (95% CI)	4.5 (–3.4, 12.3)	2.8 (–4.8, 10.5)	1.4 (–5.3, 8.1)	–3.9 (–9.7, 1.9)
Mean percent change at week 48 (95% CI)	3.1 (–7.0, 13.1)	–0.6 (–9.1, 8.0)	–0.9 (–9.1, 7.3)	–3.7 (–13.7, 6.4)
Free fatty acids				
n	141	148	139	149
Baseline mean (mmol/L)	0.6	0.5	0.6	0.6
Mean percent change at week 24 (95% CI)	14.6 (4.7, 24.6)	14.7 (4.7, 24.6)	20.9 (8.4, 33.4)	21.8 (11.0, 32.6)
Mean percent change at week 48 (95% CI)	11.8 (–4.1, 27.7)	32.8 (15.8, 49.8)	25.8 (11.7, 40.0)	24.6 (11.2, 38.1)
Fasting C-peptide				
n	141	148	139	148
Baseline mean (nmol/L)	1.02	1.02	1.04	1.02
Mean percent change at week 24 (95% CI)	0.01 (−0.06, 0.08)	−0.04 (0.09, 0.01)	−0.05 (−0.13, 0.02)	−0.07 (−0.12, −0.02)

	Placebo + glimepiride (*N* = 145)	**Dapagliflozin 2.5 mg + glimepiride (*N* = 154)**	**Dapagliflozin 5 mg + glimepiride (*N* = 142)**	**Dapagliflozin 10 mg + glimepiride (*N* = 151)**
Mean percent change at week 48 (95% CI)	−0.01 (−0.14, 0.12)	−0.09 (−0.15, −0.03)	−0.10 (−0.2, 0.01)	−0.07 (−0.14, −0.01)

N is the number of patients in the full analysis set, and *n* is the number of patients with non-missing baseline values and at least one post-baseline value in the full analysis set. *CI* confidence interval, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein. [a]Data are unadjusted mean changes from baseline ± 95% CI derived from repeated-measures analysis, and exclude data after rescue therapy.

Table S3 Neoplasms benign, malignant, and unspecified (including cysts and polyps) over 48 weeks (safety analysis set), including data after rescue therapy[a]

Preferred term, *n* (%)	**Placebo + glimepiride (*N* = 146)**	**Dapagliflozin 2.5 mg + glimepiride (*N* = 154)**	**Dapagliflozin 5 mg + glimepiride (*N* = 145)**	**Dapagliflozin 10 mg + glimepiride (*N* = 151)**
Total	2 (1.4)	6 (3.9)	4 (2.8)	2 (1.3)
Breast cancer	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
Prostatic adenoma	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)
Benign breast neoplasm	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)
Benign neoplasm of the thyroid gland	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Chronic lymphocytic leukemia	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Endometrial cancer	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Lipoma	0 (0.0)	0 (0.0)	1 (0.7)	
Lung neoplasm	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Lung neoplasm, malignant	0 (0.0)	1 (0.6)	1 (0.7)	0 (0.0)
Mediastinum neoplasm	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)
Rectal adenoma	1 (0.7)		1 (0.7)	
Seborrheic keratosis	1 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)
Uterine leiomyoma	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)

[a]Includes non-serious adverse events with onset on or after the first date of double-blind treatment and on or prior to the last day of short-term or long-term double-blind treatment plus 4 days or up to follow-up visit if earlier. Includes serious adverse events with onset on or after the first

date of double-blind treatment, and on or prior to the last day of short-term or long-term double-blind treatment, plus 30 days, or up to follow-up visit if earlier.

Table S4 Laboratory values of interest: change from baseline at weeks 24 and 48

	Placebo + glimepiride (*N* = 146)	**Dapagliflozin 2.5 mg + glimepiride (*N* = 154)**	**Dapagliflozin 5 mg + glimepiride (*N* = 145)**	**Dapagliflozin 10 mg + glimepiride (*N* = 151)**
Hematocrit (%)				
Baseline	41.83 (3.47)	41.97 (4.11)	41.98 (3.23)	42.25 (3.72)
Change at week 24	0.01 [0.17]	1.93 [0.20]	2.28 [0.22]	2.19 [0.20]
Change at week 48	–0.26 [0.22]	2.28 [0.21]	2.26 [0.26]	2.53 [0.21]
Serum creatinine (µmol/L)				
Baseline	78.3 (19.6)	77.9 (18.9)	75.3 (16.1)	75.2 (17.0)
Change at week 24	0.09 [0.97]	1.59 [0.77]	0.44 [0.83]	0.71 [0.71]
Change at week 48	–0.27 [1.03]	0.53 [0.79]	0.44 [0.82]	0.35 [0.86]
Calculated creatinine clearance (mL/min)				
Baseline	97.6 (30.5)	100.5 (37.3)	100.5 (32.3)	101.3 (32.6)
Change at week 24	–1.3 [1.06]	–3.5 [1.01]	–2.4 [1.02]	–4.8 [1.08]
Change at week 48	–1.6 [1.13]	–4.3 [1.05]	–3.1 [1.01]	–4.3 [1.31]
Estimated GFR (mL/min/1.73 m^2)				
Baseline	80.2 (19.1)	80.9 (18.6)	83.5 (19.6)	82.2 (17.9)
Change at week 24	0.0 [0.94]	–1.5 [0.89]	–0.1 [1.02]	–1.2 [1.03]
Change at week 48	–0.2 [0.96]	–0.7 [0.97]	–0.4 [1.05]	–0.3 [1.19]
Blood urea nitrogen (mmol/L)				
Baseline	5.8 (1.72)	5.6 (1.69)	5.6 (1.62)	5.5 (1.54)
Change at week 24	0.04 [0.13]	0.36 [0.12]	0.43 [0.12]	0.61 [0.11]

	Placebo + glimepiride (*N* = 146)	Dapagliflozin 2.5 mg + glimepiride (*N* = 154)	Dapagliflozin 5 mg + glimepiride (*N* = 145)	Dapagliflozin 10 mg + glimepiride (*N* = 151)
Change at week 48	0.11 [0.12]	0.39 [0.13]	0.54 [0.14]	0.68 [0.13]
Serum uric acid (µmol/L)				
Baseline	315.2 (93.6)	301.6 (81.2)	303.9 (79.8)	301.0 (82.4)
Change at week 24	1.19 [4.77]	–21.41 [4.29]	–26.17 [5.37]	–26.17 [4.90]
Change at week 48	20.22 [5.51]	–17.25 [5.41]	–17.85 [5.46]	–26.17 [4.66]
Serum cystatin-C (mmol/L)				
Baseline	0.56 (0.14)	0.56 (0.12)	0.56 (0.13)	0.55 (0.12)
Change at week 24	0.03 [0.01]	0.04 [0.01]	0.03 [0.01]	0.04 [0.01]
Change at week 48	–1.4 [0.9]	1.7 [1.1]	2.3 [1.1]	2.2 [1.1]
Urine glucose (mmol/L)				
Baseline	26.0 (58.0)	19.2 (47.7)	21.1 (55.3)	21.7 (48.4)
Change at week 24	–13.96 [5.68]	98.53 [8.40]	119.90 [8.45]	155.14 [9.28]
Change at week 48	–13.53 [5.10]	89.93 [8.88]	112.79 [8.60]	151.36 [9.27]
Urinary glucose:creatinine ratio (g/g)				
Baseline	6.21 (19.12)	3.63 (9.8)	4.55 (12.38)	4.96 (13.58)
Change at week 24	–3.4 [1.58]	20.7 [2.40]	30.0 [2.79]	35.2 [2.40]
Change at week 48	–3.4 [1.49]	18.4 [1.90]	26.9 [2.53]	34.8 [2.29]

Data are mean (standard deviation) or mean [standard error] using the safety analysis set (*full analysis set). Measures for urinary glucose and glucose:creatinine ratio were derived from a urinary spot-check performed in the morning fasting state. *N* is the number of patients at baseline in the safety analysis set. *GFR* glomerular filtration rate.