SUPPLEMENTARY DATA

Online-Only Supplementary Material

Supplementary Table S1 – Criteria for initiation of rescue therapy during the randomized treatment and extension periods

Study period	Central laboratory measure	Time window
Randomized treatment	Confirmed FPG >15 mmol/L (>270 mg/dL)	From week 8, inclusive, up to and including the day before week 12
	Confirmed FPG >13.2 mmol/L (>240 mg/dL)	From week 12, inclusive, up to and including the day before week 20
	Confirmed FPG >11.1 mmol/L (>200 mg/dL)	From week 20, inclusive, up to and including week 28 and all unscheduled visits through the day before week 36
Extension	Single HbA_{1c} >8.0% (>64 mmol/mol)	From the day of week 36 up to and including week 52 and all unscheduled visits through the day before week 65

FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin.

Supplementary Table S2 – Percent of dispensed study medication used over the 52 weeks

	Exenatide QW + dapagliflozin (*n*=231)	**Exenatide QW + placebo (*n*=230)**	**Dapagliflozin + placebo (*n*=233)**	**Total (*N*=694)**
% of dispensed exenatide QW or matching placebo used				
Mean (SD)	95.65 (17.82)	93.05 (16.08)	91.60 (15.16)	93.42 (16.45)
% received, *n* (%)				
<80%	20 (8.7)	30 (13.0)	28 (12.0)	78 (11.2)
80 to <120%	206 (89.2)	197 (85.7)	205 (88.0)	608 (87.6)
≥120%	5 (2.2)	3 (1.3)	0	8 (1.2)
% of dispensed dapagliflozin or matching placebo used				
Mean (SD)	100.81 (19.82)	99.60 (17.07)	97.21 (13.10)	99.20 (16.93)
% received, *n* (%)				
<80%	6 (2.6)	10 (4.3)	9 (3.9)	25 (3.6)
80 to <120%	209 (90.5)	205 (89.1)	218 (93.6)	632 (91.1)
≥120%	16 (6.9)	15 (6.5)	6 (2.6)	37 (5.3)

QW, once weekly; SD, standard deviation.

Supplementary Table S3 – Demographic and baseline characteristics

	Exenatide QW + dapagliflozin (*n*=228)	**Exenatide QW + placebo (*n*=227)**	**Dapagliflozin + placebo (*n*=230)**
Age, mean (SD), years	53.8 (9.8)	54.2 (9.6)	54.5 (9.2)
Male, *n* (%)	102 (44.7)	116 (51.1)	110 (47.8)
Race, *n* (%)			
White	190 (83.3)	194 (85.5)	189 (82.2)
Black	34 (14.9)	27 (11.9)	33 (14.3)
Asian	3 (1.3)	1 (0.4)	1 (0.4)
Other	1 (0.4)	5 (.22)	7 (3.0)
Hispanic ethnicity, *n* (%)	95 (41.7)	91 (40.1)	85 (37.0)
Weight, mean (SD), kg	91.8 (22.2)	89.8 (20.2)	91.1 (19.7)
BMI, mean (SD), kg/m^2	33.2 (6.8)	32.0 (5.9)	33.0 (6.1)
BMI group, *n* (%)			
<25 kg/m^2	17 (7.5)	17 (7.5)	15 (6.5)
≥25 to <30 kg/m^2	71 (31.1)	78 (34.4)	57 (24.8)
≥30 kg/m^2	140 (61.4)	132 (58.1)	158 (68.7)
HbA_{1c}, mean (SD), %	9.3 (1.1)	9.3 (1.1)	9.3 (1.0)
HbA_{1c}, mean (SD), mmol/mol	79 (11.7)	78 (11.6)	78 (11.3)
HbA_{1c} group, *n* (%)			
<8.0% [<64 mmol/mol]	14 (6.1)	13 (5.7)	14 (6.1)
≥8.0% to <9.0% [≥64 to <75 mmol/mol]	84 (36.8)	84 (37.0)	88 (38.3)
≥9.0% [≥75 mmol/mol]	130 (57.0)	130 (57.3)	128 (55.7)
Type 2 diabetes duration, mean (SD), years	7.6 (6.0)	7.4 (5.5)	7.1 (5.5)
FPG, mean (SD), mmol/L	11.0 (3.0)	10.7 (2.8)	10.6 (2.6)
SBP, mean (SD), mmHg	130.1 (12.7)	129.1 (13.1)	130.0 (12.9)
eGFR, mean (SD), mL/min/1.73 m^2*	97.7 (23.7)	99.4 (26.8)	97.5 (24.0)
eGFR group, *n* (%)			
≥30 to <60 mL/min/1.73 m^2	6 (2.6)	7 (3.1)	12 (5.2)
≥60 mL/min/1.73 m^2	222 (97.4)	220 (96.9)	218 (94.8)

To convert FPG from mmol/L to mg/dL, divide by 0.0555.

*Calculated using the Modification of Diet in Renal Disease equation.

DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin; QW, once weekly; SBP, systolic blood pressure; SD, standard deviation.

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Supplementary Table S4 – Other exploratory efficacy endpoints at week 52 in the intention-to-treat patient population

	Exenatide QW + dapagliflozin (*n*=228)	Exenatide QW + placebo (*n*=227)	Dapagliflozin + placebo (*n*=230)	Between-group difference (95% CI)	
				Exenatide QW + dapagliflozin vs. exenatide QW + placebo	Exenatide QW + dapagliflozin vs. dapagliflozin + placebo
Mean daily SMBG, mmol/L					
Baseline	11.34 (2.40)	11.01 (2.06)	11.20 (2.36)		
Week 28	8.47 (1.69)	8.89 (1.79)	8.93 (1.64)		
Change at week 28	–2.71 (0.13)	–2.18 (0.14)	–2.23 (0.13)	–0.53 (–0.85 to –0.21): *P*=0.001	–0.48 (–0.80 to –0.17); *P*=0.003
Week 52	8.26 (1.55)	8.63 (1.69)	8.86 (1.99)		
Change at week 52	–2.85 (0.15)	–2.36 (0.16)	–2.18 (0.15)	–0.49 (–0.87 to –0.11); *P*=0.011	–0.67 (–1.05 to –0.29); *P*<0.001
Waist circumference, cm					
Baseline	108.31 (15.42)	107.46 (17.05)	109.01 (16.22)		
Week 28	106.57 (15.42)	104.92 (13.78)	107.25 (15.94)		
Change at week 28	–1.60 (0.70)	–2.68 (0.74)	–1.49 (0.70)	+1.08 (–0.67 to +2.84); *P*=0.225	–0.11 (–1.83 to +1.61): *P*=0.902
Week 52	106.33 (17.63)	105.63 (15.19)	105.00 (15.23)		
Change at week 52	–2.01 (1.01)	–1.76 (1.07)	–3.58 (1.04)	–0.25 (–2.84 to +2.34); *P*=0.850	+1.57 (–0.99 to +4.13); *P*=0.229
DBP, mmHg					
Baseline	78.7 (7.7)	78.4 (8.0)	78.0 (8.1)		
Week 28	78.8 (7.5)	79.4 (7.8)	77.8 (8.4)		
Change at week 28	–0.2 (0.5)	+0.3 (0.5)	–0.8 (0.5)	–0.5 (–1.9 to +1.0); *P*=0.520	+0.6 (–0.8 to +2.0); *P*=0.404
Week 52	77.8 (7.7)	79.6 (8.1)	78.5 (9.1)		
Change at week 52	–0.7 (0.6)	+0.2 (0.7)	–0.8 (0.7)	–0.9 (–2.7 to +0.8); *P*=0.310	+0.1 (–1.7 to +1.8); *P*=0.929
Total cholesterol, mmol/L					
Baseline	4.85 (1.16)	5.00 (1.21)	4.73 (1.05)		
Week 28	4.90 (1.18)	4.96 (1.10)	4.99 (1.18)		
Change at week 28	+0.02 (0.07)	–0.04 (0.07)	+0.18 (0.07)	+0.06 (–0.12 to +0.23); *P*=0.532	–0.16 (–0.33 to +0.01); *P*=0.067
Week 52	4.88 (1.12)	4.91 (1.20)	4.86 (1.13)		
Change at week 52	+0.10 (0.08)	+0.02 (0.09)	+0.14 (0.08)	+0.08 (–0.13 to +0.28); *P*=0.458	–0.05 (–0.25 to +0.15); *P*=0.639
LDL cholesterol, mmol/L					
Baseline	2.70 (0.96)	2.79 (1.06)	2.61 (0.91)		
Week 28	2.79 (0.97)	2.81 (0.97)	2.80 (0.99)		

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	Exenatide QW + dapagliflozin (*n*=228)	Exenatide QW + placebo (*n*=227)	Dapagliflozin + placebo (*n*=230)	Between-group difference (95% CI)	
				Exenatide QW + dapagliflozin vs. exenatide QW + placebo	Exenatide QW + dapagliflozin vs. dapagliflozin + placebo
Change at week 28	+0.07 (0.06)	+0.03 (0.07)	+0.14 (0.06)	+0.04 (–0.11 to +0.20); *P*=0.602	–0.07 (–0.23 to +0.08); *P*=0.365
Week 52	2.74 (0.88)	2.70 (1.02)	2.63 (0.94)		
Change at week 52	+0.11 (0.07)	+0.02 (0.07)	+0.05 (0.07)	+0.09 (–0.08 to +0.26); *P*=0.301	+0.06 (–0.11 to +0.23); *P*=0.473
HDL cholesterol, mmol/L					
Baseline	1.22 (0.33)	1.22 (0.30)	1.17 (0.27)		
Week 28	1.27 (0.30)	1.25 (0.32)	1.24 (0.30)		
Change at week 28	+0.04 (0.02)	+0.02 (0.02)	+0.05 (0.02)	+0.02 (–0.01 to +0.06); *P*=0.230	–0.01 (–0.05 to +0.03); *P*=0.565
Week 52	1.29 (0.33)	1.26 (0.30)	1.24 (0.29)		
Change at week 52	+0.07 (0.02)	+0.02 (0.02)	+0.07 (0.02)	+0.05 (+0.01 to +0.10); *P*=0.028	+0.01 (–0.04 to +0.05); *P*=0.769
Non-HDL cholesterol, mmol/L					
Baseline	3.63 (1.11)	3.78 (1.20)	3.56 (1.04)		
Week 28	3.63 (1.13)	3.71 (1.10)	3.75 (1.14)		
Change at week 28	–0.03 (0.07)	–0.06 (0.07)	+0.12 (0.07)	+0.03 (–0.14 to +0.20); *P*=0.721	–0.15 (–0.32 to +0.01); *P*=0.074
Week 52	3.59 (1.06)	3.65 (1.22)	3.62 (1.15)		
Change at week 52	+0.01 (0.08)	–0.01 (0.09)	+0.08 (0.08)	+0.03 (–0.18 to +0.23); *P*=0.807	–0.07 (–0.27 to +0.14); *P*=0.507
Triglycerides, mmol/L					
Baseline	2.12 (1.25)	2.24 (1.31)	2.13 (1.26)		
Week 28	1.86 (1.04)	2.06 (1.21)	2.07 (1.15)		
Change at week 28	–0.31 (0.08)	–0.18 (0.08)	–0.11 (0.08)	–0.13 (–0.32 to +0.06); *P*=0.181	–0.20 (–0.39 to –0.01); *P*=0.036
Week 52	1.89 (1.09)	2.18 (1.67)	2.19 (1.46)		
Change at week 52	–0.22 (0.11)	–0.06 (0.12)	+0.01 (0.12)	–0.16 (–0.45 to 0.13); *P*=0.271	–0.23 (–0.52 to +0.06); *P*=0.114

Data exclude measurements are the initiation of rescue therapy. Baseline, week 28, and week 52 data are mean (standard deviation), change data are least-squares mean (standard error), and difference data are least-squares mean (95% CI). To convert mg/dL to mmol/L for glucose, divide by 0.0555. To convert mmol/L to mg/dL for cholesterol, divide by 0.0259. To convert mmol/L to mg/dL for triglycerides, divide by 0.0113. Mean daily SMBG, waist circumference, and DBP were analyzed using a mixed-effects model for repeated measures; lipid parameters were analyzed using ANCOVA models.

DBP, diastolic blood pressure; QW, once weekly; SMBG, self-monitored blood glucose.

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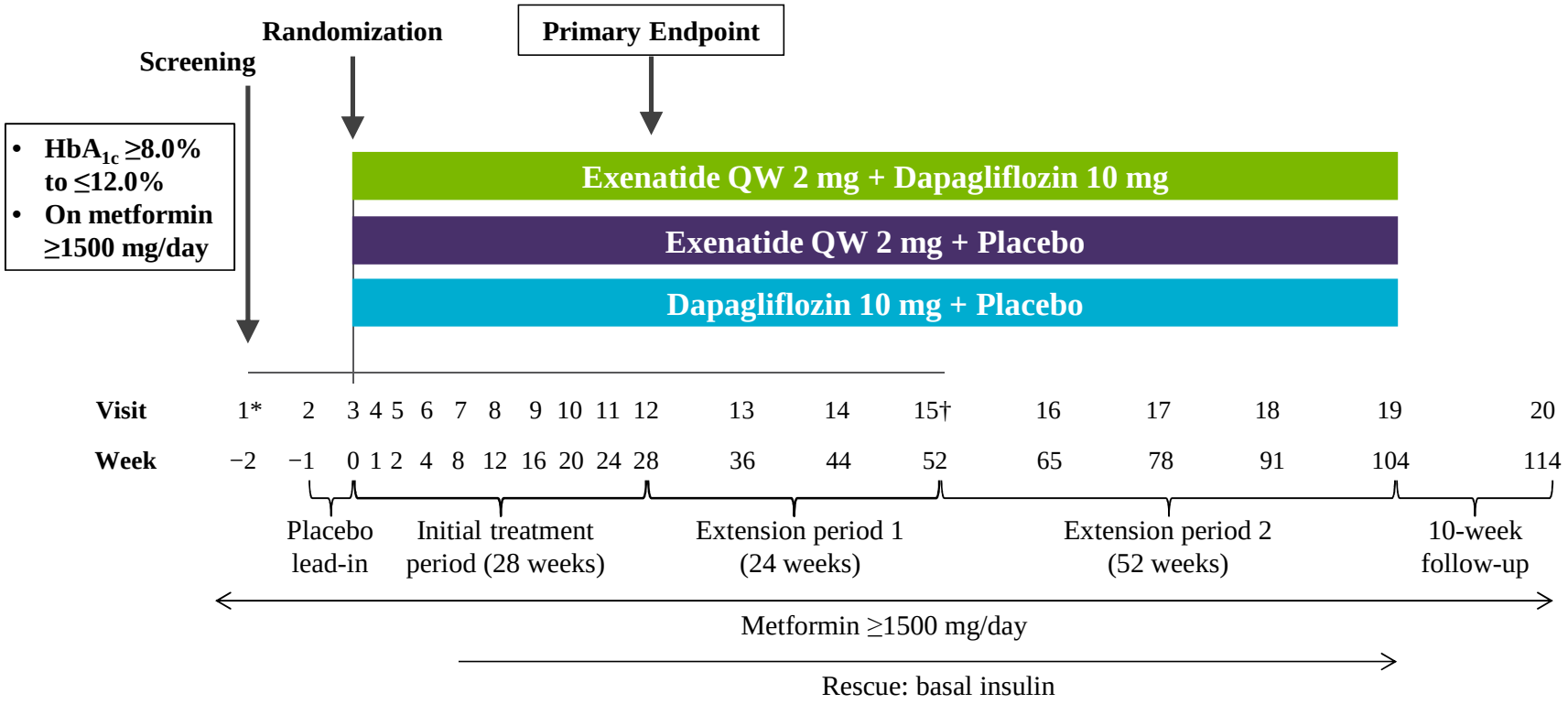
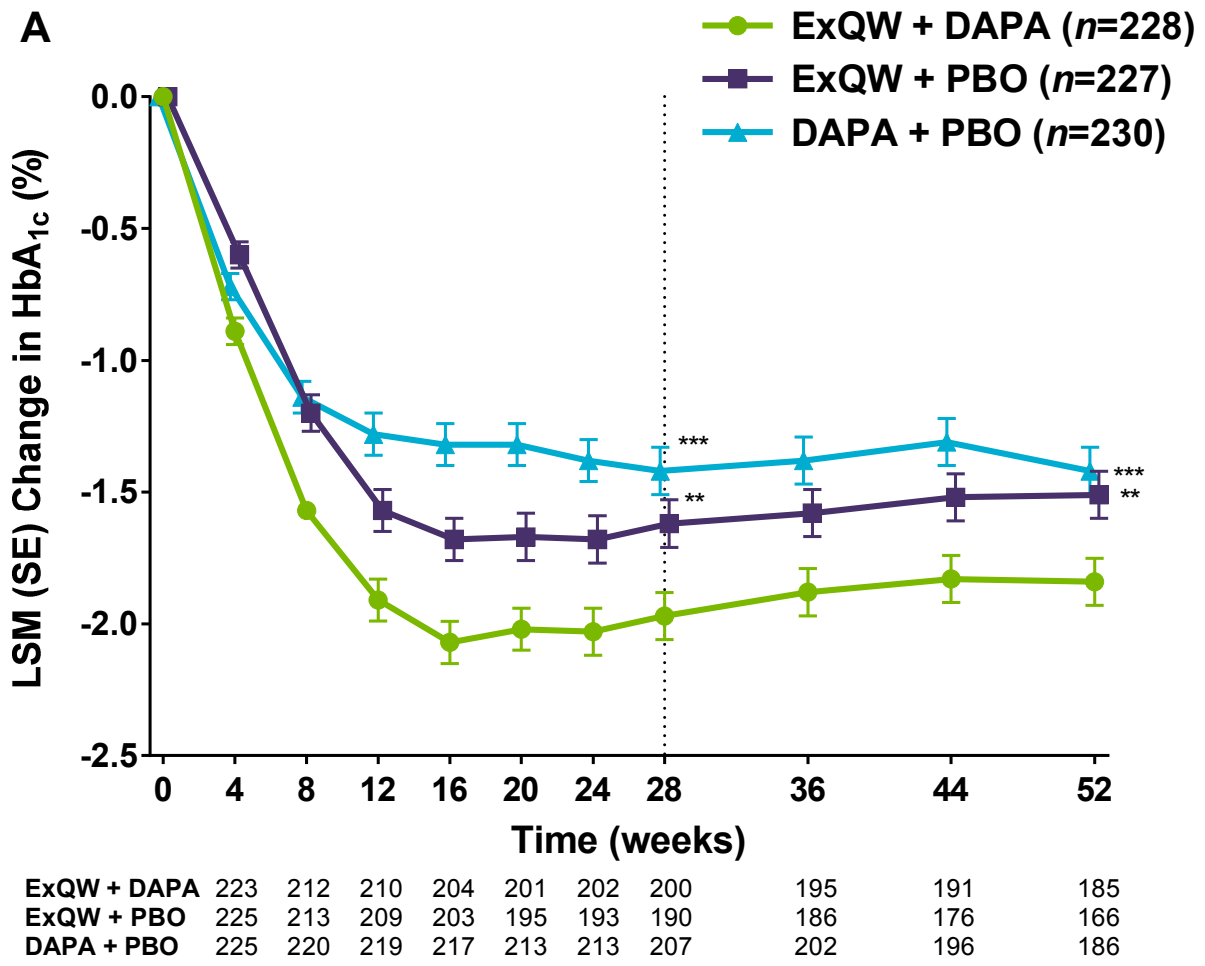
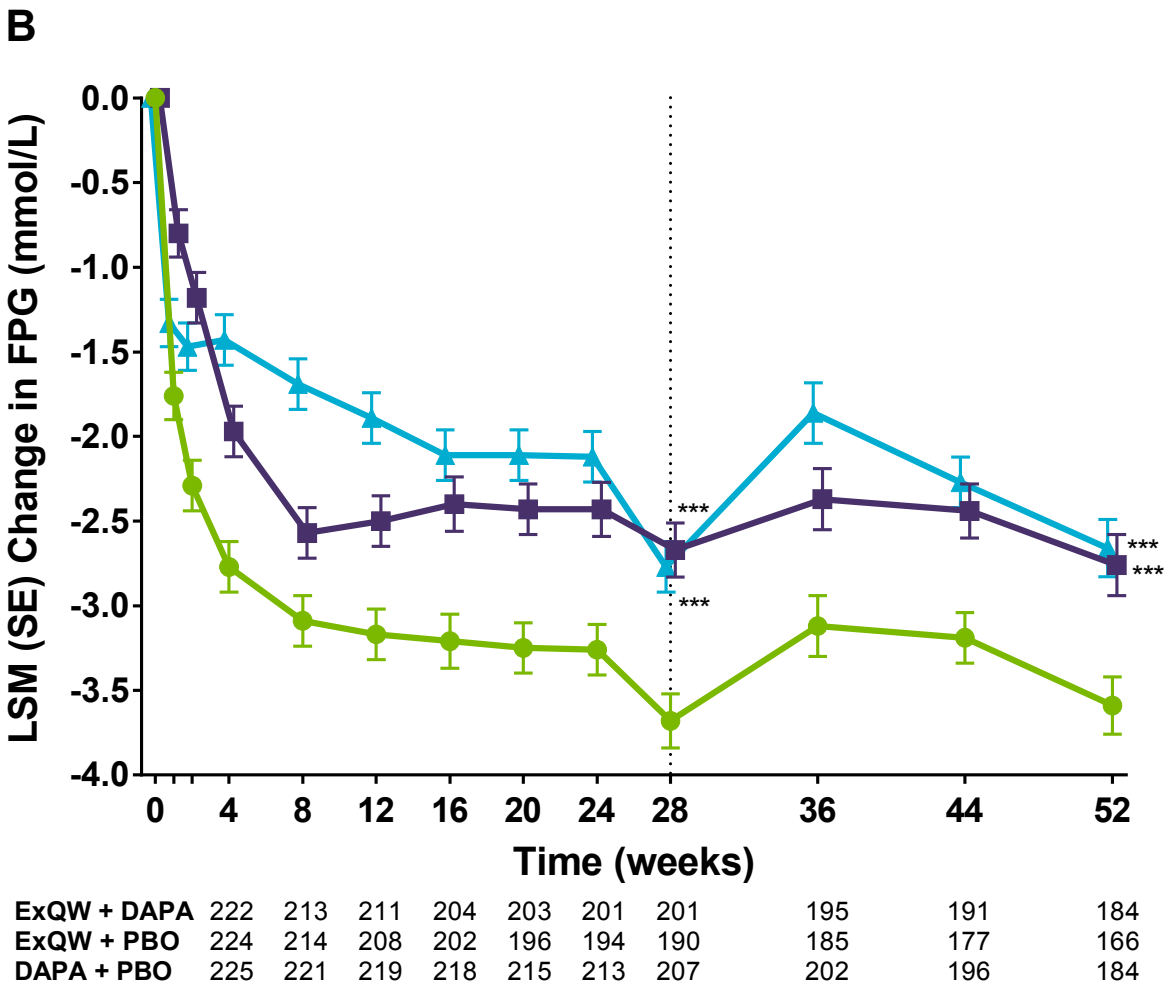
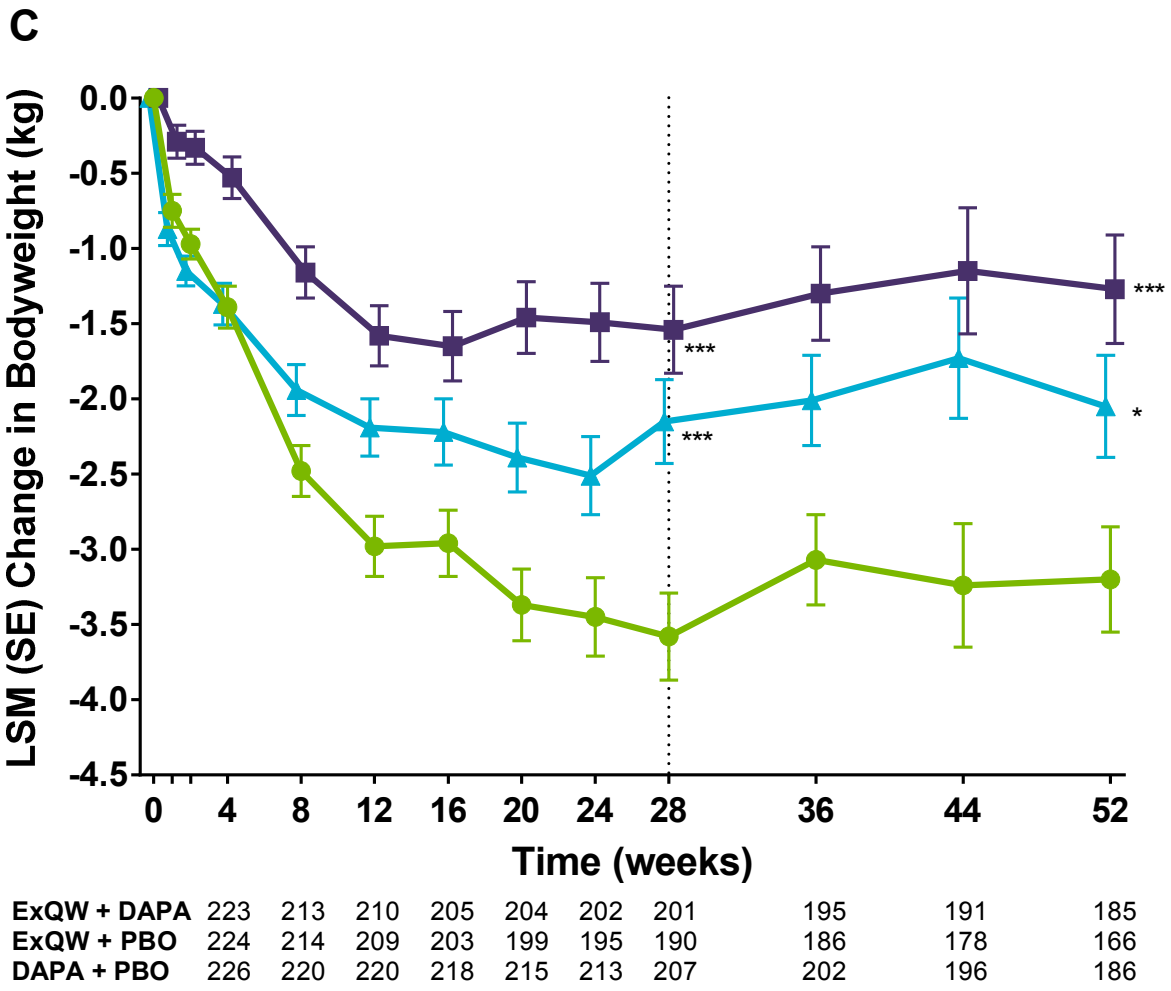
Supplementary Figure S1 – Study design. HbA_{1c}, glycated hemoglobin; ExQW, exenatide once weekly. *First patient enrolled: 04 September 2014. †Last patient last visit for initial treatment period (28 weeks) plus extension period 1 (24 weeks): 17 October 2016.



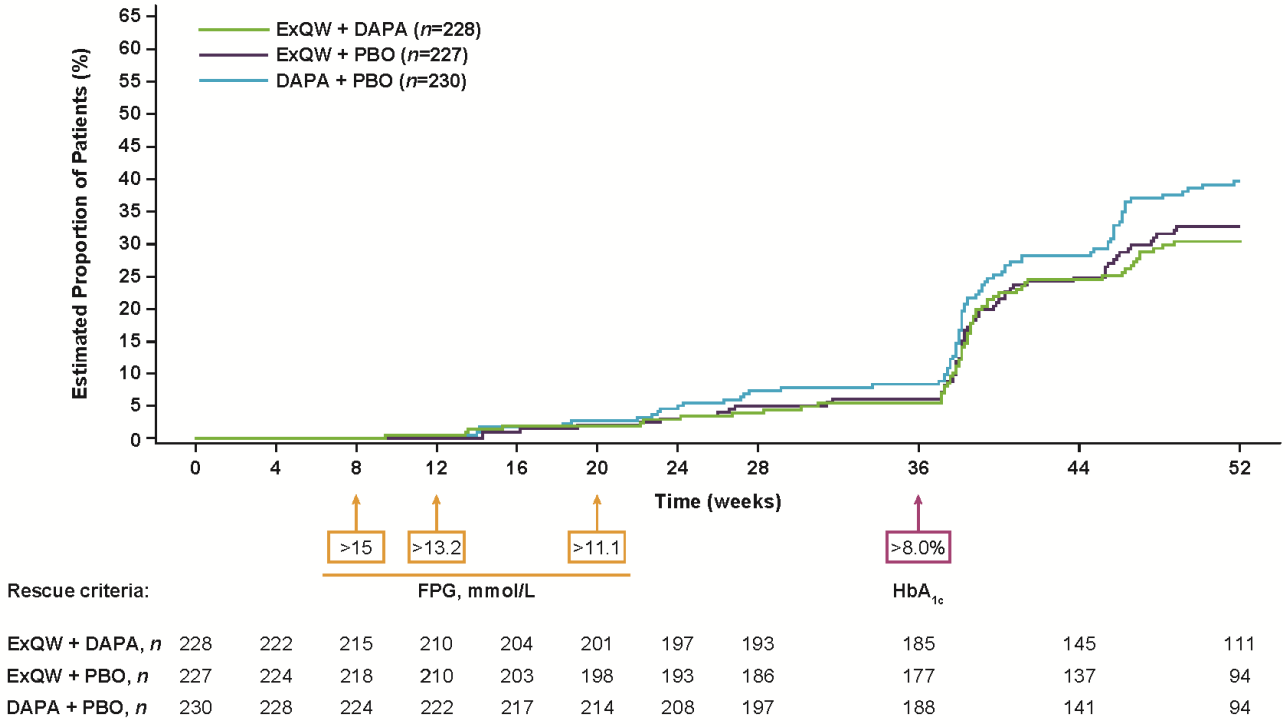
Supplementary Figure S2 – LSM (SE) change in *A*) HbA_{1c}, *B*) FPG, and *C*) weight with time including data from patients who received rescue therapy. Error bars show SEs. To convert FPG from mmol/L to mg/dL, divide by 0.0555. DAPA, dapagliflozin; ExQW, exenatide once weekly; FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin; LSM, least-squares mean; PBO, placebo; SE, standard error. **P*<0.05, ***P*<0.01, ****P*<0.001 vs. ExQW + DAPA (*P* values at week 52 are nominal).







Supplementary Figure S3 – Kaplan-Meier plot showing the proportion of patients rescued or discontinued for lack of glycemic control during the 52-week treatment period (intention-to-treat population). DAPA, dapagliflozin; ExQW, exenatide once weekly; FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin; PBO, placebo.



ExQW + DAPA, *n*	228	222	215	210	204	201	197	193	185	145	111
ExQW + PBO, *n*	227	224	218	210	203	198	193	186	177	137	94
DAPA + PBO, *n*	230	228	224	222	217	214	208	197	188	141	94

Supplementary Figure S4 – Mean (SE) change from baseline over time in *A*) eGFR, *B*) hematocrit, and *C*) heart rate. Error bars show SEs. BL, baseline; bpm, beats per minute; DAPA, dapagliflozin; eGFR, estimated glomerular filtration rate; ExQW, exenatide once weekly; PBO, placebo; SE, standard error.