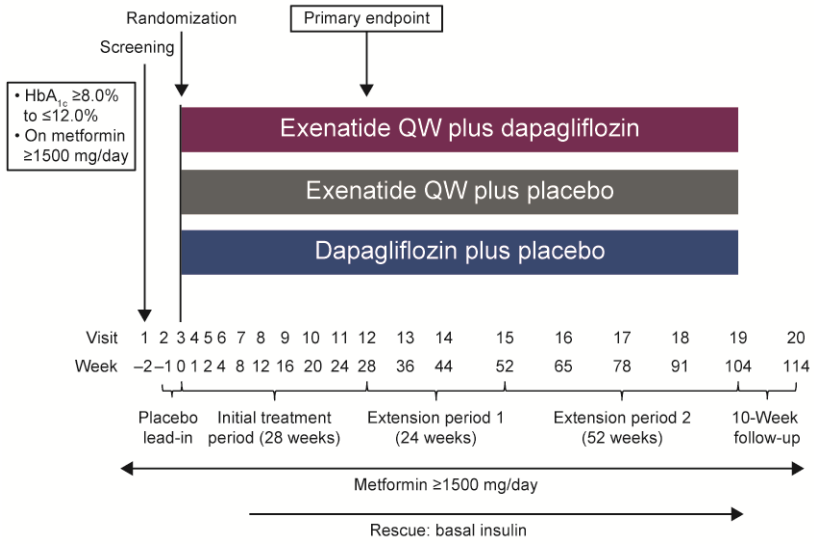
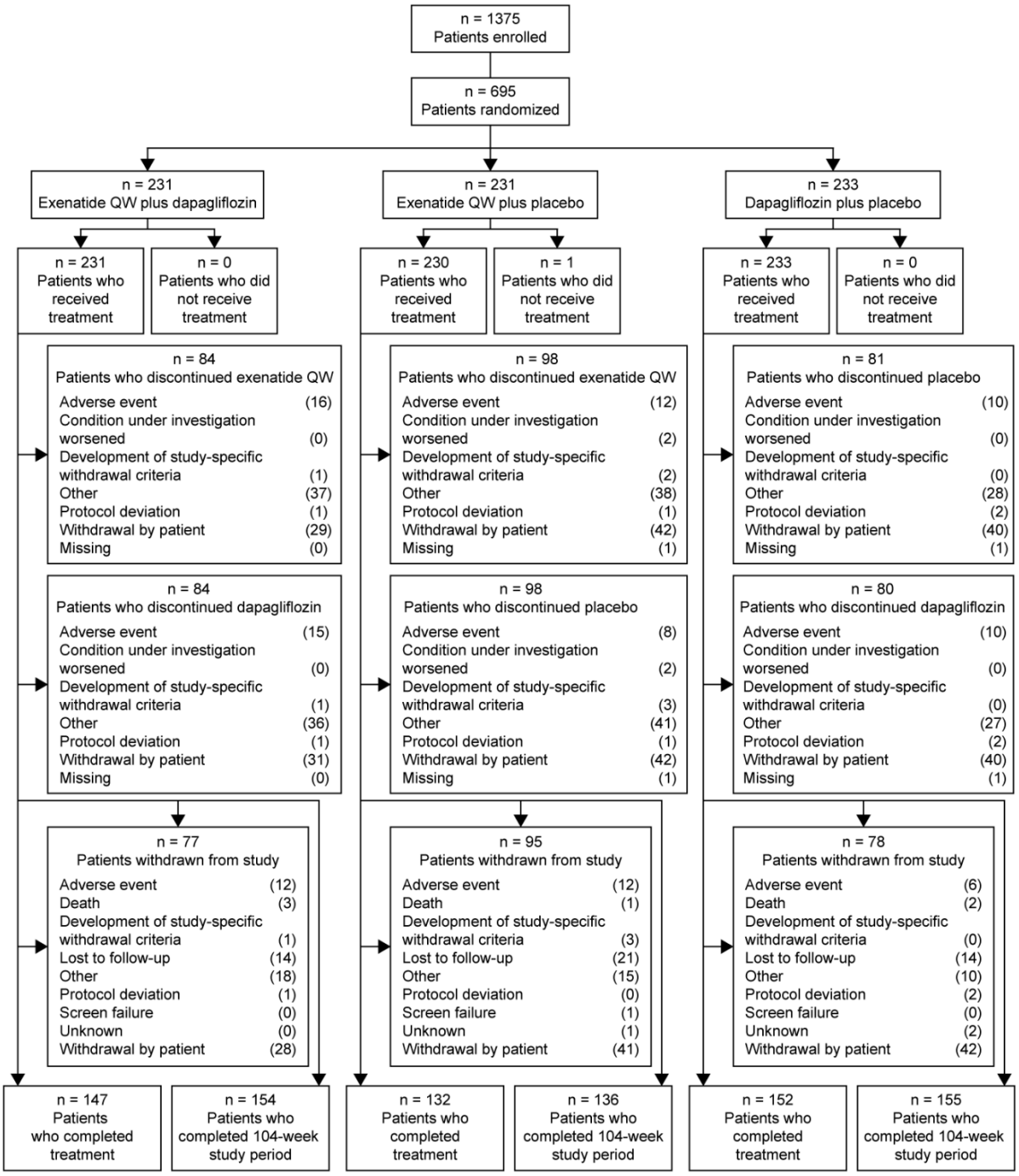
Online-only supplemental material

Supplementary Figure S1: Trial design



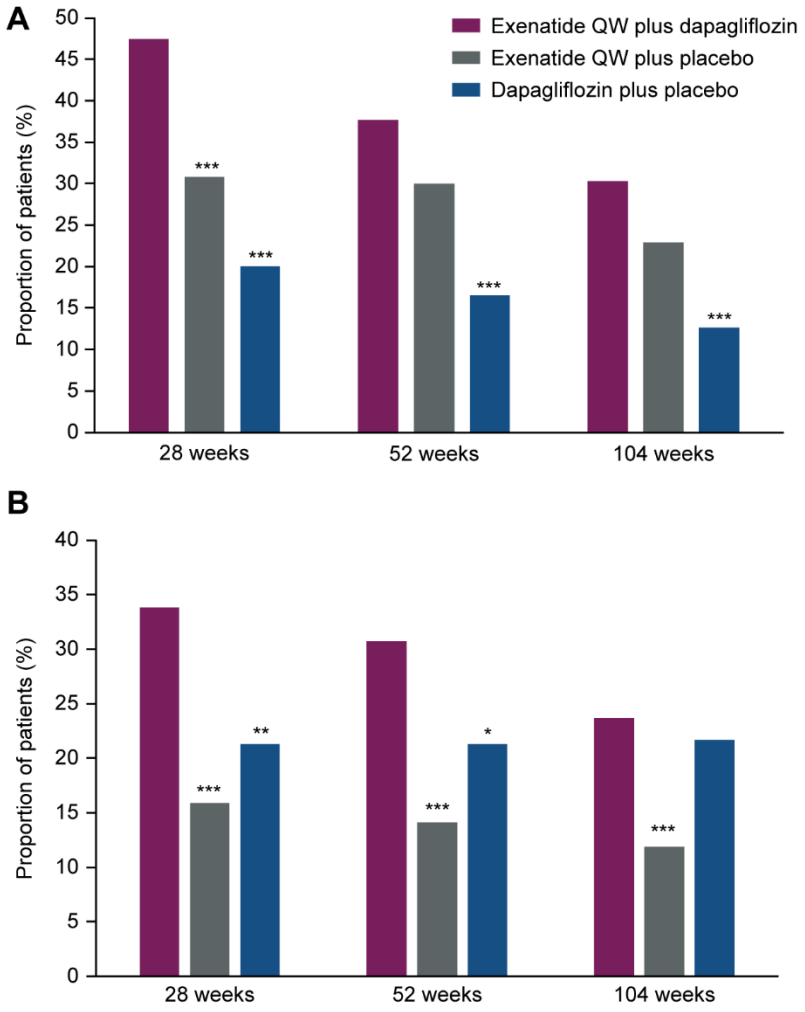
HbA_{1c}, glycated hemoglobin; QW, once weekly.

Supplementary Figure S2: Patient disposition.



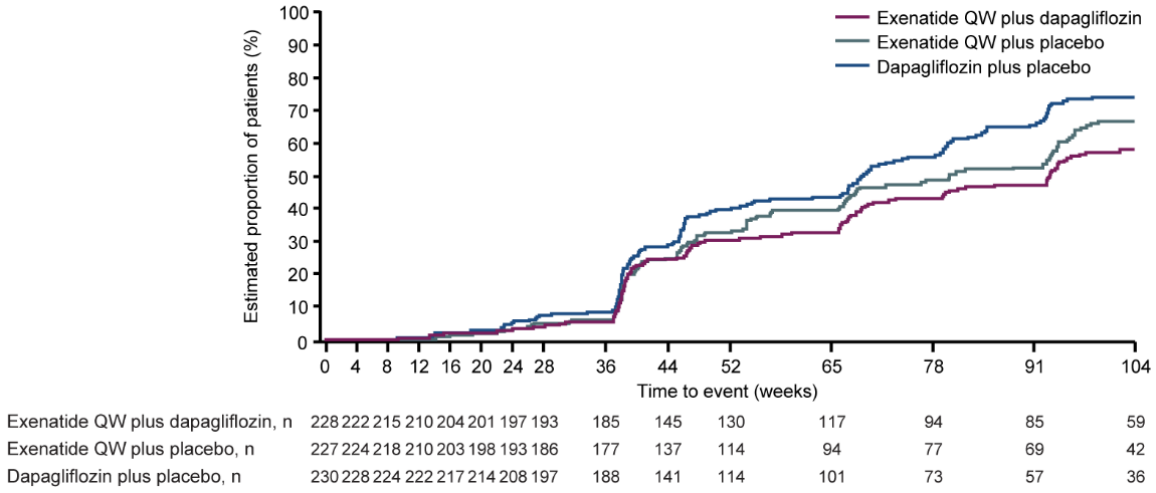
QW, once weekly

Supplementary Figure S3: Proportion of patients achieving HbA_{1c} <7.0% (<53 mmol/mol) (A), and weight loss ≥5% (B) at weeks 28, 52, and 104 (ITT population)



*P<0.05, **P<0.01, ***P<0.001 versus exenatide QW plus dapagliflozin (P values at weeks 52 and 104 are nominal). HbA_{1c}, glycated hemoglobin; QW, once weekly.

Supplementary Figure S4: Kaplan-Meier plot showing the proportion of patients rescued or discontinued due to lack of glycemic control during the 104-week treatment period (ITT population)



ITT, intention to treat; QW, once weekly.

Supplementary Table S1: Criteria for initiation of rescue therapy

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 period 1	Single HbA_{1c} >8.0% (>64 mmol/mol)	From the day of visit 13/week 36 up to and including visit 15/week 52 and all unscheduled visits through the day before visit 16/week 65
Extension period 2	Single HbA_{1c} >7.5% (>58.5 mmol/mol)	From the day of visit 16/week 65 up to and including visit 17/week 78 and all unscheduled visits through the day prior to visit 18/week 91
	Single HbA_{1c} >7.0% (>53 mmol/mol)	From the day of visit 18/week 91 up to and including the day before visit 19/week 104

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

Supplementary Table S2: Hypoglycemia definitions

Category	Definition
Major hypoglycemia	An event that results in loss of consciousness, seizure, or coma (or other mental status change consistent with neuroglycopenia in the judgment of the investigator or physician) and which resolves after at least one item of intervention recorded in the eCRF, or an event that requires third-party assistance and is associated with a plasma or capillary glucose concentration of <3 mmol/L (54 mg/dL).
Minor hypoglycemia	Non-major hypoglycemia event that has symptoms consistent with hypoglycemia and a glucose value of <3 mmol/L (54 mg/dL) prior to treating the episode.
Other hypoglycemia	If a hypoglycemia event does not meet the criteria for a major or minor event.

eCRF, electronic case report form.

Supplementary Table S3: Other exploratory efficacy endpoints at week 104

				Between-group difference (95% CI)	
	Exenatide QW plus dapagliflozin (n=228)	**Exenatide QW plus placebo (n=227)**	**Dapagliflozin plus placebo (n=230)**	**Exenatide QW plus dapagliflozin versus exenatide QW plus placebo**	**Exenatide QW plus dapagliflozin versus dapagliflozin plus placebo**
Mean daily SMBG, mmol/L					
n	76	64	49		
Baseline	10.79 (2.24)	10.46 (1.85)	10.38 (2.41)		
Week 104	7.66 (0.97)	7.90 (1.17)	8.05 (1.12)		
Change at week 104	−3.16 (0.13)	−2.99 (0.16)	−2.80 (0.17)	−0.17 (−0.52 to 0.17); *P*=0.329	−0.36 (−0.73 to 0.01); *P*=0.055
DBP, mm Hg					
n	68	50	43		
Baseline	79.3 (8.57)	78.9 (6.71)	78.5 (8.68)		
Week 104	78.5 (7.64)	79.9 (7.31)	78.7 (6.19)		
Change at week 104	0.4 (0.78)	1.1 (0.89)	−0.2 (0.95)	−0.7 (−3.0 to 1.6); *P*=0.540	0.5 (−1.8 to 2.9); *P*=0.660
Total cholesterol, mmol/L					
n	89	73	72		
Baseline	4.56 (1.06)	4.69 (1.04)	4.61 (0.97)		
Week 104	4.78 (1.15)	4.68 (0.95)	5.04 (1.31)		
Change at week 104	0.16 (0.12)	−0.03 (0.14)	0.40 (0.13)	0.19 (−0.12 to 0.50); *P*=0.217	−0.23 (−0.54 to 0.07); *P*=0.138
LDL cholesterol, mmol/L					
n	87	72	67		
Baseline	2.50 (0.86)	2.54 (0.88)	2.53 (0.84)		
Week 104	2.63 (0.99)	2.54 (0.80)	2.72 (0.91)		
Change at week 104	0.15 (0.09)	0.04 (0.11)	0.22 (0.10)	0.11 (−0.13 to 0.36); *P*=0.367	−0.07 (−0.32 to 0.18); *P*=0.568
HDL cholesterol, mmol/L					
n	89	73	72		
Baseline	1.22 (0.30)	1.25 (0.30)	1.16 (0.25)		
Week 104	1.26 (0.31)	1.31 (0.27)	1.24 (0.27)		
Change at week 104	0.03 (0.02)	0.05 (0.03)	0.05 (0.02)	−0.02 (−0.08 to 0.03); *P*=0.458	−0.03 (−0.08 to 0.03); *P*=0.349
Non-HDL cholesterol, mmol/L					
n	89	73	72		
Baseline	3.34 (0.99)	3.44 (1.05)	3.45 (0.95)		
Week 104	3.52 (1.08)	3.37 (0.90)	3.80 (1.34)		
Change at week 104	0.13 (0.12)	−0.09 (0.13)	0.35 (0.13)	0.22 (−0.08 to 0.52); *P*=0.147	−0.22 (−0.52 to 0.08); *P*=0.148
Triglycerides, mmol/L					
n	89	73	72		
Baseline	1.87 (0.87)	2.03 (1.03)	2.11 (1.04)		
Week 104	1.97 (0.95)	1.90 (0.92)	2.40 (1.95)		

Change at week 104	−0.01 (0.13)	−0.21 (0.15)	0.24 (0.14)	0.20 (−0.14 to 0.54); *P*=0.246	−0.25 (−0.59 to 0.09); *P*=0.149

Mean (SD) baseline and week 104 data for patients with observed values at both baseline and week 104. Change at week 104 data are adjusted least squares mean (standard error) and between group difference data are least squares mean (95% CI) in the ITT population. CI, confidence interval; DBP, diastolic blood pressure; ITT, intention to treat; QW, once weekly; SMBG, self-monitored blood glucose.