Semaglutide once-weekly persistence and adherence versus other GLP-1 RAs in patients with type 2 diabetes in a US real-world setting

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Supplementary Material

Supplementary Table S1. Baseline characteristics for the total adherence study population at 180 days and 360 days in patients receiving semaglutide QW versus dulaglutide after propensity score adjustment.

	Adherence population (180 days); n=17,520			Adherence population (360 days); n=7367		
	Semaglutide QW n=447	Dulaglutide n=17,073	Standardized difference x100	Semaglutide QW n=87	Dulaglutide n=7280	Standardized difference x100
Age, years (mean)	62.80	61.98	6.7	63.23	63.18	0.4
Gender, %						
Female	53.2	51.3	3.8	41.9	50.6	17.7
Male	46.8	48.7	3.7	58.1	49.3	17.7
Region, %						
Midwest	15.2	19.5	11.5	26.8	19.7	16.7
Northeast	9.1	9.2	0.1	10.5	9.1	4.9
South	57.0	54.8	4.3	45.5	53.8	16.7
West	18.3	16.1	6.0	17.2	16.8	1.1
Unknown	0.5	0.5	0.0	–	0.6	–
Medical cost, US $ (mean)	14,2228.06	15,690.90	5.1	13,740.02	15,963.65	7.5
COM/MCR, %						
COM	43.1	44.8	3.6	41.6	40.0	3.3
MCR	57.0	55.2	3.6	58.4	60.0	3.3
Insurance, %						
EPO	6.4	6.2	0.7	4.3	5.2	4.3
HMO	23.1	21.9	2.8	21.0	22.8	4.2
IND	0.3	0.5	3.2	–	0.6	–
OTH	34.5	35.5	2.2	40.6	38.6	4.1
POS	30.0	31.6	3.5	29.0	28.2	1.7
PPO	5.8	4.3	6.8	5.0	4.5	2.4
CCI score, mean	2.9	2.9	0.7	2.9	3.0	3.6

	Adherence population (180 days); n=17,520			Adherence population (360 days); n=7367		
	Semaglutide QW n=447	Dulaglutide n=17,073	Standardized difference x100	Semaglutide QW n=87	Dulaglutide n=7280	Standardized difference x100
CCI score, %						
≤1	29.9	30.8	2.0	35.0	29.0	12.9
2–3	39.0	37.6	0.4–3.4	37.3	38.2	24.8–30.4
≥4	31.1	31.6	0.8–6.6	24.7	32.82	2.0–21.6
DCSI score, mean	3.2	3.1	1.8	2.9	3.2	14.7
DCSI score, %						
≤1	25.2	24.6	6.3–7.7	26.5	23.7	6.9–17.8
2–3	35.3	37.9	1.8–8.0	39.0	37.2	1.1–3.4
≥4	39.6	37.5	1.2–9.7	34.5	39.2	1.0–13.4
ASCVD*, %	35.9	33.9	4.3	24.5	34.7	13.4
Hyperlipidemia, %	81.7	81.8	0.2	89.6	83.0	19.1
Hypertension, %	82.8	83.7	2.4	82.0	84.7	7.3
Prior antidiabetics, %						
MET	71.0	71.1	0.2	71.5	70.6	1.9
Insulin	45.4	40.6	9.7	49.4	40.8	17.3
SU	39.0	38.4	1.2	37.7	39.6	3.9
SGLT-2i	18.2	19.9	4.4	21.1	19.9	2.9
DPP-4i	25.8	26.8	2.3	49.5	27.9	14.1
TZD	7.0	8.8	6.5	7.8	9.0	4.6
MEG	1.1	1.3	1.8	0.1	1.3	14.4
AGI	0.1	0.5	8.1	–	0.6	–
AMY	0.1	0.1	0.6	–	0.0	–

The data (including costs) were taken from the Optum Clinfomatics® database. Standardized differences are presented as a range for combined CCI scores and combined DCSI scores.

*ASCVD comprised the following diagnoses: acute coronary syndrome (diagnosis code - I24, I25 ex. I25.3, I25.4), angina (I20), myocardial infarction (I21, I22, I23), peripheral artery disease (I70, I73.9, I74, I75, I99, Z86.7), revascularization (Z95.1, Z95.5, Z95.8, Z95.9, Z98.6, Z98.6), ischemic stroke (I63, I65, I66, I67.2, I67.81, I67.82, I67.83, I67.84), hemorrhagic stroke (I60, I61, I62), stroke effects (I69, R29.7 ex. R29.700) and transient ischemic attack (G45).

AGI, alpha-glucosidase inhibitors; AMY, amylinomimetics; ASCVD, atherosclerotic cardiovascular disease; CCI, Charlson comorbidity index; COM, commercial; DCSI, diabetes complications severity index; DDP-4i, dipeptidyl peptidase-4 inhibitor; EPO, exclusive provider organization; HMO, health maintenance organization; IND, indemnity; MCR, Medicare; MEG, meglitinide; MET, metformin; OTH, other; POS, point of service; PPO, preferred provider organization; QW, once-weekly; SGLT-2i, sodium glucose cotransporter-2 inhibitor, SU, sulfonylurea; TZD, thiazolidinedione.

Supplementary Table S2. Baseline characteristics stratified by commercial claim subgroup and Medicare claim subgroup.

	Commercial claim subgroup n=26,524				Medicare claim subgroup n=29,691			
	Semaglutide QW n=2698	Dulaglutide n=12,219	Liraglutide n=7513	Exenatide QW n=4094	Semaglutide QW n=581	Dulaglutide n=15,672	Liraglutide n=9673	Exenatide QW n=4265
Age, years (mean)	53.03	53.23	52.39	52.97	68.69	69.20	67.89	68.00
Gender, %								
F	47.8	45.8	53.0	45.0	55.1	55.4	56.9	54.7
M	52.2	54.1	47.0	54.9	44.9	44.6	43.1	45.3
Region, %								
Midwest	21.9	25.1	27.6	24.5	16.2	15.2	17.4	15.2
Northeast	7.6	6.9	6.9	4.2	14.6	11.2	8.7	7.4
South	58.5	53.2	49.4	54.8	52.7	55.9	55.1	59.7
West	11.9	14.8	16.0	16.5	15.8	17.1	18.1	17.02
Unknown	0.0	0.1	0.1	0.1	0.7	0.7	0.7	0.7
Medical cost, US $	11,449.55	11,361.15	13,799.84	10,311.26	20,617.23	19,996.60	22,188.32	18,363.96
Insurance, %								
EPO	13.6	14.0	13.5	14.7				
HMO	14.0	12.3	12.0	9.8	28.4	28.5	29.7	33.4
IND	0.6	1.0	0.8	0.9				
OTH	1.0	0.5	0.8	0.0	65.6	64.7	63.1	60.4
POS	70.0	71.3	72.3	74.0				
PPO	0.9	1.0	0.8	0.7	6.2	6.7	7.2	6.2
CCI score, mean	2.02	2.02	2.06	1.97	3.9	4.0	3.77	3.6
CCI score, %								
≤1	47.1	48.6	47.0	48.4	15.3	16.1	15.6	16.8

2–3	40.1	37.8	38.1	39.2	32.9	37.0	35.3	38.3
≥4	12.8	13.6	14.9	12.4	51.8	46.9	49.0	44.9
DCSI score, mean	2.11	2.13	2.09	2.05	4.01	3.98	4.02	3.91
DCSI score, %								
≤1	33.6	34.8	38.3	36.3	15.5	15.7	17.51	16.7
2–3	47.1	46.1	41.83	45.2	31.3	30.9	28.8	31.3
≥4	19.3	19.1	19.9	18.5	53.2	53.4	53.6	52.0
ASCVD*, %	17.7	17.2	20.3	17.8	47.7	48.2	50.1	46.7
Hyperlipidemia, %	77.9	75.5	72.5	76.2	89.9	86.1	85.5	98.6
Hypertension, %	74.4	74.0	73.4	74.5	93.46	91.6	91.7	91.4
Prior antidiabetics, %								
MET	76.0	75.9	71.1	75.9	61.8	66.7	63.0	67.7
Insulin	34.4	30.6	31.5	27.6	54.2	47.1	48.3	42.9
SU	25.4	34.7	28.6	33.0	34.1	42.0	36.3	42.9
SGLT-2i	28.6	25.8	17.9	29.6	22.2	14.9	11.6	17.8
DPP-4i	20.4	24.4	16.6	24.5	27.9	27.7	20.5	27.3
TZD	8.1	8.3	6.3	9.6	10.5	9.7	8.8	11.8
MEG	0.5	0.7	0.6	0.6	1.4	1.7	1.1	1.5
AGI	0.2	0.4	0.2	0.3	0.7	0.6	0.0	0.5
AMY	0.0	0.0	0.1	0.0	0.2	0.0	0.0	0.1

*ASCVD comprised the following diagnoses: acute coronary syndrome (diagnosis code - I24, I25 ex. I25.3, I25.4), angina (I20), myocardial infarction (I21, I22, I23), peripheral artery disease (I70, I73.9, I74, I75, I99, Z86.7), revascularization (Z95.1, Z95.5, Z95.8, Z95.9, Z98.6, Z98.6), ischemic stroke (I63, I65, I66, I67.2, I67.81, I67.82, I67.83, I67.84), hemorrhagic stroke (I60, I61, I62), stroke effects (I69, R29.7 ex. R29.700) and transient ischemic attack (G45).

AGI, alpha-glucosidase inhibitors; AMY, amylinomimetics; ASCVD, atherosclerotic cardiovascular disease; CCI, Charlson comorbidity index; DCSI, diabetes complications severity index; DDP-4i, dipeptidyl peptidase-4 inhibitor; EPO, exclusive provider organization; HMO, health maintenance organization; IND, indemnity; MEG, meglitinide; MET, metformin; OTH, other; POS, point of service; PPO, preferred provider organization; QW, once-weekly; SGLT-2i, sodium glucose cotransporter-2 inhibitor, SU, sulfonylurea; TZD, thiazolidinedione.

Supplementary Table S3. Baseline characteristics after propensity score adjustment for (A) commercial claim subgroup and (B) Medicare claim subgroup.

(A)

	Semaglutide QW n=2688	Dulaglutide n=12,220	Standardized difference x100
Age, years (mean)	53.2	53.2	0.4
Gender, %			
F	45.8	46.2	0.8
M	54.2	53.8	0.8
Region, %			
Midwest	23.9	24.5	1.4
Northeast	7.1	7.0	0.4
South	54.5	54.1	0.7
West	14.4	14.3	0.4
Unknown	0.1	0.1	1.2
Medical cost, US $ (mean)	11,122.91	11,368.71	0.9
Insurance, %			
EPO	13.8	13.9	0.5
HMO	12.9	12.6	0.6
IND	0.8	0.9	1.4
OTH	0.6	0.6	0.0
POS	71.0	71.0	0.0
PPO	1.0	1.0	0.7
CCI score, mean	2.0	2.0	0.5
CCI score, %			
≤1	48.3	48.3	0.0
2–3	38.2	38.3	1.5–1.8
≥4	13.6	13.5	0.9–4.2
DCSI score, mean	2.1	2.1	0.5
DCSI score, %			
≤1	34.2	34.6	0.5–0.8
2–3	45.9	46.4	1.5–3.4
≥4	19.9	19.0	0.3–2.8
ASCVD* %	17.6	17.3	0.6
Hyperlipidemia, %	75.9	75.9	0.01
Hypertension, %	74.5	74.1	0.9
Prior antidiabetics, %			
MET	76.2	75.9	0.5
Insulin	31.4	31.3	0.2
SU	32.6	33.0	0.9
SGLT-2i	26.4	26.3	0.2
DPP-4i	23.6	23.7	0.2
TZD	8.2	8.2	0.2
MEG	0.7	0.7	0.1
AGI	0.4	0.3	0.8
AMY	0.0	0.0	0.0

(B)

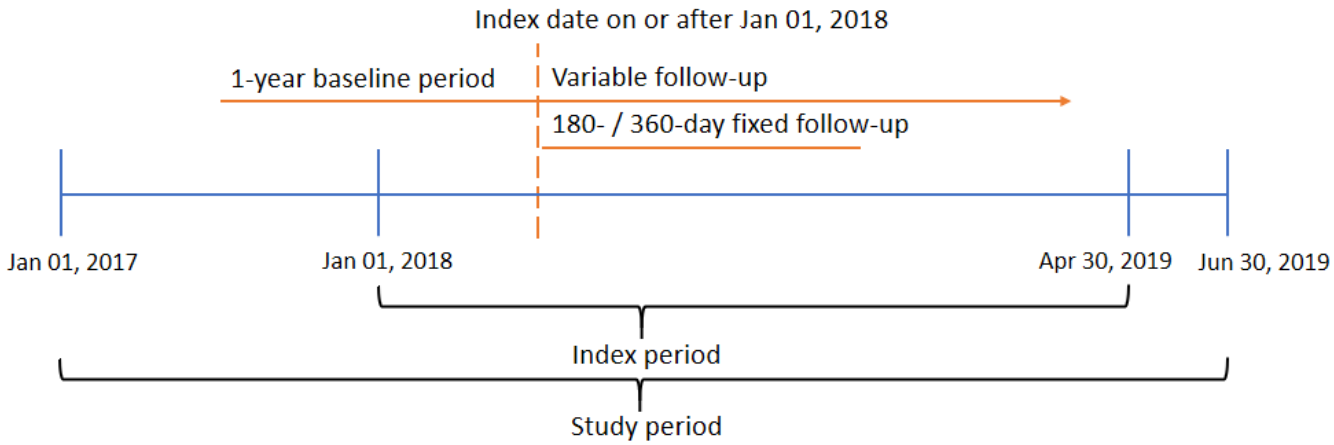
	Semaglutide QW n=582	Dulaglutide n=15672	Standardized difference x100
Age, years (mean)	68.5	69.2	7.6
Gender, %			
F	55.8	55.4	0.8
M	44.2	44.6	0.8
Region, %			
Midwest	17.1	15.2	5.1
Northeast	12.1	11.4	2.3
South	54.0	55.7	3.6
West	16.2	17.0	2.1
Unknown	0.6	0.7	0.7
Medical cost, US $ (mean)	19,598.26	20,019.14	1.2
Insurance, %			
EPO	–	–	–
HMO	30.5	28.5	4.4
IND	–	–	–
OTH	61.1	64.8	7.6
POS	–	–	–
PPO	8.4	6.7	6.2
CCI score, mean	3.6	3.7	2.4
CCI score, %			
≤1	15.5	16.1	1.6
2–3	39.1	36.9	3.1–8.0
≥4	45.4	47.0	1.3–3.1
DCSI score, mean	3.9	4.0	4.3
DCSI score, %			
≤1	17.9	15.7	3.6–4.5
2–3	32.4	30.9	5.0–9.1
≥4	49.7	53.4	1.2–8.1
ASCVD* %	46.0	48.2	4.5
Hyperlipidemia	85.3	86.2	2.7
Hypertension	91.4	91.6	1.0
Prior antidiabetics			
MET	66.8	66.6	0.6
Insulin	49.5	47.3	4.3
SU	40.3	41.7	2.8
SGLT-2i	14.3	15.20	2.6
DPP-4i	27.7	27.7	0.1
TZD	8.7	9.7	3.7
MEG	1.4	1.6	1.7
AGI	0.5	0.6	1.2
AMY	0.1	0.0	0.9

Standardized differences are presented as a range for combined CCI scores and combined DCSI scores.

*ASCVD comprised the following diagnoses: acute coronary syndrome (diagnosis code - I24, I25 ex. I25.3, I25.4), angina (I20), myocardial infarction (I21, I22, I23), peripheral artery disease (I70, I73.9, I74, I75, I99, Z86.7), revascularization (Z95.1, Z95.5, Z95.8, Z95.9, Z98.6, Z98.6), ischemic stroke (I63, I65, I66, I67.2, I67.81, I67.82, I67.83, I67.84), hemorrhagic stroke (I60, I61, I62), stroke effects (I69, R29.7 ex. R29.700) and transient ischemic attack (G45).

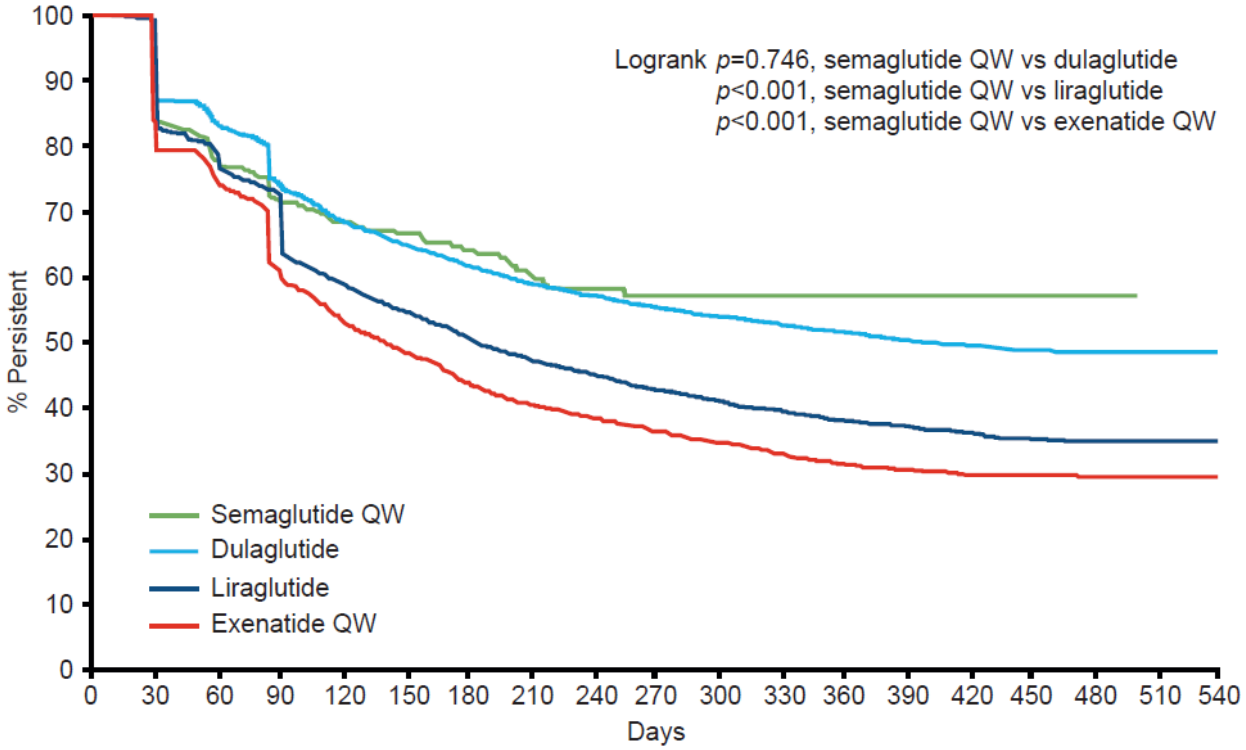
AGI, alpha-glucosidase inhibitors; AMY, amylinomimetics; ASCVD, atherosclerotic cardiovascular disease; CCI, Charlson comorbidity index; DCSI, diabetes complications severity index; DPP-4i, dipeptidyl peptidase-4 inhibitor; MEG, meglitinide; MET, metformin; QW, once-weekly; SGLT-2i, sodium glucose cotransporter-2 inhibitor, SU, sulfonylurea; TZD, thiazolidinedione.

Supplementary Figure S1. Study timeline.



The baseline period refers to the 360 days prior to the first possible index date (Jan 01, 2018). The date of a patient's first GLP-1 RA prescription was set as the index date. The dashed line represents an example index date. Patients were followed-up for varying lengths of time after the index date until they discontinued treatment (>60-day gap in supply) or reached the data cut-off (June 30, 2019). Treatment persistence was assessed after 180 and 360 days after the index date.

Supplementary Figure S2. Unadjusted Kaplan-Meier survival curve estimates for all study drugs – stratified for the Medicare claim subgroup.

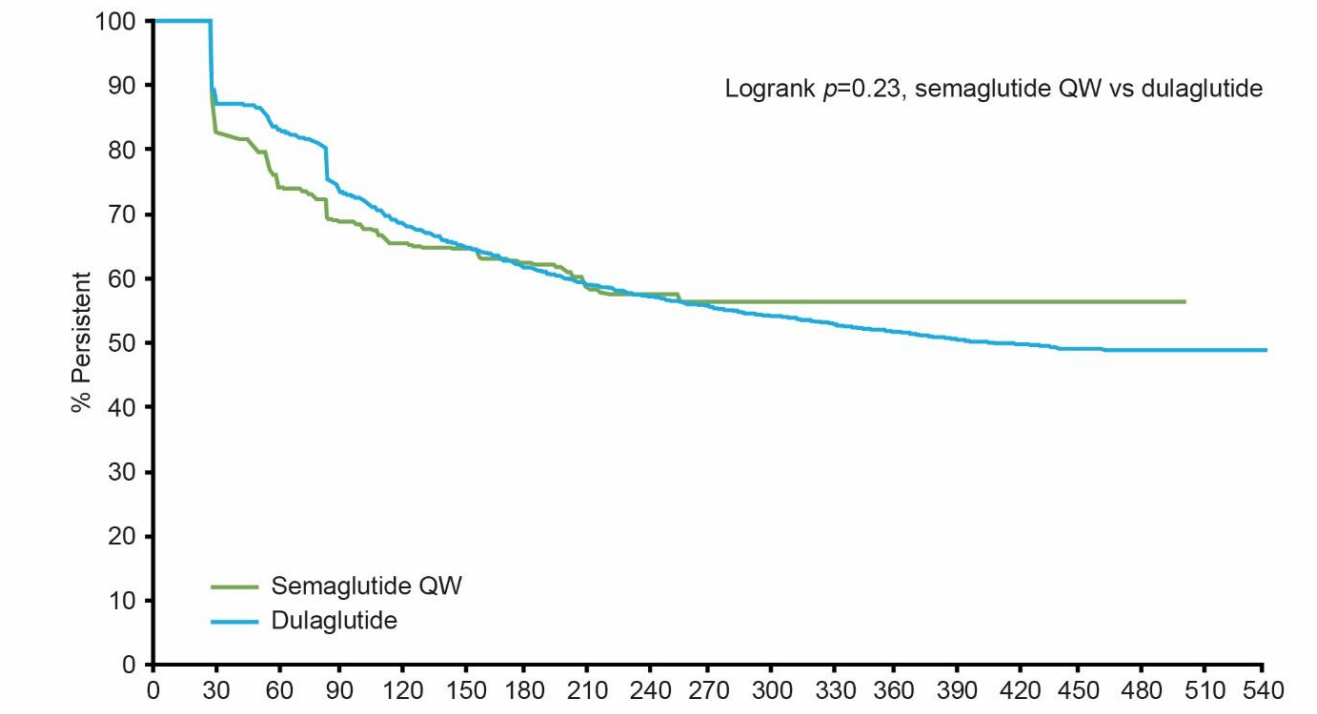


Number at risk																		
Semaglutide QW	572	406	302	209	152	118	89	69	47	30	20	14	11	6	3	2	–	–
Dulaglutide	13651	12507	9710	7791	6398	5296	4496	3819	3234	2682	2152	1777	1410	1084	790	524	510	42
Liraglutide	9493	7327	6226	4461	3766	3140	2703	2329	1967	1636	1372	1140	934	738	553	377	189	31
Exenatide QW	3497	3065	2248	1800	1493	1216	1040	887	735	603	483	386	310	246	191	113	44	5

	Estimated persistence at 180 days (%)	Estimated persistence at 360 days (%)	Discontinuation rate, HR (95% CI) vs semaglutide QW	*p*-value (semaglutide QW vs comparators)
Semaglutide QW	64.1	57.1	-	-
Dulaglutide	61.6	51.6	0.97 (0.84, 1.12)	0.746
Liraglutide	50.7	38.1	1.33 (1.15, 1.55)	<0.001
Exenatide QW	43.8	31.4	1.64 (1.41, 1.90)	<0.001

Data are presented for the unadjusted analysis set. CI, confidence interval; HR, hazard ratio; QW, once-weekly.

Supplementary Figure S3. Adjusted Kaplan–Meier survival curve estimates for semaglutide QW and dulaglutide, after propensity score adjustment – stratified for the Medicare claim subgroup.



Weighted number at risk																		
Semaglutide QW	572	397	290	201	149	117	84	65	49	33	19	13	11	5	3	2	–	–
Dulaglutide	13659	12518	9718	7804	6413	5312	4508	3828	3240	2686	2154	1778	1410	1084	790	524	251	42

	Estimated persistence at 180 days (%)	Estimated persistence at 360 days (%)	Discontinuation rate, HR (95% CI) vs semaglutide QW	*p*-value (semaglutide QW vs dulaglutide)
Semaglutide QW	62.4	56.2	-	-
Dulaglutide	61.7	51.7	0.89 (0.74, 1.08)	0.23

CI, confidence interval; HR, hazard ratio; QW, once-weekly.