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SUPPLEMENTARY DATA

Supplementary Table 1. Demographics and baseline characteristics

	EQW (N=248)	MET (N=246)	PIO (N=163)	SITA (N=163)
Age, y	54 (11)	54 (11)	55 (11)	52 (11)
Gender, n %				
Male	139 (56.0)	154 (62.6)	97 (59.5)	94 (57.7)
Female	109 (44.0)	92 (37.4)	66 (40.5)	69 (42.3)
Race/Ethnicity, n %				
Caucasian	169 (68.1)	160 (65.0)	110 (67.5)	113 (69.3)
East Asian	34 (13.7)	31 (12.6)	19 (11.7)	18 (11.0)
West Asian	21 (8.5)	20 (8.1)	15 (9.2)	15 (9.2)
Hispanic	16 (6.5)	21 (8.5)	15 (9.2)	13 (8.0)
African	7 (2.8)	11 (4.5)	4 (2.5)	3 (1.8)
Other[a]	1 (0.4)	3 (1.2)	0 (0)	1 (0.6)
Weight, kg	87.5 (18.9)	85.9 (19.6)	86.1 (17.8)	88.7 (18.7)
BMI, kg/m^2	31.4 (5.3)	30.7 (5.5)	31.1 (5.3)	31.8 (5.4)
HbA$_{1c}$, %	8.5 (1.2)	8.6 (1.2)	8.5 (1.2)	8.5 (1.3)
FSG, mmol/L	9.9 (2.9)	10.0 (3.4)	9.8 (3.0)	9.7 (2.6)
Duration of T2D, y	2.7 (3.2)	2.6 (3.6)	2.7 (3.7)	2.7 (3.7)

Data are presented as n (%) or mean (SD). [a]Native American, Aboriginal and/or Torres Strait Islander. ITT population. Abbreviations: HbA$_{1c}$ = hemoglobin HbA$_{1c}$; BMI = body mass index; EQW = exenatide once weekly; FSG = fasting serum glucose; MET = metformin; PIO = pioglitazone; SITA = sitagliptin; T2D = type 2 diabetes.

Supplementary Table 2. Resolution of ongoing treatment-emergent adverse events during the 10-week safety follow-up

	EQW (N=248)		MET (N=246)		PIO (N=163)		SITA (N=163)	
	Ongoing[a]	Resolved[b]	Ongoing[a]	Resolved[b]	Ongoing[a]	Resolved[b]	Ongoing[a]	Resolved[b]
Headache	2 (0.8)	1 (0.4)	1 (0.4)	0 (0)	0 (0)	0 (0)	1 (0.6)	1 (0.6)
Diarrhoea	2 (0.8)	1 (0.4)	10 (4.1)	1 (0.4)	0 (0)	0 (0)	1 (0.6)	0 (0)
Injection Site Nodule	18 (7.3)	8 (3.2)	17 (6.9)	8 (3.3)	3 (1.8)	1 (0.6)	9 (5.5)	2 (1.2)
Nasopharyngitis	1 (0.4)	1 (0.4)	2 (0.8)	0 (0)	0 (0)	0 (0)	1 (0.6)	0 (0)
Nausea	1 (0.4)	0 (0)	3 (1.2)	1 (0.4)	0 (0)	0 (0)	0 (0)	0 (0)
Dyspepsia	5 (2.0)	0 (0)	2 (0.8)	1 (0.4)	1 (0.6)	0 (0)	1 (0.6)	0 (0)
Constipation	1 (0.4)	0 (0)	1 (0.4)	0 (0)	0 (0)	0 (0)	2 (1.2)	0 (0)
Back Pain	0 (0)	0 (0)	5 (2.0)	1 (0.4)	2 (1.2)	0 (0)	1 (0.6)	0 (0)
Arthralgia	7 (2.8)	0 (0)	3 (1.2)	0 (0)	5 (3.1)	1 (0.6)	2 (1.2)	1 (0.6)
Hypertension	2 (0.8)	0 (0)	3 (1.2)	0 (0)	8 (4.9)	0 (0)	3 (1.8)	0 (0)
Peripheral oedema	0 (0)	0 (0)	1 (0.4)	0 (0)	2 (1.2)	0 (0)	0 (0)	0 (0)

Data are presented as n (%) of patients. [a]At 26 weeks; [b]By the end of the 10-week safety follow-up. ITT population. Abbreviations: EQW = exenatide once weekly; MET = metformin; PIO = pioglitazone; SITA = sitagliptin.

Supplementary Table 3. Change in HbA$_{1c}$ (%) from baseline by anti-exenatide antibody status at endpoint

	Endpoint HbA$_{1c}$ (LOCF)	Change from Baseline to Endpoint (LOCF)	Between-group treatment comparison
	LS mean (SE)	LS mean (SE)	LS mean difference (p-value)
Antibody to exenatide at endpoint (LOCF)			
2-level status			
Negative (n=96)	7.12 (0.12)	-1.31 (0.12)	N/A
Positive (n=135)	7.03 (0.10)	-1.39 (0.10)	0.08 (p=0.549)
3-level status			
Negative (n=96	7.10 (0.12)	-1.33 (0.12)	N/A
Positive lower (n=107)	6.92 (0.12)	-1.51 (0.12)	0.18 (p=0.214)
Positive higher (n=28)	7.40 (0.20)	-1.02 (0.20)	-0.31 (p=0.179)

Abbreviations: LOCF = last post-baseline measurement carried forward; LS mean = least-squares mean; n = number of patients having both baseline and post-baseline data; n = total number of patients; N/A = not applicable; SE = standard error.
Note: Only patients with non-missing baseline value and at least one non-missing post-baseline value of the response variable were included in analysis. Antibodies to exenatide were defined as a positive titer reported after a negative titer at baseline, or a positive titer that had increased by at least three dilutions from a detectable baseline titer.
Analysis of covariance (ANCOVA) model: Post-baseline Response Variable = Antibody to Exenatide at Endpoint + Baseline Response Variable + Pooled Country (Type III sums of squares).

Supplementary Table 4. IWQOL-Lite Total Scores

	Endpoint (LOCF)	Change from Baseline to Endpoint (LOCF)	Treatment Comparison EQW vs. Comparators	Between-group Comparison p-value
	LS mean (SE)	LS mean (SE)	LS mean difference (95% CI)	
Treatment				
EQW (n=228)	88.38 (0.77)	4.85 (0.77)	N/A	N/A
MET (n=221)	88.37 (0.77)	4.84 (0.77)	0.01 (-2.02, 2.04)	0.994
PIO (n=142)	84.84 (0.94)	1.31 (0.94)	3.54 (1.23, 5.84)	0.003
SITA (n=142)	87.55 (0.95)	4.02 (0.95)	0.83 (-1.48, 3.13)	0.482

Abbreviations: CI = confidence interval; EQW = exenatide once weekly; IWQOL-Lite = Impact of Weight on Quality of Life Questionnaire-Lite; LOCF = last post-baseline measurement carried forward; LS Mean = least-squares mean; MET = metformin; n = number of patients having both baseline and post-baseline data; N/A = not applicable; PIO = pioglitazone; SE = standard error; SITA = sitagliptin; vs. = versus.

Note: Only patients with non-missing baseline value and at least one non-missing post-baseline value of the response variable were included.

Analysis of covariance (ANCOVA) model: Post-baseline Variable = Treatment + Baseline Response Variable + Pooled Country (Type III sums of squares). The two-sided 95% confidence interval is for the LS mean difference between Exenatide, MET, PIO and SITA.

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Supplementary Table 5. BES Total Score

	Endpoint (LOCF)	Change from Baseline to Endpoint (LOCF)	Treatment Comparison EQW vs. Comparators	Between-group Comparison p-value
	LS mean (SE)	LS mean (SE)	LS mean difference (95% CI)	
Treatment				
EQW (n=212)	5.02 (0.34)	-2.66 (0.34)	N/A	N/A
MET (n=196)	5.04 (0.35)	-2.64 (0.35)	-0.02 (-0.94, 0.89)	0.961
PIO (n=163)	6.61 (0.41)	-1.07 (0.41)	-1.59 (-2.61, -0.57)	0.002
SITA (n=163)	5.99 (0.41)	-1.69 (0.41)	-0.97 (-1.98, 0.03)	0.058

Abbreviations: BES = Binge Eating Scale; CI = confidence interval; EQW = exenatide once weekly; LOCF = last post-baseline measurement carried forward; LS mean = least-squares mean; MET = metformin; n = number of patients having both baseline and post-baseline data; N/A = not applicable; PIO = pioglitazone; SE = standard error; SITA = sitagliptin; vs. = versus.
Note: Only patients with non-missing baseline value and at least one non-missing post-baseline value of the response variable were included.
Analysis of covariance (ANCOVA) model: Post-baseline Response Variable = Treatment + Baseline Response Variable + Pooled Country (Type III sums of squares). The two-sided 95% confidence interval is for the LS mean difference between Exenatide, MET, PIO and SITA.

Supplementary Table 6. DTSQc Total Scores

Treatment	Endpoint (LOCF)	Treatment Comparison EQW vs. Comparators	Between-group Comparison p-value
	LS mean (SE)	LS mean difference (95% CI)	
Treatment			
EQW (n=221)	13.08	N/A	N/A
MET (n=224)	12.42	0.65 (-0.48, 1.78)	0.257
PIO (n=143)	13.35	-0.27 (-1.55, 1.01)	0.676
SITA (n=140)	12.49	0.59 (-0.70, 1.87)	0.371

Abbreviations: CI = confidence interval; DTSQc = Diabetes Treatment Satisfaction Questionnaire (change version); EQW = exenatide once weekly; LOCF = last post-baseline measurement carried forward; LS mean = least-squares mean; MET = metformin; n = number of patients having both baseline and post-baseline data; N/A = not applicable; PIO = pioglitazone; SE = standard error; SITA = sitagliptin; vs. = versus.

Analysis of covariance (ANCOVA) model: Post-baseline Response Variable = Treatment + Pooled Country (Type III sums of squares). The two-sided 95% confidence interval is for the LS mean difference between Exenatide, MET, PIO and SITA.

Supplementary Table 7. DTSQs Total Scores

Treatment	Endpoint (LOCF)	Change from Baseline to Endpoint (LOCF)	Treatment Comparison EQW vs. Comparators	Between-group Comparison p-value
	LS mean (SE)	LS mean (SE)	LS mean difference (95% CI)	
EQW (n=222)	30.78 (0.40)	3.38 (0.40)	N/A	N/A
MET (n=210)	30.34 (0.40)	2.95 (0.40)	0.43 (-0.62, 1.49)	0.421
PIO (n=138)	31.10 (0.49)	3.70 (0.49)	-0.32 (-1.51, 0.88)	0.600
SITA (n=143)	30.01 (0.48)	2.61 (0.48)	0.77 (-0.41, 1.95)	0.200

Abbreviations: CI = confidence interval; DTSQs = Diabetes Treatment Satisfaction Questionnaire (status version); EQW = exenatide once weekly; LOCF = last post-baseline measurement carried forward; LS mean = least-squares mean; MET = metformin; n = number of patients having both baseline and post-baseline data; N/A = not applicable; PIO = pioglitazone; SE = standard error; SITA = sitagliptin; vs. = versus.
Note: Only patients with non-missing baseline value and at least one non-missing post-baseline value of the response variable were included.
Analysis of covariance (ANCOVA) model: Post-baseline Response Variable = Treatment + Baseline Response Variable + Pooled Country (Type III sums of squares). The two-sided 95% confidence interval is for the LS mean difference between Exenatide, MET, PIO and SITA.

Supplementary Table 8. EQ-5D Index Scores

UK Population-based Index Score

	Endpoint (LOCF)	Change from Baseline to Endpoint (LOCF)	Treatment Comparison EQW vs. Comparators	Between-group Comparison p-value
	LS mean (SE)	LS mean (SE)	LS mean difference (95% CI)	
Treatment				
EQW (n=232)	0.88 (0.01)	0.03 (0.01)	N/A	N/A
MET (n=227)	0.88 (0.01)	0.03 (0.01)	0.00 (-0.02, 0.03)	0.854
PIO (n=146)	0.84 (0.01)	-0.01 (0.01)	0.04 (0.01, 0.07)	0.012
SITA (n=149)	0.87 (0.01)	0.02 (0.01)	0.02 (-0.02, 0.05)	0.327

Abbreviations: CI = confidence interval; EQ-5D = EuroQol-5 dimensions; EQW = exenatide once weekly; LOCF = last post-baseline measurement carried forward; LS mean = least-squares mean; MET = metformin; n = number of patients having both baseline and post-baseline data; N/A = not applicable; PIO = pioglitazone; SE = standard error; SITA = sitagliptin; vs. = versus.
Note: Only patients with non-missing baseline value and at least one non-missing post-baseline value of the response variable were included.
Analysis of covariance (ANCOVA) model: Post-baseline Response Variable = Treatment + Baseline Response Variable + Pooled Country (Type III sums of squares). The two-sided 95% confidence interval is for the LS mean difference between Exenatide, MET, PIO and SITA.

Supplementary Table 9. EQ-5D Index Scores

US Population-based Index Score

|	Endpoint (LOCF)	Change from Baseline to Endpoint (LOCF)	Treatment Comparison EQW vs. Comparators	Between-group Comparison p-value
	LS mean (SE)	LS mean (SE)	LS mean difference (95% CI)	
Treatment				
EQW (n=232)	0.90 (0.01)	0.02 (0.01)	N/A	N/A
MET (n=227)	0.91 (0.01)	0.02 (0.01)	0.00 (-0.02, 0.02)	0.840
PIO (n=146)	0.88 (0.01)	-0.01 (0.01)	0.03 (0.00, 0.05)	0.019
SITA (n=149)	0.89 (0.01)	0.01 (0.01)	0.01 (-0.01, 0.03)	0.445

Abbreviations: CI = confidence interval; EQ-5D = EuroQol-5 dimensions; EQW = exenatide once weekly; LOCF = last post-baseline measurement carried forward; LS mean = least-squares mean; MET = metformin; n = number of patients having both baseline and post-baseline data; N/A = not applicable; PIO = pioglitazone; SE = standard error; SITA = sitagliptin; vs. = versus.
Note: Only patients with non-missing baseline value and at least one non-missing post-baseline value of the response variable were included.
Analysis of covariance (ANCOVA) model: Post-baseline Response Variable = Treatment + Baseline Response Variable + Pooled Country (Type III sums of squares). The two-sided 95% confidence interval is for the LS mean difference between Exenatide,MET, PIO and SITA.
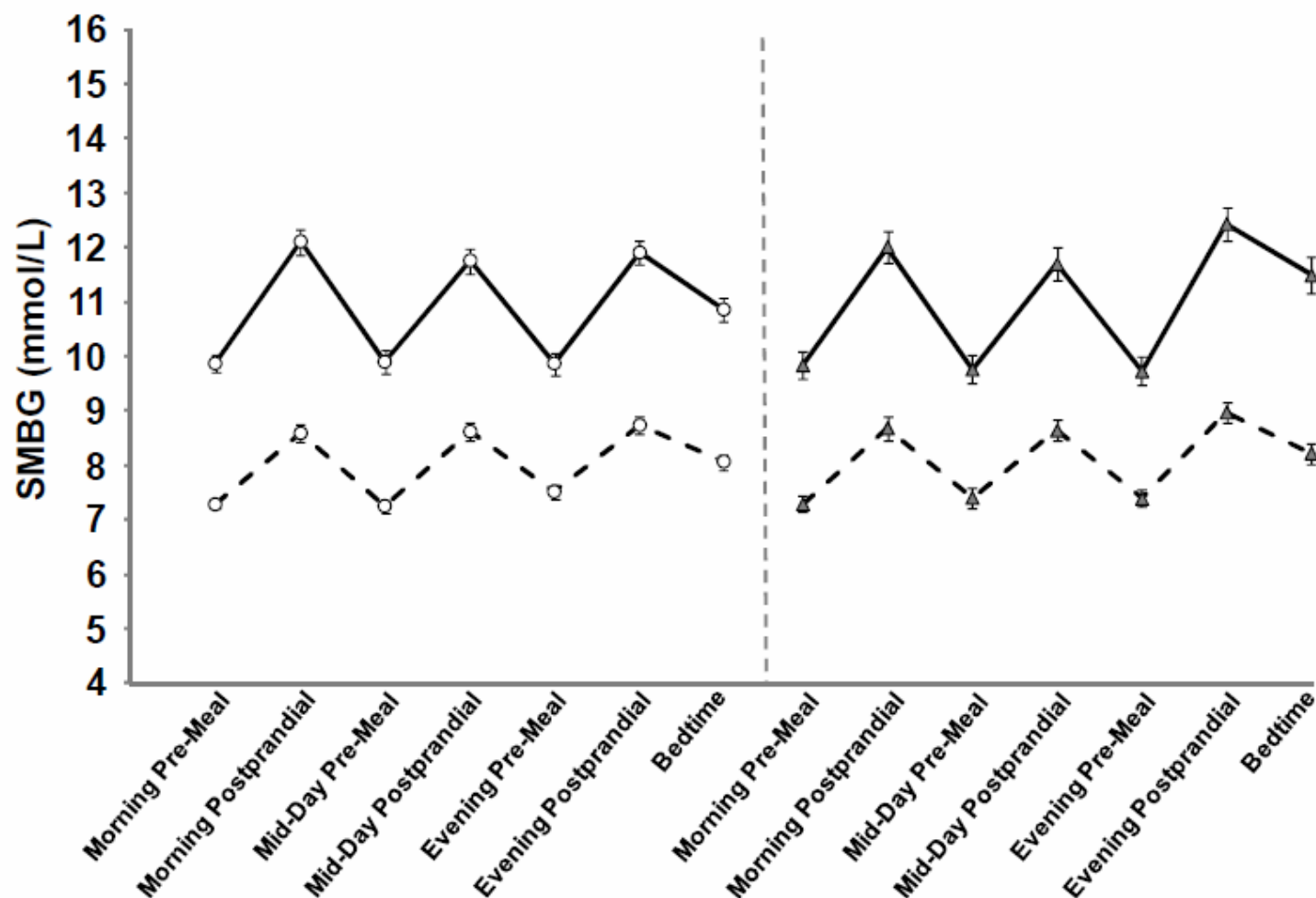
Supplementary Figure 1A. Mean (SE) 7-point SMBG at baseline (solid lines) and endpoint (LOCF) (dashed lines) with EQW (white circles) and MET (light gray squares). Postprandial was 2 hours after the start of the meal. Abbreviations: EQW = exenatide once weekly; LOCF = last observation carried forward; MET = metformin; SE = standard error; SMBG = self-monitored blood glucose.
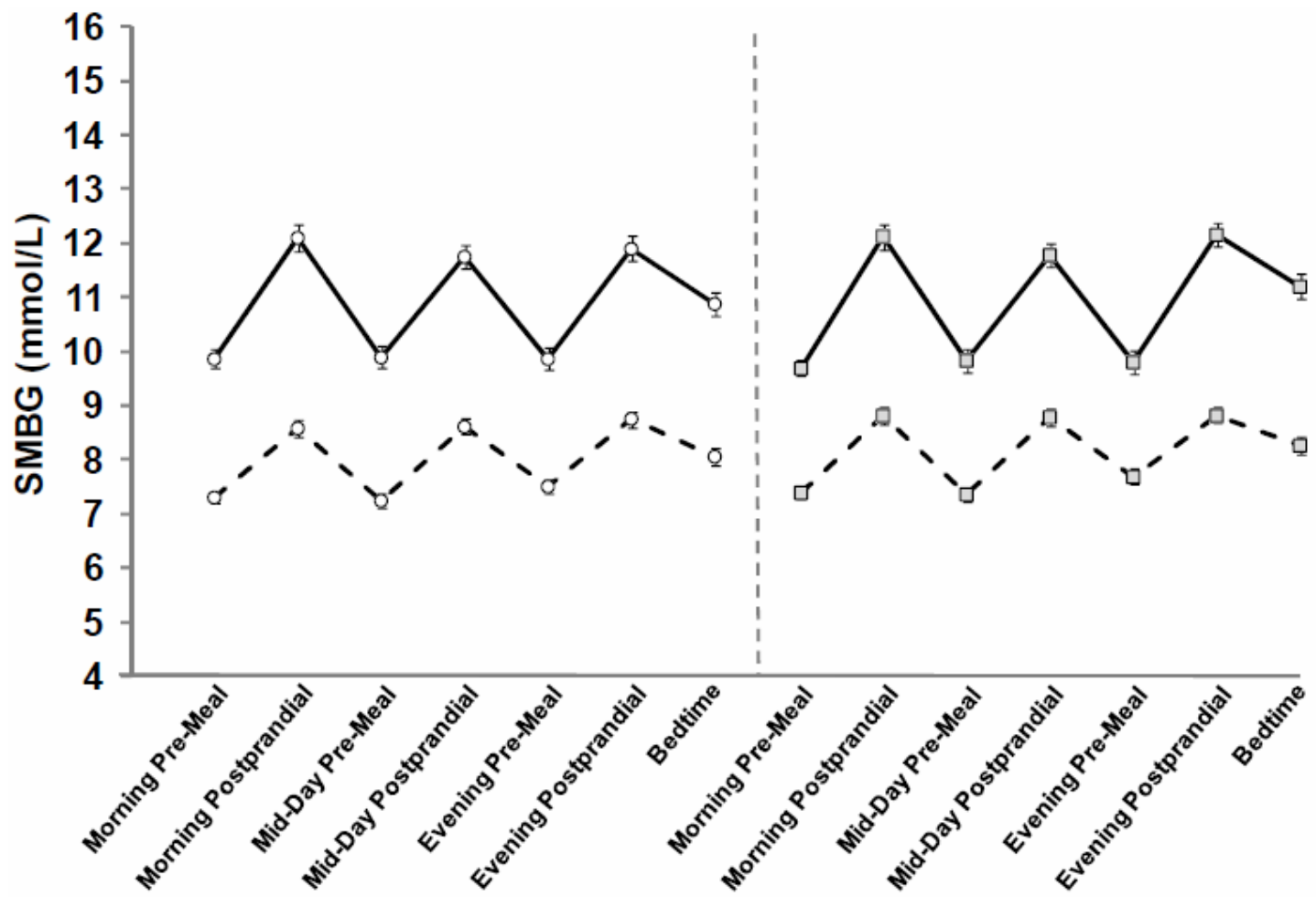
Supplementary Figure 1B. Mean (SE) 7-point SMBG at baseline (solid lines) and endpoint (LOCF) (dashed lines) with EQW (white circles) and PIO (dark gray triangles). Postprandial was 2 hours after the start of the meal. Abbreviations: EQW = exenatide once weekly; LOCF = last observation carried forward; PIO = pioglitazone; SE = standard error; SMBG = self-monitored blood glucose.
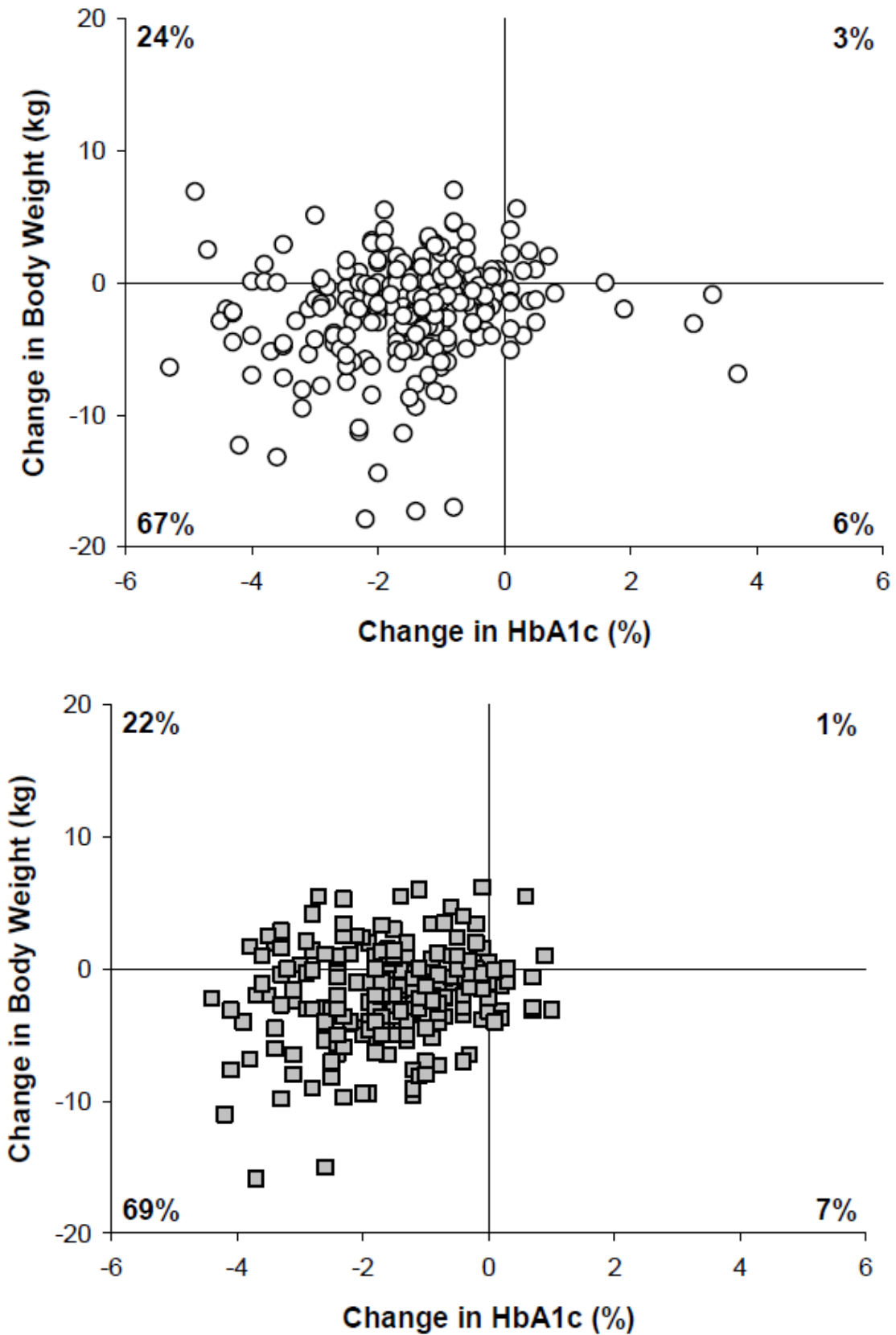
SUPPLEMENTARY DATA

Supplementary Figure 1C. Mean (SE) 7-point SMBG at baseline (solid lines) and endpoint (LOCF) (dashed lines) with EQW (white circles) and SITA (black diamonds). Postprandial was 2 hours after the start of the meal. Abbreviations: EQW = exenatide once weekly; LOCF = last observation carried forward; SE = standard error; SITA = sitagliptin; SMBG = self-monitored blood glucose.
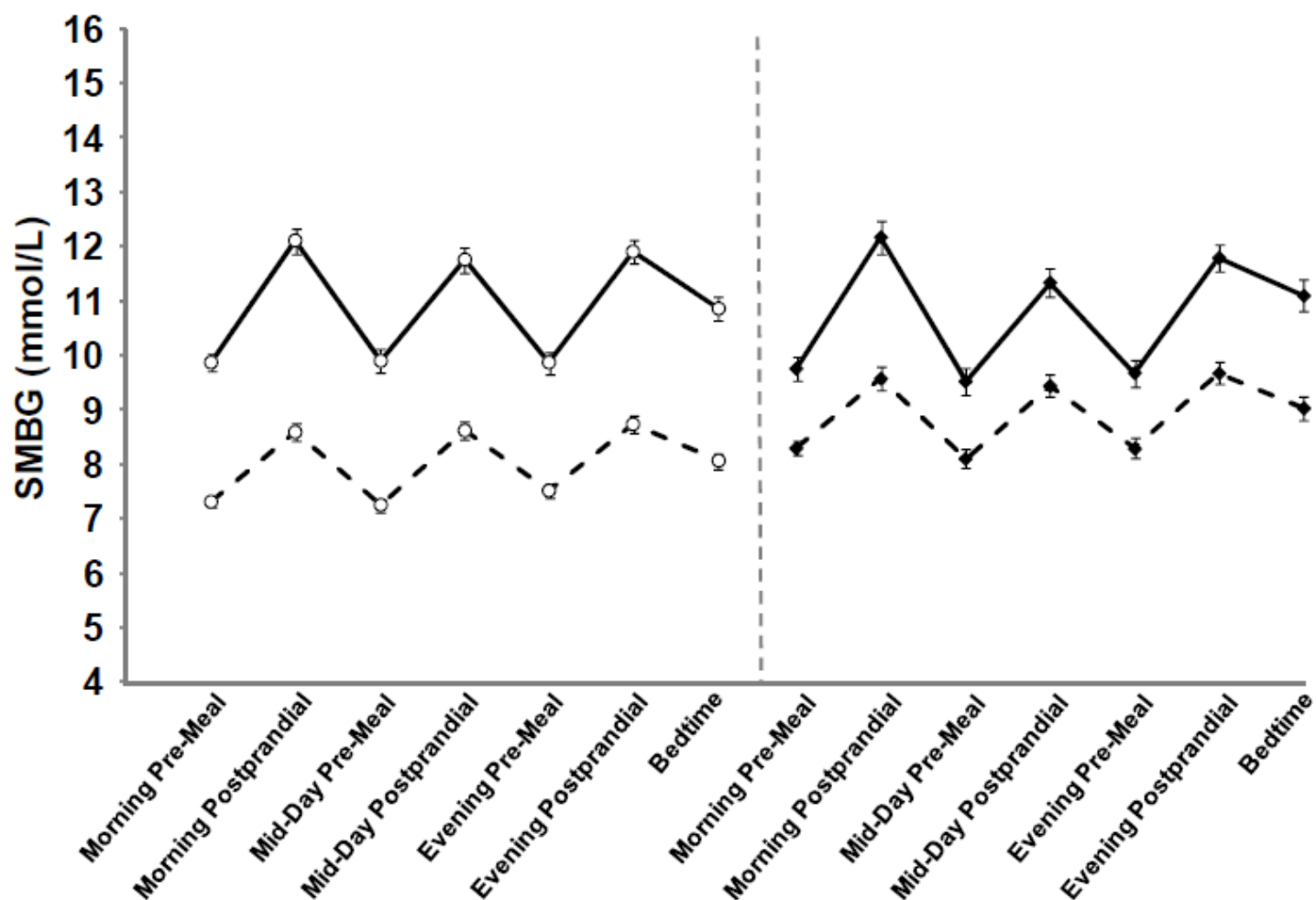
SUPPLEMENTARY DATA

Supplementary Figures 2A-D. Changes in HbA_{1c} vs. changes in weight over 26 weeks. White circles = EQW; light gray squares = MET; dark gray triangles = PIO; white diamonds = SITA.

SUPPLEMENTARY DATA