Supplementary Data

Formula S1. Calculation of IG fluctuation from continuous glucose monitoring profiles

$$\frac{1}{T}\int_{O}^{T} |IG(t) - \overline{IG}|dt$$

IG, interstitial glucose; *IG(t)*, IG value at time t; $\overline{IG}$, mean IG from the patient profile; *T*, duration of continuous glucose monitoring profile (excluding gaps with no, or invalid IG measurements).

Supplementary Table S1. DUAL I Extension Baseline Characteristics

Characteristic	*IDegLira* (n = *833*)	*IDeg* (n = *413*)	*Liraglutide* (n = *414*)
Female/male, %	48/52	52/48	50/50
Age, years	55.1 (9.9)	54.9 (9.7)	55.0 (10.2)
BMI, kg/m^2	31.2 (5.2)	31.2 (5.3)	31.3 (4.8)
Duration of diabetes, years	6.6 (5.1)	7.0 (5.3)	7.2 (6.1)
HbA_{1c}, %	8.3 (0.9)	8.3 (1.0)	8.3 (0.9)
HbA_{1c}, mmol/mol	67 (9.7)	67 (10.7)	67 (10.3)
FPG, mmol/L	9.2 (2.4)	9.4 (2.7)	9.0 (2.6)
SMBG,[a] mmol/L			
Before bedtime	10.8 (3.2)[c]	11.0 (3.3)[f]	10.7 (3.4)[i]
04:00	9.3 (2.6)[d]	9.2 (2.5)[g]	9.1 (2.8)[j]
Fasting C-peptide, nmol/L[b]	0.72 (46)[e]	0.71 (54)[h]	0.68 (51)[k]

Values are mean (SD) unless otherwise stated. Adapted from Gough et al.[15]

[a]SMBG assessed with glucose meter as plasma equivalent values of capillary whole blood glucose.

[b]Values are geometric mean (CV).

[c]$n = 788$.

[d]$n = 790$.

[e]$n = 803$.

[f]$n = 392$.

[g]$n = 397$.

[h]$n = 402$.

[i]$n = 393$.

[j]$n = 401$.

[k]$n = 398$.

BMI, body mass index; CV, coefficient of variation; FPG, fasting plasma glucose; HbA_{1c}, glycated hemoglobin; IDeg, insulin degludec; IDegLira, fixed-ratio combination of insulin degludec and liraglutide; SD, standard deviation; SMBG, self-monitored blood glucose.

Supplementary Table S2. DUAL II Baseline Characteristics

Characteristic	*IDegLira n = 199*	*IDeg n = 199*
Female/male, %	44/56	47/53
Age, years	56.8 (8.9)	57.5 (10.5)
BMI, kg/m^2	33.6 (5.7)	33.8 (5.6)
Duration of diabetes, years	10.3 (6.0)	10.9 (7.0)
HbA_{1c}, %	8.7 (0.7)	8.8 (0.7)
HbA_{1c}, mmol/mol	72 (8)	73 (8)
FPG, mmol/L	9.7 (2.9)	9.6 (3.1)
SMBG,[a] mmol/L		
Before bedtime	11.9 (3.5)[c]	11.5 (3.3)[e]
04:00	9.1 (3.2)[d]	9.2 (3.0)[f]
Fasting C-peptide, nmol/L[b]	0.54 (54)	0.50 (59)[g]

Full analysis set. Values are mean (SD) unless otherwise stated. Adapted from Buse et al.[13]

[a]SMBG assessed with glucose meter as plasma equivalent values of capillary whole blood glucose.

[b]Values are geometric mean (CV).

[c]$n = 193$

[d]$n = 191$.

[e]$n = 194$.

[f]$n = 193$.

[g]$n = 198$.

Supplementary Table S3. Overview of Missing Continuous Glucose Monitoring Data at Baseline and Week 52

Time point	*Reason for missing data*	*IDegLira (n = 131), n (%)*	*IDeg (n = 64), n (%)*	*Liraglutide (n = 65), n (%)*
Baseline	All	27 (21)	11 (17)	13 (20)
	CGM download, upload, or recording failure	6 (5)	2 (3)	4 (6)
	Technical problem with CGM sensor	2 (2)	—	1 (2)
	Withdrawal of subject[a]	—	—	2 (3)
	Other	3 (2)	—	—
	No information	16 (12)	9 (14)	6 (9)
Week 52	All	48 (37)	29 (45)	23 (35)
	CGM download, upload, or recording failure	11 (8)	7 (11)	3 (5)
	Technical problem with CGM sensor	1 (1)	1 (2)	—
	Withdrawal of subject[a]	23 (18)	13 (20)	13 (20)
	Site closed prematurely	11 (8)	5 (8)	5 (8)
	Other	1 (1)	3 (5)	2 (3)
	No information	1 (1)	—	—
Baseline or week 52	All	59 (45)	30 (47)	28 (43)

Values are number of subjects (%).

[a]Withdrawal from trial or sub-study participation.

CGM, continuous glucose monitoring.

Supplementary Table S4. Baseline Characteristics of Patients in the DUAL I Extension Sub-Study with Usable Continuous Glucose Monitoring Data at Week 52

Characteristic	*IDegLira* (n = *72*)	*IDeg* (n = *34*)	*Liraglutide* (n = *37*)
Female/male, %	43/57	27/73	41/59
Age, years	55.9 (8.5)	55.6 (9.3)	53.3 (10.7)
BMI, kg/m^2	33.0 (4.2)	32.8 (4.0)	33.1 (4.5)
Duration of diabetes, years	8.0 (5.9)	7.3 (4.7)	7.9 (4.8)
HbA_{1c}, %	8.1 (0.8)	8.0 (0.7)	8.2 (1.0)
HbA_{1c}, mmol/mol[a]	65 (9)	64 (8)	66 (11)
FPG, mmol/L	9.0 (1.9)	9.3 (2.9)	8.9 (2.0)
Fasting C-peptide, nmol/L[b]	0.69 (47)[c]	0.69 (59)	0.71 (48)[d]

Values are mean (SD) unless otherwise stated.
[a]Calculated, not measured.
[b]Values are geometric mean (CV).
[c]$n = 70$.
[d]$n = 36$.

Supplementary Table S5. Glycemic Fluctuation Assessed by MAGE, LBGI, and HBGI in Patients with Type 2 Diabetes Treated for 52 Weeks in the DUAL I Extension Continuous Glucose Monitoring Sub-Study

CGM parameter	*IDegLira* (n = *131*)	*IDeg* (n = *64*)	*ETD [95% CI]: IDegLira vs. IDeg*	*Lira* (n = *65*)	*ETD [95% CI]: IDegLira vs. Lira*
MAGE (mmol/L)					
Mean at baseline	3.6 (1.2)	3.7 (1.5)		3.7 (1.3)	
Mean Δ, w52	−1.3 (1.6)	−0.5 (2.0)	−0.7 [−1.3 to −0.1] ($P = 0.0229$)	−0.9 (2.2)	−0.3 [−0.9 to 0.3] ($P = 0.2939$)
LBGI (mmol/L)					
Mean at baseline	30.2 (20.7)	31.6 (21.0)		36.7 (20.2)	
Mean Δ, w52	17.2 (21.5)	13.2 (21.4)	0.1 [−4.1 to 4.2] ($P = 0.9819$)	7.8 (23.0)	3.8 [−0.2 to 7.9] ($P = 0.0622$)
HBGI (mmol/L)					
Mean at baseline	65.4 (4.9)	65.4 (4.5)		65.7 (5.2)	
Mean Δ, w52	−7.8 (9.4)	−5.7 (4.4)	−2.4 [−5.4 to 0.6] ($P = 0.1110$)	−5.0 (6.1)	−2.8 [−5.7 to 0.1] ($P = 0.0545$)

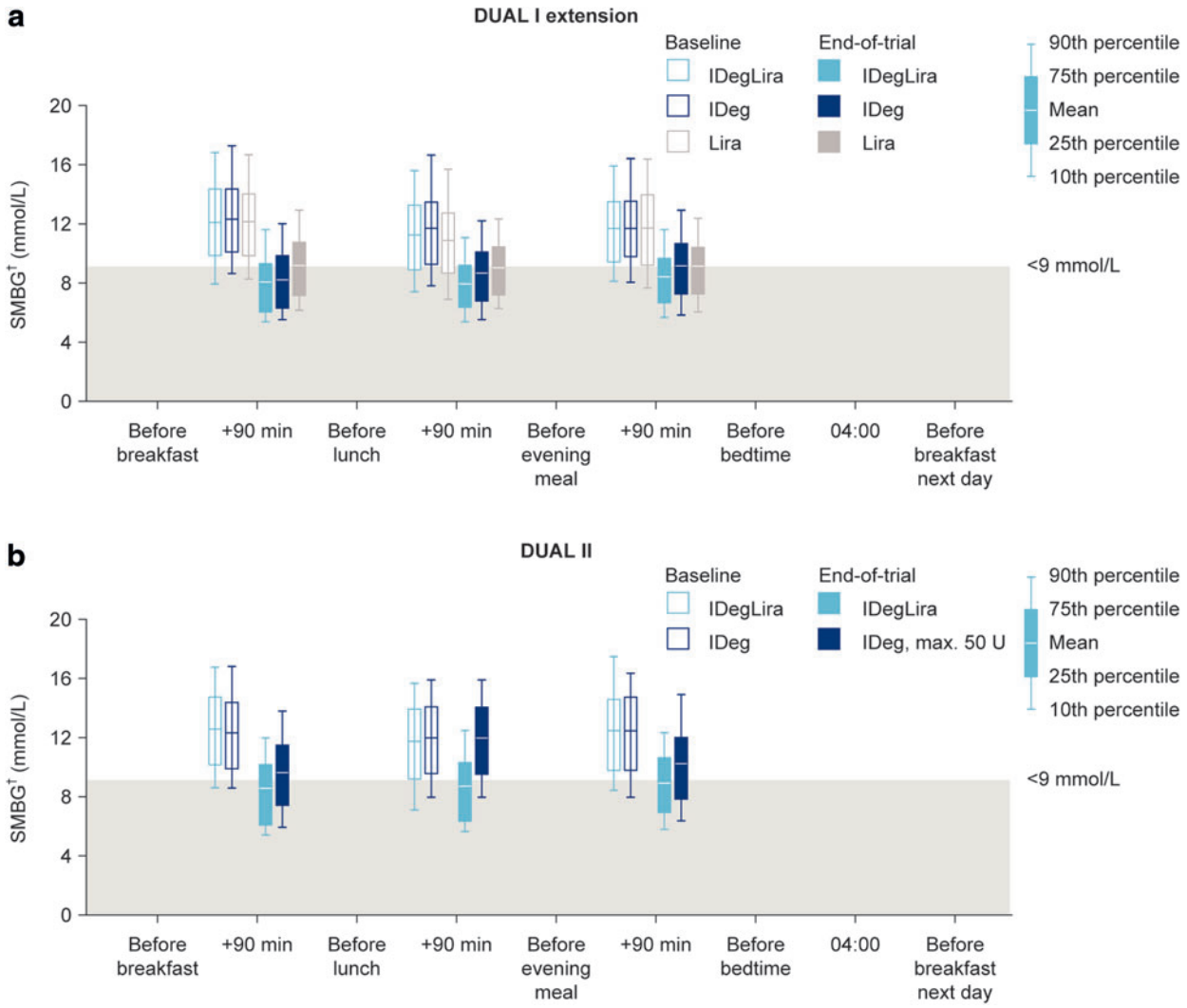
Values are mean (SD) unless otherwise stated. Parameters are analyzed based on observed data using an ANCOVA method with treatment, region, baseline HbA_{1c} stratum (≤8.3% [≤67 mmol/mol], >8.3% [>67 mmol/mol]) and previous OAD treatment as fixed effects and baseline response as covariates.

ANCOVA, analysis of covariance; CI, confidence interval; ETD, estimated treatment difference; HBGI, high blood glucose index; IG, interstitial glucose; LBGI, low blood glucose index; Lira, liraglutide; MAGE, mean amplitude of glycemic excursions; OAD, oral antidiabetic drug; w, week.

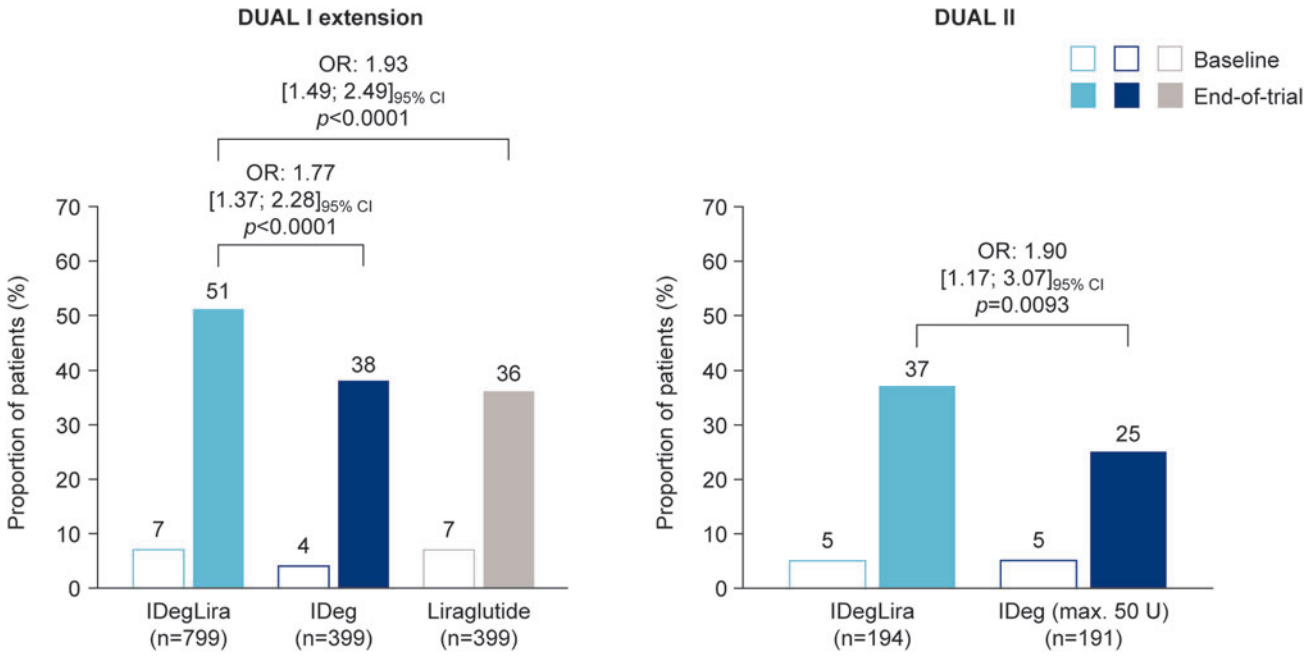
Supplementary Table S6. Episodes of Nocturnal Low Interstitial Glucose (<3.9 and <3.1 mmol/L) Among Patients in the DUAL I Extension Continuous Glucose Monitoring Sub-Study

	IDegLira	*IDeg*	*Lira*
IG <3.9 mmol/L during nocturnal period (00:01–05:59)			
Episodes, number			
Baseline	12	4	6
Week 52	29	25	5
Rate, number/100 h			
Baseline	2.0	1.4	2.1
Week 52	4.5	8.0	1.5
IG <3.1 mmol/L during nocturnal period (00:01–05:59)			
Episodes, number			
Baseline	6	6	6
Week 52	13	7	0
Rate, number/100 h			
Baseline	1.0	2.0	2.1
Week 52	2.0	2.2	0

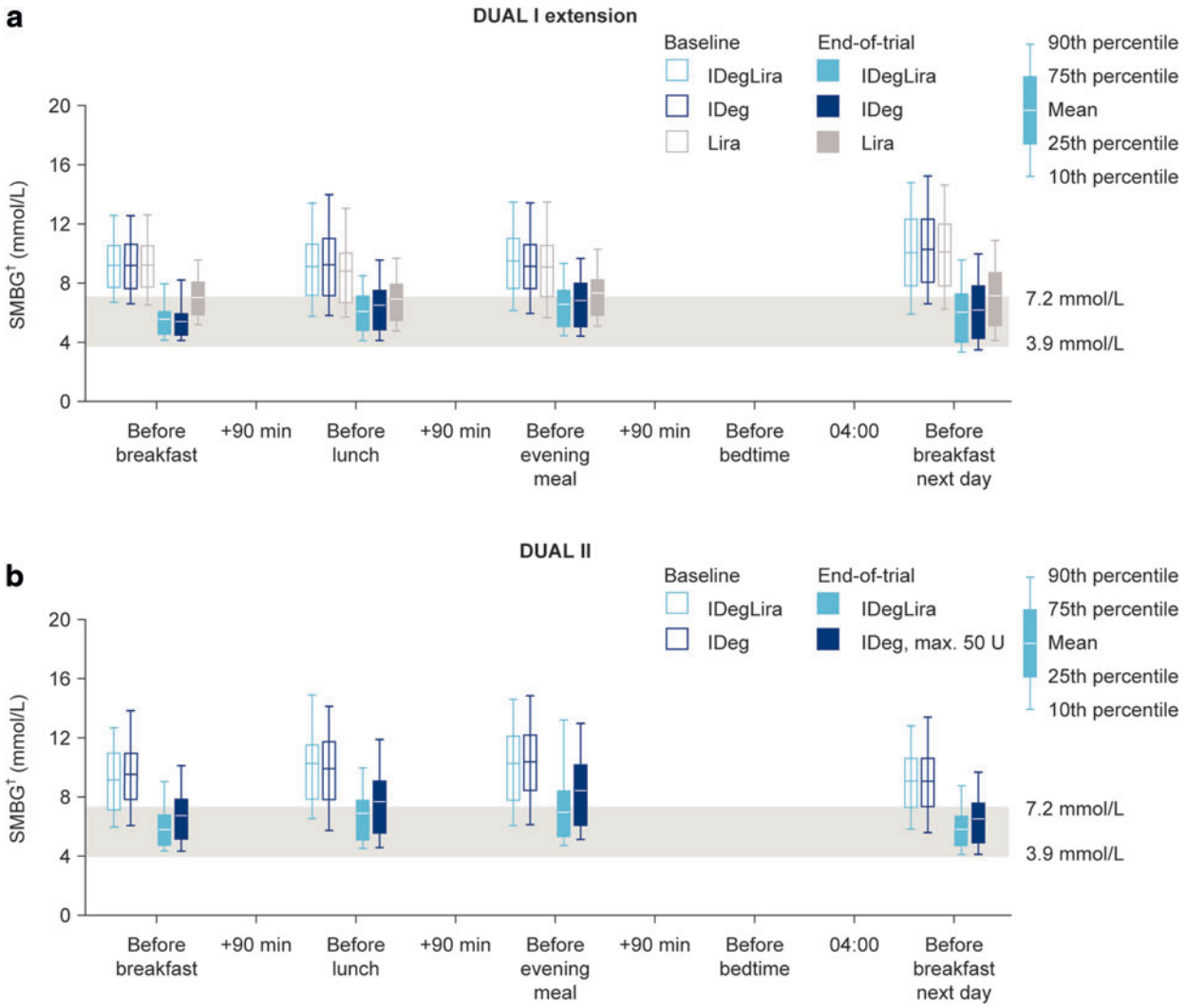
Sub-study analysis set.



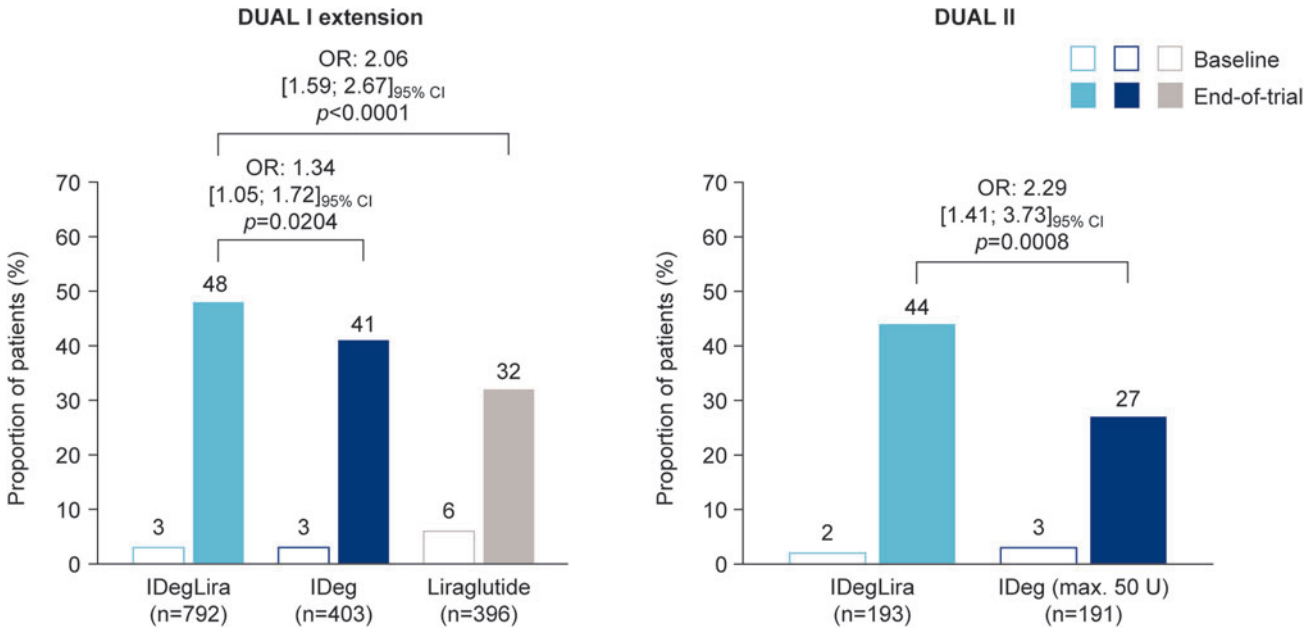
SUPPLEMENTARY FIG. S1. Distribution of postprandial SMBG* measurements across treatment arms in **(a)** DUAL I and **(b)** DUAL II at baseline and EOT. *SMBG assessed with glucose meter as plasma equivalent values of capillary whole blood glucose. Data are based on FAS, with LOCF for all subjects with a full nine-point profile at baseline. EOT, end-of-trial; FAS, full analysis set; IDeg, insulin degludec; IDegLira, fixed-ratio combination of insulin degludec and liraglutide; Lira, liraglutide; LOCF, last observation carried forward; SMBG, self-monitored blood glucose.



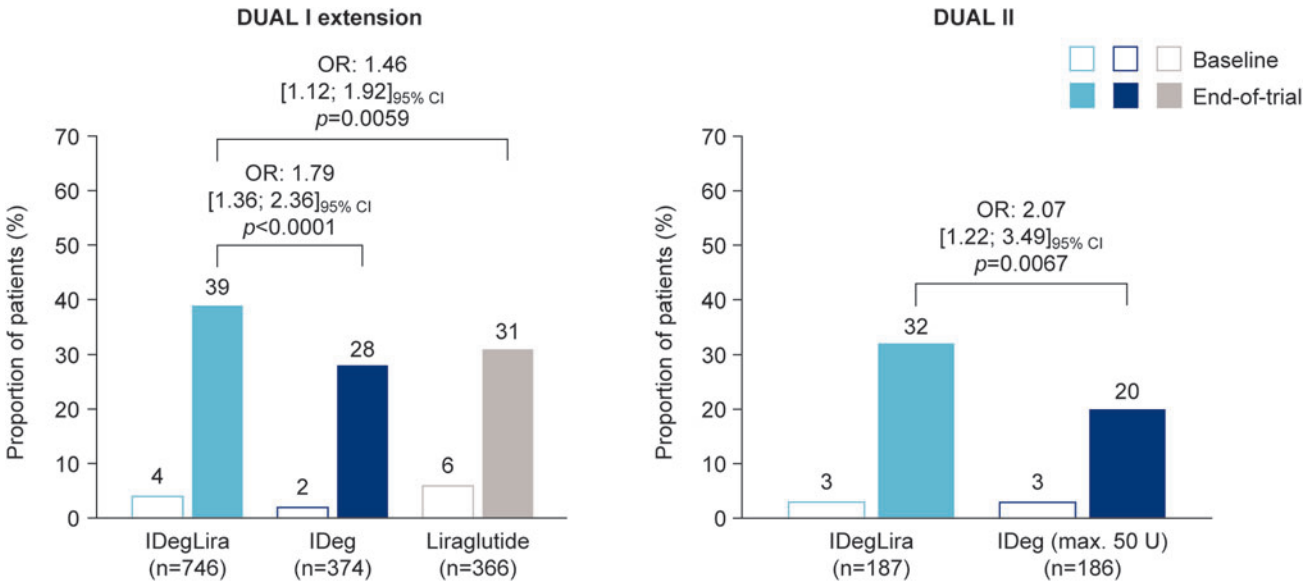
SUPPLEMENTARY FIG. S2. Proportion of patients with all three postprandial SMBG assessments <9.0 mmol/L. SMBG assessed with glucose meter as plasma equivalent values of capillary whole blood glucose. Data are based on FAS, with LOCF for all patients with a full nine-point profile at baseline; *P*-values are derived from logistic regression with treatment, region, baseline HbA_{1c} stratum (≤8.3% [≤67 mmol/mol], >8.3% [>67 mmol/mol]), and previous OAD treatment as fixed effects. HbA_{1c}, glycosylated hemoglobin; OAD, oral antidiabetic drug; OR, odds ratio.



SUPPLEMENTARY FIG. S3. Distribution of preprandial SMBG* measurements across treatment arms in **(a)** DUAL I and **(b)** DUAL II at baseline and EOT. *SMBG assessed with glucose meter as plasma equivalent values of capillary whole blood glucose. Data are based on FAS, with LOCF for all patients with a full nine-point profile at baseline..



SUPPLEMENTARY FIG. S4. Proportion of patients with all four preprandial SMBG* assessments 3.9–7.2 mmol/L. *SMBG assessed with glucose meter as plasma equivalent values of capillary whole blood glucose. Data are based on FAS, with LOCF for all patients with a full nine-point profile at baseline; *P*-values are derived from logistic regression with treatment, region, baseline HbA_{1c} stratum (≤8.3% [≤67 mmol/mol], >8.3% [>67 mmol/mol]), and previous OAD treatment as fixed effects..



SUPPLEMENTARY FIG. S5. Proportion of patients with all nine SMBG* values between 3.9 and <9 mmol/L. *SMBG assessed with glucose meter as plasma equivalent values of capillary whole blood glucose. Data are based on FAS, with LOCF for all patients with a full nine-point profile at baseline; *P*-values are derived from logistic regression with treatment, region, baseline HbA_{1c} stratum (≤8.3% [≤67 mmol/mol], >8.3% [>67 mmol/mol]) and previous OAD treatment as fixed effects..