

Supplementary Data

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Supplementary Appendix 2. Criteria for Rescue Therapy for Severe, Persistent Hyperglycemia

An additional therapeutic intervention should have been considered in patients who developed persistent, severe hyperglycemia after randomization based on the following criteria:

- During the first 8 weeks post-randomization: an average fasting plasma glucose (FPG) above 270 mg/dL (15.0 mmol/L) over at least a 2-week period,
- Between Week 8 and Week 18: an average FPG above 240 mg/dL (13.3 mmol/L) over at least a 2-week period,
- Between Week 18 and Week 26: an average FPG above 200 mg/dL (11.1 mmol/L) over at least a 2-week period or glycated hemoglobin (HbA_{1c}) above 8.0% (64 mmol/mol)
- Beginning at Week 26 (Visits 8 through 11): HbA_{1c} above 8.0% (64.0 mmol/mol) which is not at least 0.3% less than the HbA_{1c} at the previous scheduled measurement

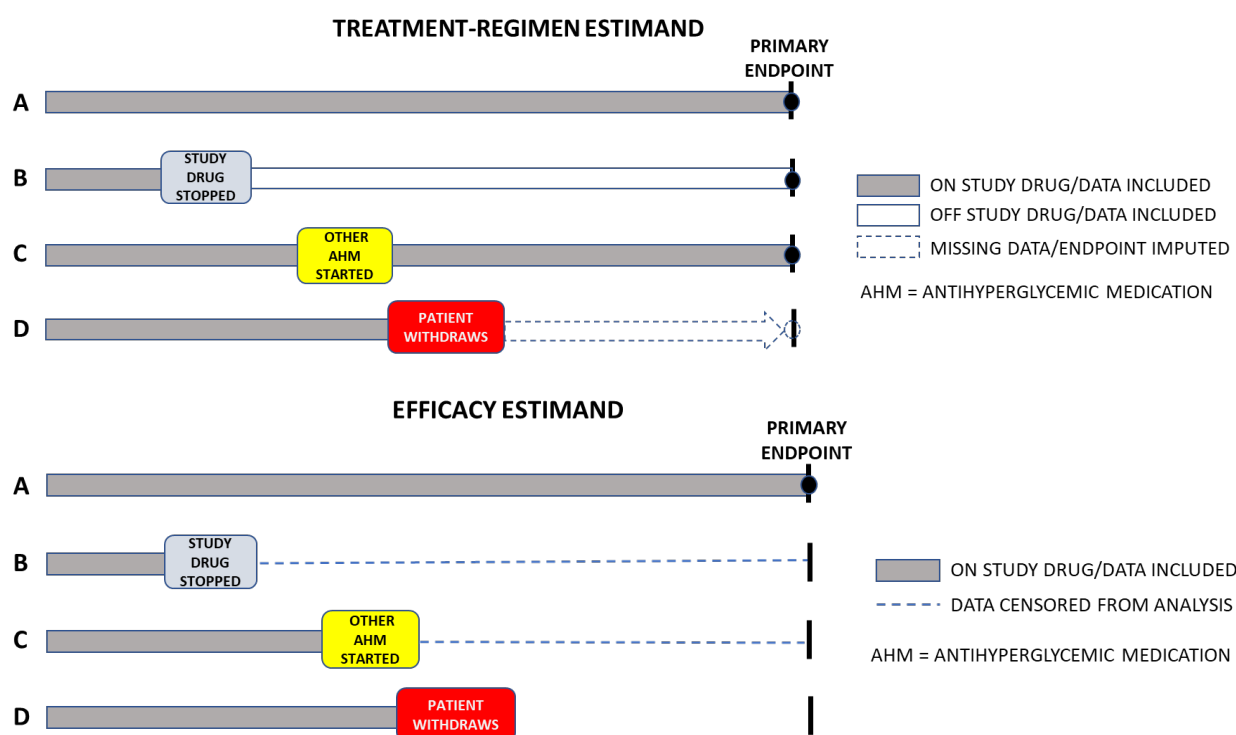
FPG criteria were to be based on at least 4 measurements taken per week.

Investigators were to first confirm that the patient was fully compliant with the assigned therapeutic regimen and that they did not have an acute condition causing severe hyperglycemia. The choice of rescue therapy was determined by the investigator, although per the protocol, preference was given to sodium-glucose co-transporter 2 inhibitor therapy as the first rescue medication. Other glucagon-like peptide-1 receptor agonists or dipeptidyl peptidase-4 inhibitors were not to be included in the rescue intervention. Patients who received a new intervention were to also continue administering study drug for the remaining period in the trial.

Supplementary Appendix 3: Statistical Considerations

Estimands

Two primary estimands were defined for analysis of the 36-week primary and secondary efficacy endpoints: a treatment-regimen estimand and an efficacy estimand. Data handling for analyses using each estimand for 4 hypothetical patients is illustrated in the graphic below.



In these examples, Patient A completed the primary 36-week endpoint on study drug, Patient B permanently stopped study drug but continued in the trial off study drug, Patient C initiated other antihyperglycemic rescue medication and continued in the trial on study drug, and Patient D withdrew from the study prior to the primary endpoint.

Details of Statistical Methods for Each Estimand

Treatment-regimen estimand: all data collected before and after either discontinuation of study drug or initiation of new antihyperglycemic therapy were included; for patients missing a primary 36 week endpoint value, an imputed value was used. Missing data at Week 36 were imputed based on retrieved dropouts defined as patients who had their HbA1c value measured at Week 36 in the same treatment group and the same status of premature treatment discontinuation (yes, no). Thus, for patients who prematurely discontinued treatment, missing data were imputed based on patients

who prematurely discontinued treatment, continued in the study, and had their HbA_{1c} value measured at Week 36. For patients who did not discontinue treatment but were missing their HbA_{1c} value at Week 36 (for example, due to missing that visit) and continued in the trial on treatment, the missing data were imputed based on patients with an HbA_{1c} value measured at Week 36 on treatment. The same approach was used to impute missing data at Week 52.

An HbA_{1c} primary endpoint value was available for 93.1% of patients at Week 36 and 89.9% of patients at Week 52. The proportion of patients with an imputed endpoint value for HbA_{1c} was similar across dose groups [Week 36: 1.5 mg, 45 (7.4%); 3.0 mg, 44 (7.1%), 4.5 mg, 39 (6.4%); Week 52: 59 (9.6%); 3.0 mg, 69 (11.2%); 4.5 mg, 58 (9.4%)].

An analysis of covariance model was applied as the primary analysis of the complete data using multiple imputation for HbA_{1c}, body weight and FSG analyses. The model terms included pooled country and treatment as fixed effects, and baseline as a covariate. For analyses of body weight and FSG, baseline HbA_{1c} stratum was added to this model as a fixed effect. A logistic regression model, including pooled country and treatment as fixed effects and baseline HbA_{1c} as a covariate, was fit to the complete data to analyze the proportions of patients achieving HbA_{1c} target <7.0% (53 mmol/mol). Missing HbA_{1c} data were imputed as not achieving the target.

Efficacy estimand: data were included up to either initiation of any new antihyperglycemic medication for more than 14 days (regardless of whether the investigator indicated that it was for severe persistent hyperglycemia) or premature study drug discontinuation, whichever occurred first. The analysis included patients with a non-missing baseline value and at least one non-missing post-baseline value of the response variable. The primary analysis model was a mixed-model for repeated measures, including pooled country, treatment, visit, treatment-by-visit interaction as fixed effects and baseline value as a covariate. Baseline HbA_{1c} stratum ($\geq 8.5\%$ and $< 8.5\%$ [69 mmol/mol]) was added in the model as a fixed effect when HbA_{1c} was not the response variable. The proportions of patients achieving HbA_{1c} targets were analyzed using a longitudinal logistic regression model for repeated measures with pooled country, treatment, visit, and the treatment-by-visit interaction included as fixed effects and baseline HbA_{1c} as a covariate.

Graphical Testing Approach

The graphical testing approach for controlling overall type I error is shown in the figure below.

The 8 hypotheses testing the superiority of dulaglutide 4.5 mg and 3.0 mg, respectively, versus dulaglutide 1.5 mg at 36 weeks were for the following endpoints:

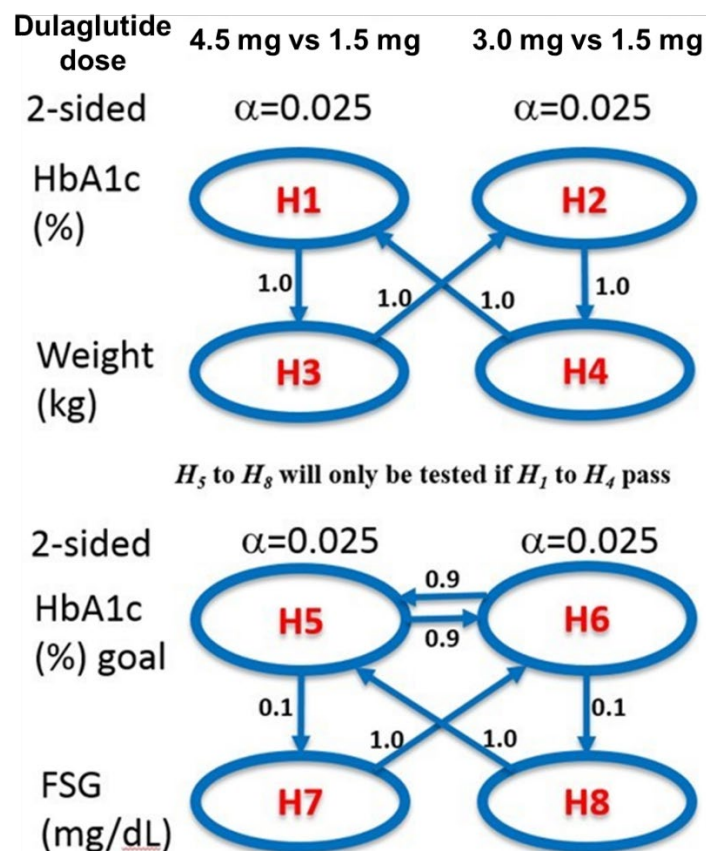
H1 and H2: mean change from baseline in HbA_{1c}.

H3 and H4: mean change from baseline in body weight.

H5 and H6: proportion of patients achieving an HbA_{1c} <7.0%.

H7 and H8: mean change from baseline in FSG.

The overall significance level of 2-sided $\alpha=0.05$ is equally split between H1 and H2 with 0.025 to H1 and 0.025 to H2. The number attached for certain edges denotes the proportion of the allocated fraction of alpha from a prespecified hypothesis (node), if it is confirmed, that will be passed to the next hypothesis. If H1 is confirmed, that α of 0.025 will be passed to H3. If H2 is confirmed, that α of 0.025 will be passed to H4. If H3 is confirmed, H2 can be tested using the full local α of 0.05 if H2 has not already been confirmed. However, if H3 cannot be confirmed, this 0.025 will be lost permanently and cannot be combined with the initial local α of 0.025 for H2. H4 can be tested only if H2 is confirmed. H5 to H8 can be tested only if H1 to H4 are confirmed. This graphical approach was conducted separately for the efficacy estimand and treatment-regimen estimand, and each was tested at the full significance level of 0.05.



Graphical approach, controlling overall type I error, when comparing the treatment effect for each of the primary and secondary efficacy objectives at 36 weeks in the ITT Population. Abbreviations: FSG = fasting serum glucose; H = hypothesis; HbA_{1c} = glycated hemoglobin.

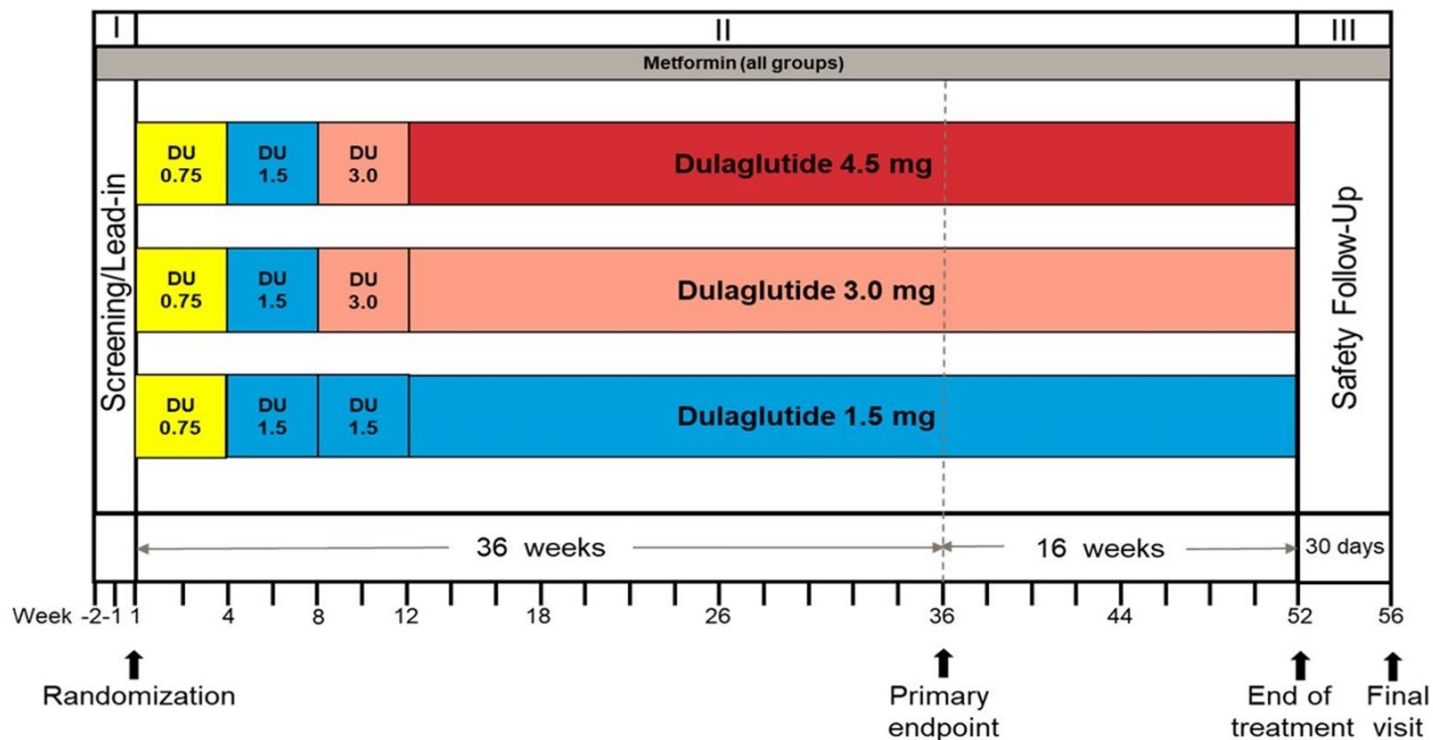
Supplementary Figure S1. Study design

Key inclusion criteria

- T2D treated with stable doses of metformin
- HbA_{1c} ≥7.5% and ≤11.0%
- Body mass index ≥25 kg/m²

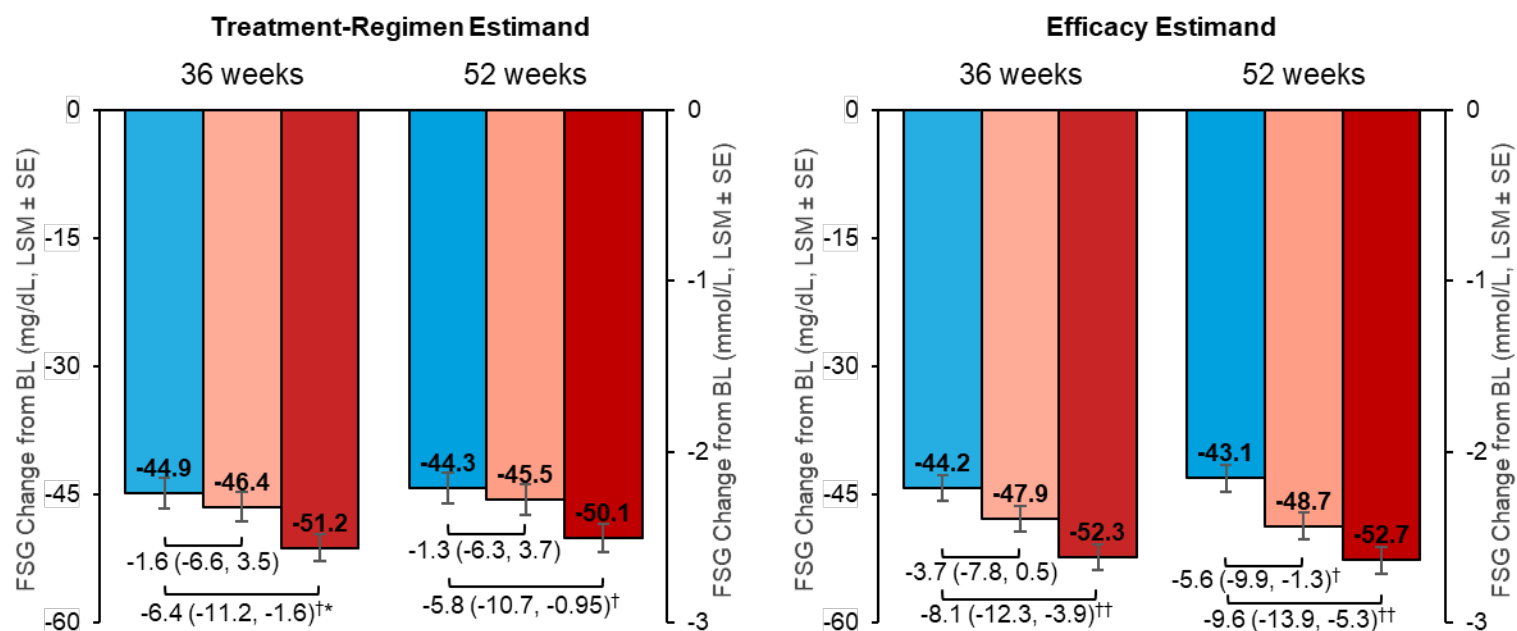
Key exclusion criteria

- Type 1 diabetes
- Treated with ANY other antihyperglycemia regimen except metformin within 3 months of screening or insulin for chronic conditions (>14 days)



Abbreviations: DU = dulaglutide; eGFR = estimated glomerular filtration rate; HbA_{1c} = glycated hemoglobin; T2D = type 2 diabetes. Note: all dulaglutide doses are once-weekly.

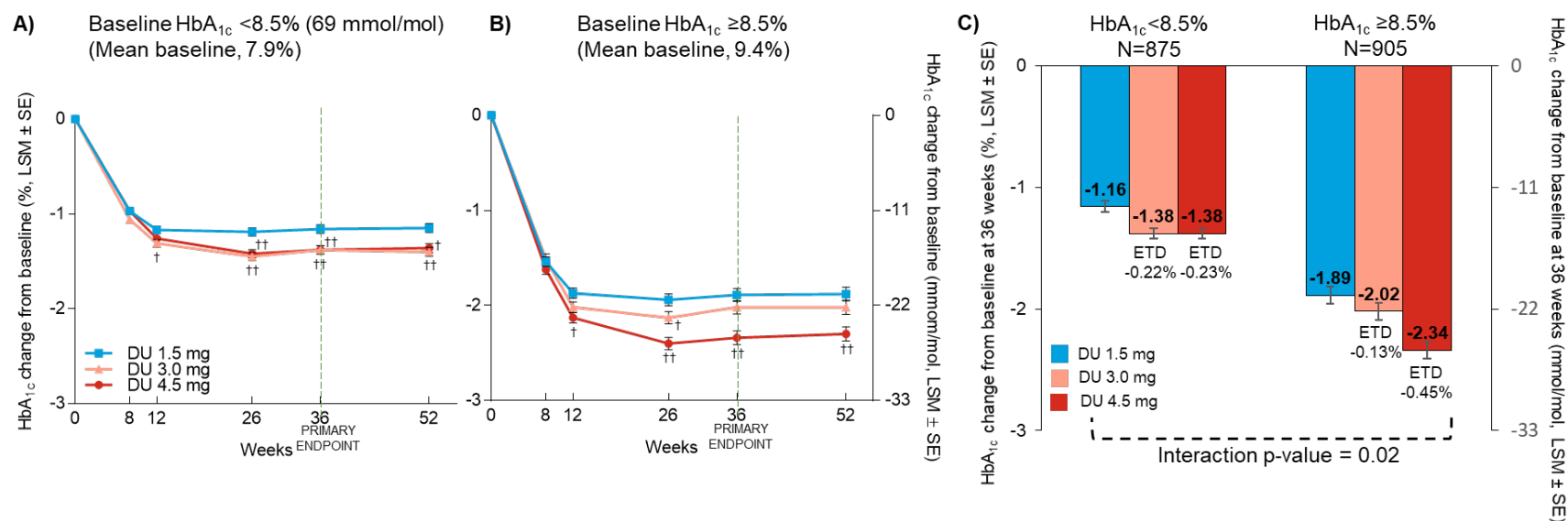
Supplementary Figure S2. Change from baseline in fasting serum glucose by estimand



Left panel: Change in FSG from baseline to 36 and 52 weeks, ANCOVA with multiple imputation (treatment-regimen estimand); right panel: change in FSG from baseline to 36 and 52 weeks, MMRM (efficacy estimand).

Data presented as LSM ± SE; ^{††}P<0.05 or P<0.001 vs dulaglutide 1.5 mg, respectively. * Nominal p-value, not adjusted for multiplicity; comparison versus dulaglutide 1.5 mg did not achieve statistical superiority under graphic testing criteria. Treatment-regimen estimand included all randomized patients with imputation of missing endpoint values. The efficacy estimand included patients with a non-missing baseline value and at least one non-missing post-baseline value of the response variable: 1743 patients (1.5 mg, n=575; 3.0 mg, n=586; 4.5 mg, n=582). Abbreviations: FSG = fasting serum glucose; BL = baseline; MMRM = mixed-model for repeated measures; ANCOVA = analysis of covariance

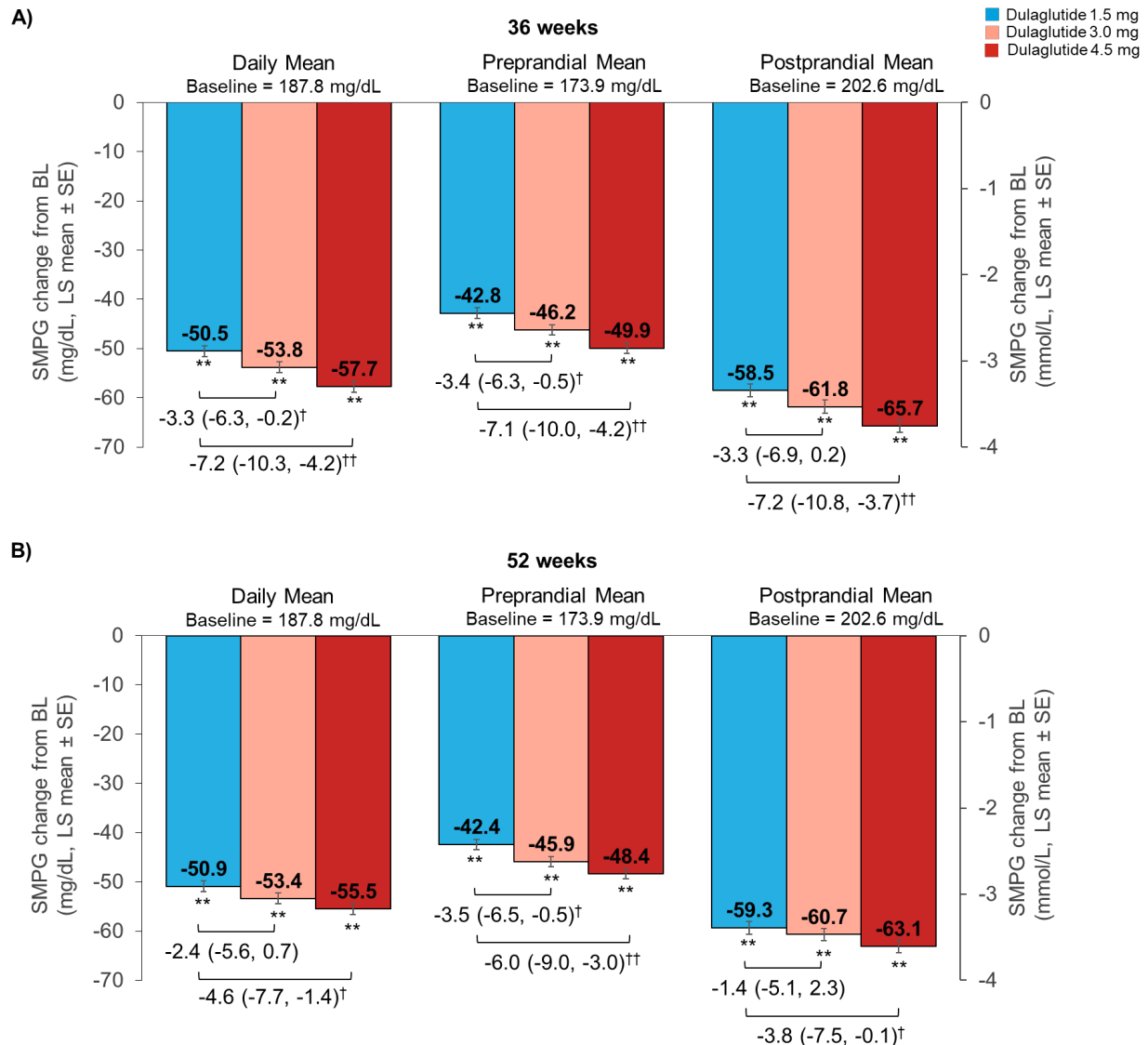
Supplementary Figure S3. Subgroup analysis of change in HbA_{1c} by baseline HbA_{1c}



A) Change in HbA_{1c} over time through 52 weeks in patients with baseline HbA_{1c} <8.5%, MMRM (efficacy estimand), B) Change in HbA_{1c} over time through 52 weeks in patients with baseline HbA_{1c} ≥8.5%, MMRM (efficacy estimand), C) Change from baseline to primary 36-week time point by baseline HbA_{1c}; N= patients with non-missing baseline value and at least one non-missing post-baseline value of the response variable. P-value is for interaction of subgroup and treatment at 36 weeks evaluated using a significance level of 0.10, unadjusted.

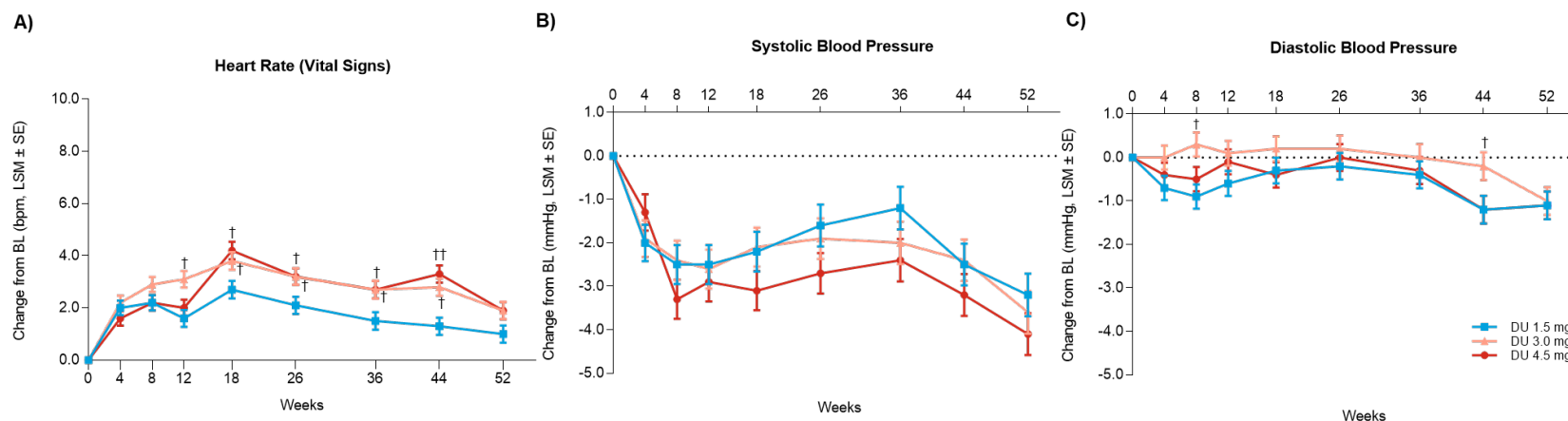
†, †† P < 0.05 or P < 0.001 vs dulaglutide 1.5 mg, respectively. Analyses included data collected up to either initiation of any new antihyperglycemic medication for more than 14 days (regardless of whether the investigator indicated that it was for severe persistent hyperglycemia) or premature treatment discontinuation, whichever occurred first. Abbreviations: ETD = estimated treatment difference vs. 1.5 mg; HbA_{1c} = glycated hemoglobin; MMRM = mixed-model for repeated measures.

Supplementary Figure S4. SMPG at 36 and 52 weeks



Six-point SMPG daily mean, preprandial mean, and postprandial changes at A) 36 weeks, and B) 52 weeks (efficacy estimand). Data presented as LSM ± SE; *,**P<0.05 or P<0.001 vs baseline, respectively; †,††P<0.05 or P<0.001 vs dulaglutide 1.5 mg, respectively. MMRM analysis. The efficacy estimand included data collected up to either initiation of any new antihyperglycemic medication for more than 14 days (regardless of whether the investigator indicated that it was for severe persistent hyperglycemia) or premature treatment discontinuation, whichever occurred first. Abbreviations: LSM = least-squares mean; MMRM = mixed-model for repeated measures; SE = standard error; SMPG = self-monitored plasma glucose

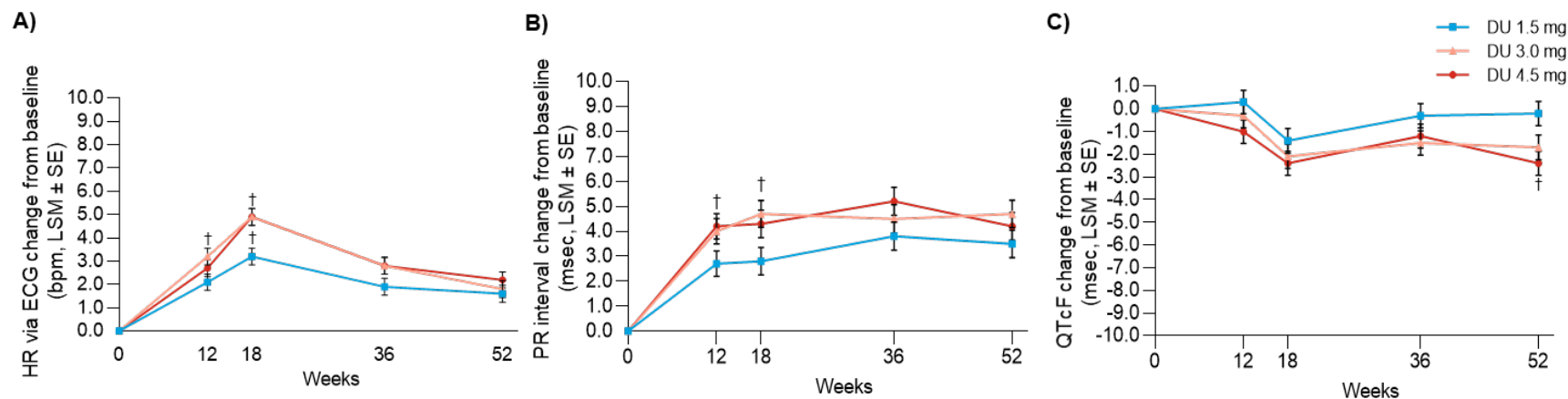
Supplementary Figure S5. Vital signs



A) Seated HR change over time, MMRM. B) Seated SBP change over time, MMRM. C) Seated DBP change over time, MMRM. Data presented are least-squares mean \pm SE. †, †† $P < 0.05$ or $P < 0.001$ vs dulaglutide 1.5 mg, respectively. Safety Population. Only patients with non-missing baseline values and at least 1 non-missing postbaseline value of the response variable were included in the analysis. Abbreviations: BL = baseline; DBP = diastolic blood pressure; DU = dulaglutide; HR = heart rate; LSM = least-squares mean; MMRM = mixed-model for repeated measures; SBP = systolic blood pressure.

Significant LSM increases in seated HR were observed across all dose groups over time (Panel A), including at the 36-week primary time point (1.5 mg, 1.5 beats per minute (bpm); 3.0 mg, 2.7 bpm; 4.5 mg, 2.7 bpm) and the 52 week final time point (1.5 mg, 1.0 bpm; 3.0 mg, 1.9 bpm; 4.5 mg, 1.9 bpm). The peak LSM change in seated HR occurred at 18 weeks across all dose groups (1.5 mg, 2.7 bpm; 3.0 mg, 3.8 bpm; 4.5 mg, 4.2 bpm), and declined thereafter through 52 weeks. The treatment differences versus the 1.5 mg group in LSM change in HR at 52 weeks were not significant for either the 3.0 mg group (0.9 bpm, $P = 0.057$) or the 4.5 mg group (0.9 bpm, $P = 0.059$).

Supplementary Figure S6. ECG parameters



A) HR via ECG change over time, MMRM. B) PR interval change over time, MMRM. C) QTcF change over time, MMRM. Data presented are LSM \pm SE. $^{\dagger}P < 0.05$ vs dulaglutide 1.5 mg. Safety Population. Only patients with non-missing baseline values and at least 1 non-missing postbaseline value of the response variable were included in the analysis. Abbreviations: ECG = electrocardiogram; HR = heart rate; LSM = least-squares mean; MMRM = mixed-model for repeated measures.

Supplementary Table S1. Key inclusion and exclusion criteria

Key Inclusion Criteria	Key Exclusion Criteria
<ul style="list-style-type: none"> • Men and nonpregnant women aged ≥ 18 years • T2D for ≥ 6 months • $HbA_{1c} \geq 7.5\%$ (58 mmol/mol) and $\leq 11.0\%$ (97 mmol/mol) • Treated with stable doses of metformin for at least 3 months prior to Visit 1 and between Visit 1 and Visit 3: <ul style="list-style-type: none"> ◦ The metformin dose was considered stable for this period if all prescribed daily doses were in the range between the minimum required dose (≥ 1500 mg/day) and the maximum approved dose per country-specific label. ◦ Lower doses were allowed only with documented GI intolerance in the required dose range or a documented eGFR (measured by CKD-EPI) or other renal function measure which requires lower doses per country-specific labeling. • Stable body weight for at least 3 months prior to Visit 1 (not changed by more than 5% in the past 3 months) • BMI ≥ 25 kg/m² 	<ul style="list-style-type: none"> • T1D • Used: <ul style="list-style-type: none"> ◦ any glucose-lowering medication other than metformin 3 months prior to study entry or during the Screening and Lead-In Period, or ◦ any GLP-1 RA at any time in the past, or ◦ insulin for chronic conditions (>14 days) • Treated with prescription or OTC drugs that promote weight loss: <ul style="list-style-type: none"> ◦ within 3 months prior to screening (Visit 1), or ◦ between study entry and randomization (Visit 3), or ◦ both; or ◦ was currently (or within the last 3 months) participating in, or planned to initiate within the timeframe of the study, an organized diet and/or exercise weight reduction program other than the lifestyle and dietary measures for diabetes treatment; • Treated with any other excluded medication: <ul style="list-style-type: none"> ◦ within 3 months prior to screening (Visit 1), or ◦ between study entry and randomization (Visit 3), or ◦ both; ◦ Excluded glucocorticoids must not have been used for >14 days within 1 month prior to Visit 1 or between Visits 1 and 3; • Discontinued metformin therapy, or changed metformin dose or formulation, between Visit 1 and Visit 3; • ≥ 1 episode of severe hypoglycemia, ≥ 1 episode of hypoglycemia unawareness within the 6 months, or both;

	<ul style="list-style-type: none"> • Had any of the following CV conditions within 2 months prior to Visit 1: <ul style="list-style-type: none"> ○ acute MI, or ○ NYHA Class III or Class IV heart failure, or ○ cerebrovascular accident (stroke) • Had: <ul style="list-style-type: none"> ○ a known clinically significant gastric emptying abnormality (eg, severe diabetic gastroparesis or gastric outlet obstruction), or ○ undergone gastric bypass (bariatric) surgery or restrictive bariatric surgery, or ○ chronically taken drugs that directly reduce GI motility; • Had: <ul style="list-style-type: none"> ○ acute or chronic hepatitis, or ○ signs and symptoms of any other liver disease other than NAFLD, or ○ ALT level >2.5 times the upper limit of the reference range, as determined by the central laboratory at study entry; • Chronic or acute pancreatitis any time prior to study entry • Known proliferative retinopathy or maculopathy requiring acute treatment according to the opinion of the investigator; • eGFR <30 mL/min/1.73 m² (or lower than the country-specific threshold for discontinuing metformin therapy per local label), calculated by CKD-EPI, as determined by the central laboratory at Visit 1 and confirmed at Visit 2; • Personal or family history of MTC or personal history of multiple endocrine neoplasia syndrome type 2 • Serum calcitonin ≥20 ng/L, as determined by the central laboratory at study entry;
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	<ul style="list-style-type: none"> • Evidence of significant, active autoimmune abnormality (for example, lupus, rheumatoid arthritis) that, in the opinion of the investigator, was likely to require concurrent treatment with systemic glucocorticoids in the next 12 months; • Active or untreated malignancy, or had been in remission from clinically significant malignancy (other than basal cell or squamous cell skin cancer) for less than 5 years; or • Any hematologic condition that may have interfered with HbA_{1c} measurement (for example, hemolytic anemias, sickle cell disease).
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Abbreviations: ALT = alanine aminotransferase; BMI = body mass index; CKD-EPI = Chronic Kidney Disease-Epidemiology Collaboration equation; CV = cardiovascular; eGFR = estimated glomerular filtration rate; GI = gastrointestinal; GLP-1 RA = glucagon-like peptide-1 receptor agonist; HbA_{1c} = glycated hemoglobin; MI = myocardial infarction; MTC = medullary thyroid cancer; NAFLD = nonalcoholic fatty liver disease; NHYA = New York Heart Association; OTC = over-the-counter; T1D = type 1 diabetes; T2D = type 2 diabetes

Supplementary Table S2. Proportion of patients achieving HbA_{1c} treatment goals at 36 and 52 weeks (efficacy estimand)

	36 Weeks (Primary Endpoint)			52 Weeks		
	DU 1.5 mg (N=612)	DU 3.0 mg (N=616)	DU 4.5 mg (N=614)	DU 1.5 mg (N=612)	DU 3.0 mg (N=616)	DU 4.5 mg (N=614)
Glycemic target						
% achieving HbA _{1c} <7% (53 mmol/mol)	57.0	64.7	71.5	58.6	65.4	71.7
OR (95% CI) vs. DU 1.5 mg		1.5 (1.1, 2.0)	2.2 (1.7, 3.0)		1.4 (1.1, 1.9)	2.0 (1.5, 2.7)
P value		0.006	<0.001		0.02	<0.001
% achieving HbA _{1c} ≤6.5% (48 mmol/mol)	38.1	48.4	51.7	40.4	49.2	51.3
OR (95% CI) vs. DU 1.5 mg		1.6 (1.2, 2.1)	2.0 (1.5, 2.6)		1.5 (1.1, 2.0)	1.7 (1.3, 2.2)
P value		<0.001	<0.001		0.004	<0.001

Odds Ratio, CI, and p-value for baseline measures are from logistic regression model with treatment as a factor. Proportion calculated based on observed data for all randomized patients excluding data collected after treatment discontinuation or initiation of other antihyperglycemic medication. Abbreviations: CI = confidence interval; DU = dulaglutide; OR = odds ratio; % achieving = proportion of patients achieving.

Supplementary Table S3. Summary of ratio at 36 and 52 weeks to baseline in HOMA2-IR, HOMA2-%B, C-peptide, and fasting glucagon (efficacy estimand)

Parameter	DU 1.5 mg (N=612)	DU 3.0 mg (N=616)	DU 4.5 mg (N=614)
HOMA2-IR			
Baseline mean	2.49	2.44	2.45
Geometric LSM ratio to baseline at 36 Weeks	0.92	0.91	0.89
Geometric LSM ratio to baseline at 52 Weeks	0.89	0.89	0.88
HOMA2-%B			
Baseline mean (%)	50.55	53.14	48.42
Geometric LSM ratio to baseline at 36 Weeks	1.66	1.75	1.91 ^{††}
Geometric LSM ratio to baseline at 52 Weeks	1.60	1.76 [†]	1.85 ^{††}
Fasting C-peptide			
Baseline mean (µg/L)	2.90	2.77	2.78
Geometric LSM ratio to baseline at 36 Weeks	0.92	0.91	0.92
Geometric LSM ratio to baseline at 52 Weeks	0.91	0.92	0.90
Fasting glucagon			
Baseline mean (pg/mL)	48.06	46.91	50.57
Geometric LSM ratio to baseline at 36 Weeks	0.78	0.79	0.73 [†]
Geometric LSM ratio to baseline at 52 Weeks	0.77	0.77	0.77
Fasting glucagon×FSG			
Baseline mean (pg/mL×mg/dL)	8810.21	8647.69	9335.30
Geometric LSM ratio to baseline at 36 Weeks	0.59	0.58	0.51 ^{††}
Geometric LSM ratio to baseline at 52 Weeks	0.59	0.56	0.54 [†]
Fasting insulin			
Baseline mean (mU/L)	18.61	18.06	18.55
Geometric LSM ratio to baseline at 36 Weeks	0.95	0.97	0.98
Geometric LSM ratio to baseline at 52 Weeks	0.94	0.96	0.93

^{†,††}P<0.05 and P<0.001 vs dulaglutide 1.5 mg, respectively. The efficacy estimand included data collected up to either initiation of any new antihyperglycemic medication for more than 14 days (regardless of whether the investigator indicated that it was for severe persistent hyperglycemia) or premature treatment discontinuation, whichever occurred first. MMRM analysis. Abbreviations: DU = dulaglutide; FSG = fasting serum glucose; HOMA2-%B = homeostatic assessment of β -cell function; HOMA2-IR = homeostatic assessment of insulin resistance; LSM = least-squares mean; MMRM = mixed-model for repeated measures.

Supplementary Table S4. Summary of nausea, diarrhea, and vomiting adverse events and treatment discontinuations due to these events through 36 weeks and 52 weeks

	36 Weeks (Primary Timepoint)				52 Weeks		
Variable, n (%)	DU 1.5 mg (N=612)	DU 3.0 mg (N=616)	DU 4.5 mg (N=614)		DU 1.5 mg (N=612)	DU 3.0 mg (N=616)	DU 4.5 mg (N=614)
TEAE							
Nausea	82 (13.4)	96 (15.6)	101 (16.4)		87 (14.2)	99 (16.1)	106 (17.3)
Diarrhea	43 (7.0)	70 (11.4)	66 (10.7)		47 (7.7)	74 (12.0)	71 (11.6)
Vomiting	34 (5.6)	51 (8.3)	57 (9.3)		39 (6.4)	56 (9.1)	62 (10.1)
Severe TEAE							
Nausea	3 (0.5)	3 (0.5)	3 (0.5)		3 (0.5)	3 (0.5)	3 (0.5)
Diarrhea	0 (0.0)	3 (0.5)	2 (0.3)		0 (0.0)	4 (0.6)	2 (0.3)
Vomiting	0 (0.0)	4 (0.6)	2 (0.3)		0 (0.0)	4 (0.6)	2 (0.3)
Treatment discontinuation due to AE							
Nausea	6 (1.0)	7 (1.1)	6 (1.0)		8 (1.3)	8 (1.3)	9 (1.5)
Diarrhea	1 (0.2)	6 (1.0)	5 (0.8)		1 (0.2)	6 (1.0)	6 (1.0)
Vomiting	0 (0.0)	5 (0.8)	8 (1.3)		0 (0.0)	5 (0.8)	8 (1.3)

All values presented as n (%). Abbreviations: AE = adverse event; CV = cardiovascular; DU = dulaglutide; GI = gastrointestinal; TEAE = treatment-emergent adverse events

Supplementary Table S5: Adverse events reported in ≥2% patients through 52 weeks:
MedDRA Gastrointestinal Disorders System Organ Class (SOC)

Event, n (%)	DU 1.5 mg (N=612)	DU 3.0 mg (N=616)	DU 4.5 mg (N=614)	Total (N=1842)
TEAEs ≥2% patients in SOC <i>Gastrointestinal Disorders</i>				
Nausea	87 (14.2)	99 (16.1)	106 (17.3)	292 (15.9)
Diarrhea	47 (7.7)	74 (12.0)	71 (11.6)	192 (10.4)
Vomiting	39 (6.4)	56 (9.1)	62 (10.1)	157 (8.5)
Constipation	19 (3.1)	26 (4.2)	24 (3.9)	69 (3.7)
Dyspepsia	17 (2.8)	31 (5.0)	17 (2.8)	65 (3.5)
Abdominal Pain Upper	18 (2.9)	21 (3.4)	16 (2.6)	55 (3.0)
Abdominal Pain	17 (2.8)	15 (2.4)	17 (2.8)	49 (2.7)
Gastroesophageal Reflux Disease	12 (2.0)	15 (2.4)	18 (2.9)	45 (2.4)
Abdominal Distension	9 (1.5)	11 (1.8)	22 (3.6)	42 (2.3)

All values presented as n (%). Abbreviations: TEAE = treatment emergent adverse event; DU = dulaglutide; MedDRA = Medical Dictionary for Regulatory Activities

Supplementary Table S6. Change from baseline to 52 weeks in serum lipid parameters

Parameter/Statistic	DU 1.5 mg (N=612)	DU 3.0 mg (N=616)	DU 4.5 mg (N=614)
Total cholesterol			
Baseline mean (mg/dL)	177.36	176.65	178.58
Mean change from baseline (mg/dL) to Week 52	-3.27**	-4.89**	-7.87**
HDL-C			
Baseline mean (mg/dL)	46.35	45.44	45.05
Mean change from baseline (mg/dL) to Week 52	0.27	0.32	0.68**
LDL-C^a			
Baseline mean (mg/dL)	91.91	93.25	95.12
Mean change from baseline (mg/dL) to Week 52	2.15	0.00	-1.78
VLDL-C^a			
Baseline mean (mg/dL)	33.95	34.22	35.34
Mean change from baseline (mg/dL) to Week 52	-3.22**	-3.77**	-6.04**,†
Triglycerides			
Baseline mean (pg/mL)	207.22	198.11	201.78
Mean change from baseline (mg/dL) to Week 52	-33.47**	-29.71**	-40.48**,†

^aCalculated value based on Friedewald equation. **P-value <0.05 versus baseline, from Wilcoxon signed-rank test; †P<0.05 versus dulaglutide 1.5 mg, from ANOVA on rank-transformed data. Abbreviations: ANOVA = analysis of variance; DU = dulaglutide; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; VLDL-C= very-low-density lipoprotein cholesterol.