SUPPLEMENTARY DATA

Criteria for Discontinuation Due to Hyperglycemia

Supplementary Table 1. Thresholds for FPG and HbA_{1c} by Visit.

Variable	Visits 5-7 (2-8 wks)	Visit 8 (9-12 wks)	Visit 9 (13-26 wks)	Visit 10 (27-39 wks)	Visits 11-15 (40-104 wks)
FPG (mg/dL)	>270	>240	>220	>220	--
				or	
HbA_{1c} (% [mmol/mol])	--	--	--	>8.5% (69)	>8.0% (64)

Abbreviations: -- = not applicable; HbA_{1c} = glycosylated hemoglobin A_{1c}; FPG = fasting plasma glucose; wks = weeks.

Patients were to be discontinued from the study if they developed persistent or worsening hyperglycemia beyond the thresholds for FPG or HbA_{1c} as specified in Table S1 above, and the criteria outlined below.

- If fasting self-monitored plasma glucose (SMPG) values meeting the above thresholds were consistently recorded by the patient for at least 2 weeks and not secondary to a readily identifiable illness or pharmacological treatment, in the opinion of the investigator, the patient was to be discontinued from the trial.

- If a patient had a FPG value (central laboratory) that met the criteria above, but the patient's fasting SMPG and/or HbA_{1c} values were inconsistent with this random FPG, the patient would receive intensified dietary counseling and have a repeat FPG measurement in 1 month. If the FPG value still met the above criteria, the patient was to be discontinued from the trial.

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Supplementary Table 2. Other endpoints of interest, change from baseline at 26 and 52 weeks.

	26 weeks				52 weeks		
	DU1.5 mg (N=304)	DU 0.75 mg (N=302)	SITA (N=315)	PL (N=177)	DU 1.5 mg (N=304)	DU 0.75 mg (N=302)	SITA (N=315)
Insulin and HOMA Parameters							
Fasting insulin (pmol/L)[a]	11.6 (6.6)	10.2 (6.5)	8.5 (6.7)	-6.9 (9.2)	10.6 (6.0)	13.0 (5.9)	4.2 (6.0)
HOMA2-%B	32.3 (2.7)[##**]	27.0 (2.6)[##**]	10.8 (2.7)	1.6 (4.0)	33.6 (2.5)[##]	22.3 (2.5)[##]	6.7 (2.5)
HOMA2-%S[a]	5.8 (2.3)	0.8 (2.3)[*]	2.3 (2.3)	9.8 (3.5)	4.7 (2.4)	2.3 (2.3)	4.3 (2.4)
Lipid Parameters, median (mmol/L)							
Total cholesterol	-0.21[##**]	-0.02	0.11	0.07	-0.03	-0.03	0.10
LDL cholesterol	-0.18[##*]	-0.05[#]	0.10	0.02	-0.06[#]	0.02	0.12
HDL cholesterol	0.02	0.03	0.03	0.05	0.05	0.07	0.05
Triglycerides	-0.19	-0.14	-0.09	-0.07	-0.16	-0.15	-0.06
Pancreatic Enzymes, median [Q1,Q3] (U/L)[b]							
Lipase	6 [-2,17][#**]	5 [-1, 16][**]	4 [-2,11][**]	-1 [-7,7]	6 [-2,15]	5 [-1,15]	4 [-2,11]
Total Amylase	7 [-1,14][#**]	6 [0,15][#**]	4 [-2,11]	2 [-6, 10]	6 [0,15][#]	6 [0,15][#]	4 [-3,12]
p-Amylase	4 [1,10][##**]	3 [0,9][#**]	2 [-1,6][**]	0 [-3,4]	4 [1,10][#]	3 [0,9]	3 [0,7]
Patients with TE Abnormal (n, %)[c]							
Lipase	109 (43)[**]	92 (37)[*]	97 (36)[*]	37 (25)	124 (49)	111 (45)	110 (41)
Total Amylase	33 (12)	33 (13)	27 (10)	13 (9)	38 (14)	42 (16)	36 (13)
p-Amylase	54 (19)[*]	55 (20)[*]	42 (14)	18 (11)	67 (24)	70 (25)	55 (19)
Pancreatic Enzymes, n (%) of patients with ≥3x ULN[d]							
Lipase	19 (6.3)	21 (7.0)	20 (6.3)	11 (6.3)	22 (7.3)	26 (8.7)	27 (8.6)
p-Amylase	2 (0.7)	1 (0.3)	1 (0.3)	1 (0.6)	2 (0.7)	4 (1.3)	1 (0.3)

[a]Measurements collected after completion of dose-finding portion of the trial.

[b]The normal range of serum values for lipase, total amylase, and p-amylase are 0-60 U/L, 20-112 U/L, and 13-53 U/L, respectively.

[c]Cumulative number (%) of patients with at least one treatment emergent abnormality.

[d]Percentages are based on the number of patients with baseline and at least 1 postbaseline result in specified treatment arm during the time period assessed.

All data are LS mean (SE) unless otherwise noted. [#, *]$P < 0.05$ vs. sitagliptin and placebo, respectively. [##,**]$P < 0.001$ vs. sitagliptin and placebo, respectively. Abbreviations: DU = dulaglutide; HOMA2-B= updated homeostasis model beta cell function; HOMA2-S= updated homeostasis model insulin sensitivity; p-amylase= pancreatic amylase; PL = placebo; $Q_{x=}$ quartile number; SITA = sitagliptin; TE= treatment-emergent; ULN= upper limit of normal for central laboratory reference range.