Improved Treatment Satisfaction with Dulaglutide and Insulin Glargine in Patients with T2D and Chronic Kidney Disease

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OBJECTIVE

Patient reported outcomes were assessed to capture worry and behavioral changes associated with concerns and experiences of hypoglycemia as measured by the Adult Low Blood Sugar Survey (ALBSS). Patients’ satisfaction with their diabetes treatment and perceived frequency of hyperglycemia and hypoglycemia was evaluated using the Diabetes Treatment Satisfaction Questionnaire (DTSQ).

Is there a difference in the hypoglycemia concerns or treatment satisfaction reported by patients with T2D and CKD treated with dulaglutide compared to glargine?

STUDY DESIGN

KEY RESULT

Change from baseline in PRO measures

	Week	Dulaglutide 1.5 mg (N=183)	Dulaglutide 0.75 mg (N=180)	Insulin glargine (N=186)
Adult Low Blood Sugar Survey (ALBSS)^a				
Total Score	Baseline	23.3 (16.78)	22.0 (18.00)	25.4 (17.92)
	26	-4.3 (1.15)**	-3.1 (1.13)*	-1.6 (1.09)
	52	-2.5 (1.20)*	-3.8 (1.19)*	-3.5 (1.17)*
Behavior Scale	Baseline	27.2 (18.36)	26.5 (21.87)	30.4 (20.63)
	26	-4.3 (1.40)*	-3.3 (1.38)*	-2.5 (1.33)
	52	-2.1 (1.44)	-4.0 (1.42)*	-3.5 (1.40)*
Worry Scale	Baseline	20.1 (20.92)	18.5 (19.21)	21.4 (21.23)
	26	-4.3 (1.33)*	-3.4 (1.31)*	-1.1 (1.26)
	52	-2.9 (1.38)*	-4.2 (1.37)*	-3.7 (1.35)*
Diabetes Treatment Satisfaction Questionnaire (DTSQ)				
Total Score	Baseline	27.5 (7.32)	28.3 (7.02)	26.7 (8.19)
	26	4.5 (0.46)**	4.0 (0.46)**	4.0 (0.44)**
	52	4.1 (0.48)**	3.6 (0.48)**	4.8 (0.47)**
Hyperglycemia Scale	Baseline	3.5 (1.84)	3.5 (1.81)	3.4 (1.88)
	26	-1.1 (0.15)**	-1.0 (0.15)***	-1.4 (0.15)**
	52	-1.1 (0.16)**	-1.2 (0.16)**	-1.3 (0.15)**
Hypoglycemia Scale	Baseline	1.8 (1.67)	1.5 (1.77)	1.6 (1.72)
	26	-0.1 (0.13)	-0.0 (0.13)	-0.1 (0.13)
	52	-0.2 (0.14)	-0.2 (0.14)	0.0 (0.13)

- ^aTransformed scores (0 to 100). All baseline scores presented as mean (SD). All change from baseline scores presented as least squares mean (SE). *, ** 2-sided p<.05 and p<.001 versus baseline; # 2-sided p<.05 vs insulin glargine.
- Significant decreases from baseline (improvements) in all 3 ALBSS scores were observed with dulaglutide at both 26 and 52 weeks (except for the Behavior score at 52 weeks in the dulaglutide 1.5 mg arm) and with glargine only at 52 weeks
 - Significant increases from baseline (improvements) in the DTSQ Total score and significant decreases from baseline (improvements) in the DTSQ Hyperglycemia score were observed with dulaglutide and glargine at 26 and 52 weeks
 - At 26 weeks, the decrease from baseline in the DTSQ Hyperglycemia score in the dulaglutide 0.75 mg arm was significantly smaller than the decrease in the insulin glargine arm
 - Dulaglutide treatment and the implemented insulin dose adjustment algorithms (targeting fasting PG of 100-150 mg/dL and preprandial PG between 120-180 mg/dL) may have contributed to these improvements
 - No significant differences between dulaglutide and glargine were observed

CONCLUSION

In patients with T2D and CKD stages 3 and 4, dulaglutide and glargine were associated with less worry and concern regarding hypoglycemia, Improvements in treatment satisfaction, and a decrease in perceived frequency of hyperglycemia with no significant difference between dulaglutide and glargine.

BACKGROUND

- Many diabetes medications, including insulin, are primarily cleared by the kidneys; therefore, medications used to treat T2D often require dose adjustments or are contraindicated in patients with CKD^{2,3}
- No dose adjustment for dulaglutide is needed for patients with varying degrees of renal impairment
- Beneficial clinical outcomes associated with dulaglutide and prandial insulin lispro combination therapy in patients with T2D and CKD can be further assessed through patient-reported outcome (PRO) measures
 - ALBSS includes behavior and worry items; behavior items ask patients to rate how often they engaged in each behavior during their daily routine and worry items ask how often they worried about certain factors/events associated with low blood sugar^{4,5}
 - DTSQ evaluates absolute treatment satisfaction and includes scales to measure patients’ perceived hypoglycemia and hyperglycemia^{6,7}

BASELINE CHARACTERISTICS

Demographics (safety population, except FBG [mITT population])	Dulaglutide 1.5 mg N=192	Dulaglutide 0.75 mg N=190	Insulin Glargine N=194
Sex, women	88 (45.8)	86 (45.3)	101 (52.1)
Age, years	64.7 ± 8.8	64.7 ± 8.6	64.3 ± 8.4
Duration of diabetes, years	17.6 ± 8.7	18.0 ± 8.8	18.7 ± 8.7
A1c, % (mmol/mol)	8.6 ± 0.9 (70.5 ± 9.8)	8.6 ± 1.1 (70.5 ± 12.0)	8.6 ± 1.0 (70.5 ± 10.9)
FBG, mg/dL (mmol/L)	161.5 ± 55.6 (9.0 ± 3.1)	166.6 ± 70.6 (9.3 ± 3.9)	170.7 ± 72.2 (9.5 ± 4.0)
Weight, kg	88.1 ± 16.0	90.9 ± 18.3	88.2 ± 18.5
BMI, kg/m²	32.1 ± 4.8	33.0 ± 5.5	32.4 ± 5.3
Daily total insulin dose, U	58.8 ± 30.1	56.6 ± 31.2	59.3 ± 34.2
Daily total insulin dose, U/kg	0.7 ± 0.3	0.6 ± 0.3	0.7 ± 0.3
Duration of CKD Stage 3 or higher, years	4.2 ± 5.6	4.0 ± 4.9	3.5 ± 4.0
eGFR⁸, ml/min/1.73m²	38.1 ± 13.2	38.3 ± 12.3	38.5 ± 13.0
60 ≤ Baseline eGFR <90	9 (4.7)	7 (3.7)	14 (7.2)
45 ≤ Baseline eGFR <60	53 (27.6)	53 (27.9)	51 (26.3)
30 ≤ Baseline eGFR <45	73 (38.0)	75 (39.5)	67 (34.5)
15 ≤ Baseline eGFR <30	55 (28.6)	55 (28.9)	61 (31.4)
Baseline eGFR <15	2 (1.0)	0 (0.0)	1 (0.5)
UACR, g/kg (mean [median])	779.1 (213.7)	842.2 (233.6)	919.5 (195.6)
Microalbuminuria (30 ≤ UACR ≤ 300)	74 (38.5)	61 (32.3)	56 (28.9)
Macroalbuminuria (UACR >300)	84 (43.8)	84 (44.4)	90 (46.4)

Data presented as mean ± SD or n (%), unless otherwise noted, MMRM analysis. eGFR was calculated based on the CKD-EPI equation⁸. Abbreviations: A1c=glycated A1c; BMI=body mass index; DU=dulaglutide; FBG=fasting blood glucose.

ADDITIONAL RESULTS

Glycemic measures at 26 and 52 weeks				
	Weeks	Dulaglutide 1.5 mg (N=183)	Dulaglutide 0.75 mg (N=180)	Insulin glargine (N=186)
Δ HbA1c, %	26	-1.2 (0.1)†††	-1.1 (0.1)††	-1.1 (0.1)**
	52	-1.1 (0.1)†††	-1.1 (0.1)††	-1.0 (0.1)**
Δ HbA1c, mmol/mol	26	-13.1 (1.1)†††	-12.0 (1.1)††	-12.0 (1.1)**
	52	-12.0 (1.1)†††	-12.0 (1.1)††	-10.9 (1.1)**
Δ Weight, kg	26	-2.8 (0.4)***	-2.0 (0.4)***	1.1 (0.3)*
	52	-2.7 (0.5)***	-1.7 (0.4)***	1.6 (0.4)**
Total Hypoglycemia rate, events/participant/year^a	26	5.5 ± 12.5##	7.8 ± 20.4##	17.1 ± 27.7
	52	5.8 ± 13.7##	7.6 ± 17.8#	14.4 ± 22.2
Documented Symptomatic Hypoglycemia rate, events/participant/year^a	26	4.2 ± 11.6##	4.9 ± 13.4##	11.3 ± 22.0
	52	4.4 ± 12.2#	4.3 ± 9.3##	9.6 ± 17.7

^aPlasma glucose ≤70 mg/dL. Values presented as least squares mean (SE) for HbA1c and weight or mean ± SD for hypoglycemia.
†, †† Multiplicity adjusted 1-sided p<0.001 for noninferiority versus insulin glargine with a 0.4% margin or 0.3% margin, respectively; *, ** 2-sided p<0.05 or p<.001 vs baseline, respectively; #, ## 2-sided p<0.05 or p<.001 vs insulin glargine, respectively.

References:

1. Tuttle et al. Poster presented at ADA 2017. Abstract LB36 (138-LB).
2. National Kidney Foundation. *Am J Kidney Dis.* 2012;60(5):850-886.
3. Tuttle et al. *Am J Kidney Dis.* 2014;64(4):510-533.
4. Cox et al. *Diabetes Care.* 1987;10(5):617-21.
5. Stargardt et al. *HQOL.* 2009;7:91. doi:10.1186/1477-7525-7-91.
6. Bradley C. In: Handbook of Psychology and Diabetes. 1994; 111-32.
7. Bradley C. *Diabetes Care.* 1999;22(3):530-2.
8. Levey et al. *Ann Intern Med.* 2009;150(9):604-612