Poster 0162

WCIRDC 2021
December 2–4

Real-World Outcomes in People With Type 2 Diabetes (PWD2) and Renal Impairment Receiving Insulin Glargine 300 U/mL (Gla-300) and Insulin Degludec 100 U/mL or 200 U/mL (IDeg): The DELIVER-R Study

Timothy Bailey[1], Scott Urquhart[2], Jukka Westerbacka[3], Jasvinder Gill[4], Charlie Nicholls[5]

[1]AMCR Institute, Escondido, CA, USA; [2]Diabetes and Thyroid Associates, Fredericksburg, VA, USA; [3]Sanofi, Paris, France; [4]Sanofi, Bridgewater, NJ, USA; [5]Sanofi, Reading, UK

Presenting Author: Timothy Bailey (tbailey@amcrinstitute.com)

Scan here to view a PDF of this poster

ABSTRACT

Background: Insulin is commonly used in the treatment of PWD2 with renal impairment, but is associated with increased risk of hypoglycemia which may compromise achievement of glycemic control.

Objectives: To compare real-world clinical outcomes in PWD2 with renal impairment receiving Gla-300 or IDeg.

Methods: Insulin-naïve adult US PWD2 with estimated glomerular filtration rate 15–60 mL/min/1.73 m^2 who received Gla-300 or IDeg between Mar 1, 2015–Sep 30, 2019 were identified using electronic medical records (IBM Explorys). Index date was first prescription of Gla-300/IDeg, and patients were required to have data available for ≥12 months before, and ≥6-month after, index. Gla-300 and IDeg cohorts were then propensity-score matched on baseline characteristics. Glycated hemoglobin (HbA1c) change from baseline to last measure 3–6 months after index, proportion of patients achieving target HbA1c (<7% and <8%), and incidence of hypoglycemia (%; indicated by international classification of diseases-9/10 codes) were assessed.

Results: After matching, baseline characteristics in the Gla-300 (n=300) and IDeg (n=300) cohorts were similar (male: 51.3% vs 49.7%; mean age: 68.2 vs 68.4 years; hypoglycemia in the past 6 m: 11.3% vs 10.3%; HbA1c: 9.3% vs 9.3%). At 6-month follow-up, HbA1c reductions (−1.45% vs −1.33%), proportion of patients achieving target HbA1c (<7%: 24.7% vs 25.3%; <8%: 61.3% vs 58.3%), and incidence of hypoglycemia (16.0% vs 15.3%) were similar between the Gla-300 and IDeg cohorts, respectively.

Conclusion: In insulin-naïve PWD2 with renal impairment, Gla-300 demonstrated a trend towards slightly greater, but not statistically significant, reductions in HbA1c; hypoglycemia incidence was similar.

INTRODUCTION

- Second-generation basal insulin (BI) analogs, including Gla-300 and IDeg, are associated with less glycemic variability and reduced hypoglycemia compared with first-generation BIs, and are frequently used to achieve glycemic control in PWD2[1]
- A substantial proportion of PWD2 also have renal impairment; a recent report estimated that approximately 21% of PWD2 in the United States (US) had concomitant renal impairment[2]
- However, BIs must be used with caution in PWD2 who also have renal impairment; the increased risk of hypoglycemia in these patients may lead to discontinuation and consequently may compromise achievement of glycemic control
- Since PWD2 who also have renal impairment are typically not well represented in randomized controlled trials, analysis of real-world data provides an opportunity to evaluate clinical outcomes in this setting

METHODS

Study Population and Design

- Insulin-naïve adult PWD2 and renal impairment who received Gla-300 or IDeg between March 1, 2015 and August 31, 2019 were identified using electronic medical records (EMR) from IBM Explorys® in the US
- The index date was the first prescription of Gla-300/IDeg during the identification period (**Figure 1**)

Figure 1: Study overview

Gla-300, insulin glargine 300 U/mL; HbA1c, glycated hemoglobin; IDeg, insulin degludec 100/200 U/mL; PWD2, people with type 2 diabetes.

- Eligible participants had:
  - ≥1 diagnosis of type 2 diabetes (identified using International Classification of Diseases, 9th/10th Revision [ICD-9/-10] codes)
  - EMR data for ≥12 months before index ("baseline") and ≥6 months after index ("follow-up")
  - Estimated glomerular filtration rate of 15–60 mL/min/1.73 m^2
  - History of oral antidiabetic medication or glucagon-like peptide-1 receptor agonist use before index
- People with a record of insulin prescription, end-stage renal disease or dialysis in the 12 months before index, or a record of type 1 diabetes at any point, were excluded
- Once eligible PWD2 had been identified, the Gla-300 and IDeg cohorts were propensity-score matched on baseline characteristics

Study Assessments

- Study assessments included:
  - Change in HbA1c from baseline to last measurement 3–6 months after index
  - Proportion of patients achieving target HbA1c (<7% and <8%)
  - Any and emergency department (ED)/inpatient-associated incidence and rates (per person per year [PPPY]) of hypoglycemia (identified by ICD-9/-10 codes, or a blood glucose recording ≤70 mg/dL) during the 6-month baseline and 6-month follow-up periods
- A subgroup analysis assessed change in HbA1c in PWD2 stratified by whether they had HbA1c ≤9% or >9% at baseline

Statistical Analyses

- Propensity-score matching was used to match the Gla-300 and IDeg cohorts to account for the underlying differences in baseline characteristics
- Baseline characteristics were analyzed descriptively; means and standard deviations (SDs) were provided for continuous variables
- Logistic regression, Student's t-test, and generalized linear model were used to compare outcomes in the 2 cohorts
- Fisher's exact test and McNemar's test were used to evaluate the statistical significance of differences in categorical variables; Student's t-tests were used for the means of continuous variables, and corresponding *P*-values and confidence intervals (CIs) were provided

RESULTS

Baseline Characteristics

- In total, 784 PWD2 (Gla-300, n=461; IDeg, n=323) were identified; after matching, 300 PWD2 were retained in each cohort
- Baseline characteristics were similar between the 2 cohorts (male: 51.3% vs. 49.7%; mean age: 68.2 vs. 68.4 years; hypoglycemia in the past 6 months: 11.3% vs. 10.3%; **Table 1**)

Table 1: Baseline characteristics for matched patients

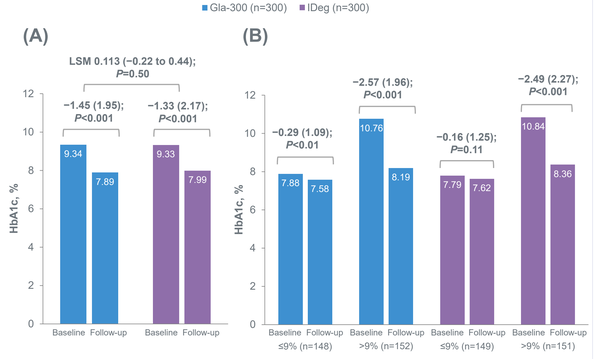
	Gla-300 (n=300)	IDeg (n=300)	SMD
Age, years, mean (SD)	68.20 (10.02)	68.38 (10.24)	0.02
Male, n (%)	154 (51.33)	149 (49.67)	0.03
HbA1c, %, mean (SD)	9.34 (1.83)	9.33 (1.99)	0.01
BMI, kg/m^2, mean (SD)	33.18 (6.76)	32.84 (6.72)	0.05
eGFR, mL/min/1.73 m^2, mean (SD)	45.81 (10.34)	45.95 (9.75)	0.01
GLP-1 RAs in 12 months before index, n (%)	68 (22.67)	73 (24.33)	0.04
OADs in 12 months before index, n (%)			
OADs	254 (84.67)	256 (85.33)	0.02
Sodium-glucose cotransporter-2 inhibitors	70 (23.33)	72 (24.00)	0.02
Dipeptidyl peptidase-4 inhibitors	136 (45.33)	136 (45.33)	0.00
Sulfonylureas	168 (56.00)	162 (54.00)	0.04
Metformin	150 (50.00)	146 (48.67)	0.03
Number of OADs, mean (SD)	1.873 (1.18)	1.880 (1.23)	0.01
Hypoglycemia within 6 months before index event, n (%)	34 (11.33)	31 (10.33)	0.03

BMI, body mass index; eGFR, estimated glomerular filtration rate; Gla-300, insulin glargine 300 U/mL; GLP-1 RA, glucagon-like peptide-1 receptor agonist; HbA1c, glycated hemoglobin; IDeg, insulin degludec 100/200 U/mL; OAD, oral antidiabetic medication; SD, standard deviation; SMD, standardized mean difference.

HbA1c Reduction and Goal Attainment

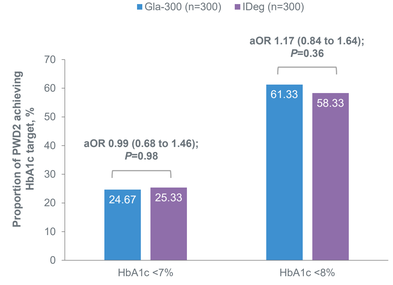
- HbA1c values decreased significantly during the 6-month follow-up period in both the Gla-300 (baseline: 9.34% vs. 6 months: 7.89%; *P*<0.001) and IDeg cohorts (baseline: 9.33% vs. 6 months: 7.99%; *P*<0.001; **Figure 2A**)
  - Reductions in HbA1c values were comparable between the 2 cohorts (1.45% for Gla-300 vs. 1.33% for IDeg; *P*=0.50; **Figure 2A**)
  - When stratified by baseline HbA1c, reduction in HbA1c at 6-month follow-up was statistically significant in both subgroups receiving Gla-300 (**Figure 2B**); reduction in HbA1c in PWD2 receiving IDeg was significant in the >9% subgroup but not in the ≤9% subgroup
  - After the 6-month follow-up period, patients receiving Gla-300 and IDeg had comparable HbA1c goal attainment with similar proportions achieving the target of <7% (Gla-300: 24.7%; IDeg: 25.3%) and <8% (Gla-300: 61.3%; IDeg: 58.3%) (**Figure 3**)

Figure 2: Change in HbA1c from baseline to 6-month follow-up (A) overall; (B) stratified by baseline HbA1c



Gla-300, insulin glargine 300 U/mL; HbA1c, glycated hemoglobin; IDeg, insulin degludec 100/200 U/mL; LSM, least square mean.

Figure 3: Proportion of patients achieving target HbA1c goals (<7% and <8%) at 6-month follow-up

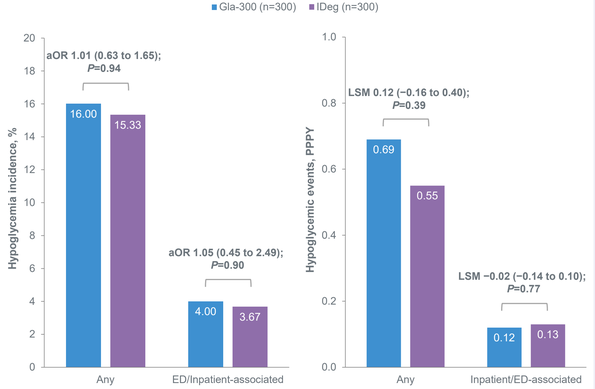


aOR, adjusted odds ratio; Gla-300, insulin glargine 300 U/mL; HbA1c, glycated hemoglobin; IDeg, insulin degludec 100/200 U/mL; PWD2, people with type 2 diabetes.

Incidence of Hypoglycemia

- During the 6-month follow-up period, the incidence of hypoglycemia was similar for Gla-300 (16.0%) versus IDeg (15.3%) (**Figure 4**)
  - Hypoglycemia events in the 6-month follow-up period were not significantly different with Gla-300 (0.69 PPPY) versus IDeg (0.55 PPPY)
- Similar results were observed for hypoglycemia events associated with inpatient/ED visits
  - The incidence of inpatient/ED hypoglycemia in Gla-300 patients was 4.0% versus 3.7% in IDeg patients (**Figure 4**) and the exposure-adjusted incidence rate of inpatient/ED hypoglycemia events was 0.12 versus 0.13 PPPY

Figure 4: Hypoglycemic outcomes at 6-month follow-up for the Gla-300 and IDeg cohorts



aOR, adjusted odds ratio; ED, emergency department; Gla-300, insulin glargine 300 U/mL; IDeg, insulin degludec 100/200 U/mL; LSM, least square mean; PPPY, per patient per year.

DISCUSSION

- This real-world study assessed glycemic control and hypoglycemic outcomes with 2 frequently used BIs in PWD2 who also had renal impairment
- Hypoglycemic events were identified by ICD-9/-10 codes and/or lab results; consequently, some underreporting was possible, and severity of hypoglycemia could not be fully assessed
- The second-generation BIs Gla-300 and IDeg are associated with improved glycemic outcomes compared with first-generation BIs in PWD2.[1] This study showed that in insulin-naïve PWD2 with renal impairment, Gla-300 demonstrated a trend towards slightly greater, but not statistically significant, reductions in HbA1c; hypoglycemia incidence was similar

REFERENCES

1. Cheng AYY, et al. *Diabet Ther.* 2020;11:2555–93.
2. Saran R, et al. *Am J Kidney Dis.* 2018;71(3 Suppl 1):A7.

ACKNOWLEDGMENTS

This study was sponsored by Sanofi. Medical writing support was provided by Martin Bell of Curo (a division of Envision Pharma Group) and funded by Sanofi.

DISCLOSURES

Timothy Bailey — Research support: Abbott Diabetes, Abbott Rapid Diagnostics, Bioliinq, Capillary Biomedical, Dexcom, Eli Lilly, Kowa, Lexicon, Livongo, Mannkind, Medtronic, Novo Nordisk, REMD, Sanofi, Sanvita, Senseonics, Viacyte, vTv Therapeutics, Zealand Pharma; Consultant's honoraria: Abbott, Lifescan, Mannkind, Medtronic, Sanofi; Speaker's honoraria: BD, Medtronic, Sanofi.
Scott Urquhart — Advisory boards: AstraZeneca, Dexcom, Novo Nordisk, Sanofi; Speakers' bureaus: AstraZeneca, Dexcom, Novo Nordisk.
Jukka Westerbacka, Jasvinder Gill, Charlie Nicholls — Employees and stockholders: Sanofi.