

# CLINICAL OUTCOMES OF PATIENTS WITH TYPE 2 DIABETES (T2D) WHO SWITCHED TO INSULIN GLARGINE 300 U/ML (GLA-300) FROM INSULIN GLARGINE 100 U/ML (GLA-100) IN REAL-WORLD US TREATMENT SETTINGS

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## BACKGROUND

- Insulin glargine 300 units (U)/mL (Gla-300) delivers the same dose of insulin as insulin glargine 100 U/mL (Gla-100), with the same active metabolite, but in one-third of the volume.<sup>1</sup>
- Gla-300 has a prolonged, more constant, pharmacokinetic/pharmacodynamic profile than Gla-100.<sup>2</sup>
- The EDITION programme compared the efficacy and safety of Gla-300 with that of Gla-100 in patients with type 2 diabetes (T2D) and using basal insulin plus mealtime insulin ± metformin (EDITION 1) or basal insulin plus oral antidiabetes drugs (OADs) (EDITION 2).<sup>3-6</sup>
- In the EDITION 1 and 2 clinical trials, the efficacy of Gla-300 in reducing glycated haemoglobin A<sub>1c</sub> (A1C) levels has been shown to be comparable with that of Gla-100, but with similar or less weight gain, and reduced risk of confirmed and/or severe hypoglycaemia.<sup>3-6</sup>
- In the EDITION 1 and 2 trials, patients randomized to Gla-300 used 10% more basal insulin than patients randomized to Gla-100.<sup>3,5</sup>
- It has been suggested that this may be related to the slightly lower bioavailability of Gla-300 that results from its longer residence time in the subcutaneous space, potentially leading to increased enzymatic inactivation.<sup>4</sup>
- Real-world data describing the dosing differences between Gla-100 and Gla-300 in patients with T2D are lacking.

## OBJECTIVE

- To compare insulin dose changes in a real-world setting in adult patients with T2D using prior Gla-100, and who either switched to Gla-300 or remained on Gla-100.

## METHODS

### Study Design and Data Source

- This was a retrospective claims study using data from the Clinformatics™ Data Mart (CDM) database for the period 1 October 2014 to 31 March 2016 inclusive.
  - The database includes administrative health claims for members of a large national managed-care company affiliated with Optum®.
  - Administrative claims submitted for payment by providers and pharmacies are verified, adjudicated, adjusted, and de-identified prior to inclusion in the CDM.
  - The CDM also includes results for outpatient laboratory tests processed by large national lab vendors under contract with the managed-care organization; data are included only for those with both medical and prescription-drug coverage to enable users to evaluate the complete healthcare experience.

### Patient Selection

- Eligible patients were adults (≥ 18 years of age) with a diagnosis of T2D using prior Gla-100, and who had:
  - no use of other basal insulin at baseline
  - continuous enrollment during 6 months' baseline and 6 months' follow-up
  - ≥ 2 Gla-100 claims in the 6 months' baseline period
  - either ≥ 1 Gla-100 or ≥ 1 Gla-300 claim during the identification period (1 April to 31 December 2015).

### Definition and Measurement of Persistence

- The index date for switching from Gla-100 to Gla-300 was the date of the first Gla-300 claim; for patients remaining on Gla-100, the index date was the date of a random claim between the third and the last claim during the identification period (Figure 1).
- Patients were defined as "persistent" if they remained on the index insulin (Gla-100 or Gla-300) during the follow-up period and without discontinuation after the index date.
- Index insulin was considered discontinued if the prescription was not refilled within the expected time of medication coverage (the 90th percentile of the time, stratified by the metric quantity supplied, between the first and second fills for patients with at least 1 refill).

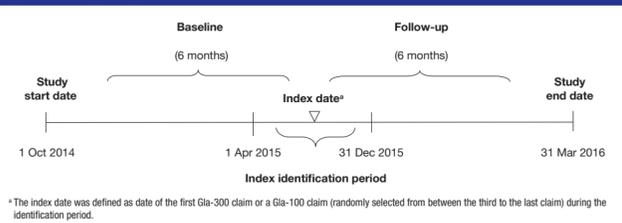
### Study Outcomes

- Outcomes evaluated during the follow-up period were:
  - daily average consumption (DACON) of basal insulin, calculated as the total number of study-drug units dispensed from initiation to the last refill during follow-up, divided by the number of days in that period (0-6 months)
  - average percent change in DACON per patient from baseline to follow-up
  - mean A1C reduction from baseline to follow-up (3-6 months).

### Statistical Analyses

- Patients switching to Gla-300 were matched to those continuing Gla-100 via propensity score matching (PSM) at a ratio of 1: up to 3.
- PSM was based on the baseline characteristics of the patients, which included:
  - demographics – age, gender, race, insurance, payer, region
  - clinical characteristics – baseline A1C, baseline antidiabetes drug use, comorbidities and diabetic complications (including Charlson Comorbidity Index score), DACON, baseline hypoglycaemia incidence, healthcare utilization, cost at baseline.

Figure 1. Study Design.



## RESULTS

- A total of 34,267 patients with T2D were eligible for this study (Figure 2).
- Patient baseline demographics and clinical characteristics are shown in Table 1.
- PSM yielded 443 and 1,241 patients using Gla-300 and Gla-100, respectively, with matched baseline characteristics.

- Within the matched sample, Gla-300 and Gla-100 cohorts had comparable DACON at baseline (56.0 U/day vs 53.6 U/day, respectively;  $P = 0.212$ ) (Table 1, Figure 3A) and follow-up (58.8 U/day vs 55.0 U/day, respectively;  $P = 0.097$ ) (Figure 3B), corresponding to comparable percent changes in DACON (13.8% vs 12.6%, respectively;  $P = 0.753$ ) (Figure 3C).
- In persistent patients, DACON increased from baseline to follow-up with both Gla-300 (from 56.5 U/day to 59.2 U/day;  $n = 346$ ) and Gla-100 (from 54.7 U/day to 55.0 U/day;  $n = 1,090$ ), with no statistical difference in percent change in DACON between cohorts (9.7% for Gla-300 vs 7.3% for Gla-100;  $P = 0.467$ ) (Figure 3).
- For the subset of patients with available A1C measures, both cohorts showed comparable mean A1C at baseline and follow-up (Figure 4).

Figure 2. Patient Attrition for Clinformatics™ Study.

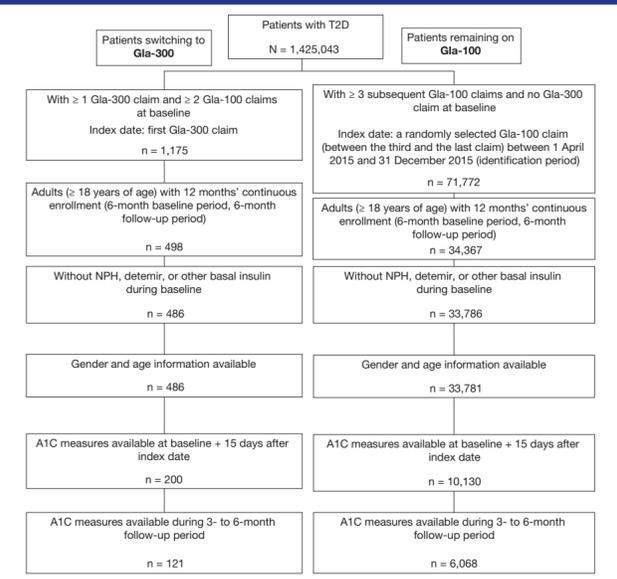


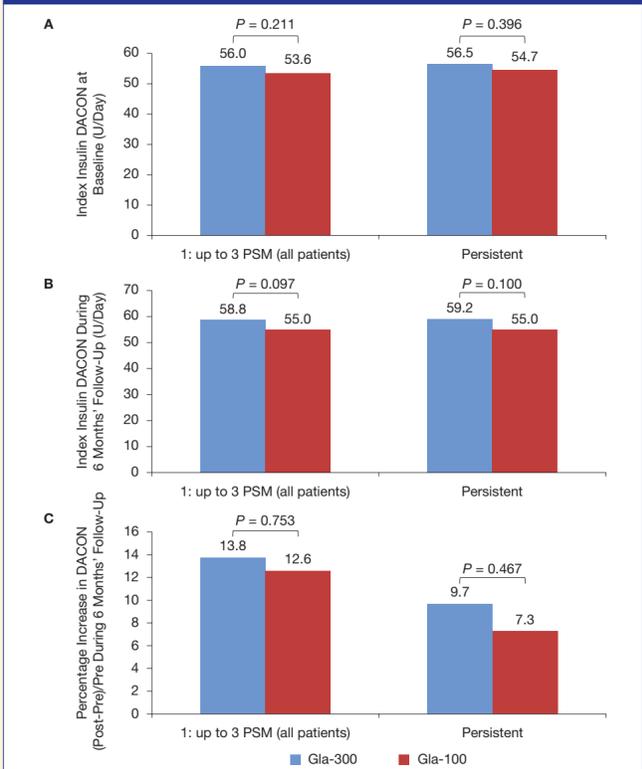
Table 1. PSM of Baseline Characteristics of Patients Switching to Gla-300 and Those Continuing on Gla-100 in the USA.

Overall	Gla-300 Switchers N = 443	Gla-100 Continuers N = 1,241	P value	Standardized Difference
<b>Demographic characteristics</b>				
Age in years, mean (SD)	66.4 (10.8)	66.5 (10.9)	0.843	1.1
<b>Age by group, n (%)</b>				
18-44	15 (3.4)	38 (3.1)	0.737	1.8
45-54	44 (9.9)	128 (10.3)	0.820	1.3
55-64	103 (23.3)	287 (23.1)	0.958	0.3
65-74	188 (42.2)	538 (43.4)	0.739	1.8
≥ 75	93 (21.0)	250 (20.1)	0.704	2.1
<b>Gender, n (%)</b>				
Male	235 (53.0)	601 (48.4)	0.095	9.2
Female	208 (47.0)	640 (51.6)	0.095	9.2
<b>Health plan type, n (%)</b>				
Indemnity	9 (2.0)	21 (1.7)	0.643	2.5
Non-capitated point of service	41 (9.3)	108 (8.7)	0.725	1.9
Health maintenance organization	145 (32.7)	433 (34.9)	0.411	4.6
Preferred provider organization	37 (8.4)	94 (7.6)	0.600	2.9
Exclusive provider organization	6 (1.4)	17 (1.4)	0.981	0.1
Others	205 (46.3)	568 (45.8)	0.855	1.0
<b>Payer type, n (%)</b>				
Commercial	75 (16.9)	203 (16.4)	0.781	1.5
Medicare	368 (83.1)	1,038 (83.6)	0.781	1.5
<b>Race, n (%)</b>				
White	267 (60.3)	744 (60.0)	0.906	0.7
Black	52 (11.7)	168 (13.5)	0.335	5.4
Hispanic	62 (14.0)	174 (14.0)	0.989	0.1
Other	62 (14.0)	155 (12.5)	0.417	4.4
<b>Geographic location, n (%)</b>				
Northeast	68 (15.3)	176 (14.2)	0.549	3.3
North central	76 (17.2)	223 (18.0)	0.701	2.1
South	195 (44.0)	534 (43.0)	0.719	2.0
West	101 (22.8)	303 (24.4)	0.494	3.8
Unknown	3 (0.7)	5 (0.4)	0.471	3.7
<b>Comorbidities and severity indicators</b>				
Charlson Comorbidity Index, score (SD)	4.2 (1.9)	4.1 (1.8)	0.332	5.3
Hospitalization within the 30 days before index date, n (%)	9 (2.0)	23 (1.9)	0.814	1.3
<b>Baseline comorbidities, n (%)</b>				
Hypertension	371 (83.7)	1,024 (82.5)	0.555	3.3
Dyslipidaemia	348 (78.6)	969 (78.1)	0.836	1.1
Hyperlipidaemia	347 (78.3)	965 (77.8)	0.804	1.4
Neuropathy	158 (35.7)	431 (34.7)	0.723	2.0
Obesity	127 (28.7)	353 (28.4)	0.929	0.5
Mental illness	103 (23.3)	304 (24.5)	0.599	2.9
Renal disease	101 (22.8)	257 (20.7)	0.356	5.1
Chronic pulmonary disease	100 (22.6)	264 (21.3)	0.568	3.1
Retinopathy	93 (21.0)	240 (19.3)	0.453	4.1
Nephropathy	86 (19.4)	215 (17.3)	0.325	5.4
Peripheral vascular disease	69 (15.6)	193 (15.6)	0.991	0.1
Depression	64 (14.4)	188 (15.1)	0.722	2.0
Congestive heart failure	62 (14.0)	158 (12.7)	0.498	3.7
Cerebrovascular disease	52 (11.7)	137 (11.0)	0.689	2.2
Severe mental illness	41 (9.3)	123 (9.9)	0.689	2.2
Liver disease (mild)	27 (6.1)	78 (6.3)	0.887	0.8
Cancer	27 (6.1)	60 (4.8)	0.304	5.5
Myocardial infarction	24 (5.4)	49 (3.9)	0.192	7.0
<b>DACON, A1C, and OADs</b>				
<b>Baseline A1C values (A1C at baseline + 15 days post index date)</b>				
Mean baseline A1C values, % (SD)	8.8 (1.7)	8.7 (1.8)	0.411	7.4
Missing, n (%)	273 (61.6)	772 (62.2)	0.828	1.2
< 8%, n (%)	63 (14.2)	176 (14.2)	0.984	0.1
≥ 8% and < 9%, n (%)	41 (9.3)	116 (9.3)	0.954	0.3
≥ 9%, n (%)	66 (14.9)	177 (14.3)	0.744	1.8
OAD use, n (%)	270 (60.9)	754 (60.8)	0.944	0.4
<b>OAD use by drug class, n (%)</b>				
Biguanide	204 (46.0)	536 (43.2)	0.298	5.7
Sulphonylureas	103 (23.3)	284 (22.9)	0.875	0.9
DPP-4 inhibitors	60 (13.5)	194 (15.6)	0.292	5.9
Thiazolidinediones	18 (4.1)	36 (2.9)	0.233	6.3
Meglitinide derivatives	7 (1.6)	11 (0.9)	0.223	6.3
α-glucosidase inhibitors	3 (0.7)	5 (0.4)	0.471	3.7
<b>Number of unique OADs, n (SD)</b>				
0.9 (0.9)	0.9 (0.8)	0.485	3.8	
<b>Baseline Gla-100 DACON, U/day (SD)</b>				
56.0 (33.9)	53.6 (36.8)	0.212	6.8	
<b>Co-payment for index basal insulin, n (%)</b>				
\$0-15	443 (100)	1,241 (100)		0.0
\$16-30	0 (0.0)	0 (0.0)		0.0
≥ \$31	0 (0.0)	0 (0.0)		0.0
<b>Baseline hypoglycaemic events, n (%)</b>				
Any hypoglycaemia	36 (8.1)	91 (7.3)	0.587	3.0

DPP-4, dipeptidyl peptidase-4; SD, standard deviation.

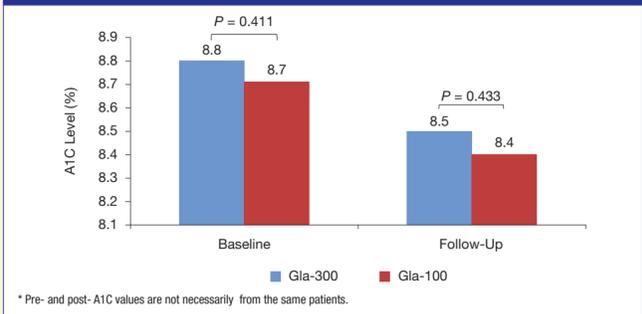
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Figure 3. Index Insulin DACON at Baseline (A), During Follow-Up (B), and Percentage Increase in DACON at 6 Months' Follow-Up (C) for Patients Who Switched to Gla-300 (n = 443) and Patients Who Remained on Gla-100 (n = 1,241).



Values are presented for all patients after PSM, and for the subgroup of "persistent" patients (Gla-300: n = 346; Gla-100: n = 1,090) at 6 months' follow-up using the 90th percentile. Patients were defined as persistent if they remained on the index insulin (Gla-100 or Gla-300) during the follow-up period without discontinuation after the index date. Index insulin was considered discontinued if the prescription was not refilled with the expected time of medication coverage (the 90th percentile of the time, stratified by the metric quantity supplied, between first and second fills among patients with at least 1 refill).

Figure 4. A1C Levels at Baseline and Follow-Up for Patients Who Switched to Gla-300 and Patients Who Remained on Gla-100 with Available A1C Measures\* (Baseline, Gla-300 [n = 170], Gla-100 [n = 469]; Follow-Up, Gla-300 [n = 107], Gla-100 [n = 254]).



\* Pre- and post-A1C values are not necessarily from the same patients.

## LIMITATIONS

- This is a retrospective database analysis; no causal relationship can be established.
- Selection bias is a limitation of claims database analyses.
- Prescription claims were used for the study, but prescription orders do not necessarily mean the medication was taken as directed.
- The 2 cohorts were matched using PSM (based on demographics and clinical characteristics) to provide balanced cohorts for the comparison.
  - The data reflect the comparison of this population of patients, and may not be representative of all patients with T2D.
- It is not mandatory to report lab information in claims data; as such, only a proportion of patients in the cohorts had A1C data available at baseline and follow-up.
- Missing A1C data may have impacted PSM.
  - To account for missing A1C data:
    - baseline A1C was matched for those patients with data available
    - other clinical characteristics were balanced.
- Missing A1C data in the follow-up limited the analysis when evaluating A1C reduction.
  - Additional analysis on A1C outcome is warranted when sample size permits.

## CONCLUSIONS

- In a real-world clinical setting, switching to Gla-300, compared with continuing on Gla-100, was not associated with a higher basal insulin dose in patients with T2D; similar changes in DACON and A1C were observed between cohorts.
- Patients switching to Gla-300 and those continuing on Gla-100 up-titrated their dose by only 7-9%, with mean A1C remaining elevated in both, confirming the need for more appropriate titration for patients with T2D.
- Sample size permitting, additional analyses on A1C outcomes and hypoglycaemia rates would provide additional valuable information from this real-world assessment.

## REFERENCES

- Steintraesser A, et al. Diabetes Obes Metab. 2015;17:835-42. 2014;16:873-6.
- Becker RH, et al. Diabetes Care. 2015;38:637-43.
- Riddle MC, et al. Diabetes Care. 2014;37:2755-62.
- Riddle MC, et al. Diabetes Obes Metab. 2015;17:835-42.
- Yki-Järvinen H, et al. Diabetes Care. 2014;37:2325-43.
- Yki-Järvinen H, et al. Diabetes Obes Metab. 2015;17:1142-19.

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## DISCLOSURES

Ye is an employee of Sanofi US, Inc. Zhou is an employee and stockholder of Sanofi US, Inc. Xie and Kariburyo are employees of STATINMED Research, which is under contract with Sanofi US, Inc to conduct this study. Meneghini is a consultant and advisory board member for Novo Nordisk and Sanofi Aventis.