

# Intensification With Insulin Glargine 300 U/mL (Gla-300) or First-Generation Basal Insulins (BIs) in People With Type 2 Diabetes (T2D) on Once-Weekly Glucagon-Like Peptide-1 Receptor Agonists (GLP-1 RAs): DELIVER New-G

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## INTRODUCTION

- In people with T2D, GLP-1 RA treatment can lower HbA1c, alongside having a low risk of hypoglycemia<sup>1</sup>; however, some patients require intensification with BI to achieve glycemic targets<sup>1,2,3</sup>
- Insulin glargine 300 U/mL (Gla-300), a second-generation BI analogue, provides similar efficacy with lower rates of hypoglycemia than first-generation BIs<sup>4</sup>

## OBJECTIVE

To compare effectiveness of intensification with Gla-300 or first-generation BIs on glycemic outcomes, healthcare resource utilization (HCRU), and costs in adults with T2D receiving GLP-1 RA with or without oral antihyperglycemic drugs (OADs)

## METHODS

- Retrospective, observational study using the US Optum Clinformatics<sup>®</sup> Data Mart Claims database (4/1/2015–12/30/2021)
- Insulin-naïve adults with T2D receiving once-weekly GLP-1 RA therapy who intensified treatment (index date) with Gla-300 or a first-generation BI (Neutral Protamine Hagedorn [NPH], detemir, insulin glargine 100 U/mL), were propensity score matched, 1:2, by baseline demographics and clinical characteristics
- Primary endpoint was noninferiority of HbA1c reduction from baseline to 6 months between treatments. Secondary endpoints including hypoglycemia, achievement of HbA1c <7 % and HbA1c <7 % without hypoglycemia, HCRU, and costs, were analyzed descriptively

## RESULTS

- After matching, 605 people intensified with Gla-300 and 1210 with first-generation BIs; in both groups ~60% were dulaglutide users (Table 1). Mean time to intensification with insulin was <1 year after GLP-1 RA initiation
- Mean HbA1c at baseline was 9.06 % for Gla-300 and 9.17 % for first-generation BI. Mean HbA1c reduction from baseline was -0.96 % for Gla-300 versus -1.02 % for first-generation BIs (Figure 1)
- Noninferiority was demonstrated at a significance level of 0.025 (noninferiority p-value=0.0003; upper 95% confidence interval [CI] <0.4 so the null hypothesis of the paired one-sided t-test with margin of 0.4 was rejected)
  - Similar glycemic outcomes were seen for the subgroup with HbA1c ≥9 % at baseline (Table 2)



**POSTER HIGHLIGHT:** In this US real-world study of people with T2D receiving weekly GLP-1 RA therapy with or without OADs, intensification with Gla-300 was associated with similar HbA1c reduction and low hypoglycemia rates, and lower HCRU versus first-generation BIs

**Table 1: Baseline characteristics of people intensifying with Gla-300 or first-generation BI<sup>a</sup>**

|   | Intensified with Gla-300 (N=605) | Intensified with first-generation BI (N=1210) |
|---|----------------------------------|---|
| <b>Age, mean (SD), years</b>  | 63.2 (10.7)                      | 63.4 (10.9)                                   |
| <b>Gender, n (%), male</b>  | 318 (52.6)                       | 578 (47.8)                                    |
| <b>Weekly GLP-1 RA use, n (%)</b>   |                                  |   |
| Dulaglutide   | 353 (58.3)                       | 732 (60.5)                                    |
| Semaglutide injectable  | 152 (25.1)                       | 304 (25.1)                                    |
| Exenatide LA  | 135 (22.3)                       | 255 (21.1)                                    |
| <b>Time to intensification with insulin, mean (SD), days</b>                                | 295.8 (184.3)                    | 279.1 (178.7)                                 |
| <b>Type of first-generation BI at index date, n (%)</b>                                     |                                  |   |
| Gla-100   | -                                | 959 (79.3)                                    |
| Insulin detemir   | -                                | 193 (16.0)                                    |
| NPH   | -                                | 58 (4.8)                                      |
| <b>Use of ≥1 antihyperglycemic medication during the baseline period, n (%)<sup>b</sup></b> |                                  |   |
| Metformin   | 513 (84.8)                       | 1021 (84.4)                                   |
| Sulfonylureas   | 383 (63.3)                       | 766 (63.3)                                    |
| DPP-4i  | 213 (35.2)                       | 415 (34.3)                                    |
| SGLT-2 inhibitor  | 102 (16.9)                       | 223 (18.4)                                    |
| SGLT-2 inhibitor  | 192 (31.7)                       | 367 (30.3)                                    |
| Thiazolidinediones  | 68 (11.2)                        | 109 (9.0)                                     |
| Alpha-glucosidase inhibitors  | 7 (1.2)                          | 8 (0.7)                                       |
| Meglitinides  | 11 (1.8)                         | 18 (1.5)                                      |
| <b>HbA1c, mean (SD), %</b>  | 9.06 (1.93)                      | 9.17 (1.88)                                   |
| <b>Healthcare utilization during the baseline period, n (%)<sup>b</sup></b>                 |                                  |   |
| ≥1 hospitalization  | 66 (10.9)                        | 117 (9.7)                                     |
| ≥1 emergency room visit   | 111 (18.3)                       | 242 (20.0)                                    |

<sup>a</sup>Cohorts were matched using a greedy nearest neighbor matching algorithm, with a caliper and without replacement.

<sup>b</sup>The baseline period covered the 6 months prior to the index date.

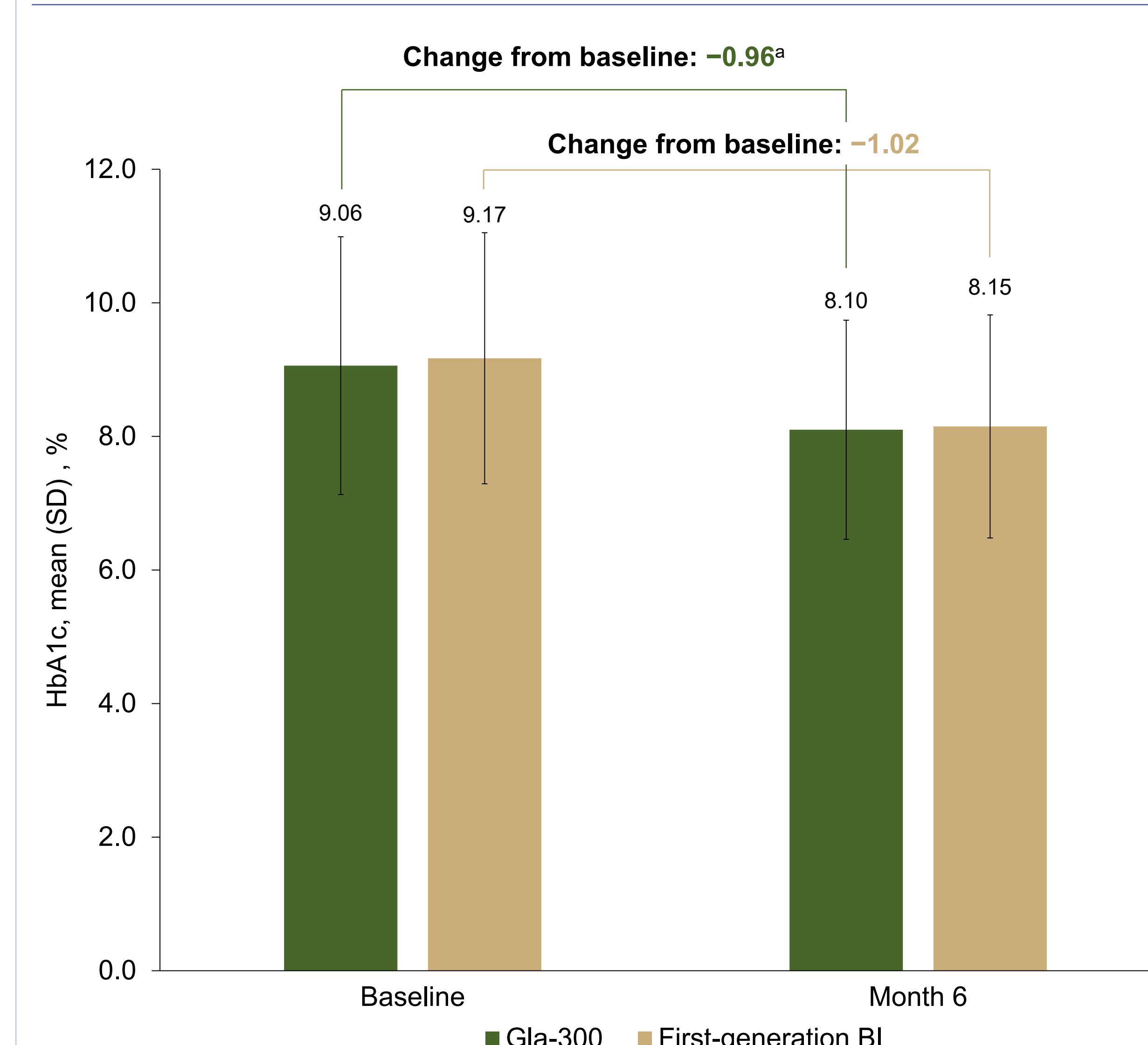
BI, basal insulin; DPP-4i, dipeptidyl peptidase 4 inhibitors; Gla-100, insulin glargine 100 U/mL; Gla-300, insulin glargine 300 U/mL; GLP-1 RA, glucagon-like peptide-1 receptor agonist; NPH, Neutral Protamine Hagedorn; SD, standard deviation; SGLT-2, sodium glucose co-transporter-2.

**Table 2: Secondary endpoints**

|  | Intensified with Gla-300 (N=605) | Intensified with first-generation BI (N=1210) |
|--|----------------------------------|---|
| <b>HbA1c ≥9 % subgroup analysis</b>                |                                  |   |
| HbA1c at baseline, mean (SD)                       | 10.73 (1.40)                     | 10.69 (1.40)                                  |
| HbA1c at Month 6, mean (SD)                        | 8.67 (1.79)                      | 8.84 (1.83)                                   |
| Change in HbA1c from baseline to Month 6           | -2.05 (2.04)                     | -1.85 (2.22)                                  |
| Mean of differences (one-sided 97.5% CI)           | -0.2029 (-inf, 0.1499)           |   |
| <b>Hypoglycemia outcomes</b>                       |                                  |   |
| Number of people with ≥1 event, n (%)              | 11 (1.82)                        | 22 (1.82)                                     |
| Total number of events, n                          | 19                               | 73  |
| Total person years                                 | 295.01                           | 591.16  |
| Event rate, per 100 person years                   | 6.4                              | 12.3  |
| Rate ratio (95% CI) <sup>a</sup>                   | 0.50 (0.19, 1.29)                |   |
| <b>Target achievement</b>                          |                                  |   |
| HbA1c <7 % achievement, n (%)                      | 152 (25.1)                       | 285 (23.6)                                    |
| Odds ratio (95% CI) <sup>b</sup>                   | 1.09 (0.87, 1.37)                |   |
| HbA1c <7 % achievement without hypoglycemia, n (%) | 148 (24.5)                       | 277 (22.9)                                    |
| Odds ratio (95% CI) <sup>b</sup>                   | 1.09 (0.87, 1.37)                |   |

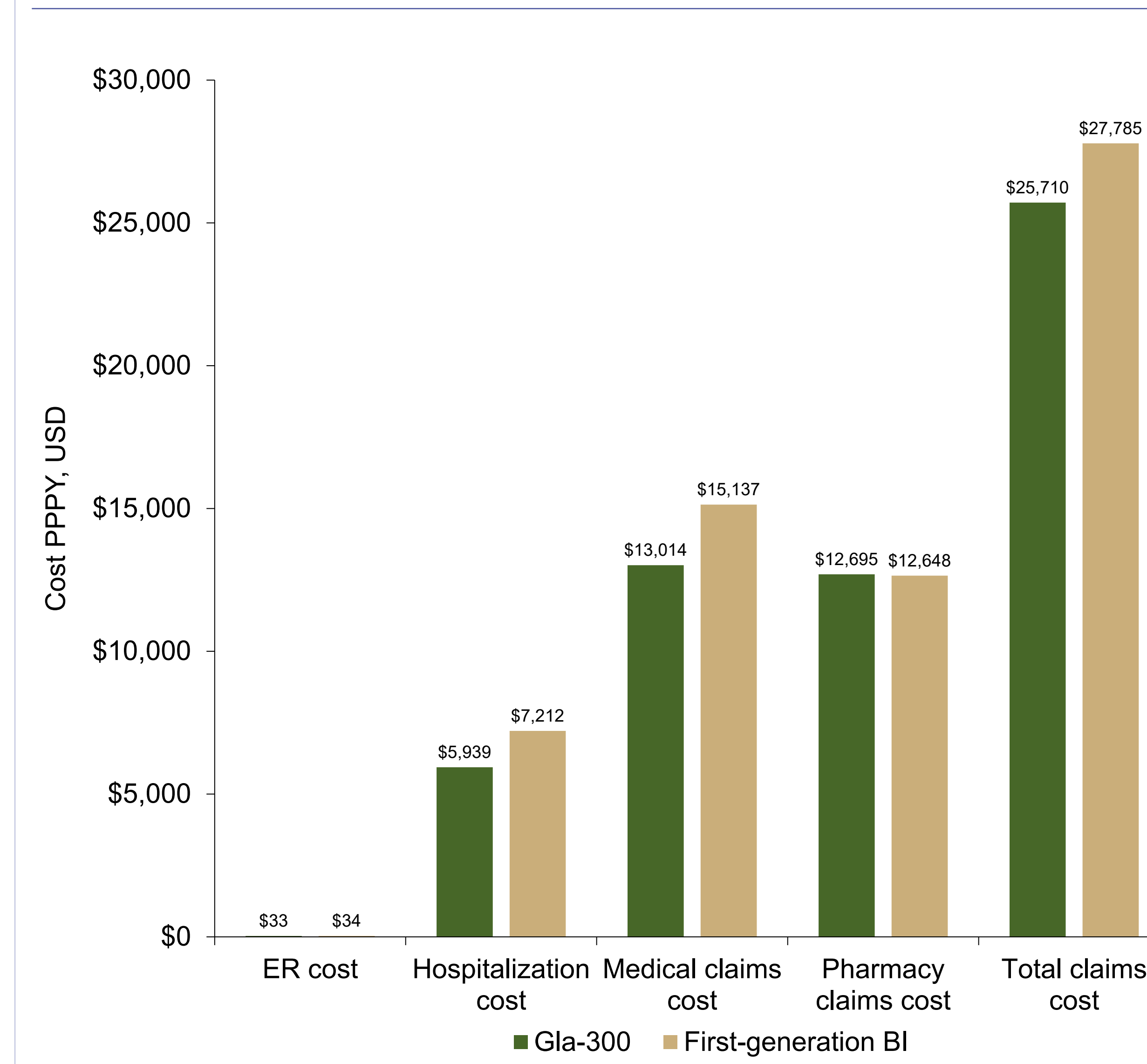
<sup>a</sup>Event rate ratio (95% CI) from Poisson regression. <sup>b</sup>Odds ratio (95% CI) from logistic regression. BI, basal insulin; CI, confidence interval; Gla-300, insulin glargine 300 U/mL; SD, standard deviation.

**Figure 1: Change from baseline in HbA1c at Month 6**



<sup>a</sup>Mean of differences Gla-300 versus first-generation BIs (one-sided 97.5% CI): 0.0637 (-inf, 0.2543), noninferiority p-value=0.0003. BI, basal insulin; CI, confidence interval; Gla-300, insulin glargine 300 U/mL; SD, standard deviation.

**Figure 2: Diabetes-related healthcare costs**



BI, basal insulin; ER, emergency room; Gla-300, insulin glargine 300 U/mL; PPPY, per person per year.

## RESULTS (continued)

- Hypoglycemia event rates/100 person-years (PY) were 6.4 versus 12.3 (rate ratio 0.50) with Gla-300 and first-generation BIs, respectively (Table 2)
- Similar proportions of Gla-300 and first-generation BI users achieved HbA1c <7 % (25.1% and 23.6%) and HbA1c <7 % without hypoglycemia (24.5% and 22.9%; Table 2)
- Diabetes-related event rates/100 PY were lower with Gla-300 than first-generation BIs:
  - Hospitalizations/100 PY: Gla-300, 22.7 versus first-generation BIs, 27.6, rate ratio (95% CI) 0.82 (0.61, 1.09)
  - Emergency room visits/100 PY: Gla-300, 11.2 versus first-generation BIs, 13.4, rate ratio (95% CI) 0.89 (0.59, 1.34)
- Diabetes-related annual costs per person were lower with Gla-300 versus first-generation BIs by \$1,272.35 for hospitalization and \$2,074.83 for total healthcare claims costs (Figure 2)

## CONCLUSIONS

- Similar HbA1c reductions, target achievement, and low hypoglycemia incidence were achieved for both Gla-300 and first-generation BIs when used for intensification after GLP-1 RA therapy
- Diabetes-related health costs were lower with Gla-300 versus first-generation BIs
- These results are consistent with data from the DELIVER series of studies that glycemic control with a low risk of hypoglycemia is seen on intensification with Gla-300 results in real-world clinical practice<sup>5,6</sup>

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## DISCLOSURES

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