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# Impact of background antihyperglycemic therapy on insulin glargine 300 U/mL (Gla-300) vs insulin degludec 100 U/mL (IDeg-100) in insulin-naïve people with T2DM from the BRIGHT randomised study

BRIGHT

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## INTRODUCTION

- Insulin glargine 300 U/mL (Gla-300) and insulin degludec 100 U/mL (IDeg-100) are two second-generation basal insulin analogs which have a longer duration of action,[1,2] and provide similar glycemic control with lower risk of hypoglycemia[3,4] compared with the first-generation basal insulin, insulin glargine 100 U/mL (Gla-100).
- The BRIGHT study is the first head-to-head randomised controlled trial comparing the efficacy and safety of Gla-300 and IDeg-100 in combination with oral antihyperglycemic drugs (OADs) with or without glucagon-like peptide-1 receptor agonists (GLP-1RAs) in 929 people with type 2 diabetes (T2DM).
- Primary results of BRIGHT showed:[5]
  - Non-inferiority of $HbA_{1c}$ reduction over 24 weeks with Gla-300 versus IDeg-100 (primary endpoint).
  - Incidence and rates of anytime (24 h) hypoglycemia were comparable with both treatments over 24 weeks, and lower with Gla-300 during the 0–12 week initial active titration period.

**OBJECTIVE**

**To determine the impact of background OAD/GLP-1 RA therapy on the efficacy and safety of Gla-300 versus IDeg-100 in insulin-naïve people with T2DM.**

## METHODS

- BRIGHT (NCT02738151) was a multicenter, open-label, randomised, parallel-group, 24-week actively controlled study in insulin-naïve participants aged ≥18 years with T2DM for ≥1 year prior to screening and uncontrolled ($HbA_{1c}$ ≥7.5 to ≤10.5 %) on current OAD therapy with or without GLP-1 RAs (stable dose for ≥3 months).
- Participants continued background OAD/GLP-1 RA therapy at their previous dose throughout the study unless they were not approved for use with insulin therapy or safety concerns necessitated a reduction or cessation of background therapy.
- Participants were randomised 1:1 to receive either Gla-300 or IDeg-100, with randomization stratified by $HbA_{1c}$ at screening (<8/≥8 %), and sulfonylurea (SU) or glinide use before the day of screening (Yes/No), and titrated to a target fasting self-measured plasma glucose of 80–100 mg/dL.
- Pre-specified analyses investigated reduction in $HbA_{1c}$ from baseline to week 24, and incidence of hypoglycemia (based on ADA guidelines)[6] according to use of OAD/GLP-1 RA therapy at screening; a post hoc analysis on hypoglycemia rates according to background therapy was also performed.
- $HbA_{1c}$ was assessed using a mixed model of repeated measures. Incidence of hypoglycemia was compared between treatment groups using logistic regression analysis and the annualized rates of hypoglycemia were assessed using an overdispersed Poisson regression model.

## RESULTS

### Demographics:

- Baseline characteristics were comparable across all background therapy groups (**Table 1**).
- At baseline, 65.7% of participants were using SUs, 24.4% were on DPP-4 inhibitors, 13.3% used SGLT-2 inhibitors, and 11.9% were receiving GLP-1 RAs.
  - The proportion of participants using each background therapy remained stable throughout the study.
- As 91.5% of participants received metformin at baseline, comparisons of efficacy and safety were not performed according to metformin use.

### Glycemic control:

- Reductions in mean $HbA_{1c}$ were similar between Gla-300 and IDeg-100 groups across all background OAD/GLP-1 RA therapy groups (no evidence of heterogeneity of treatment effect; all p>0.05) (**Figure 1**).

### Hypoglycemia:

- The incidence of confirmed hypoglycemia at any time of day (24 h) was comparable for both basal insulin treatment groups at both glycemic thresholds, irrespective of background OAD/GLP-1 RA therapy; no evidence of heterogeneity of treatment effect according to use of background therapy was detected (all p>0.05) (**Figure 2**).
- Similarly to the results observed for incidence of hypoglycemia, rates of confirmed hypoglycemia at any time of day (24 h) were comparable for both basal insulin treatments, irrespective of background therapy; no evidence of heterogeneity of treatment effect (all p>0.05; data not shown).

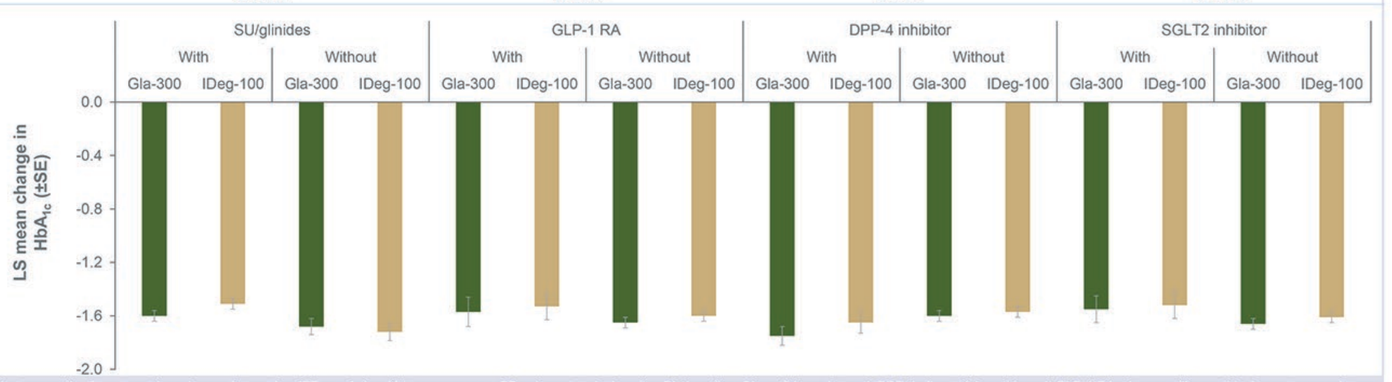
**Table 1: Baseline characteristics by background therapy**

| | SU/glinides | | | | GLP-1 RA | | | | DPP-4 inhibitor | | | | SGLT-2 inhibitor | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | With | | Without | | With | | Without | | With | | Without | | With | | Without | |
| | Gla-300 N=318 | IDeg-100 N=316 | Gla-300 N=148 | IDeg-100 N=147 | Gla-300 N=46 | IDeg-100 N=65 | Gla-300 N=420 | IDeg-100 N=398 | Gla-300 N=121 | IDeg-100 N=106 | Gla-300 N=345 | IDeg-100 N=357 | Gla-300 N=62 | IDeg-100 N=62 | Gla-300 N=404 | IDeg-100 N=401 |
| Age, years | 60.8 ±9.9 | 60.8 ±9.5 | 60.0 ±8.9 | 59.9 ±10.3 | 59.4 ±8.6 | 59.7 ±10.4 | 60.7 ±9.7 | 60.6 ±9.7 | 62.5 ±10.1 | 62.3 ±10.0 | 59.9 ±9.3 | 59.9 ±9.6 | 59.8 ±10.7 | 58.0 ±7.9 | 60.7 ±9.4 | 60.9 ±10.0 |
| Gender, male, n (%) | 163 (51.3) | 173 (54.7) | 84 (56.8) | 79 (53.7) | 26 (56.5) | 26 (40.0) | 221 (52.6) | 226 (56.8) | 68 (56.2) | 67 (63.2) | 179 (51.9) | 185 (51.8) | 32 (51.6) | 34 (54.8) | 215 (53.2) | 218 (54.4) |
| BMI, kg/m² | 31.8 ±4.3 | 31.6 ±4.4 | 31.6 ±4.5 | 30.7 ±4.4 | 33.0 ±3.8 | 32.6 ±4.5 | 31.6 ±4.4 | 31.1 ±4.4 | 31.4 ±4.3 | 30.5 ±4.3 | 31.8 ±4.3 | 31.6 ±4.4 | 31.7 ±4.4 | 31.4 ±5.0 | 31.7 ±4.3 | 31.3 ±4.3 |
| Diabetes duration, years | 10.8 ±6.1 | 11.0 ±6.4 | 9.7 ±6.2 | 10.0 ±6.7 | 11.9 ±6.0 | 12.1 ±7.2 | 10.3 ±6.1 | 10.5 ±6.4 | 11.9 ±6.7 | 10.9 ±7.1 | 10.0 ±5.8 | 10.6 ±6.3 | 11.6 ±6.5 | 11.4 ±5.7 | 10.3 ±6.0 | 10.6 ±6.6 |
| $HbA_{1c}$, % | 8.73 ±0.85 | 8.59 ±0.79 | 8.66 ±0.81 | 8.52 ±0.81 | 8.85 ±0.71 | 8.48 ±0.75 | 8.69 ±0.85 | 8.58 ±0.81 | 8.71 ±0.91 | 8.48 ±0.79 | 8.71 ±0.81 | 8.60 ±0.80 | 8.74 ±0.71 | 8.70 ±0.88 | 8.70 ±0.85 | 8.55 ±0.79 |
| FPG, mg/dL | 192 ±50 | 184 ±53 | 189 ±48 | 178 ±48 | 191 ±42 | 185 ±62 | 190 ±50 | 181 ±50 | 199 ±52 | 179 ±45 | 188 ±48 | 183 ±53 | 182 ±50 | 171 ±48 | 192 ±49 | 184 ±52 |
| Pre-breakfast SMPG, mg/dL | 178 ±40 | 172 ±38 | 179 ±41 | 171 ±38 | 184 ±40 | 176 ±43 | 177 ±41 | 171 ±37 | 176 ±41 | 166 ±35 | 179 ±40 | 173 ±39 | 171 ±37 | 172 ±40 | 179 ±41 | 172 ±38 |
| eGFR, mL/min/1.73 m² | 92.1 ±27.3 | 89.4 ±25.8 | 93.0 ±25.7 | 93.9 ±26.2 | 96.1 ±26.7 | 85.7 ±24.2 | 92.0 ±26.8 | 91.6 ±26.2 | 87.9 ±28.0 | 84.7 ±22.9 | 94.0 ±26.2 | 92.6 ±26.6 | 93.5 ±30.6 | 95.0 ±22.2 | 92.2 ±26.2 | 90.1 ±26.5 |

Randomized population. Data are mean ± SD, unless otherwise stated. BMI, body mass index; DDP-4, dipeptidyl peptidase-4; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; GLP-1 RA, glucagon-like peptide-1 receptor agonist; SD, standard deviation; SGLT-2, sodium-glucose co-transporter-2; SMPG, self-measured plasma glucose; SU, sulfonylureas

**Figure 1: Mean $HbA_{1c}$ and change from baseline to week 24**

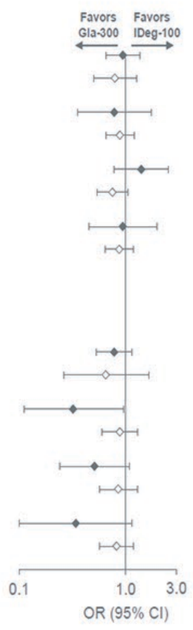
| | SU/glinides | | | | GLP-1 RA | | | | DPP-4 inhibitor | | | | SGLT-2 inhibitor | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | With | | Without | | With | | Without | | With | | Without | | With | | Without | |
| | Gla-300 | IDeg-100 | Gla-300 | IDeg-100 | Gla-300 | IDeg-100 | Gla-300 | IDeg-100 | Gla-300 | IDeg-100 | Gla-300 | IDeg-100 | Gla-300 | IDeg-100 | Gla-300 | IDeg-100 |
| N | 310 | 310 | 143 | 143 | 46 | 65 | 407 | 388 | 117 | 105 | 336 | 348 | 59 | 61 | 394 | 392 |
| Baseline | 8.75 ±0.84 | 8.60 ±0.80 | 8.67 ±0.81 | 8.50 ±0.80 | 8.85 ±0.71 | 8.48 ±0.75 | 8.71 ±0.84 | 8.59 ±0.81 | 8.72 ±0.92 | 8.48 ±0.79 | 8.73 ±0.80 | 8.60 ±0.80 | 8.73 ±0.72 | 8.68 ±0.87 | 8.72 ±0.85 | 8.55 ±0.79 |
| Week 24 | 7.06 ±0.79 | 7.09 ±0.75 | 6.96 ±0.79 | 6.89 ±0.78 | 7.11 ±0.72 | 7.04 ±0.63 | 7.02 ±0.80 | 7.02 ±0.79 | 6.90 ±0.68 | 6.95 ±0.72 | 7.07 ±0.82 | 7.05 ±0.78 | 7.10 ±0.66 | 7.11 ±0.65 | 7.01 ±0.81 | 7.01 ±0.78 |
| LS mean difference in change from BL (95% CI) | −0.09 (0.21 to 0.03) | | 0.04 (−0.14 to 0.22) | | −0.03 (−0.32 to 0.26) | | −0.05 (−0.16 to 0.06) | | −0.09 (−0.30 to 0.11) | | −0.03 (−0.15 to 0.09) | | −0.03 (−0.30 to 0.25) | | −0.05 (−0.16 to 0.06) | |
| p-value* | 0.626 | | | | 0.762 | | | | 0.957 | | | | 0.779 | | | |




*p value to test heterogeneity of treatment-by-subgroup interaction. ITT population. Values are mean ± SD unless stated otherwise. BL, baseline; CI, confidence interval; DDP-4, dipeptidyl peptidase-4; GLP-1 RA, glucagon-like peptide-1 receptor agonist; ITT, intent-to-treat; SD, standard deviation; SE, standard error; SGLT-2, sodium-glucose co-transporter-2; SU, sulfonylureas

**Figure 2: Incidence of hypoglycemia at any time of day (24 h)**

| | | Incidence Gla-300 n (%) | IDeg-100 n (%) | OR (95% CI) | p-value* |
|---|---|---|---|---|---|
| Confirmed hypoglycemia (≤70 mg/dL) | | | | | |
| SU/glinides | With | 237 (75.0) | 240 (76.2) | 0.94 (0.65 to 1.35) | 0.5776 |
| | Without | 70 (47.9) | 79 (53.7) | 0.79 (0.50 to 1.26) | |
| GLP-1 RA | With | 27 (58.7) | 43 (66.2) | 0.78 (0.35 to 1.75) | 0.7758 |
| | Without | 280 (67.3) | 276 (69.5) | 0.88 (0.65 to 1.20) | |
| DPP-4 inhibitor | With | 87 (72.5) | 71 (67.0) | 1.40 (0.77 to 2.52) | 0.0735 |
| | Without | 220 (64.3) | 248 (69.7) | 0.75 (0.54 to 1.04) | |
| SGLT-2 inhibitor | With | 34 (54.8) | 36 (58.1) | 0.94 (0.45 to 1.97) | 0.8337 |
| | Without | 273 (68.3) | 283 (70.8) | 0.87 (0.64 to 1.18) | |
| Confirmed hypoglycemia (<54 mg/dL) | | | | | |
| SU/glinides | With | 60 (19.0) | 73 (23.2) | 0.78 (0.53 to 1.14) | 0.7328 |
| | Without | 8 (5.5) | 12 (8.2) | 0.65 (0.26 to 1.65) | |
| GLP-1 RA | With | 5 (10.9) | 19 (29.2) | 0.32 (0.11 to 0.95) | 0.0854 |
| | Without | 63 (15.1) | 66 (16.6) | 0.88 (0.60 to 1.29) | |
| DPP-4 inhibitor | With | 14 (11.7) | 22 (20.8) | 0.51 (0.24 to 1.08) | 0.2374 |
| | Without | 54 (15.8) | 63 (17.7) | 0.85 (0.57 to 1.28) | |
| SGLT-2 inhibitor | With | 4 (6.5) | 11 (17.7) | 0.34 (0.10 to 1.14) | 0.1713 |
| | Without | 64 (16.0) | 74 (18.5) | 0.82 (0.57 to 1.19) | |




*p-value to test heterogeneity of treatment-by-subgroup interaction. Safety population. CI, confidence interval; DDP-4, dipeptidyl peptidase-4; GLP-1 RA, glucagon-like peptide-1 receptor agonist; OR, odds ratio; SGLT-2, sodium-glucose co-transporter-2; SU, sulfonylureas

## DISCUSSION

- Overall, BRIGHT showed that Gla-300 and IDeg-100 provided similar $HbA_{1c}$ reductions, with comparable incidence and rates of hypoglycemia at any time of day (24 h) over the 24-week treatment period.[5]
- The present analysis showed that this similar $HbA_{1c}$ reduction (~1.6 %) and comparable hypoglycemia frequency observed with Gla-300 and IDeg-100 is evident regardless of background OAD/GLP-1 RA therapy.

**CONCLUSION**

**Both second-generation basal insulins (Gla-300 and IDeg-100) provide similar $HbA_{1c}$ reductions (~1.6 %) and low risk of hypoglycemia at any time of day (24 h) over 24 weeks, irrespective of the use of background non-insulin antihyperglycemic drug therapy.**

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