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Similar variability of fasting and 24-h self-measured plasma glucose (SMPG) with insulin glargine 300 U/mL (Gla-300) vs insulin degludec 100/mL (IDeg-100) in insulin-naïve adults with T2DM: the randomised BRIGHT trial

BRIGHT

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INTRODUCTION

- Insulin glargine 300 U/ml (Gla-300) and insulin degludec (IDeg) are second-generation basal insulins, with improved pharmacodynamic (PD) and pharmacokinetic (PK) properties compared with the first-generation basal insulin, insulin glargine 100 U/ml (Gla-100).[1,2]
- Two studies comparing the PK/PD properties of Gla-300 and IDeg in people with type 1 diabetes (T1DM) yielded conflicting results:
  - Bailey *et al.* 2018[3]: Gla-300 provided less fluctuating steady-state PD profiles (lower within-day variability) and more evenly distributed PK profiles compared with IDeg 100 U/ml (IDeg-100).
  - Heise *et al.* 2017[4]: IDeg 200 U/ml had lower within-day and day-to-day variability in glucose-lowering effect compared with Gla-300.
- BRIGHT is the first head-to-head randomised controlled trial comparing the efficacy and safety of Gla-300 and IDeg-100 in people with T2DM (N=929).[5]

- Results showed:
  - Non-inferiority of HbA_{1c} reduction over 24 weeks (primary endpoint), and similar 8-point self-measured plasma glucose (SMPG) profiles at baseline and week 24, with Gla-300 versus IDeg-100.
  - Similar changes in HbA_{1c} (nominal p-value = 0.667) and fasting SMPG after the 0–12 week active titration period.
  - Incidence and rates of anytime (24 h) hypoglycaemia were comparable with both treatments over 24 weeks, and lower with Gla-300 during the 0–12 week active titration period.

OBJECTIVE

To compare glycaemic variability of Gla-300 and IDeg-100 using variability of 24-h SMPG, based on 8-point SMPG profiles, and variability of fasting SMPG.

METHODS

- BRIGHT (NCT02738151) was a multicentre, 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 oral antihyperglycemic drug (OAD) therapy with or without glucagon-like peptide-1 receptor agonist (GLP-1 RA) therapy.
- Participants were randomised 1:1 to receive either Gla-300 or IDeg-100 and titrated to a target fasting SMPG of 4.4–5.6 mmol/l.
- The primary endpoint of BRIGHT was change in HbA_{1c} from baseline to week 24. This analysis presents data for the following secondary endpoints: change in 8-point SMPG profiles; variability of 24-h SMPG (within-day intra-subject variability); and variability of fasting SMPG (day-to-day intra-subject variability).
- Variability of 24-h SMPG was assessed as the mean coefficient of variation (CV; calculated as: [standard deviation (SD)/mean] × 100]) over 8-point SMPG profiles taken at least once within the 5 days prior to baseline, weeks 12 and week 24. Variability of fasting SMPG was determined using the CV of ≥3 fasting SMPG measurements over 7 days prior to baseline and the visits at weeks 2, 4, 8, 12, 20 and 24.
- A mixed model of repeated measures was used to assess the change in variability of 24-h and fasting SMPG, with fixed categorical effects of: treatment group; visit; treatment-by-visit interaction; and randomisation stratum of sulfonylurea/meglitinide use (Yes/No) and HbA_{1c} (<8/≥8 %) at screening. Continuous fixed covariates of corresponding baseline value and baseline value-by-visit interaction were also included.

RESULTS

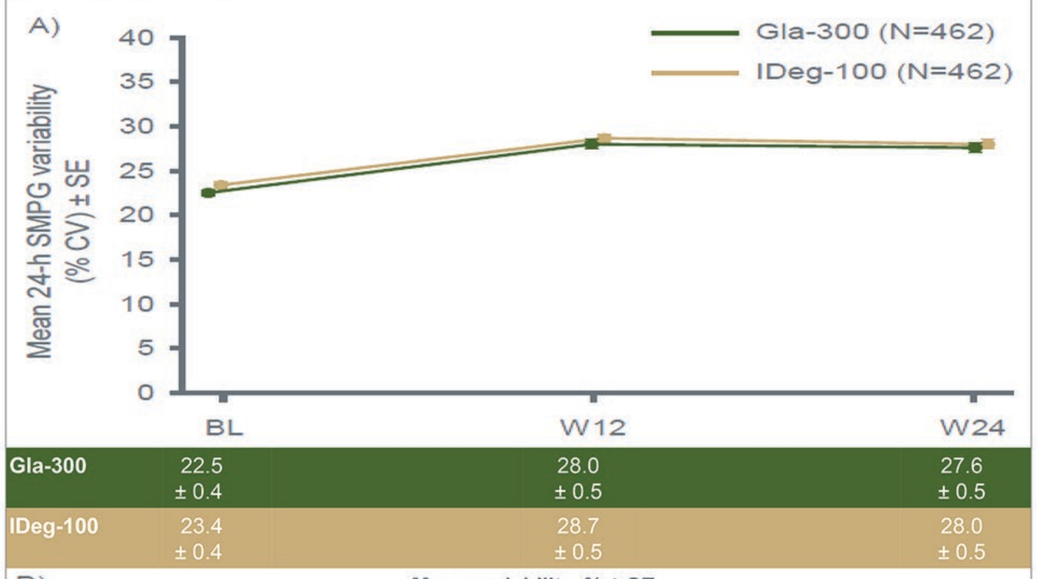
- **Demographics:**
  - Baseline characteristics were comparable in both treatment groups (**Table 1**).

Table 1: Baseline characteristics (randomised population)

	Gla-300 (N=466)	IDeg-100 (N=463)	Total (N=929)
Age, years	60.6 ± 9.6	60.5 ± 9.8	60.5 ± 9.7
Gender, % (male/female)	53/47	54/46	54/46
BMI, kg/m²	31.7 ± 4.3	31.3 ± 4.4	31.5 ± 4.4
Known T2DM duration, years	10.5 ± 6.1	10.7 ± 6.5	10.6 ± 6.3
HbA_{1c}, %	8.71 ± 0.83	8.57 ± 0.80	8.64 ± 0.82
FPG, mmol/l	10.6 ± 2.7	10.1 ± 2.9	10.3 ± 2.8
Fasting SMPG, mmol/l	9.9 ± 2.3	9.5 ± 2.1	9.7 ± 2.2
eGFR, ml/min/1.73 m²	92.4 ± 26.8	90.8 ± 26.0	91.6 ± 26.4

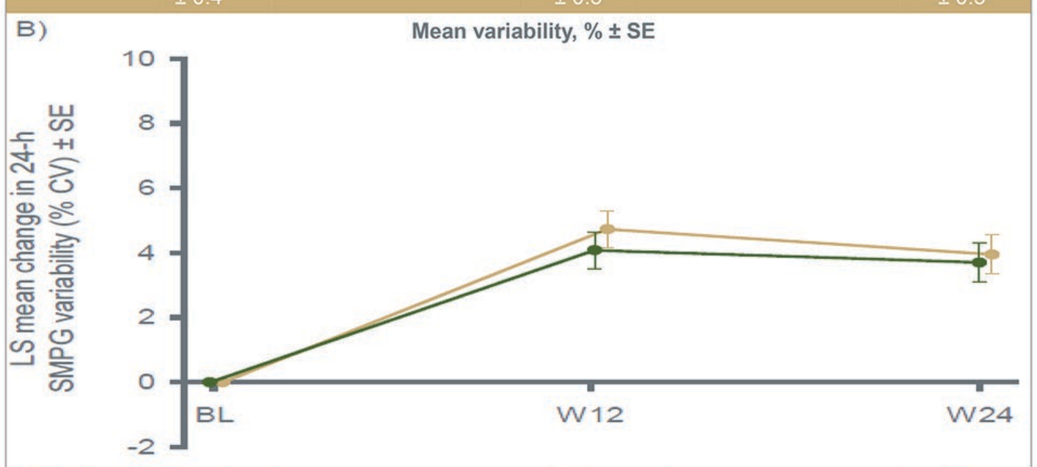
Data are presented as mean ± SD, unless otherwise stated. BMI, body mass index; eGFR, estimated glomerular filtration rate; FPG, fasting plasma glucose; SD, standard deviation; SMPG, self-measured plasma glucose

Figure 1: A) variability and B) change in variability of 24-h SMPG (based on 8-point profiles) by study visit



	BL	W12	W24
Gla-300	22.5 ± 0.4	28.0 ± 0.5	27.6 ± 0.5
IDeg-100	23.4 ± 0.4	28.7 ± 0.5	28.0 ± 0.5

Mean variability, % ± SE



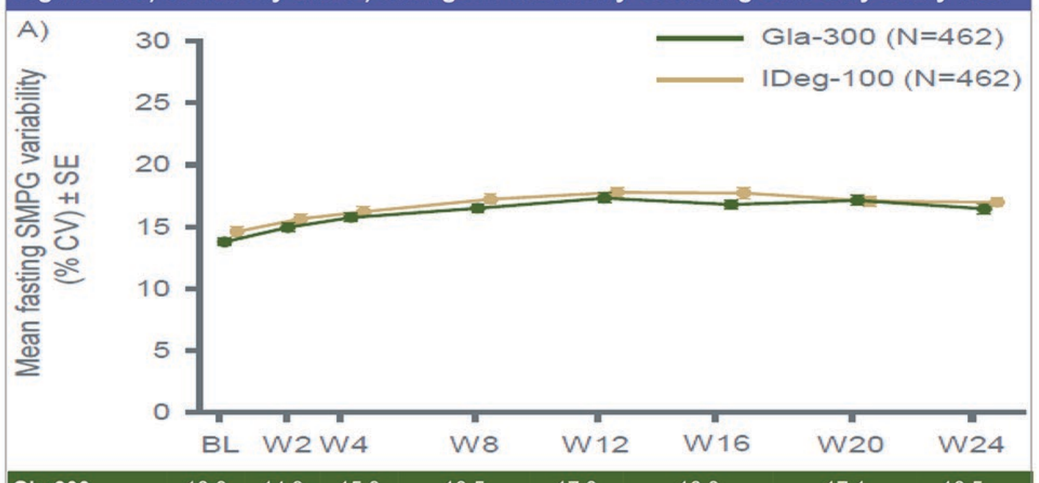
	BL	W12	W24
Gla-300	0	4.1 ± 0.6	3.7 ± 0.6
IDeg-100	0	4.7 ± 0.6	4.0 ± 0.6

LS mean change in variability, % ± SE

ITT population. BL, baseline; CV, coefficient of variation; ITT, intent-to-treat; LS, least squares; SE, standard error; W, week

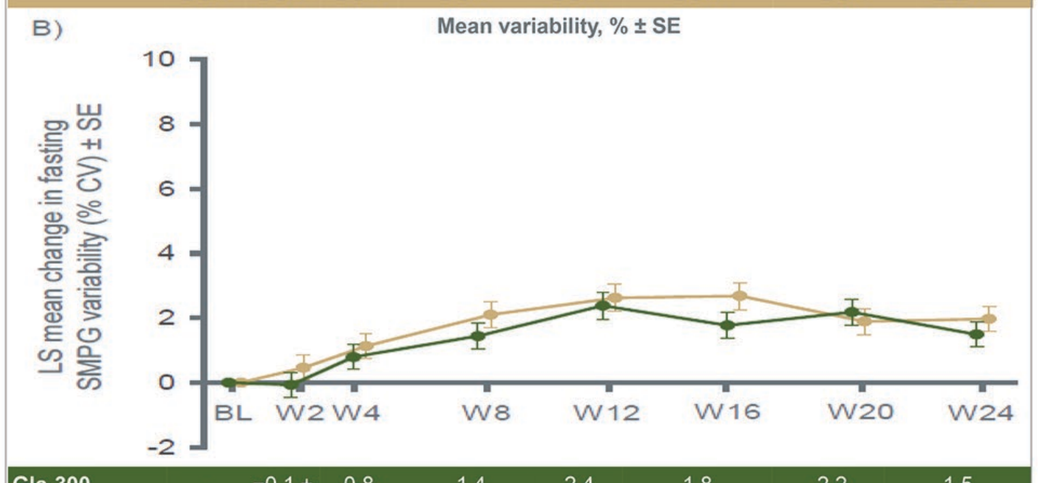
- **Variability of 24-h 8-point SMPG profiles:**
  - Mean (SD) baseline variability (CV) for 24-h SMPG (taken from 8-point profiles) was similar for Gla-300 (22.52% [8.33]) and IDeg-100 (23.40% [8.74]).
  - Similar increases in mean 24-h SMPG variability were seen in both treatment groups from baseline to week 24, with a mean (SE) change of 3.70% (0.59) and 3.95% (0.60) for Gla-300 and IDeg-100, respectively. Least squares (LS) mean difference between treatment groups was −0.25% (95% CI: −1.72 to 1.23) (**Figure 1**).

Figure 2: A) variability and B) change in variability of fasting SMPG by study visit



	BL	W2	W4	W8	W12	W16	W20	W24
Gla-300	13.8 ± 0.3	14.9 ± 0.4	15.8 ± 0.4	16.5 ± 0.4	17.3 ± 0.4	16.8 ± 0.4	17.1 ± 0.4	16.5 ± 0.4
IDeg-100	14.6 ± 0.4	15.6 ± 0.4	16.2 ± 0.4	17.2 ± 0.4	17.8 ± 0.4	17.7 ± 0.4	17.1 ± 0.4	17.0 ± 0.4

Mean variability, % ± SE



	BL	W2	W4	W8	W12	W16	W20	W24
Gla-300	0	−0.1 ± 0.4	0.8 ± 0.4	1.4 ± 0.4	2.4 ± 0.4	1.8 ± 0.4	2.2 ± 0.4	1.5 ± 0.4
IDeg-100	0	0.5 ± 0.4	1.1 ± 0.4	2.1 ± 0.4	2.6 ± 0.4	2.7 ± 0.4	1.9 ± 0.4	2.0 ± 0.4

LS mean change in variability, % ± SE

ITT population. BL, baseline; CV, coefficient of variation; ITT, intent-to-treat; LS, least squares; SE, standard error; W, week

- **Variability of fasting SMPG:**
  - Mean (SD) baseline variability (CV) for fasting SMPG was also similar for Gla-300 (13.77% [6.98]) and IDeg-100 (14.61% [7.70]).
  - Similar increases in mean fasting SMPG variability were seen in both treatment groups from baseline to week 24, with a mean change of 1.49% (0.39) and 1.97% (0.39) for Gla-300 and IDeg-100, respectively. LS mean difference between treatment groups was: −0.48 (−1.49 to 0.53) (**Figure 2**).

DISCUSSION

- The present analysis indicates that the differences in glycaemic variability between Gla-300 and IDeg-100, reported in previous PK/PD studies,[3,4] do not translate into meaningful clinical differences in variability of 24-h and fasting SMPG.
- Glycaemic variability was similar between treatment groups at baseline and after initiation of either Gla-300 or IDeg-100.
  - As expected in these previously insulin-naïve participants, a slight increase in within-day and day-to-day intra-subject variability was observed after insulin initiation and titration, for both basal insulins.
  - Despite Gla-300 showing within-day and day-to-day plasma glucose variability as low as that of IDeg-100, Gla-300 provided lower incidence and rates of anytime (24 h) hypoglycaemia during the 0–12 week active titration period.
- Gla-300 or IDeg-100 are both suitable treatment options for people with T2DM and, through their effect on glycaemic variability, they may be equally effective in reducing the risk of complications associated with hypo- and hyperglycaemia.

CONCLUSION

Similar variability in 24-h SMPG and fasting SMPG was observed with Gla-300 and IDeg-100 over the 24-week treatment period.

REFERENCES

1. Becker R, *et al. Diabetes Care* 2015; 38: 637–43.
2. Heise T, *et al. Diabetes Obes Metab* 2012; 14: 859–64.
3. Bailey TS, *et al. Diabetes Metab* 2018; 44: 15–21.
4. Heise T, *et al. Diabetes Obes Metab* 2017; 19: 1032–9.
5. Rosenstock J, *et al. Diabetes Care* 2018; 41: 2147–54.

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DISCLOSURE

Robert Ritzel — **Honoraria, consultation fees or speaker's bureau fees:** AstraZeneca, Berlin-Chemie, Eli Lilly, Merck, Novartis, Novo Nordisk, Sanofi, Servier. Alice Cheng — **Lecture fees or advisory board honorarium:** Abbott, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Janssen, Merck, Novo Nordisk, Sanofi, Takeda. Zsolt Bosnyak, Emmanuelle Boëlle-Le Corfec, Anna M.G. Cali and Xiangling Wang — **Employee:** Sanofi. Juan Frias — **Advisory board honorarium, research funding and consulting fees:** AbbVie, Allergan, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Elcelyx, Eli Lilly, Genetech, IONIS, Janssen, Johnson & Johnson, Lexicon, Ligand, Madrigal, Merck, Mylan, Myovant, Novartis, Novo Nordisk, Ogeda, Pfizer, Sanofi, TaiwanJ, Theracos, Viking. Ronan Roussel — **Honoraria, consultation fees, research funding or speaker's bureau fees:** Amgen, AstraZeneca, Danone Research, Eli Lilly, Johnson & Johnson, Merck, Novo Nordisk, Physiogenex Sanofi. Geremia Bolli — **Advisory board honoraria, research funding or speaker's bureau fees:** Menarini, Sanofi.

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