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RESEARCH ARTICLE

Comparison of insulin detemir and insulin glargine using a basal-bolus regimen in a randomized, controlled clinical study in patients with type 2 diabetes

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Abstract

Background This treat-to-target study compared the efficacy and safety of insulin detemir (IDet) and insulin glargine (IGla) in a basal-bolus (insulin aspart) regimen in type 2 diabetes.

Methods 385 patients were randomized 2 : 1 (IDet : IGla). Non-inferiority of IDet to IGla was determined by HbA_{1c} 95% CI upper limit <0.4.

Results IDet and IGla showed similar efficacy in HbA_{1c} reduction at 26 weeks, as the non-inferiority criterion was met at 26 weeks (LS mean [Det−Gla]: 0.207; 95% CI: 0.0149,0.3995). It appeared that IGla in some cases did better than IDet in terms of HbA_{1c}, but the difference (0.207%) was not clinically meaningful. Based on the CONSORT guideline, non-inferiority analysis using the LOCF approach was inconclusive regarding possible inferiority of delta 0.4 (LS mean of [Det−Gla]: 0.307; 95% CI: 0.1023, 0.5109). HbA_{1c} decreased significantly from baseline in IDet (−1.1% [26 weeks], −0.9% [LOCF], $p < 0.001$) and in IGla (−1.3% [26 weeks, LOCF], $p < 0.001$). Final HbA_{1c} were 7.1% (26 weeks) and 7.3% (LOCF) in IDet, and 6.9% (26 weeks) and 7.0% (LOCF) in IGla. Final FPG were 130 mg/dL (26 weeks) and 135 mg/dL (LOCF) in IDet, and 134 mg/dL (26 weeks) and 137 mg/dL (LOCF) in IGla. There was significantly less weight gain in IDet-treated patients (1.2 ± 3.96 kg *versus* 2.7 ± 3.94 kg, $p = 0.001$). Hypoglycemia risk was comparable between groups. The majority of IDet-treated patients (87.4%) remained on a once-daily basal insulin regimen throughout the study.

Conclusions IDet and IGla were both effective and safe treatments for glycemic control in a basal-bolus regimen for type 2 diabetes. Clinically significant reductions in HbA_{1c} were achieved in both groups, but with significantly less weight gain in the IDet group at comparable basal insulin dosage.

Keywords insulin detemir; insulin glargine; type 2 diabetes; glycemic control; weight gain; hypoglycemia

Introduction

Type 2 diabetes is a progressive disease that in many cases will require insulin in order to achieve or sustain satisfactory glycemic control and to consequently

reduce the risk of associated complications. Intensive glucose control with insulin therapy was shown in the landmark UKPDS study to reduce long-term complications, but also to be commonly associated with weight gain and increased risk of hypoglycemia [1]. Several studies, including the STENO-2, ADVANCE and the 10-year follow-up UKPDS studies have provided further evidence of the importance of good glycemic control in reducing morbidity and mortality [2–6].

Both insulin detemir (IDet) and insulin glargine (IGla) are soluble long-acting insulin analogs, with comparable pharmacodynamic profiles, and prolonged durations of effect compared with NPH insulin in patients with type 2 diabetes [7–9]. IDet has also been shown to be associated with less weight gain, compared with NPH insulin [10,11], and IGla [12,13], and after transition from IGla [14].

This current study compared the efficacy and safety of the basal insulins IDet and IGla used in combination with insulin aspart as bolus insulin in patients with type 2 diabetes.

Materials and methods

This was a multi-center, randomized, open-label, parallel-group, treat-to-target trial with a 26-week treatment period to compare the efficacy and safety of IDet to IGla with insulin aspart in a basal-bolus regimen in patients with type 2 diabetes. Patients who were at least 18 years old, with a body mass index (BMI) of $\leq$ 40 kg/m^2 and an HbA_{1c} ranging from 7 to 11% and who had previously received any OAD, insulin, or insulin plus OAD treatment regimens were randomized 2 : 1 to IDet and IGla treatment groups. Patients were excluded from the trial if they had proliferative retinopathy or maculopathy that required acute treatment six months before the start of the study, recurrent major hypoglycemia, anticipated change in medication known to interfere with glucose metabolism, impaired hepatic or renal function believed to interfere with study participation, cardiac problems or uncontrolled hypertension.

There were 9 visits and 13 telephone contacts. All patients followed a basal-bolus insulin treatment regimen throughout the trial. IDet and IGla were used as basal treatment and insulin aspart as bolus treatment. IDet and insulin aspart (Levemir® and NovoLog®, Novo Nordisk A/S, Bagsvaerd, Denmark) were supplied individually as 3 mL (100 U/mL) solutions for injection in pre-filled disposable pens (FlexPen®). IGla (Lantus®, Sanofi-Aventis, USA) was supplied in 10 mL vials (100 U/mL) delivered with syringe and needle. IDet and IGla were injected subcutaneously preferably in the thigh, and insulin aspart was injected in the abdomen. All patients started with a once-daily basal treatment regimen in the evening at the same time each day (anytime from one hour before the last main meal until bedtime). For patients randomized to IDet, an optional second daily morning dose could be added at the discretion of the investigator when pre-defined plasma glucose criteria were met. Pre-dinner bolus and evening basal insulin doses were given within a four-hour period to avoid relative hypoinsulinemia.

For insulin-naive patients, the starting dose of IDet or IGla was 12 U. Patients who previously followed a once-daily basal insulin regimen were transferred to the trial product on a unit-to-unit basis. For patients whose previous regimen was more than once daily, the total daily dose was reduced by 30% and administered in one evening injection. Basal insulin was titrated at the instruction of the investigator according to titration guidelines (Table 1) with the aim of reaching the pre-breakfast plasma glucose (PG) targets of $\leq$ 108 mg/dL without significant hypoglycemia. However, if the average pre-breakfast PG was $\leq$ 108 mg/dL, but the average pre-dinner PG remained $>$ 108 mg/dL after titration of the evening dose and optimization of the bolus doses, a second basal morning dose of IDet was introduced at a starting dose of 4 U. If at least one pre-breakfast or pre-dinner PG value was $<$ 56 mg/dL or between 56 and 72 mg/dL without any obvious explanation, the evening or morning dose of basal insulin was reduced by 4 and 2 U, respectively. Treatment with insulin secretagogues (sulphonylureas, repaglinide, nateglinide) or α-glucosidase inhibitors was discontinued prior to initiating trial drug. Treatment with thiazolidinediones or metformin was continued without any change of dose and was used according to label. These OAD products were not provided by Novo Nordisk.

Statistical analysis

All analyses of study endpoints were based on a pre-planned statistical analysis plan. The intention-to-treat (ITT) analysis set consisted of all randomized subjects who were exposed to at least one dose of trial product. Summary data were presented using descriptive statistics (n, mean, standard deviation [SD] or %). The primary efficacy endpoint was HbA_{1c} after 26 weeks of treatment.

Table 1. Algorithms for titration of evening basal insulin dose of IDet or IGla and morning basal insulin dose of IDet

Average pre-dinner or pre-breakfast PG	Change in evening dose of IDet or IGla based on pre-breakfast PG (Units)	Change in morning dose of IDet based on pre-dinner PG (Units)
$\leq$ 108 mg/dL (target)	No adjustment	No adjustment
109–126 mg/dL	+2 U	+2 U
127–144 mg/dL	+4 U	+2 U
145–162 mg/dL	+6 U	+4 U
163–180 mg/dL	+8 U	+6 U
$>$ 180 mg/dL	+12 U	+8 U
If one or more pre-breakfast or pre-dinner PG values for both algorithms		
$<$ 56 mg/dL	−4U	−4U
56–72 mg/dL	−2U	−2U

PG, plasma glucose.

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Summary of data at week 26 with or without the last observation carried forward (LOCF) imputation for missing values were presented. The secondary efficacy endpoints were FPG during the trial and body weight. Safety endpoints were the incidence of hypoglycemic events and adverse events. Hypoglycemic events occurring between 23 : 00 h (included) and 06 : 00 h (excluded) were classified as nocturnal events, and those occurring between 06 : 00 h (included) and 23 : 00 h (excluded) were classified as daytime events.

HbA_{1c} measurements were analyzed using an analysis of covariance (ANCOVA) model, with treatment as fixed effect and baseline HbA_{1c} as covariate. Patients with incomplete or missing observations for week 26 had their data imputed using the LOCF procedure. A two-sided 95% confidence interval was constructed for treatment differences between IDet and IGla. IDet was non-inferior to IGla if the upper limit of this confidence interval was lower than 0.4. The CONSORT reporting guideline was followed for reporting the non-inferiority results [15]. Differences in final HbA_{1c} among non-completers and completers in each treatment groups were presented using descriptive statistics. FPG and body weight measurements were also analyzed using ANCOVA models, with treatment as fixed effect and baseline FPG or body weight as covariate, respectively. Hypoglycemic events that occurred during the treatment period were assumed to follow a Poisson distribution. The difference in the rate of hypoglycemic events (events/patient/year) between treatment groups was analyzed using a Poisson regression model.

Results

Demographics and baseline characteristics

A total of 254 patients (99.2% of 256 randomized) and 131 patients (100.0%) made up the ITT population in the IDet and IGla groups, respectively. The majority of patients in both groups completed the study at 26 weeks (82.0% and 86.3% in the IDet and IGla groups, respectively). Of the 46 withdrawals in the IDet group, the most frequently reported reason was non-compliance (32% [15 patients]). Of the 18 withdrawals in the IGla group, the most frequently reported reasons were non-compliance (22% [4 patients]) and withdrawal of consent (22% [4 patients]).

The IGla group had a slightly higher proportion of males and Caucasians, compared with the IDet group (Table 2). All other baseline characteristics were comparable between treatment groups. Baseline glycemic control was comparable between treatment groups. HbA_{1c} was 8.4% in both groups and FPG was 174.0 mg/dL and 172.2 mg/dL in the IDet and IGla groups, respectively (Table 3).

Table 2. Baseline characteristics of the ITT population

	IDet ($n = 254$)	IGla ($n = 131$)	Total ($n = 385$)
Age, mean (SD), years	55.8 (10.0)	55.9 (11.0)	55.8 (10.3)
Gender, *n* (%) males	131 (51.6)	79 (60.3)	210 (54.5)
Race, *n* (%)			
Caucasian	193 (76.0)	108 (82.4)	301 (78.2)
African American	37 (14.6)	14 (10.7)	51 (13.2)
Asian	7 (2.8)	3 (2.3)	10 (2.6)
American Indian or Alaskan Native	4 (1.6)	0 (0.0)	4 (1.0)
Others	13 (5.1)	6 (4.6)	19 (4.9)
Ethnicity, *n* (%)			
Hispanic/Latino	41 (16.1)	23 (17.6)	64 (16.6)
Non-Hispanic/Latino	213 (83.9)	108 (82.4)	321 (83.4)
Weight, mean (SD), kg	94.4 (18.1)	97.8 (18.3)	95.5 (18.2)
BMI, mean (SD), kg/m^2	32.6 (4.8)	33.0 (4.4)	32.7 (4.7)
HbA_{1c}, mean (SD), %	8.4 (1.0)	8.4 (1.0)	8.4 (1.0)
FPG, mean (SD), mg/dL	174.0 (59.3)	172.2 (58.5)	173.4 (59.0)
Duration of DM, mean (SD), years	12.5 (6.8)	11.9 (7.4)	12.3 (7.0)
Pre-trial therapy, *n* (%)			
OAD monotherapy	9 (3.5)	6 (4.6)	15 (3.9)
OAD combination therapy	42 (16.5)	20 (15.3)	62 (16.1)
Insulin without OAD	83 (32.7)	41 (31.3)	124 (32.2)
Insulin with OAD	120 (47.2)	64 (48.9)	184 (47.8)

SD, standard deviation; BMI, body mass index; FPG, fasting plasma glucose; OAD, oral anti-diabetic drug; DM, diabetes mellitus; IDet, insulin detemir; IGla, insulin glargine.

Insulin exposure

The majority of patients in both groups had received insulin treatment before entering the study (79.9 and 80.2% in the IDet and IGla groups, respectively). The mean ± SD basal insulin doses at 26 weeks were comparable between treatment groups (0.81 ± 0.456 U/kg and 0.75 ± 0.324 U/kg for the IDet and IGla groups, respectively) ($p = 0.100$).

The majority of the IDet-treated patients (87.4%) remained on a once-daily basal insulin regimen throughout the study. The mean ± SD daily IDet dose was 0.80 ± 0.460 U/kg for patients on a once-daily IDet regimen, and 0.89 ± 0.429 U/kg for patients on a twice-daily IDet regimen. The mean ± SD daily dose at 26 weeks was lower among insulin-naïve patients treated with IDet (0.70 ± 0.349 U/kg) and IGla (0.67 ± 0.249 U/kg), compared with non-insulin-naïve patients treated with IDet (0.84 ± 0.475 U/kg) and IGla (0.77 ± 0.338 U/kg).

Glycemic control

The non-inferiority criterion of baseline-adjusted HbA_{1c} in the IDet group to the IGla group was met at 26 weeks (LS mean of [Det-Gla]: 0.207; 95% CI: 0.0149, 0.3995). Based on the CONSORT reporting guideline [15], the result of the non-inferiority analysis using the LOCF approach was inconclusive regarding possible inferiority of delta 0.4 (LS mean of [Det-Gla]: 0.307; 95% CI: 0.1023, 0.5109) (Table 3). HbA_{1c} showed significant

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Table 3. Change in HbA_{1c} from baseline in the ITT population

	IDet			IGla					
	n	LS Mean (SE)	Change from baseline	*n*	LS Mean (SE)	Change from baseline	ANCOVA IDet-IGla	*p*-value	Non-inferiority criteria met (95% CI)
HbA_{1c} (%)									
Baseline[a]	254	8.42 (0.063)		131	8.42 (0.085)				
26 weeks	216	7.13 (0.073)	−1.08 (1.077)	115	6.92 (0.091)	−1.28 (1.117)	0.207	0.035	Yes[b] (0.0149, 0.3995)
LOCF	251	7.33 (0.076)	−0.94 (1.117)	128	7.02 (0.096)	−1.25 (1.141)	0.307	0.004	Inconclusive[b] (0.1023, 0.5109)
FPG (mg/dL)									
Baseline[a]	253	174.0 (3.73)		131	172.2 (5.11)				
26 weeks	215	129.7 (3.16)	−43.2 (3.16)	115	134.3 (4.32)	−38.7 (4.32)	−4.54	0.397	N.A.
LOCF	250	135.4 (3.15)	−37.9 (3.15)	128	136.7 (4.40)	−36.5 (4.40)	−1.32	0.808	N.A.

IDet, insulin detemir; IGla, insulin glargine; LS mean, least square mean (baseline-adjusted mean) estimated from an analysis of covariance (ANCOVA) model with treatment as fixed effect and baseline values as covariate; CI, confidence interval; LOCF, using data from last observation carried forward (end of study).
[a]Baseline values are mean (SE).
[b]Non-inferiority outcomes were interpreted based on the CONSORT reporting guideline [15]. The value of the delta (treatment difference) used in determining the non-inferiority outcome was 0.4. The results based on the 26-week data showed that non-inferiority criteria was met, since the upper confidence limit was less than delta (0.4). The results based on the LOCF approach was inconclusive regarding possible inferiority of magnitude 0.4 (delta), since the confidence interval included delta (0.4) [15].

decreases from baseline in both treatment groups (−1.1% [26 weeks], −0.9% [LOCF] in the IDet group, and −1.3% [26 weeks and LOCF] in the IGla group, $p < 0.001$ for all changes from baseline) (Figure 1). Mean final HbA_{1c} of patients who did not complete the 26-week treatment was 8.6% in the IDet group (18% of patients) and 7.9% in the IGla group (14% of patients) ($p = 0.013$). Among patients in the IDet group, 39% (LOCF) and 43% (26 weeks) achieved target $HbA_{1c} < 7\%$ overall, and 37% (LOCF) and 41% (26 weeks) achieved target without hypoglycemic episodes. Among the patients in the IGla group, 54% (LOCF) and 57% (26 weeks) achieved HbA_{1c} target overall, and 52% (LOCF) and 56% (26 weeks) achieved target without hypoglycemic episodes.

Mean laboratory-measured FPG showed comparable decreases in both treatment groups, from 174 to 130 mg/dL (26 weeks) and 135 mg/dL (LOCF) in the IDet group, and from 172 to 134 mg/dL (26 weeks) and 137 mg/dL (LOCF) in the IGla group (Table 3). Mean pre-dinner glucose levels in the IDet group were 142.9 ± 46.34 mg/dL (26 weeks) and 149.7 ± 54.07 mg/dL (LOCF), and in the IGla group were 135.0 ± 44.65 mg/dL (26 weeks) and 139.3 ± 45.40 mg/dL (LOCF) ($p > 0.05$, NS). The 9-point self-measured plasma glucose (SMPG) profiles for both treatment groups were not statistically different (Figure 2).

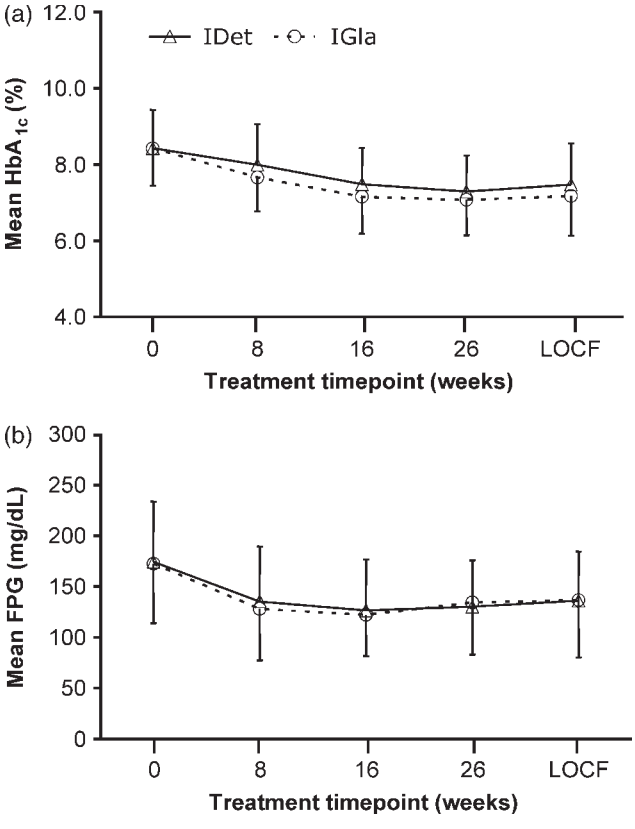

Figure 1. Mean (± SD) HbA_{1c} and FPG values over time.
HbA_{1c} (A) and fasting plasma glucose (FPG) values (B) from baseline to 26 weeks and end of study (LOCF) are presented. IDet is represented by a solid line and triangle, and IGla by a dashed line and circle

Body weight

By the end of the study, patients treated with IDet had gained significantly less weight compared with patients treated with IGla (1.2 ± 3.96 kg *versus* 2.7 ± 3.94 kg, $p = 0.001$; 95% CI: −2.19, −0.56). The difference in weight gain between treatment groups was 1.37 kg.

Hypoglycemic events

The rates of hypoglycemic events (all, daytime, nocturnal and all major events) were comparable between treatment groups (Table 4). A total of 76.2% of patients in the IDet

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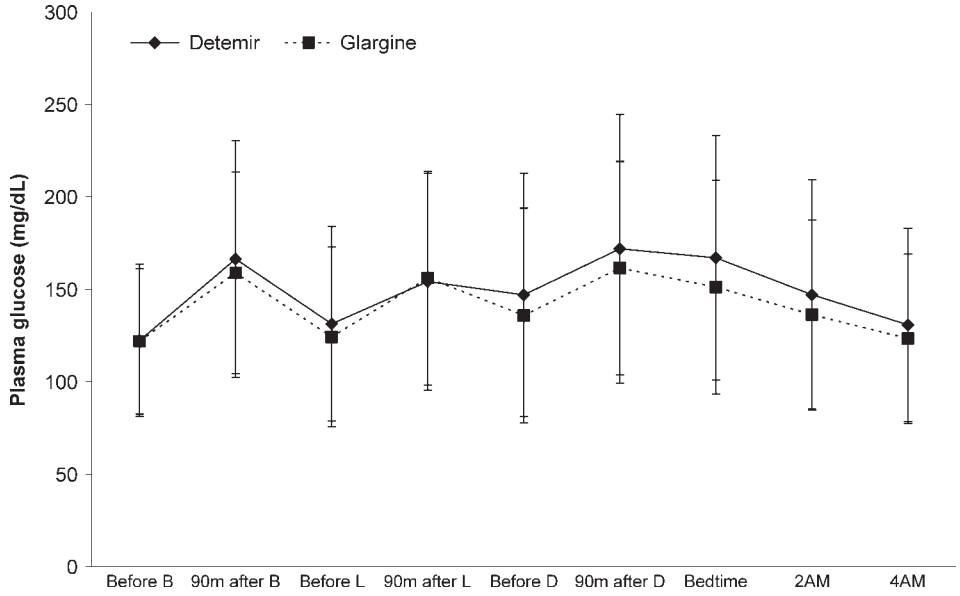

Figure 2. Mean 9-point plasma glucose profiles.
IDet is represented by a solid line and square, and IGla by a dashed line and square. B, breakfast; L, lunch; D, dinner

Table 4. Hypoglycemic events in the safety population

	IDet ($n = 256$)		IGla ($n = 131$)		
Hypoglycemic Events	*n* (%) patients	Events per patient-year	*n* (%) patients	Events per patient-year	*p* value[a]
All events	195 (76.2)	19.30	98 (74.8)	17.94	0.653
Daytime events	175 (68.4)	14.15	88 (67.2)	13.80	0.888
Nocturnal events	118 (46.1)	4.23	56 (42.7)	3.38	0.299
All major events	10 (3.9)	0.09	5 (3.8)	0.12	0.709

IDet, insulin detemir; IGla, insulin glargine.
[a]Between-group *p* values were estimated from Poisson regression (rate ratio = 1).

group reported hypoglycemic events at a rate of 19.3 events per subject-year and 74.8% of patients in the IGla group reported events at a rate of 17.9 events per subject-year ($p = 0.653$). The most frequently reported hypoglycemic events in both groups were daytime events. Major hypoglycemic events were reported by 3.9% of patients and 3.8% of patients in the IDet and IGla groups, respectively. Nocturnal events were reported by 46.1% of patients and 42.7% of patients in the IDet and IGla groups, respectively.

Adverse events

A total of 66.0% (169 out of 256 patients) in the IDet safety population reported 605 treatment emergent adverse events (TEAEs) and 71.0% (93 out of 131 patients) in the IGla safety population reported 273 TEAEs. The most commonly reported TEAEs in the IDet group were peripheral edema (19 events), and in the IGla group were upper respiratory tract infection (15 events). Overall, 3.9% (10) patients and 2.3% (3) patients withdrew from the trial due to adverse events in the IDet and IGla groups, respectively.

A total of 27 serious adverse events (SAEs), including one possibly related to the trial drug and one probably related to the trial drug (both hypoglycemia), were reported by 23 patients in the IDet group. A total of eight SAEs were reported by five patients in the IGla group.

Discussion

This study showed that treatment with IDet or IGla in a basal-bolus regimen resulted in significant improvements in the glycemic control of patients with type 2 diabetes. Epidemiological analysis of the UKPDS study has demonstrated a curvilinear relationship between HbA_{1c} and diabetes-related complications [16]. Each 1% reduction in HbA_{1c} was associated with reductions in risk by 21% for death or any outcome related to diabetes, 14% for myocardial infarction and 37% for microvascular complications. These benefits of good glycemic control with intensive therapy have been reinforced by findings from recent studies [2,5,6], including the STENO-2 study, in which a 50% reduction in the risk of cardiovascular and microvascular events was reported in patients with type

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2 and microalbuminaria who received intensive therapy and had a decrease of 0.5% in HbA_{1c} levels [3]. Therefore, the improvements of more than 1% point in HbA_{1c} of both groups in this current study were clinically significant in terms of reducing the risk of diabetes-related mortality and complications.

Nevertheless, the majority of patients in both treatment groups did not achieve the recommended glycemic targets, although this was a treat-to-target study. It is possible that the beta-cell function of the majority of the patient population was at an advanced stage of deterioration, as the average duration of diabetes was 12 years and 80% of patients had previously been exposed to insulin, hence presenting a challenge for treatment to target. It should be noted here that although the difference was significant between treatment groups, the rate of target achievement in the current study was not consistent with the outcomes reported in other trials, which showed comparable target HbA_{1c} achievement without hypoglycemic episodes in patients with type 2 diabetes treated with IDet or IGla: 36.2% (IDet) *versus* 36.7% (IGla) [13] and 33% (IDet) *versus* 35% (IGla) [12]. The low rates of hypoglycemic events observed in the current study suggest that the titration could have been more aggressive, as improvements in glycemic control and frequency of hypoglycemic events are expected to increase with intensification of insulin treatment [1].

This study adopted the well-established non-inferiority clinical margin of 0.4% (according to the 2008 FDA Guidance for Industry on Diabetes Mellitus: Developing Drugs and Therapeutic Biologics for Treatment and Prevention). Based on the CONSORT reporting guideline [15], the outcome of the current study based on the LOCF approach was classified as inconclusive regarding possible inferiority of magnitude delta (0.4), because the confidence interval spanned the predetermined delta (0.4) required for non-inferiority, despite having a statistically significant difference. Based on the 26-week data, the upper limit of the confidence interval was below 0.4, indicating that IDet was non-inferior to IGla. It appeared that IGla in some cases did better than IDet in terms of HbA_{1c} in this trial. However, the difference of 0.207% observed in the current study was much smaller than the well-established margin of 0.4% and was therefore not clinically meaningful. The *p*-value and confidence interval in this study were most likely a result of the large sample size, which was a possible reason cited by the CONSORT guideline for such scenarios. Thus, by strict statistical and clinical criteria, these results showed that IDet was not inferior to IGla. One bias in interpreting results using the LOCF approach lies in its dependence on the delicate balance between the number of patients who complete the planned treatment for a study and those who do not, and their clinical outcome at the various stages of completion. One would expect only the patients who complete the full course of treatment to reap its full benefits. This appears to be the case in this study, in which the HbA_{1c} levels of the non-completers in both treatment groups were higher than those of the completers. This difference was bigger in the IDet group (1.5%) than the IGla group (1.0%). Further, there were proportionally more non-completers in the IDet group (18%), compared with the IGla group (14%), implying that more patients in the IDet group received treatment for fewer than 26 weeks. (It should be noted that most of the patients withdrew due to non-compliance, and that only a small proportion (15%) withdrew due to ineffective therapy. The high incidence of non-compliance could have been affected by the unfamiliarity of the patients to IDet, since one-fifth of the patients in the IDet group were previously treated with IGla and could have been reluctant to continue with the IDet treatment, which was considered to be the newer treatment at the time of the study.) When these patients were included in the LOCF analysis, the overall effect of IDet was expectedly smaller, compared with that of IGla. However, when only patients who completed 26 weeks of treatment were included, there was no clinical difference in the efficacy of IDet and IGla. This could account for the disagreement between the 26-week *versus* the LOCF non-inferiority analyses. The LOCF analysis was essentially inconclusive and could possibly have been different had the non-completion rates been similar between treatment groups. The 26-week results represent the effects of insulin to their full effect and are, therefore, a more accurate reflection of the 'real-world' clinical experience. The conclusion of non-inferiority of IDet to IGla based on the 26-week results is also consistent with the clinical experience with detemir reported in other studies [12–14]. Future studies having more stringent patient compliance with study completion could provide more conclusive evidence for these comparisons. Another limitation of the study was the different devices in each treatment group, which precluded blinding and could have introduced a bias into the study.

Patients in the IDet and IGla groups received comparable basal insulin doses throughout the study. Further, approximately 88% of patients in the IDet group remained on a once-daily regimen, with comparable glycemic improvements to IGla. Despite the similarity in insulin dosage and HbA_{1c} reduction, there was significantly less weight gain in the IDet group, compared with the IGla group in the current study. These results support earlier findings that showed less weight gain in IDet-treated patients compared with IGla-treated patients (2.7 *versus* 3.5 kg [12] and 2.8 *versus* 3.8 kg [13]) and compared with NPH-treated patients (0.7 *versus* 1.6 kg [17], 1.0 *versus* 1.8 kg [11] and 0.5 *versus* 1.1 kg [18]). In contrast, a recent meta-analysis of 12 randomized controlled trials showed significantly more weight gain in IGla-treated patients, compared with NPH-treated patients, despite comparable glycemic control [19]. Several mechanisms have been hypothesized to explain this weight-sparing effect of IDet [20–22], including preferential hepatic insulin action and appetite regulation [23].

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Conclusion

This study showed that IDet and IGla were both effective and safe treatments for glycemic control when used in a basal-bolus regimen in patients with type 2 diabetes. Clinically significant reductions in HbA_{1c} were achieved in both groups, with a once-daily dosing regimen adopted in the majority of patients. Despite the similarity in basal insulin dosage received in both groups, there was significantly less weight gain in the IDet group.

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Conflict of interest

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