

# A New-Generation Ultra-Long-Acting Basal Insulin With a Bolus Boost Compared With Insulin Glargine in Insulin-Naïve People With Type 2 Diabetes

A randomized, controlled trial

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**OBJECTIVE**—Insulin degludec/insulin aspart (IDegAsp) is a soluble coformulation of the novel basal analog insulin degludec (IDeg; 70%) and insulin aspart (IAsp; 30%). We compared the safety and efficacy of IDegAsp, an alternative formulation (AF) (55% IDeg and 45% IAsp), and insulin glargine (IGlar) in insulin-naïve subjects with type 2 diabetes inadequately controlled with oral antidiabetic drugs.

**RESEARCH DESIGN AND METHODS**—In this 16-week, open-label trial, subjects (mean age 59.1 years, A1C 8.5%, BMI 30.3 kg/m<sup>2</sup>) were randomized to once-daily IDegAsp ( $n = 59$ ), AF ( $n = 59$ ), or IGlar ( $n = 60$ ), all in combination with metformin. Insulin was administered before the evening meal and dose-titrated to a fasting plasma glucose (FPG) target of 4.0–6.0 mmol/L.

**RESULTS**—After 16 weeks, mean A1C decreased in all groups to comparable levels (IDegAsp: 7.0%; AF: 7.2%; IGlar: 7.1%). A similar proportion of subjects achieved A1C <7.0% without confirmed hypoglycemia in the last 4 weeks of treatment (IDegAsp: 51%; AF: 47%; IGlar: 50%). Mean 2-h postdinner plasma glucose increase was lower for IDegAsp (0.13 mmol/L) and AF (0.24 mmol/L) than IGlar (1.63 mmol/L), whereas mean FPG was similar (IDegAsp: 6.8 mmol/L; AF: 7.4 mmol/L; IGlar: 7.0 mmol/L). Hypoglycemia rates were lower for IDegAsp and IGlar than AF (1.2, 0.7, and 2.4 events/patient year). Nocturnal hypoglycemic events occurred rarely for IDegAsp (1 event) and IGlar (3 events) compared with AF (27 events).

**CONCLUSIONS**—In this proof-of-concept trial, once-daily IDegAsp was safe, well tolerated, and provided comparable overall glycemic control to IGlar at similar low rates of hypoglycemia, but better postdinner plasma glucose control.

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Although currently available basal insulin analogs have advantages over NPH insulin, they fail to completely mimic the physiological basal insulin secretion profile; at higher doses in particular, their profile is not completely flat, but shows a gentle rise and fall (1). Furthermore, lower doses do not achieve 24-h insulin coverage in all individuals (2), and there remains some within-subject variability in the metabolic effect impeding optimal insulin titration. These limitations, together with a lack in postprandial insulin coverage, may partly explain why a large proportion of patients with type 2 diabetes fail to reach and maintain recommended A1C targets (3–5) considered to minimize the risk for microvascular complications (6–8).

To provide more optimal basal insulin coverage, insulin degludec (IDeg), a new-generation ultra-long-acting basal insulin, was developed. Primarily as a result of the formation of soluble multimeric hexamers at the injection site, IDeg has a smooth and stable pharmacokinetic profile at steady state (9) that gives rise to a considerably longer action profile than current basal insulin formulations (10) as well as lower within-subject variability (11).

IDeg can be coformulated with insulin aspart (IAsp) (12) resulting, for the first time, in a soluble preparation comprising two different insulin analogs (IDegAsp: 70% v/v IDeg as basal insulin and 30% v/v IAsp as prandial insulin). By providing both basal and rapid-acting insulin analogs in one injection, IDegAsp could be an attractive alternative to the common strategy of initiating insulin therapy with basal insulin only on top of oral antidiabetic drugs (OADs). Indeed, for many patients, simultaneously targeting fasting and postmeal plasma glucose could be a more suitable approach to

achieving and sustaining optimal glycemic control (13).

In this exploratory, clinical proof-of-concept trial, we compared the safety and efficacy of IDegAsp with insulin glargine (IGlar), both given once-daily in combination with metformin in insulin-naïve subjects with type 2 diabetes inadequately controlled on OAD therapy. To establish the optimal ratio of IDeg to IAsp, an alternative formulation of IDegAsp (AF) containing a higher percentage of IAsp (45%) was also evaluated.

## RESEARCH DESIGN AND METHODS

**RESEARCH DESIGN AND METHODS**—Twenty-two sites in five European countries (France, Germany, Norway, Romania, and Spain) participated in this phase 2, open-label, randomized, controlled 16-week trial. The trial protocol was approved by local institutional review boards, and all subjects gave written informed consent. The study was conducted in accordance with the Declaration of Helsinki (14) and Good Clinical Practice guidelines (15).

### Trial population

Adults with type 2 diabetes were enrolled if they were 18–75 years of age, had an A1C of 7–11%, and had a BMI of 25–37 kg/m<sup>2</sup>. Subjects had to be insulin-naïve (no previous insulin treatment or insulin treatment for ≤14 days in the 3 months prior to trial), and had to be treated with up to two OADs in the 2 months prior to trial at stable maximum doses or at least half maximum allowed doses. Subjects were excluded if they had been treated with thiazolidinediones in the 3 months preceding the trial. Other exclusion criteria included cardiac disease (heart failure: New York Heart Association class III or IV, unstable angina pectoris, or a myocardial infarction) within 12 months of the trial, severe hypertension (systolic blood pressure ≥180 mmHg or sitting diastolic blood pressure ≥100 mmHg), recurrent severe hypoglycemia or hypoglycemia unawareness, use of drugs likely to affect glycemia, impaired hepatic function (alanine aminotransferase >2.5-fold the upper local reference limit), pregnancy, and breast-feeding.

### Treatments

Prior to randomization, eligible subjects discontinued their pretrial OAD treatment and underwent a 2-week forced metformin titration period (dose increased up to 2,000 mg/day: 1,000 mg each at breakfast and the evening meal) followed by a

1-week metformin maintenance period. Subjects taking metformin at enrollment could undergo a modified titration period or advance directly to the metformin maintenance period. Metformin could be decreased to a minimum of 1,500 mg/day in the case of unacceptable hypoglycemia or other adverse events. Subjects were eligible for randomization provided the maximum daily metformin dose (2,000 mg) or maximum tolerated dose (1,500 mg) remained unchanged in the maintenance period and the median prebreakfast self-measured plasma glucose (SMPG) value (measured on the 3 days prior to randomization) was ≥7.5 mmol/L (135 mg/dL).

Randomization was carried out using a telephone- or web-based randomization system, with subjects stratified according to pretrial OAD treatment (Table 1). Eligible subjects were randomized (1:1:1) to receive once-daily subcutaneous injections of either IDegAsp (70% IDeg and 30% IAsp; Novo Nordisk A/S, Bagsværd, Denmark; 100 U/mL), AF (55% IDeg and 45% IAsp; Novo Nordisk A/S, Bagsværd, Denmark; 100 U/mL) or IGLar (Lantus; sanofi-aventis, Paris, France; 100 U/mL) for 16 weeks, all in combination with metformin.

The insulin starting dose was 10 units administered in the abdomen (IDegAsp,

AF) or thigh (IGlar) before the evening meal. IDegAsp and AF were administered using a 3 mL FlexPen device (Novo Nordisk A/S, Bagsværd, Denmark); IGLar was administered using a 3 mL Optiset device (sanofi-aventis, Paris, France). Based on SMPG levels before breakfast (lowest FPG value from 3 consecutive days), insulin doses were individually titrated once a week throughout the trial (by clinic or telephone contacts) aiming at an FPG level of 4.0–6.0 mmol/L (72–108 mg/dL). Doses were increased by 2 units if FPG was 6.1–8.0 mmol/L (109–144 mg/dL), by 4 units if FPG was 8.1–9.0 mmol/L (145–162 mg/dL), or by 6 units if FPG was >9.0 mmol/L (>162 mg/dL); doses were decreased by 2 units (or 5% reduction if dose >45 units) if FPG was 3.1–3.9 mmol/L (56–71 mg/dL), and by 4 units (or 10% reduction if dose >45 units) if FPG was <3.1 mmol/L (<56 mg/dL). If the FPG target was reached, IDegAsp and AF doses could be further adjusted (in suggested increments of 2 units) to achieve a dinner postprandial plasma glucose target value of <8.0 mmol/L (<145 mg/dL), provided that no hypoglycemia had occurred.

### Outcome measures

The primary end point was A1C (%) after 16 weeks of treatment. Other efficacy end

**Table 1—Characteristics of randomized population and subject disposition**

	IGlar	IDegAsp	AF
Sex: male/female (%)	73/27	63/37	58/42
Age (years)	58.4 ± 8.4	58.7 ± 8.8	60.2 ± 8.2
Weight (kg)	86.8 ± 11.3	85.1 ± 11.7	83.9 ± 15.7
Height (m)	1.69 ± 0.07	1.68 ± 0.09	1.66 ± 0.10
BMI (kg/m <sup>2</sup> )	30.5 ± 3.5	30.2 ± 3.4	30.3 ± 4.3
Duration of diabetes (years)	8.5 ± 4.8	9.1 ± 8.0	9.5 ± 5.8
Prestudy OAD treatment			
Met and/or α-gluc	30 (50)	30 (51)	30 (51)
SU with/without α-gluc	0 (0)	1 (2)	0 (0)
Met and SU	30 (50)	28 (47)	29 (49)
A1C (%)	8.4 ± 1.3	8.3 ± 1.2	8.6 ± 1.5
FPG (mmol/L)	12.1 ± 3.5	11.1 ± 3.3	11.5 ± 3.2
Randomized	60	59	59
Exposed	60	59	59
Completers	55 (92)	55 (93)	53 (90)
Withdrawals (%)	5 (8)	4 (7)	6 (10)
Adverse events	0 (0)	1 (2)*	0 (0)
Noncompliance	1 (2)	2 (3)	2 (3)
Ineffective therapy	2 (3)	0 (0)	0 (0)
Other	2 (3)	1 (1.7)	4 (7)

Data are means ± SD or n (%) unless otherwise indicated. All subjects were white. \*Serious adverse event of “transient ischemic attack” considered by the investigator to be unlikely related to trial product. α-gluc, α-glucosidase inhibitor; Met, metformin; SU, sulphonylurea.

points included changes in laboratory-measured FPG and 9-point SMPG profile. The proportion of subjects achieving A1C <7.0% and  $\leq 6.5\%$  at end of trial, and the proportion reaching these A1C targets without confirmed hypoglycemia (confirmed by a plasma glucose measurement of <3.1 mmol/L [56 mg/dL] or if classified as “severe”) in the last 4 weeks of treatment (subjects treated for  $\geq 8$  weeks) were also determined.

Safety variables included adverse events, hypoglycemic episodes, vital signs, physical examination, funduscopy, electrocardiogram, standard biochemical and hematology measures, and insulin antibodies (IDeg-specific, IAsp-specific and antibodies cross-reacting between IDeg and IAsp and between IDeg and human insulin). Hypoglycemia was classified as “severe” (if assistance from another person was required) or “confirmed” (if confirmed by a plasma glucose measurement of <3.1 mmol/L [56 mg/dL] irrespective of symptoms, or if classified as “severe”). Hypoglycemia was considered “nocturnal” if the time of onset was between 2300 and 0559 h.

Laboratory analyses were performed by Quintiles Central Laboratories (Edinburgh, Scotland). A1C was assayed using a validated high-performance liquid chromatography method certified by the National Glycohemoglobin Standardization Program. FPG was measured using the Gluco-quant system (Roche, Mannheim, Germany). Insulin antibodies were analyzed by Celerion (Fehraltorf, Switzerland) using a subtraction radioimmunoassay method (16), validated according to standard procedures (17). Subjects determined SMPG using glucose meters (Abbott Diabetes Care, Alameda, CA) and recorded values in diaries.

### Statistical analyses

The statistical evaluation of A1C, FPG, and 2-h postprandial plasma glucose increment was based on all randomized subjects following the intention-to-treat principle. Missing values for A1C and FPG were imputed using last observation carried forward. Treatment differences in A1C and FPG values after 16 weeks of treatment were estimated by a linear model, in which the estimates were adjusted by country, sex, OAD therapy at screening, age, and baseline values. Mean 2-h postprandial plasma glucose increments (plasma glucose concentration measured 2 h after a meal minus the plasma glucose concentration measured

immediately prior to the meal) were analyzed in an identical fashion to the primary end point except for the inclusion of the premeal plasma glucose value as an additional covariate.

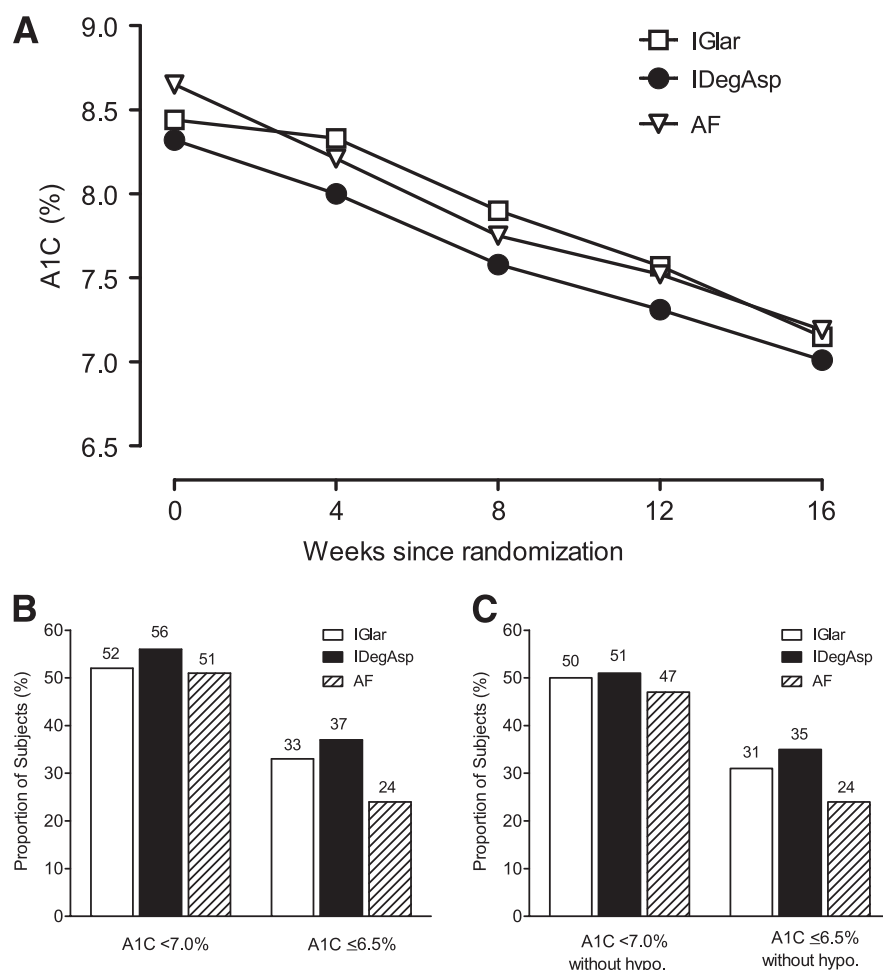
Testing for superiority or noninferiority was not the aim of this exploratory trial; no confirmatory hypotheses were prespecified, and no formal statistical testing was undertaken. Instead, the aim was to estimate a treatment difference in A1C with sufficient precision: a 95% CI for the treatment difference with a total width of 0.8% (absolute) was considered sufficient for this proof-of-concept trial and would be obtained with 50 completed subjects per treatment arm. On the basis of the chosen precision for A1C and an expected dropout rate of 15%, 60 subjects were to be randomized to each treatment arm. Values are presented as mean  $\pm$  SD for descriptive statistics and

as estimated mean (95% CI) for inferential statistics from the linear model.

**RESULTS**—A total of 226 people were screened for the trial, of which 46 failed screening criteria, and 2 were run-in failures. The remaining 178 subjects were randomized and exposed to treatment following the metformin run-in period (Table 1). Baseline characteristics at randomization were comparable across treatment groups, with the exception of a higher percentage of males in the IGlar group (Table 1). A similar proportion (7–10%) of subjects withdrew from each treatment group during the trial (Table 1).

### Glycemic control

Mean A1C values decreased over the course of the 16-week trial (Fig. 1A); after 16 weeks, A1C had decreased by  $1.3 \pm 1.0$  %-point (IDegAsp),  $1.5 \pm 1.4$  %-point



**Figure 1**—Mean A1C over time (A), percentage of subjects achieving A1C targets of <7.0% and  $\leq 6.5\%$  at end of study (B), and percentage of subjects treated for at least 8 weeks achieving A1C targets of <7.0% and  $\leq 6.5\%$  at end of study in the absence of confirmed hypoglycemia (hypo.) in the last 4 weeks of treatment (C).

(AF), and  $1.3 \pm 1.1$  %-point (IGlar) to similar end-of-trial values ( $7.0 \pm 1.0$ ,  $7.2 \pm 1.0$ , and  $7.1 \pm 1.3\%$ , respectively). IDegAsp was associated with a 0.11 %-point greater reduction in A1C compared with IGlar (estimated mean treatment difference [IDegAsp-IGlar]:  $-0.11$  [95% CI  $-0.41$  to  $0.19$ ]) and a 0.08 %-point greater reduction in A1C compared with AF (estimated mean treatment difference [AF-IDegAsp]:  $0.08$  [95% CI  $-0.22$  to  $0.38$ ]).

Overall, more subjects in the IDegAsp group achieved glycemic targets (Fig. 1B and C). For all treatments, a similar proportion of subjects ( $\sim 50\%$ ) reached an A1C of  $<7.0\%$  by trial end, whereas a higher proportion of subjects in the IDegAsp and IGlar groups achieved an A1C value of  $\leq 6.5\%$  compared with AF (Fig. 1B). Treatments were comparable in terms of the percentage of subjects reaching an A1C of  $<7.0\%$  in the absence of confirmed hypoglycemia in the last 4 weeks of treatment (Fig. 1C). However, compared with AF, a greater percentage of subjects in the IDegAsp and IGlar groups reached an A1C of  $\leq 6.5\%$  in the absence of confirmed hypoglycemia in the last 4 weeks of treatment (Fig. 1C).

All treatment groups had improvements from baseline in mean 9-point SMPG profile (Fig. 2). Mean 2-h postprandial plasma glucose increments (plasma glucose concentration measured 2 h after a meal minus the plasma glucose concentration measured immediately prior to the meal) were similar for all treatments after breakfast and lunch. However,

the increase in mean 2-h postdinner plasma glucose was substantially lower for IDegAsp ( $0.13 \pm 3.43$  mmol/L) and AF ( $0.24 \pm 3.48$  mmol/L) compared with IGlar ( $1.63 \pm 3.18$  mmol/L). The estimated mean treatment difference was  $-1.34$  mmol/L [95% CI  $-2.45$  to  $-0.23$ ] for IDegAsp-IGlar and  $0.01$  mmol/L [95% CI  $-1.09$  to  $1.12$ ] for AF-IDegAsp.

Mean FPG values decreased over the course of the 16-week trial. After 16 weeks, mean FPG levels had decreased by  $4.3 \pm 3.5$  mmol/L in the IDegAsp group, by  $4.1 \pm 3.1$  mmol/L in the AF group, and by  $5.1 \pm 3.9$  mmol/L in the IGlar group to comparable end-of-trial values ( $6.8 \pm 2.5$ ,  $7.4 \pm 2.8$ , and  $7.0 \pm 2.5$  mmol/L, respectively). IDegAsp was associated with a 0.13 mmol/L greater reduction in FPG compared with IGlar (estimated mean treatment difference [IDegAsp-IGlar]:  $-0.13$  mmol/L [95% CI  $-1.03$  to  $0.77$ ]) and a 0.64 mmol/L greater reduction in FPG compared with AF (estimated mean treatment difference [AF-IDegAsp]:  $0.64$  mmol/L [95% CI  $-0.25$  to  $1.53$ ]).

The self-monitored FPG titration target of 4.0–6.0 mmol/L was reached by 43, 54, and 51% of participants on IGlar, IDegAsp, and AF, respectively, at trial end; the postdinner plasma glucose target ( $<8.0$  mmol/L) was reached by 42, 76, and 76%, respectively. The median time to reach the FPG target for the first time was similar for all treatments (5 weeks). There was no obvious difference in baseline characteristics between subjects

who did or did not meet FPG targets other than a slightly higher ( $\sim 0.4$ – $0.9$  mmol/L) baseline FPG in the latter group (Supplementary Table 1).

### Insulin dose

Baseline (starting) insulin doses were comparable across treatment arms ( $\sim 0.12$  units/kg), with doses increasing for all groups during the trial. At end-of-trial, mean daily insulin doses were  $\sim 20\%$  lower for IDegAsp and AF than IGlar ( $0.38 \pm 0.16$ ,  $0.36 \pm 0.16$ , and  $0.45 \pm 0.20$  units/kg, respectively).

### Body weight

Only small changes in mean body weight were observed from baseline to week 16 for IDegAsp ( $-0.4 \pm 2.3$  kg), AF ( $0.3 \pm 2.2$  kg), and IGlar ( $-0.1 \pm 3.2$  kg).

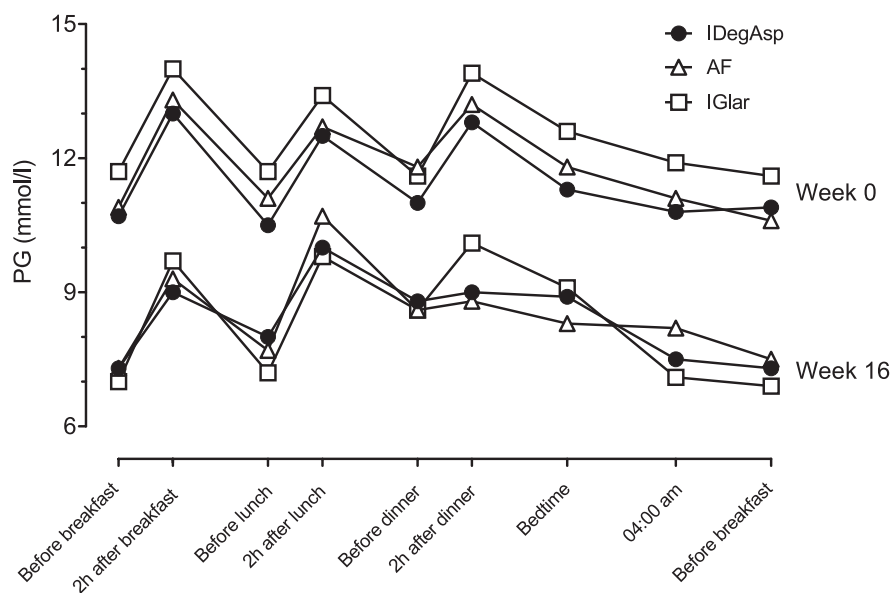
### Hypoglycemic events

No severe hypoglycemic events were reported. Confirmed hypoglycemia (plasma glucose  $<3.1$  mmol/L) was infrequent and reported for 22% (13 subjects; 20 events), 31% (18 subjects; 41 events) and 15% (9 subjects; 12 events) of subjects in the IDegAsp, AF, and IGlar groups, respectively; rates of confirmed hypoglycemia were lower for IDegAsp and IGlar than AF (1.2, 0.7, and 2.4 events/patient year). Nocturnal hypoglycemia occurred rarely for IDegAsp (1 subject; 1 event) and IGlar (3 subjects; 3 events) compared with AF (10 subjects; 27 events).

### Adverse events and other safety measures

The majority of adverse events were mild or moderate in severity. Three serious adverse events were reported: two for IDegAsp (2 subjects; 2 events: depression, transient ischemic attack; the latter leading to the subject's discontinuation) and one for AF (epistaxis), none of which was considered to be related to trial product by the investigator. Adverse events judged to have possible or probable relation to insulin were only reported for AF (5 subjects; 5 events: diarrhea, nausea, diabetic retinopathy, ecchymosis, and hematoma).

Overall, levels of antibodies specific to IAsp and IDeg remained low or undetectable during the trial. Small increases were observed from baseline to end-of-trial (to a median level of  $\leq 0.1\%$  B/T at end-of-trial) in antibodies cross-reacting between IDeg and IAsp (for both IDegAsp and AF groups) and between



**Figure 2**—Mean 9-point SMPG profiles.

IDeg and human insulin (IDegAsp group only). There was no apparent association between these minor changes in antibodies and A1C, hypoglycemia, insulin dose, or body weight (results not shown).

No clinically relevant differences were observed between treatments in physical examination findings, vital signs, standard laboratory analyses (hematology and biochemistry), funduscopy, or electrocardiogram.

**CONCLUSIONS**—The main objective of this exploratory, clinical proof-of-concept trial was to assess the feasibility of insulin initiation with once-daily administration of IDegAsp, the first available soluble coformulation of distinct rapid-acting and basal insulin analogs, as add-on therapy to metformin in patients with type 2 diabetes insufficiently controlled with OADs.

IDegAsp achieved clinically meaningful improvements in A1C of  $\sim 1.4$  %-point that were comparable to those seen with IGlax. The reduction in A1C was slightly (nonsignificantly) greater with IDegAsp (estimated mean treatment difference [IDegAsp-IGlax]:  $-0.11$  [95% CI  $-0.41$  to  $0.19$ ]) but confirmatory trials are needed to establish potential treatment differences. Nevertheless, the observation that  $\sim 50\%$  of subjects achieved an A1C target of  $<7.0\%$  with IDegAsp, and that rates of hypoglycemia were similar to IGlax despite greater reductions in 2-h postdinner plasma glucose increment, is promising and warrants further investigation in larger, longer-term trials.

In principle, initiation of insulin therapy with a coformulation of two distinct insulin analogs, such as IDegAsp, has the potential to combine the simplicity of one insulin injection with the advantages of the more physiological profiles of both prandial and basal insulin analogs. Insulin regimens with prandial components have been shown to achieve lower A1C levels than basal insulin alone, but at the expense of higher rates of hypoglycemia and greater weight gain (13,18,19). Until now, it has not been feasible to combine rapid-acting prandial insulin analogs with a long-acting basal analog in one injection. This might be convenient not only for insulin initiation but also for intensification of insulin therapy because many patients will require prandial insulin on top of basal insulin therapy (13,20,21). Indeed, by addressing both prandial and basal insulin needs from the outset, glycemic control is expected

to be achieved in more subjects and sustained for longer, thereby delaying the need to intensify treatment with additional injections. Therefore, it should be tested in adequately powered studies whether or not the benefits previously seen with basal and rapid-acting insulin analogs (e.g., better postprandial glucose control, less [nocturnal] hypoglycemia) can be achieved through the early introduction of and long-term treatment with a coformulation such as IDegAsp. It is important, though, to choose the right proportions of rapid-acting and basal insulin; in this trial we also tested a formulation of IDegAsp containing a higher proportion of IAsp (45%). This AF was associated with a twofold higher rate of confirmed, mostly nocturnal, hypoglycemia and, consequently, fewer subjects achieved A1C targets without hypoglycemia in the last 4 weeks of treatment. In view of these findings, the clinical development of the AF has been discontinued.

In contrast to AF, the overall safety profile of IDegAsp was comparable to IGlax: no relevant changes in safety assessments occurred, hypoglycemia rates were low (only one nocturnal hypoglycemic event was reported for IDegAsp), and no increases in mean body weight were observed. With respect to efficacy, IDegAsp provided markedly better postdinner plasma glucose control than IGlax (at a similarly low level of nocturnal hypoglycemia). However, this did not translate into improved overall glycemic control; at end of trial, no apparent difference in A1C was found between treatments. It cannot be ruled out that the period of time when postdinner plasma glucose levels differed between treatments was of too short a duration to translate into a significant reduction in A1C, but it should be noted that the lack of an A1C difference is in accordance with early trials with other novel insulin preparations. In fact, initial studies with short-acting insulin analogs did not show a superior effect on A1C lowering compared with human insulin despite lower postprandial glucose levels, and it was not before basal insulin therapy was optimized that beneficial effects on A1C and/or hypoglycemia were observed (22). Because this was the first trial of IDegAsp in a clinical setting, a relatively conservative titration algorithm was used, which resulted in  $\sim 50\%$  of subjects in each treatment arm achieving the FPG target after 16 weeks of treatment. It therefore seems conceivable that a more

intense titration algorithm, over a longer time period, may lead to greater glucose and A1C improvements with IDegAsp. In addition, it is possible that glycemic control could have been further optimized by tailoring the dosing of IDegAsp to coincide with the meal inducing the largest postprandial glucose excursion (in the present trial, mean postmeal glucose excursions at baseline were greatest after breakfast). It is noteworthy that similar glycemic control was achieved with lower doses of IDegAsp, although this needs to be confirmed in larger studies. The design of ongoing phase 3 trials with IDegAsp will take many of the limitations of the current trial into account: more intense treatment algorithms will be applied so that more subjects are anticipated to reach titration targets. This is not expected to lead to higher rates of hypoglycemia than in this study because dosing of IDegAsp will be targeted to the most appropriate meal of the day rather than fixed to a certain meal.

Despite the limitations of this proof-of-concept study with a small sample size, a relatively short treatment duration and an open study design, it did show IDegAsp to be a promising treatment option for initiating (and potentially intensifying) insulin therapy in subjects with type 2 diabetes inadequately controlled with OADs. IDegAsp was safe and well tolerated, providing comparable overall glycemic control to IGlax with lower doses and with the additional benefit of postdinner plasma glucose control that did not result in an increased risk of nocturnal hypoglycemia.

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T.H., C.J.T., R.C., J.D., D.G., A.L., E.R., H.M., P.D., and R.J. researched data, contributed to discussion, and reviewed and edited the manuscript. P.D. conducted the statistical analyses.

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