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Review

Current status of insulin degludec in type 1 and type 2 diabetes based on randomized and observational trials

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ABSTRACT

Insulin degludec is a new ultra-long-action basal insulin. Using treat-to-target protocols, controlled trials have shown comparable HbA_{1c} reductions with insulin degludec and comparators in both type 1 and type 2 diabetes. Most studies identify, however, better control of fasting plasma glucose with insulin degludec vs. either insulin glargine U100 or detemir, and all have consistently demonstrated clinically relevant decreases in (nocturnal) hypoglycaemic episodes. These characteristics have provided added therapeutic value for insulin degludec in clinical practice. Thus, the aim of this review is to discuss, within the context of randomized and observational studies, the clinical effects of insulin degludec use in type 1 and type 2 diabetes.

Introduction

Long-acting insulin analogues represent a major advance over neutral protamine Hagedorn (NPH) insulin, and have now become a standard of care in the treatment of both type 1 (T1D) and type 2 diabetes (T2D), even though their clinical benefit in T2D is still a subject of debate, as recently mentioned by Lipska et al. [1]. Insulin degludec (IDeg; Tresiba®), a new ultra-long-acting basal insulin analogue used in patients with either T1D or T2D [2], has an added hexadecanedioic acid to lysine at the B29 position, and is the only insulin analogue to self-associate into multihexamers after subcutaneous injection, resulting in a soluble depot from which monomers are slowly and continuously absorbed into the bloodstream [2]. As a result, IDeg has a prolonged action profile with a half-life of 25.4 h [vs. 12.5 h for insulin glargine 100 U/mL (IGlar-U100; Lantus®)], thereby providing a consistent, stable, flat delivery level of basal insulin over 42 h, with no peaks [2]. This observation was confirmed by Heise et al. [3] in clamp studies showing a similar glucose-lowering effect over both the first and last 12 h of exposure, whereas the greatest effect of IGlar-U100 occurred in the first 12–18 h after dosing. However, recent data have indicated a comparable flat profile with insulin glargine 300 U/mL (IGlar U300; Toujeo®) [4].

IDeg is also characterized by less variability in its glucose-lowering effects vs. comparators in both T1D and T2D. Thus, in T1D patients during clamp studies, Heise et al. [3] elegantly demonstrated a lower within-subject coefficient of variation for IDeg vs. IGlar-U100 (20% vs. 82%, respectively; $P < 0.001$), as well as significantly lower day-to-day and within-day variability [3,5,6]. Compared with IGlar-U300, day-to-day variability was also approximately four times lower with IDeg [4,5]. Interestingly, however, higher doses of IGlar-U300 relative to IDeg were needed to achieve the same glycaemic level [4]. Nevertheless, contradictory results were reported in 2018 by Bailey et al. [7] in T1D, showing that IGlar-U300 was associated with less glycaemic variability than IDeg at a dose of 0.4 U/kg/day [treatment ratio: 0.80, 95% confidence interval (CI): 0.66–0.96; $P = 0.047$], but with no significant difference at a dose of 0.6 U/kg/day. In addition, the pharmacokinetic specificities of IDeg are preserved in patients with hepatic or renal impairment [8,9], and in both the elderly and in children [10,11].

Given this context, the aim of the present review is to lay out a state-of-the-art report concerning the clinical effects of IDeg in T1D and T2D on the basis of recent scientific data, 5 years after its approval in Europe by the European Medicines Agency (EMA).

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Table 1
Key studies with insulin degludec (IDeg) in type 1 diabetes.

Studies [reference]	Treatment arms	Duration (weeks)	HbA_{1c} at inclusion (%; mean ± SD)	Treatment difference in HbA_{1c} at end of study: IDeg vs. comparator	Treatment difference in FPG at end of study: IDeg vs. comparator	Overall hypoglycaemia ERR: IDeg vs comparator	Nocturnal hypoglycaemia ERR:IDeg vs. comparator	Severe hypoglycaemia ERR: IDeg vs. comparator
BEGIN Basal–Bolus Type 1 [13]	IDeg (n = 472)	52	7.7 ± 0.9	−0.01%	−5.9 mg/dL	1.07	0.75	1.38
	IGlar-U100 (n = 157)		7.7 ± 1.0	[−0.14–0.11] (NS)	[−18.5–6.5] (P = 0.35)	[0.89–1.28] (P = 0.48)	[0.59–0.96] (P = 0.021)	[0.72–2.64] (P = 0.34)
BEGIN Flex T1 [14]	IDeg Free Flex (n = 239)	26 +	7.7 ± 1.0	0.07%	−19.3 mg/dL	1.02	0.73	0.47
	IGlar-U100 (n = 133)	26	7.7 ± 0.9	[−0.05–0.19] (NS)	[−32.8–5.8] (P = 0.005)	[0.84–1.24] (NS)	[0.54–0.98] (P = 0.035)	[0.23–0.94] (P = 0.033)
SWITCH 1 [15]	IDeg, then IGlar-U100 (n = 249)	32 +	7.7 ± 1.0	0.11%	−17.0 mg/dL	0.94	0.75	0.74
	IGlar-U100, then IDeg (n = 252)	32	7.5 ± 1.0	[−0.00–0.23] (NS)	[−25.5–−8.41] (P < 0.001)	[0.91–0.98] (P = 0.002)	[0.68–0.83] (P < 0.001)	[0.61–0.90] (P = 0.003)
EU-TREAT [16]	IDeg (n = 1717)	26 + 26	8.0 ± 1.3	−0.22% [−0.27–−0.18] (P < 0.001)	−21.0 mg/dL [−27.4–−14.7] (P < 0.001)	0.79 [0.68–0.92] (P < 0.001)	0.48 [0.34–0.67] (P < 0.001)	0.17 [0.11–0.27] (P < 0.001)
IDeg vs. IDet [17]	IDeg (n = 302)	26 + 26	8.0 ± 1.0	−0.01%	−20.0 mg/dL	0.95	0.67	0.86
	IDet (n = 153)		8.0 ± 0.9	[−0.17–0.14] (NS)	[−32.9–7.2] (P < 0.05)	[0.78–1.17] (NS)	[0.51–0.88] (P < 0.05)	[0.46–1.62] (NS)
Children ages 1–17 years [10]	IDeg (n = 174)	26 + 26	8.2 ± 1.1	−0.04%	−29.2 mg/dL	1.11	0.99	1.30
	IDet (n = 176)		8.0 ± 1.1	(NS)	[−51.1–−7.4] (P = 0.009)	[0.89–1.38] (NS)	[0.72–1.34] (NS)	[0.64–2.64] (NS)

Data in square brackets are 95% confidence intervals (CI).
FPG: fasting plasma glucose; ERR: estimated rate ratio; IGlar-U100: insulin glargine 100 U/mL; IDet: insulin detemir; NS: not statistically significant.

Synopsis of the main results

HbA_{1c} and fasting plasma glucose in type T1D

Global glycaemic control [HbA_{1c}, fasting plasma glucose (FPG)] with IDeg was first investigated *vs* IGlar-U100 in the BEGIN trial programme, which included seven randomized, controlled, open-label, treat-to-target clinical trials designed to demonstrate IDeg non-inferiority in the primary outcome (reduction in HbA_{1c}) [12]. In the BEGIN Basal–Bolus Type 1 trial, after 52 weeks of follow-up (Table 1), reductions in HbA_{1c} were identical in patients treated with once-daily IDeg and IGlar-U100 (−0.40 ± 0.03% for IDeg and −0.39 ± 0.07% for IGlar-U100). Percentages of patients achieving their glycaemic targets at the end of the study were also comparable between the two insulins: 40% and 43% of participants, respectively, achieved HbA_{1c} targets of < 7.0% [13]. Similar results were reported in the BEGIN Flex T1 trial, in which the timing of IDeg injections ranged from a minimum of 8 h to a maximum of 40 h between doses; in this study, FPG was slightly lower with IDeg than with IGlar-U100 (−19.3 mg/dL; *P = 0.005*; Table 1) [14].

The SWITCH 1 trial was a treat-to-target double-blind study designed to demonstrate the superiority of IDeg in the primary outcome (reduction in hypoglycaemic episodes) [15]. The study included T1D patients at high risk of hypoglycaemia randomized to receive either once-daily IDeg for 32 weeks, followed by IGlar-U100 for the remaining 32 weeks, or IGlar-U100 followed by IDeg instead [15]. As indicated in Table I, treatment changes in HbA_{1c} were again comparable between the two arms, although FPG was again lower with IDeg than with IGlar-U100 (−17.0 mg/dL; P < 0.001). In this study, as with the BEGIN Basal–Bolus Type 1 trial, statistically lower doses of IDeg were used compared with IGlar-U100 [13,15].

In a real-life retrospective study, reductions in both HbA_{1c} and FPG were reported at 1 year in patients who switched from IGlar-U100 or insulin detemir (IDet; Levemir®) to IDeg [HbA_{1c}: −0.22% (P < 0.001); FPG: −21.0 mg/dL (P < 0.001; Table 1) [16]. In a study comparing IDeg and IDet, comparable effects on HbA_{1c}, but greater reductions in FPG, were reported in the IDeg group [17]. Similarly, in a paediatric population, Thalange et al. [10] also observed comparable HbA_{1c} levels, but lower FPG, with IDeg *vs* IDet (-29.2 mg/dL; P = 0.0090). Of note, in that study, hyperglycaemia and ketosis events were decreased in the IDeg arm [treatment ratio IDeg vs. IDet: relative risk (RR): 0.41, 95% CI: 0.22–0.78; P = 0.0066] [10].

HbA_{1c} and fasting plasma glucose in T2D

In the open-label, treat-to-target, non-inferiority BEGIN Basal–Bolus Type 2 study comparing IDeg and IGlar-U100 in a cohort of > 1000 subjects, HbA_{1c} reductions after 52 weeks of treatment were comparable: HbA_{1c} decreased by 1.10% in the IDeg group and by 1.19% in the IGlar group (Table 2) [18]. Percentages of patients achieving glycaemic targets at the end of the study were also comparable with the two insulins: 49% and 50% of participants, respectively, reached HbA_{1c} targets of < 7.0% [18]. In addition, no differences in FPG were observed [18].

In contrast, a lower FPG was reported in an insulin-naïve population in the BEGIN Once Long study (−7.7 mg/dL vs. IGlar-U100; P = 0.005) [19]. Compared with sitagliptin, treatment differences in HbA_{1c} of −0.43% (P < 0.0001) and in FPG of −39.1 mg/dL (P < 0.0001) were reported in favour of IDeg (Table 2) [20]. In the SWITCH 2 trial, which involved 720 subjects at high risk of hypoglycaemia, glycaemic control (HbA_{1c}, FPG) was comparable at the end of the trial despite lower insulin doses with IDeg relative to IGlar-U100 [21]. In the DEVOTE trial, designed to evaluate cardiovascular safety of IDeg in T2D at high risk of cardiovascular events, mean FPG levels were also somewhat lower with IDeg *vs* IGlar-U100 after 2 years of follow-up (−7.2 mg/dL; P < 0.001), but with no significant differences in HbA_{1c} [22].

In the European Tresiba Audit (EU-TREAT) trial, switching to IDeg was associated with reductions in both HbA_{1c} (−0.52%; P < 0.001) and FPG (-26.4 mg/dL; P < 0.001) after 1 year of follow-up [16]. More recently, in the open-label, non-inferiority BRIGHT study, Rosenstock et al. [23] reported no differences in glycaemic control (HbA_{1c}, FPG) between IDeg and IGlar-U300 in an insulin-naïve population (Table 2). Comparable improvements in

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Table 2
Key studies with insulin degludec (IDeg) in type 2 diabetes.

Studies [reference]	Treatment arms	Duration (weeks)	HbA_{1c} at inclusion (%; mean ± SD)	Treatment difference in HbA_{1c} at end of study: IDeg vs. comparator	Treatment difference in FPG at end of study: IDeg vs. comparator	Overall hypoglycaemia ERR:IDeg vs. comparator	Nocturnal hypoglycaemia ERR:IDeg vs. comparator	Severe hypoglycaemia ERR: IDeg vs. comparator
BEGIN Basal–Bolus Type 2 [18]	IDeg + IAsp ± Met ± Pio (n = 744)	52	8.3 ± 0.8	0.08% [−0.05–0.21] (NS)	−5.9 mg/dL [−11.7–1.1] (NS)	0.82 [0.69–0.99] (P = 0.0359)	0.75 [0.58–0.99] (P = 0.0399)	NA
	IGlar-U100 + IAsp ± Met ± Pio (n = 248)		8.4 ± 0.9					
BEGIN Once Long [19]	IDeg + Met ± DPP-4i (n = 766)	52	8.2 ± 0.8	0.09% [−0.04–0.22] (NS)	−7.7 mg/dL [−13.3–2.3] (P = 0.005)	0.82 [0.64–1.04] (P = 0.106)	0.64 [0.42–0.98] (P = 0.038)	0.14 [0.03–0.70] (P = 0.017)
	IGlar-U100 + Met ± DPP-4i (n = 257)		8.2 ± 0.8					
BEGIN Early [20]	IDeg ± Met/S/ glinides ± Pio (n = 225)	26	8.8 ± 1.0	−0.43% [−0.61–−0.24] (P < 0.0001)	−39.1 mg/dL [−46.7–−31.4] (P = 0.034)	3.81 [2.40–6.05] (P < 0.0001)	1.93 [0.90–4.1] (P = 0.09)	NA
	Sitagliptin ± Met/ S/ glinides ± Pio (n = 222)		9.0 ± 1.0					
SWITCH 2 [21]	IDeg, then IGlar-U100 (n = 360)	32 +	7.6 ± 1.1	0.09% [−0.04–0.23] (NS)	NA	0.77 [0.70–0.85] (P < 0.001)	0.75 [0.64–0.89] (P < 0.001)	0.49 [0.26–0.94] (P = 0.03)
	IGlar-U100, then IDeg (n = 360)	32	7.6 ± 1.1					
EU-TREAT [16]	IDeg (n = 833)	26 + 26	8.4 ± 1.4	−0.52% [−0.61–−0.42] (P < 0.001)	−26.4 mg/dL [−36.0–−16.8] (P < 0.001)	0.49 [0.26–0.91] (P = 0.025)	0.09 [0.04–0.20] (P < 0.001)	NA
DEVOTE [22]	IDeg (n = 3818) IGlar-U100 (n = 3819)	103	8.4 ± 1.7	0.01% [−0.05–0.07] (NS)	−7.2 mg/dL [−10.3–−4.1] (P < 0.001)	NA	NA	0.60 [0.48–0.76] (P < 0.001)
BRIGHT [23]	IGlar-U300 (n = 462)	24	8.7 ± 0.8	IGlar-U300 vs. IDeg: -0.05% [-0.15–0.05] (NS)	IGlar-U300 vs. IDeg: 7.7 mg/dL [2.7–12.7] (NS)	IGlar-U300 vs. IDeg: 0.86 [0.71–1.04] (NS)	IGlar-U300 vs. IDeg: 0.81 [0.58–1.12] (NS)	NA
	IDeg (n = 462)		8.6 ± 0.8					

Data in square brackets are 95% confidence intervals (CI).
FPG: fasting plasma glucose; ERR: estimated rate ratio; IAsp: insulin aspart; Met: metformin; Pio: pioglitazone; IGlar-U100/U300: insulin glargine 100/300 U/mL; DPP-4i: dipeptyl peptidase-4 inhibitor; S: sulphonylureas; NA: not available; NS: not statistically significant.

glycaemic control were demonstrated in the DELIVER D + cohort observational study in patients switching from a first-generation basal analogue (IGlar-U100/IDet) to either IGlar-U300 or IDeg [24]. On the other hand, in the Clinical Outcome Assessment of the Effectiveness of Insulin Degludec in Real-life Medical Practice (CONFIRM), Tibaldi et al. [25] reported a greater reduction in HbA_{1c} with IDeg than with IGlar-U300 (−0.27% between groups; P = 0.03), again in insulin-naïve patients.

Hypoglycaemia in T1D patients

In the BEGIN Basal–Bolus Type 1 trial, nocturnal hypoglycaemias at 1 year were reduced by 25% in the IDeg vs. IGlar-U100 group: 4.41 vs. 5.86 episodes per patient-years of exposure (P = 0.021; Table 1) [13]. Rates of overall confirmed plasma glycaemia (< 56 mg/dL) or severe hypoglycaemia were comparable. Interestingly, the risk of hypoglycaemia was not increased by flexible timing of IDeg injections, as demonstrated in the BEGIN Flex T1 study [14]. In SWITCH 1, the rate ratio of overall symptomatic hypoglycaemia throughout the entire trial was 6% lower with IDeg vs. IGlar-U100 (RR: 0.94, P = 0.002). In addition, rates of nocturnal hypoglycaemic events were 25% lower in the IDeg group (RR: 0.75, P < 0.001), and a smaller proportion of patients using IDeg experienced severe hypoglycaemia (RR: 0.74, P = 0.003; Table 1) [15].

These results were largely confirmed by the EU-TREAT trial in real-life conditions, with reductions of 21%, 52% and 83% of all, nocturnal and severe hypoglycaemic events, respectively (P < 0.001) [16]. The risk of nocturnal hypoglycaemia was also 33% lower with IDeg compared with IDet (P < 0.05) [17]. Thalange et al. [10], however, observed no such statistical benefit with IDeg vs. IDet in a paediatric population.

Hypoglycaemia in T2D

In the BEGIN Basal–Bolus Type 2 trial, rates of overall confirmed hypoglycaemia were lower with IDeg than with IGlar-U100 (11.1 vs. 13.6 episodes per patient-years; P = 0.0359), as were also rates of nocturnal events (1.4 vs. 1.8 episodes per patient-years; P = 0.0399). Yet, rates of severe hypoglycaemias were identical [18]. Flexibility in injection timing resulted in no changes in hypoglycaemic events between groups [26]. In the SWITCH 2 study, the rate of overall symptomatic hypoglycaemia was lower with IDeg vs. IGlar-U100 (RR: 0.77, P < 0.001), as were also rates of nocturnal (RR: 0.75, P < 0.001) and severe (RR: 0.49, P = 0.03) hypoglycaemias (Table 2) [21].

Similarly, the DEVOTE reported a lower rate of severe hypoglycaemia in the IDeg *vs* IGlar-U100 arm (RR: 0.60, P = 0.017) [22], while comparable results for hypoglycaemic events were observed in the real-life EU-TREAT trial (Table 2)

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[16]. In the BRIGHT study, hypoglycaemic events were likewise comparable in both groups (IGlar-U300 vs. IDeg) throughout the entire study period. However, during the titration phase, fewer overall (RR: 0.77, $P = 0.023$) and nocturnal (RR: 0.65, $P = 0.040$) hypoglycaemic events were observed with IGlar-U300 than with IDeg, despite the use of larger basal insulin doses of IGlar-U300 (+0.11 U/kg; Table 2) [23]. Also, switching from IGlar-U100 or IDet to either IDeg or IGlar-U300 in the DELIVER D+ study similarly decreased hypoglycaemia incidence and event rates after adjusting for baseline hypoglycaemia [24]. Nevertheless, in the CONFIRM trial, IDeg treatment resulted in a greater reduction in rates and likelihood of hypoglycaemia than did IGlar-U300 (RR: 0.70, 95% CI: 0.50–0.99; $P < 0.05$) [25].

Cardiovascular and general safety

As already mentioned, the cardiovascular safety of IDeg was the primary objective of the DEVOTE study, which included 7637 T2D patients at high cardiovascular risk randomized to receive either IDeg or IGlar-U100 [22]. After 2 years of follow-up, the risk of a major cardiovascular event (MACE), defined as death due to cardiovascular causes, non-fatal myocardial infarction and/or non-fatal stroke, was similar in both groups [hazard ratio (HR): 0.91, 95% CI: 0.78–1.06; $P < 0.001$ for non-inferiority], thereby confirming IDeg cardiovascular safety.

Consistent with this, a recent meta-analysis by Zhang et al. [26] reported no differences in rates of cardiovascular events and total mortality between IDeg and IGlar-U100 in T1D and T2D. In addition, serious adverse events rates overall were similar for IDeg and comparators; the number of neoplasms was also similar between IDeg and IGlar-U100 [22]. Concerning weight changes, no significant differences between IDeg and comparators were reported during the follow-up of patients with either T1D or T2D [13,15,16,18,21,23,26].

Quality of life

Quality of life (QoL) was analyzed in the BEGIN programme trials by a 36-item short-form (SF-36) questionnaire [13,18]. Responses mapped onto the EuroQol health utility scale covering five dimensions (EQ-5D) showed that IDeg was associated with improvement in health status (+0.005 points vs. IGlar-U100, 95% CI: 0.0006–0.009; $P < 0.024$) [27], although these results need to be interpreted with caution as the study was not double-blinded. Nevertheless, a Japanese trial confirmed that, after switching from basal insulin (IGlar-U100 or IDet) to IDeg, the QoL (mainly mental stress and anxiety over treatment), as evaluated by a diabetes-related QoL questionnaire, improved in T2D patients [28]. These results are consistent with the findings of Rodbard et al. [29], who found evidence of improvement in QoL in T2D patients evaluated by the SF-36 questionnaire after 2 years of IDeg use.

Discussion and conclusion

IDeg in 2019 represents an alternative to other basal insulin analogues. In terms of HbA_{1c} levels, randomized controlled trials using a treat-to-target protocol have indeed demonstrated the non-inferiority (but not superiority) of IDeg vs. comparators (most often IGlar-U100) in T1D and T2D, with similar percentages of patients achieving glycaemic targets at the end of follow-up. Observational studies (not necessarily using a treat-to-target design) indicated lower HbA_{1c} levels with IDeg vs. other basal insulins. As regards FPG, most of the treat-to-target trials found evidence of slightly, yet significantly, lower values with IDeg vs. IGlar-U100 or IDet in T1D and T2D patients.

Many patients using insulin therapy fail to reach glycaemic targets in part due to the occurrence of hypoglycaemic events. In this context, IDeg administration in both randomized and observational studies was systematically associated with lower rates of nocturnal hypoglycaemic events in patients with either T1D or T2D. This robust observation is mostly related to less day-to-day and within-day glycaemic variability after IDeg injections, thus allowing clinicians to highly and securely titrate insulin doses to better target FPG levels, as observed in most trials. In addition, specific trials have also shown fewer overall and severe hypoglycaemic events with IDeg treatment *vs* comparators. Such a global reduction in risk of hypoglycaemias is associated with improvement in QoL, as confirmed by questionnaires, and potentially also with the prevention of cardiovascular disease. In fact, a substantial number of studies have demonstrated a close relationship between (severe) hypoglycaemias and cardiovascular events [30–34]. Consistent with these previous reports, a subanalysis of DEVOTE showed a doubling in risk of all-cause mortality for patients experiencing severe hypoglycaemias during follow-up (HR: 2.51, 95% CI: 1.79–3.50; $P < 0.001$) [35].

More recently, comparable results on glycaemic control and hypoglycaemic events have been reported in T1D and T2D patients in the EDITION programme of trials comparing the effects of IGlar-U300 vs. IGlar-U100 [36]. Likewise, in patients with T2D, a meta-analysis by Roussel et al. [37] found similar HbA_{1c} and FPG reductions with IGlar-U300 vs. IGlar-U100 [mean differences: 0.01%, 95% CI: −0.06–0.08 (not significant, NS) and 3.2 mg/dL, 95% CI: −0.5–6.8 (NS), respectively], whereas IGlar-U300 was associated with fewer anytime and nocturnal hypoglycaemias than IGlar-U100 [36,37].

To our knowledge, the BRIGHT study is the only randomized prospective comparison of IDeg and IGlar-U300 in insulin-naïve T2D patients [23]. At 24 weeks, HbA_{1c} was similarly improved from baseline in both groups, demonstrating non-inferiority of IGlar-U300 vs. IDeg (Table 2). As already mentioned, hypoglycaemia prevalence was comparable in both treatment groups except for fewer anytime and nocturnal hypoglycaemic events with IGlar-U300 specifically during the titration phase, but not throughout the entire treatment period [23].

High price tags can restrict access to new medicines. In addition, cost-effectiveness analysis has shown that, in a T1D population, switching from an "older" basal insulin to IDeg was associated with cost savings for the healthcare system too by decreasing hospitalizations for hypoglycaemic events, and improving quality-adjusted life-years (QALYs) in terms of life expectancy and health-related QoL [38]. In agreement with these results, a UK study by Evans et al. [39] confirmed that switching to IDeg could be cost-effective in T1D patients, especially those experiencing nocturnal hypoglycaemia and/or hypoglycaemia unawareness. Similar conclusions were reported in T2D patients treated with basal insulin, especially those with episodes of recurrent hypoglycaemia [40].

In conclusion, IDeg is an effective alternative treatment to IGlar-U100 in terms of HbA_{1c} improvement in randomized trials. Indeed, some studies highlighted better control of FPG with IDeg *vs* either IGlar-U100 or IDet. Moreover, all of the available data are consistent in showing significant reductions in nocturnal hypoglycaemic episodes as well as potential reductions of severe events with IDeg, as indicated by some studies. Such a reduced risk of (nocturnal) hypoglycaemias and better FPG control with IDeg clearly result in additional positive benefits with the long-acting insulin analogue *vs* comparators in daily practice, allowing safer titration of basal insulin by patients.

Up to now, comparisons between IDeg and IGlar-U300 have resulted in globally comparable results in a T2D patient population throughout the entire treatment period. Other head-to-head and

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observational studies, particularly in T1D populations, are now needed to extend the currently available positive data. Such future findings may even help clinicians to broaden the use of this new therapeutic tool in our insulin armamentarium.

Disclosure of interest

VP has participated in advisory panels and been an investigator in clinical studies for Novo Nordisk and Sanofi. MB has been a speaker and/or provided research support for AstraZeneca, Boehringer Ingelheim, Mundi Pharma, MSD, Mylan, Novo Nordisk, Sanofi and Servier.

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