

# Insulin degludec 200 U/mL is ultra-long-acting and has a flat and stable glucose-lowering effect

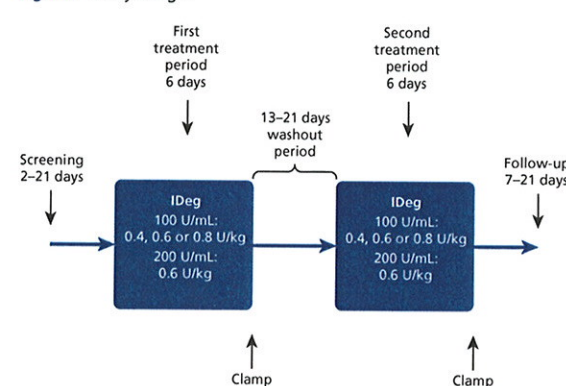
## Introduction

- Insulin degludec (IDeg) is a new-generation, ultra-long-acting basal insulin, with a half-life ( $t_{1/2}$ ) twice as long as that of insulin glargine.<sup>1,2</sup>
- In pharmacokinetic (PK) and pharmacodynamic (PD) studies in patients with type 1 diabetes (T1D) IDeg has demonstrated a flat and stable action profile with blood glucose control lasting beyond 42 h.<sup>2</sup>
- In order to accommodate the wide range of insulin dose requirements characteristic of diabetes, especially type 2 diabetes (T2D), IDeg has been developed as both 100 U/mL and 200 U/mL formulations.<sup>3</sup> The PK and PD data for the 100 U/mL formulation have already been published.<sup>1</sup>
- The 200 U/mL formulation of IDeg allows up to 160 U to be administered in a single injection using a newly developed prefilled pen compared with a maximum of 80 U with the 100 U/mL formulation.<sup>3</sup>
- This should allow patients with large insulin dose requirements to achieve acceptable basal insulin levels with one rather than two injections and may prove preferable for patients who wish to change their injection pen less frequently.
- The objective of this study was to investigate the PD and PK properties of IDeg 200 U/mL in patients with T2D.

## Methods

- Subjects aged 18–70 years, with insulin-treated T2D not on OAD, received 0.6 U/kg IDeg 200 U/mL once daily over 6 days (Figure 1). Patients were included as part of a randomised two-way crossover study including both the 200 U/mL formulation and three doses of the 100 U/mL formulation.
- Subjects underwent a 26-h euglycaemic clamp (Biostator; clamp blood glucose level: 5 mmol/L [90 mg/dL]) after the last dose at the end of each treatment period (Day 6).
- Blood samples for assessment of steady-state pharmacokinetics were drawn for 120 h after the last dose.

Figure 1 Study design.



## Statistical analyses

- Distribution of the glucose-lowering effect over the 24-h dosing interval was quantified by estimating the ratio between the  $AUC_{GIR}$  for the first 12 h versus the total  $AUC_{GIR}$  for the entire 24-h dosing interval ( $AUC_{GIR,0-12h,SS}/AUC_{GIR,total,SS}$ ) (50:50 split).
- Terminal  $t_{1/2}$  was estimated from the individual log-insulin profiles.

## Results

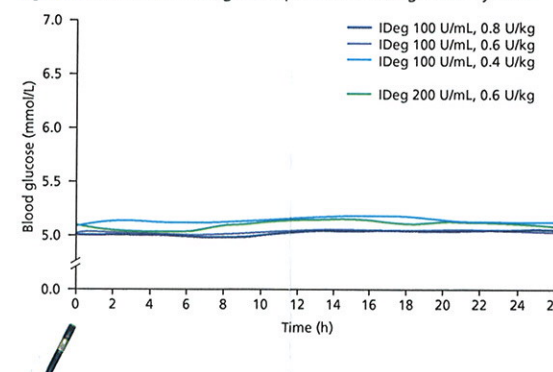
- Patient characteristics are detailed in Table 1.
- Blood glucose stayed close to the target level throughout the clamp with the effect of IDeg extending beyond 26 h in all patients; results for IDeg 200 U/mL were similar to those seen for IDeg 100 U/mL (Figure 2).
- As previously shown for IDeg 100 U/mL, the GIR profile for IDeg 200 U/mL was flat and stable over the dosing interval (Figure 3).

Table 1 Baseline characteristics of patients receiving IDeg 200 U/mL.

Characteristic	
Number of patients randomised, n	16
Age, years	59.4 (±6.0)
White Caucasian (%)	16 (100.0)
Male, n (%)	14 (87.5)
Body mass index, kg/m <sup>2</sup>	30.0 (±2.5)
Duration of diabetes, years	14.2 (±5.6)
HbA <sub>1c</sub> , %	7.3 (±0.8)
Fasting C-peptide, nmol/L	0.4 (±0.2)

Values are mean (standard deviation) unless otherwise stated

Figure 2 26-h mean blood glucose profiles with IDeg at steady state.



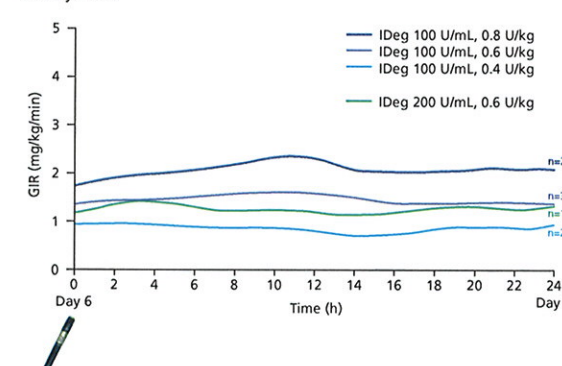
- The glucose-lowering effect of IDeg was evenly distributed over the dosing interval, with  $AUC_{GIR}$  for each of the two 12-h intervals being approximately 50% of the total  $AUC_{GIR,SS}$ . Results with IDeg 200 U/mL were comparable to those seen with IDeg 100 U/mL (Table 2).

Table 2 Distribution of glucose-lowering effect at steady state over 24 h.

	IDeg 100 U/mL, 0.4 U/kg (n=22)	IDeg 100 U/mL, 0.6 U/kg (n=37)	IDeg 100 U/mL, 0.8 U/kg (n=21)	IDeg 200 U/mL, 0.6 U/kg (n=16)
$AUC_{GIR,0-12h,SS}/AUC_{GIR,total,SS}$	49%	53%	50%	54%

$AUC_{GIR,0-12h,SS}$ , area under the glucose infusion rate curve for the first 12 h;  $AUC_{GIR,total,SS}$ , area under the glucose infusion rate curve over the whole 24-h dosing interval

Figure 3 24-h glucose infusion rate (GIR) mean profiles with IDeg at steady state.



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Table 3 Terminal half-life ( $t_{1/2}$ ) of IDeg.

	IDeg 100 U/mL, 0.4 U/kg (n=22)	IDeg 100 U/mL, 0.6 U/kg (n=37)	IDeg 100 U/mL, 0.8 U/kg (n=21)	IDeg 200 U/mL, 0.6 U/kg (n=16)
$t_{1/2}$ (h)	24.6	24.4	26.8	26.2
Mean $t_{1/2}$ (h)	25.1			

## References

- Heise et al. *Diabetes Obes Metab* 2012;14:859–64
- Heise et al. *Diabetologia* 2011;54(Suppl. 1):S425
- Heise et al. *Diabetes* 2012;61 (Suppl. 1):A91(349-OR)
- Korsatko et al. *Diabetologia* 2011;54(Suppl. 1):S427

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## Conclusions

- IDeg 200 U/mL has a flat, stable and evenly distributed glucose-lowering effect, an ultra-long duration of action with a terminal  $t_{1/2}$  >26 h and controlled blood glucose fully in all subjects in this study.
- IDeg 200 U/mL has similar characteristics to IDeg 100 U/mL. Formal bioequivalence has been established in a study in people with type 1 diabetes.<sup>4</sup>