Insulin degludec (IDeg) is an ultra-long-acting basal insulin that forms soluble multi-hexamers after injection. These release monomers slowly and continuously to produce a flat and stable glucose-lowering effect. We describe the pharmacokinetic and pharmacodynamic properties of IDeg compared with insulin glargine (IGlar) under steady-state conditions in patients with type 1 diabetes (T1D). This was a randomised, double-blind, two-period crossover study in 66 patients with T1D. Patients (mean, 37 years old, BMI 24.9 kg/m², HbA1c 8.1%) received one of three fixed doses (0.4, 0.6, 0.8 U/kg) of IDeg and IGlar once daily for 8 days with a 7–21 day wash-out period. A euglycaemic glucose clamp (glucose level: 5.5 mmol/L) was performed at the end of each treatment period with PK sampling throughout and for 120 h after last dose. Total exposure to IDeg at steady state was stable and increased proportionally with increasing dose. The serum exposure to IDeg was equally distributed between the first and second 12 hours post-dosing (AUC[IDeg, 0-12h]/AUC[IDeg, total] = 0.5) whereas 60% of exposure to IGlar occurred during the first 12 hours (AUC[IGlar,0-12h]/AUC[IGlar, total] = 0.6) for all doses. Likewise, the cumulated AUC below and above the average glucose infusion rate (AUCF[GIR]) was considerably lower for all doses of IDeg (0.25, 0.37, 0.38 mg/kg/min) than with IGlar (0.39, 0.54, 0.73 mg/kg/min). The estimated molar dose ratio (AUC[GIR, total]) was 1.03 [95% CI: 0.95; 1.12]. IDeg was detectable in the serum for at least 120 h post-dosing, whereas IGlar fell below the lower limit of quantification 36–48 h post-dosing. Mean terminal half-lives were 25.4 and 12.5 h for IDeg and IGlar, respectively. Both treatments were well tolerated with no safety concerns. IDeg has a half-life that is twice as long as IGlar with a more evenly distributed and stable pharmacokinetic exposure and glucose-lowering effect, over 24 hours at steady state in patients with T1D.

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Insulin degludec has a two-fold longer half-life and a more consistent pharmacokinetic profile compared with insulin glargine

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Insulin degludec has a two-fold longer half-life and a more consistent pharmacokinetic profile compared with insulin glargine (<1 min ago)
Insulin degludec has an ultra-long duration of action that extends beyond 42 hours with a flat and stable profile. Once-daily insulin degludec has been studied in a large-scale clinical trial programme, BEGIN®, examining its impact on glucose control, hypoglycaemia and the possibility to flexibly adjust the insulin degludec dosing time to suit patient needs. Insulin degludec has been submitted for once-daily use to the European Medicines Agency (EMA) and the US Food and Drug Administration (FDA) in September 2011 for regulatory review. Insulin degludec: two-fold longer half-life and a more consistent pharmacokinetic profile compared to insulin glargine. IDF 2011 21th World Congress Abstract Book. IDF: Dubai, 2011; p 471 (Poster P-1444). Nosek L et al.