# Reduction of glycemic variability at 12 weeks of treatment with insulin degludec in patients with diabetes with high glycemic variability and hypoglycemia

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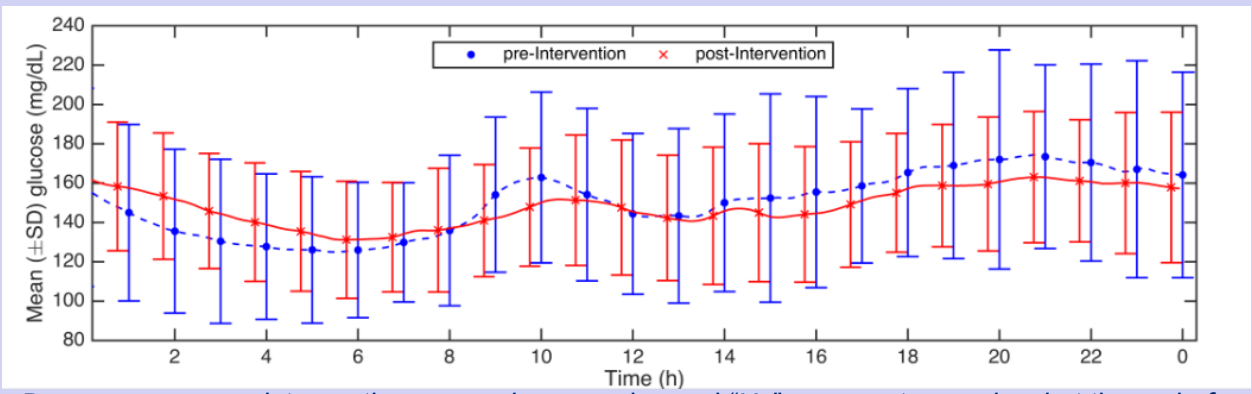
**Introduction:** Degludec (IDeg) is an ultra-long-acting insulin, with stable pharmacodynamic profile which leads to lower fluctuations in glucose levels. The effect of IDeg has not been specifically assessed in patients with increased basal glycemic variability (GV).

**Objetive:** to assess the impact of the switch from a Glargine or Detemir insulin to IDeg on GV, measured by continuous glucose monitoring (CGM), on metabolic control and on the incidence of hypoglycemia episodes in a group of patients with and without increased baseline GV.

**Methods:** A prospective before-after pilot study was conducted. The impact of the switch from a Glargine or Detemir insulin to a basal insulin regimen with IDeg for 12 weeks on GV measured by continuous glucose monitoring (figure 1), on A1c levels, and on the incidence of episodes of global and nocturnal hypoglycemia was assessed in a group of patients with (coefficient of variation >34 %) or without increased baseline GV using a Generalized Estimating Equation (GEE) analysis.

**Results:** 60 patients with basal bolus therapy and history of hypoglycemia were included. Most patients had type 2 diabetes (72.4 %).

**Figure 1.** Pre-intervention and End-of-The-Study 24-hour Mean Glucose Profile as Measured by Continuous Glucose Monitoring.




Dots represent pre-intervention mean glucose value and "Xs" represent mean level at the end of study, after 12 weeks of treatment with insulin degludec. Mean and SD are calculated based on glucose measures at specific hours.

18 patients had high GV (HGV). In this group a significant reduction of 11.1% of CV (95%CI:6.3,15.9,p=0.01) was found (figure 1). In table 2, GEE analysis confirmed a higher impact on patients with HGV (p<0.001).

**Table 1.** Glycemic variability for IDeg pre-treatment and 12 weeks post-treatment.

| GV Metrics. | Low glycemic variability n=42 | | | High glycemic variability n=18 | | |
|---|---|---|---|---|---|---|
| | Baseline | 12 weeks | p- value | Baseline | 12 weeks | p- value |
| Mean of glucose | 142.6 ± 32 | 143.1± 37 | 0.93 | 161.1±45 | 149.0±49 | 0.23 |
| %CV | 24.4± 5.01 | 26.2 ± 9.1 | 0.21 | 44.7±7.3 | 33.6±10.1 | <0.001 |
| SD: | 35.4 ± 12.5 | 37.6 ±15.6 | 0.37 | 71.3±19.5 | 49.8±20.0 | <0.001 |
| MODD | 33.5 ±11.2 | 39.1 ± 18.0 | 0.03 | 73.9±30.0 | 57.1±29.1 | 0.01 |
| CONGA1 | 24.2 ± 7.45 | 25.2 ±10.4 | 0.51 | 43.6±12.4 | 34.1±10.8 | 0.004 |
| CONGA2 | 35.1 ± 11.1 | 36.2 ±15.4 | 0.62 | 66.1±17.8 | 50.3±17.9 | 0.001 |
| CONGA4 | 44.7 ± 15.3 | 46.6 ± 20.9 | 0.57 | 89.0±25.6 | 64.6±23.4 | <0.001 |
| IQR | 49.5 ± 21.0 | 53.4 ± 24.1 | 0.35 | 104.6±42.4 | 69.8±34.2 | <0.001 |
| LBGI | 1.41 ±1.17 | 2.21 ± 2.51 | 0.06 | 8.05±5.58 | 4.64±4.39 | 0.06 |

Basal A1c was 8.28 % ± 1.74 % and after 12 weeks of treatment with IDeg was 7.16 % ± 1.54 %. The mean difference was -1.04 % (95 % CI, -0.42, -1.67), p = 0.0013.

The percentage of patients with at least 1 episode of hypoglycemia <54 mg/dL decreased from 66.6 % to 22.2 % (p=0.02) and from 37.14 % to 5.71 % (p<0.01) for global and nocturnal hypoglycemia, respectively. Changes were not significant in patients with low GV. A reduction of A1c was observed in both groups (p<0.001).

**Conclusions**: The results suggest that treatment with IDeg reduces GV, A1c levels and the incidence of global and nocturnal hypoglycemia events in patients with HGV.

## References

1. Zinman B, Philis-Tsimikas A, Cariou B, Handelsman Y, Rodbard HW, Johansen T, et al. Insulin degludec versus insulin glargine in insulin-naive patients with type 2 diabetes: a 1-year, randomized, treat-to-target trial (BEGIN Once Long). Diabetes Care 2012 Dec;35(12):2464-71.
2. Liebl A, Davidson J, Mersebach H, Dykiel P, Tack CJ, Heise T. A novel insulin combination of insulin degludec and insulin aspart achieves a more stable overnight glucose profile than insulin glargine: results from continuous glucose monitoring in a proof-of-concept trial. J Diabetes Sci Technol 2013 Sep 1;7(5):1328-36.
3. Hidetaka Hamasaki, Takaaki Nakayama, Arisa Yamaguchi, Sumine Moriyama, Hisayoki Katsuyama, Masafumi Kakei, et al. Comparison of Glycemic Variability by Using Insulin Glargine and Insulin Degludec in Japanese Patients With Type 1 Diabetes, Monitored by Continuous Glucose Monitoring: A Preliminary Report. Journal of Endocrinology & Metabolism 2013 Nov 28;3(6):138-46.

(CV) coefficient of variation, (SD) standard deviation, (MOOD) mean of daily difference, (CONGA) continuous overall net glycemic action, (IQR) interquartile range, (IQR) interquartile range, (LBGI) low blood glucose index, (MAG) mean absolute glucose change, (MAGE) mean amplitude of glycemic excursion.